AUTHENTICATED
U.S. GOVERNMENT
INFORMATION
GPO

12-24-85
Vol. 50 No. 247
Pages 52435-52756

# federal register

Tuesday
December 24, 1985

**Briefings on How To Use the Federal Register—**
For information on briefings in Washington, DC, see announcement on the inside cover of this issue.

## Selected Subjects

**Air Pollution Control**
Environmental Protection Agency

**Authority Delegations (Government Agencies)**
Small Business Administration

**Aviation Safety**
Federal Aviation Administration

**Blood**
Food and Drug Administration

**Cable Television**
Federal Communications Commission

**Customs Duties and Inspection**
Customs Service

**Fair Housing**
Housing and Urban Development Department

**Government Procurement**
Defense Department
General Services Administration
National Aeronautics and Space Administration
Small Business Administration

**Income Taxes**
Internal Revenue Service

**Military Personnel**
Army Department

**Milk Marketing Orders**
Agricultural Marketing Service

CONTINUED INSIDE

# Selected Subjects

**FEDERAL REGISTER** Published daily, Monday through Friday, (not published on Saturdays, Sundays, or on official holidays), by the Office of the Federal Register, National Archives and Records Administration, Washington, DC 20408, under the Federal Register Act (49 Stat. 500, as amended; 44 U.S.C. Ch. 15) and the regulations of the Administrative Committee of the Federal Register (1 CFR Ch. I). Distribution is made only by the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

The **Federal Register** provides a uniform system for making available to the public regulations and legal notices issued by Federal agencies. These include Presidential proclamations and Executive Orders and Federal agency documents having general applicability and legal effect, documents required to be published by act of Congress and other Federal agency documents of public interest. Documents are on file for public inspection in the Office of the Federal Register the day before they are published, unless earlier filing is requested by the issuing agency.

The **Federal Register** will be furnished by mail to subscribers for $300.00 per year, or $150.00 for 6 months, payable in advance. The charge for individual copies is $1.50 for each issue, or $1.50 for each group of pages as actually bound. Remit check or money order, made payable to the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

There are no restrictions on the republication of material appearing in the **Federal Register.**

Questions and requests for specific information may be directed to the telephone numbers listed under INFORMATION AND ASSISTANCE in the READER AIDS section of this issue.

**How To Cite This Publication:** Use the volume number and the page number. Example: 50 FR 12345.

**Organization and Functions (Government Agencies)**
Consumer Product Safety Commission
Transportation Department

**Postal Service**
Postal Service

**Radio**
Federal Communications Commission

**Savings and Loan Associations**
Federal Home Loan Bank Board

**Securities**
Securities and Exchange Commission

**Water Pollution Control**
Environmental Protection Agency

## THE FEDERAL REGISTER: WHAT IT IS AND HOW TO USE IT

FOR: Any person who uses the Federal Register and Code of Federal Regulations.

WHO: The Office of the Federal Register.

WHAT: Free public briefings (approximately 2 1/2 hours) to present:
1. The regulatory process, with a focus on the Federal Register system and the public's role in the development of regulations.
2. The relationship between the Federal Register and Code of Federal Regulations.
3. The important elements of typical Federal Register documents.
4. An introduction to the finding aids of the FR/CFR system.

WHY: To provide the public with access to information necessary to research Federal agency regulations which directly affect them. There will be no discussion of specific agency regulations.

### WASHINGTON, DC

WHEN: January 17; at 9 am.

WHERE: Office of the Federal Register, First Floor Conference Room, 1100 L Street NW., Washington, DC.

RESERVATIONS: Howard Landon 202-523-5227 (Voice)
Melanie Williams 202-523-5229 (TDD)

FUTURE WORKSHOPS: Additional workshops are scheduled bimonthly in Washington and on an annual basis in Federal regional cities. Dates and locations will be announced later.

**NOTE: There will be a sign language interpreter for hearing impaired persons at this briefing.**

# Contents

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

**The President**
PROCLAMATIONS
52755 Generalized System of Preferences; amendment (Proc. 5423)

**Executive Agencies**

**Agricultural Marketing Service**
RULES
Milk marketing orders:
52435 Southern Illinois

**Agriculture Department**
*See* Agricultural Marketing Service; Federal Grain Inspection Service.

**Alcohol, Drug Abuse, and Mental Health Administration**
NOTICES
52561 Acquired Immunodeficiency Syndrome (AIDS); alcohol, drug abuse, and mental health aspects

**Antitrust Division**
NOTICES
National cooperative research notifications:
52568 Portland Cement Association
52568 Semiconductor Research Corp.

**Army Department**
RULES
52447 Family support, child custody, and paternity

**Coast Guard**
PROPOSED RULES
Ports and waterways safety:
52534 Port access routes; Santa Barbara Channel area; study; correction

**Commerce Department**
*See* National Bureau of Standards; National Oceanic and Atmospheric Administration.

**Commodity Futures Trading Commission**
NOTICES
52583 Meetings; Sunshine Act (6 documents)

**Consumer Product Safety Commission**
RULES
Organization, functions, and authority delegations:
52440 Media Relations Office and Information and Public Affairs Office

**Copyright Office, Library of Congress**
RULES
52458 Coin-operated phonorecord players; recordation and certification

**Customs Service**
PROPOSED RULES
Merchandise entry:
52532 Consolidated shipments; designation of brokers

**Defense Department**
*See also* Army Department.
RULES
52443 Contractors receiving negotiated contract awards ($10 million or more)
PROPOSED RULES
Federal Acquisition Regulation (FAR):
52727 Selling costs
NOTICES
Meetings:
52550 Electron Devices Advisory Group
52550 Military Personnel Testing Advisory Committee

**Education Department**
NOTICES
Grants; availability, etc.:
52550 Postsecondary education improvement fund; comprehensive program
Meetings:
52552 Women's Educational Programs National Advisory Council

**Energy Department**
NOTICES
Atomic energy agreements; subsequent arrangements:
52552 Energy Department
Environmental statements; availability, etc.:
52553 Lakeview Uranium Mill Tailings Site, OR
Floodplain and wetlands protection; environmental review determinations; availability, etc.:
52555 Lakeview Uranium Mill Tailings Site, Lakeview, OR

**Environmental Protection Agency**
RULES
Air quality implementation plans; approval and promulgation; various States:
52460 Florida
52461 Rhode Island; correction
PROPOSED RULES
Water quality standards:
52540 Kentucky
NOTICES
Air quality; prevention of significant deterioration (PSD):
52556 Permit determinations, etc.; Region IX
Air quality criteria:
52556 Ozone and other photochemical oxidants

**Federal Aviation Administration**
RULES
52439 Airport radar service areas; correction
Airworthiness directives:
52437 Bell
52438 Sikorsky
52439 Restricted areas; correction
PROPOSED RULES
52532 Terminal control areas; correction
NOTICES
52578 Airport noise compatibility program:
Jackson Hole Airport, WY

**Federal Communications Commission**
RULES
Frequency allocations and radio treaty matters:
52462 Fixed and mobile services and radio astronomy services; footnotes removed
Television broadcasting:
52462 Cable television systems; technical and operational requirements review
PROPOSED RULES
Radio services; special:
52543 Satellite communications; direct broadcast satellite service; technical standards; comment period extended

**Federal Deposit Insurance Corporation**
NOTICES
52557 Banking system; disclosure by FDIC of statutory enforcement actions; policy statement; effective date deferred

**Federal Grain Inspection Service**
PROPOSED RULES
52469 Standards for inspection and certification of certain agricultural commodities and products

**Federal Highway Administration**
PROPOSED RULES
Engineering and traffic operations:
52534 Uniform Traffic Control Devices Manual; extension of time

**Federal Home Loan Bank Board**
PROPOSED RULES
Federal savings and loan system:
52482 Corporate governance; reorganization

**Federal Maritime Commission**
NOTICES
52557 Agreements filed, etc.

**Federal Mediation and Conciliation Service**
NOTICES
Grants; availability, etc.:
52558 Labor-management cooperation program

**Federal Railroad Administration**
NOTICES
Exemption petitions, etc.:
52579 Atchison, Topeka & Santa Fe Railway Co.
52579 Canadian Pacific, Ltd.
52580 Chicago & North Western Transportation Co.
52580 Natchez Trace Railroad (NTR) et al.
52581 Seaboard System Railroad

**Federal Reserve System**
NOTICES
52583 Meetings; Sunshine Act (2 documents)

**Federal Trade Commission**
NOTICES
52560 Premerger notification waiting periods; early terminations

**Fish and Wildlife Service**
NOTICES
52565 Endangered and threatened species permit applications

**Food and Drug Administration**
PROPOSED RULES
Biological products:
52602 Blood and blood derivatives; efficacy review implementation
NOTICES
Food additive petitions:
52562 Kureha Chemical Industry Co., Ltd.; withdrawal
Human drugs:
52561 Regulatory review period determination; Fortaz; correction
52562 Regulatory review period determination; Hexabrix injection; correction
52564 Regulatory review period determination; Sulcosyn solution
Meetings:
52562 Advisory committees, panels, etc.

**General Services Administration**
PROPOSED RULES
Federal Acquisition Regulation (FAR):
52727 Selling costs

**Health and Human Services Department**
*See* Alcohol, Drug Abuse, and Mental Health Administration; Food and Drug Administration.

**Housing and Urban Development Department**
RULES
Fair housing:
52441 Nondiscrimination and equal opportunity in housing

**Interior Department**
*See* Fish and Wildlife Service; Land Management Bureau; National Park Service.

**Internal Revenue Service**
RULES
Income taxes:
52443 Fringe benefits; listed property; reporting and recordkeeping requirements; temporary; correction

**Interstate Commerce Commission**
NOTICES
Railroad services abandonment:
52567 Burlington Northern Railroad Co.
52568 Chicago & North Western Transportation Co.
52567 Illinois Central Gulf Railroad Co.

**Justice Department**
*See* Antitrust Division; National Institute of Justice.

**Labor Department**
*See also* Mine Safety and Health Administration; Occupational Safety and Health Administration.
NOTICES
Meetings:
52569 Trade Negotiations and Trade Policy Labor Advisory Committee

**Land Management Bureau**
NOTICES
Environmental statements; availability, etc.:
52565 Kemmerer Resource Area, WY
52565 Public lands; National Wildlife Federation v. Burford; court order publication

**Library of Congress**
*See* Copyright Office, Library of Congress.

**Management and Budget Office**
NOTICES
52730 Federal information management (Circular A–130)

**Mine Safety and Health Administration**
NOTICES
Safety standard petitions:
52570 Union Oil Co. of California

**National Aeronautics and Space Administration**
PROPOSED RULES
Federal Acquisition Regulation (FAR):
52727 Selling costs

**National Bureau of Standards**
NOTICES
Information processing standards, Federal:
52546 Minimal BASIC and FORTRAN

**National Commission on Employment Policy**
NOTICES
52570 Business careers; hearing

**National Foundation on Arts and Humanities**
NOTICES
52571 Agency information collection activities under OMB review

**National Highway Traffic Safety Administration**
PROPOSED RULES
Motor vehicle safety standards:
52544 Lamps, reflective devices, and associated equipment; removable transparent headlamp covers; petition denied
NOTICES
Motor vehicle safety standards; exemption petitions, etc.:
52581 Alfa Romeo, Inc.

**National Institute of Justice**
NOTICES
52569 Adult property offenders, ethnographic study; report availability

**National Oceanic and Atmospheric Administration**
NOTICES
Permits:
52549 Marine mammals

**National Park Service**
NOTICES
Historic Places National Register; pending nominations:
52566 Alabama et al.
52566 Florida

**National Transportation Safety Board**
NOTICES
52584 Meetings; Sunshine Act

**Nuclear Regulatory Commission**
NOTICES
Meetings
52572 Reactor Safeguards Advisory Committee (3 documents)

**Occupational Safety and Health Administration**
NOTICES
Meetings:
52570 Occupational Safety and Health Federal Advisory Council

**Pacific Northwest Electric Power and Conservation Planning Council**
NOTICES
Power plan amendments:
52575 Columbia River Basin fish and wildlife program

**Personnel Management Office**
NOTICES
Excepted service:
52573 Schedules A, B, and C; positions placed or revoked; update

**Postal Service**
PROPOSED RULES
Domestic Mail Manual:
52534 Plant-Load Operations

**Securities and Exchange Commission**
RULES
Securities:
52440 Broker-dealers; registration; applicability to banks; request for exemptions

**Small Business Administration**
RULES
Organization, functions, and authority delegations:
52436 Program activities in field offices; certificate of competency approval
52436 Procurement assistance; certificate of competency program; approval authority
NOTICES
Applications, etc.:
52577 Magna Pacific Investments
Disaster loan areas:
52577 Arkansas
52577 Florida
52577 Florida; correction
52577 New York

**State Department**
NOTICES
Meetings:
52578 International Radio Consultative Committee

**Textile Agreements Implementation Committee**
NOTICES
Cotton, wool, and man-made textiles:
52549 Turkey

**Transportation Department**
*See also* Coast Guard; Federal Aviation Administration; Federal Highway Administration; Federal Railroad Administration; National Highway Traffic Safety Administration.
RULES
Organization, functions, and authority delegations:
52467 Assistant Secretary for Policy and International Affairs; aviation consumer protection regulations, etc.
52439 Director, Office of Community and Consumer Affairs; aviation economic functions

NOTICES
Aviation proceedings:
52578 Standard foreign fare level; index adjustment factors

**Treasury Department**
*See* Customs Service; Internal Revenue Service.

**Veterans Administration**
NOTICES
52582 Agency information collection activities under OMB review

---

**Separate Parts in This Issue**

**Part II**
52602 Department of Health and Human Services, Food and Drug Administration

**Part III**
52727 Department of Defense
General Services Administration
National Aeronautics and Space Administration

**Part IV**
52730 Office of Management and Budget

**Part V**
52755 The President

---

**Reader Aids**
Additional information, including a list of public laws, telephone numbers, and finding aids, appears in the Reader Aids section at the end of this issue.

## CFR PARTS AFFECTED IN THIS ISSUE

A cumulative list of the parts affected this month can be found in the Reader Aids section at the end of this issue.

**3 CFR**
**Proclamations:**
5423 ..... 52755

**7 CFR**
1032 ..... 52435
**Proposed Rules:**
68 ..... 52469

**12 CFR**
**Proposed Rules:**
543 ..... 52482
544 ..... 52482

**13 CFR**
101 ..... 52436
125 ..... 52436

**14 CFR**
39 (2 documents) ..... 52437, 52438
71 ..... 52439
73 ..... 52439
385 ..... 52439
**Proposed Rules:**
71 ..... 52532

**16 CFR**
1000 ..... 52440

**17 CFR**
240 ..... 52440

**19 CFR**
**Proposed Rules:**
141 ..... 52532

**21 CFR**
**Proposed Rules:**
606 ..... 52602
610 ..... 52602
640 ..... 52602

**23 CFR**
**Proposed Rules:**
625 ..... 52534
655 ..... 52534

**24 CFR**
107 ..... 52441

**26 CFR**
1 ..... 52443
602 ..... 52443

**32 CFR**
166 ..... 52443
584 ..... 52447

**33 CFR**
**Proposed Rules:**
166 ..... 52534
167 ..... 52534

**37 CFR**
201 ..... 52458

**39 CFR**
**Proposed Rules:**
111 ..... 52534

**40 CFR**
52 (2 documents) ..... 52460, 52461
**Proposed Rules:**
131 ..... 52540

**47 CFR**
2 ..... 52462
76 ..... 52462
**Proposed Rules:**
100 ..... 52543

**48 CFR**
**Proposed Rules:**
31 ..... 52727

**49 CFR**
1 ..... 52467
**Proposed Rules:**
571 ..... 52544

# Rules and Regulations

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

This section of the FEDERAL REGISTER contains regulatory documents having general applicability and legal effect, most of which are keyed to and codified in the Code of Federal Regulations, which is published under 50 titles pursuant to 44 U.S.C. 1510.
The Code of Federal Regulations is sold by the Superintendent of Documents. Prices of new books are listed in the first FEDERAL REGISTER issue of each week.

## DEPARTMENT OF AGRICULTURE

### Agricultural Marketing Service

### 7 CFR Part 1032

### Milk in the Southern Illinois Marketing Area; Order Suspending Certain Provisions of the Order

**AGENCY:** Agricultural Marketing Service, USDA.

**ACTION:** Suspension of rules.

**SUMMARY:** This action suspends certain provisions of the Southern Illinois order concerning the shipping standards for regulating supply plants under the order. The suspension lowers the proportion of milk receipts (from 50 to 40 percent) that must be shipped from supply plants to bottling plants during December 1985. The suspension was requested by Mid-America Dairymen, Inc., a cooperative association that represents a substantial number of the producers who supply the market. The action is necessary because higher production and seasonally decreasing sales of fluid milk products during the December holiday season reduce the need for bottling plants to rely on supply plant milk for fluid milk needs. Absent a suspension, costly and inefficient shipments of milk would be made solely for the purpose of assuring that dairy farmers, who regularly supply the fluid milk needs of the market, would continue to have their milk priced under the order.

**EFFECTIVE DATE:** December 24, 1985.

**FOR FURTHER INFORMATION CONTACT:** John F. Borovies, Marketing Specialist, Dairy Division, Agricultural Marketing Service, U.S. Department of Agriculture, Washington, DC 20250, (202) 447-2089.

**SUPPLEMENTARY INFORMATION:** Prior document in this proceeding:

Notice of Proposed Suspension: Issued November 26, 1985; published December 2, 1985 (50 FR 49395).

The Administrator of the Agricultural Marketing Service has determined that this rule will not have a significant economic impact on a substantial number of small entities. The action lessens the regulatory impact of the order on certain milk handlers and tends to insure that dairy farmers will continue to have their milk priced under the order and thereby receive the benefits that accrue from such pricing.

This order of suspension is issued pursuant to the provisions of the Agricultural Marketing Agreement Act of 1937, as amended (7 U.S.C. 601 *et seq.*), and of the order regulating the handling of milk in the Southern Illinois marketing area.

Notice of proposed rulemaking was published in the **Federal Register** on December 2, 1985 (50 FR 49395) concerning a proposed suspension of certain provisions of the order. Interested persons were given an opportunity to file written data, views, and arguments thereon. No comments opposing the proposed action were received.

After consideration of all relevant material, including the proposal in the notice and other available information, it is hereby found and determined that for the month of December 1985 the following provisions of the order do not tend to effectuate the declared policy of the Act:

In § 1032.7(b), the words "which have at least 50 percent Class I use (not including filled milk) of the total of such supply plant milk and producer milk receipts" and the words "through February".

**Statement of Consideration**

This action suspends certain provisions concerning the shipping standards for regulating supply plants under the Southern Illinois order. The suspension lowers the proportion of milk receipts (from 50 to 40 percent) that supply plants must ship to pool distributing plants to attain pool plant status during December 1985.

The suspension was requested by Mid-America Dairymen, Inc., a cooperative association that represents a substantial number of producers who supply the market. Mid-Am contends that the action is necessary to recognize the lesser need for supply plant shipments to meet the fluid milk requirements of distributing plants during December 1985.

The suspension is necessary because of production increases by producers over year-earlier levels. The higher level of production has reduced the degree to which distributing plants need to rely on supply plant shipments for milk requirements. As sales of fluid milk products decline during the December holiday season, the need for milk from supply plants will be further reduced. In the absence of a suspension action to recognize the declining need for supply plant milk during December, costly and inefficient shipments of milk from supply supply plants would be made solely for the purpose of assuring that the milk of dairy farmers who have regularly supplied the fluid needs of the market would continue to be priced under the order.

Interested parties were given an opportunity to submit written data, views, or arguments concerning this action. No comments in opposition to the suspension were received.

It is hereby found and determined that thirty days' notice of the effective date hereof is impractical, unnecessary and contrary to the public interest in that:

(a) This suspension is necessary to reflect current marketing conditions and to assure the orderly marketing of milk in the marketing area in that without the suspension costly and inefficient shipments of milk would be made solely for the purpose of assuring that dairy farmers would continue to have their milk priced under the order;

(b) This suspension does not require of persons affected substantial or extensive preparation prior to the effective date; and

(c) Notice of proposed rulemaking was given interested parties and they were afforded opportunity to file written data, views, or arguments concerning this suspension. No opposing views were received.

Therefore, good cause exists for making this order effective upon publication in the **Federal Register.**

**List of Subjects in 7 CFR Part 1032**

Milk marketing orders, Milk, Dairy products.

The authority citation for 7 CFR Part 1032 continues to read as follows:

**Authority:** (Secs. 1-19, 48 Stat. 31, as amended; 7 U.S.C. 601-674).

*It is therefore ordered,* That the following language in § 1032.7 of the order is hereby suspended for the month of December 1985.

## PART 1032—MILK IN THE SOUTHERN ILLINOIS MARKETING AREA

**§ 1032.7 [Amended]**

In 7 CFR Part 1032 in § 1032.7(b), the words "which have at least 50 percent Class I use (not including filled milk) of the total of such supply plant milk and producer milk receipts" and the words "through February".

Effective date: December 24, 1985.

Signed at Washington, DC on: December 18, 1985.

Alan T. Tracy,

*Deputy Assistant Secretary, Marketing and Inspection Services.*

[FR Doc. 85-30332 Filed 12-23-85; 8:45 am]

BILLING CODE 3410-02-M

## SMALL BUSINESS ADMINISTRATION

### 13 CFR Part 101

**[Revision 2—Amdt. 41]**

### Delegation of Authority To Conduct Program Activities in Field Offices; Certificate of Competency Approval Authority

**AGENCY:** Small Business Administration.

**ACTION:** Final rule.

**SUMMARY:** Increases the Regional Administrators' authority to approve applications for Certificates of Competency from $2,000,000 to $5,000,000 and allows the regional office COC specialists approval authority on COC cases valued less than $250,000. Increasing the monetary approval authority of Regional Administrators will improve and speed program delivery by placing the authority in the regional office which has direct responsibility of delivering SBA assistance. Delegating COC decision authority on cases valued less than $250,000 to Regional Office COC specialists will expedite the process procedure on small dollar value cases and improve program delivery at the regional office level. Prior to the expiration date of this change, SBA will evaluate if benefits accrued to the SBA and small businesses would merit extension of this rule.

**EFFECTIVE DATE:** December 24, 1985, for the period of one year.

**FOR FURTHER INFORMATION CONTACT:** John Whitmore, Director, Office of Industrial Assistance, Small Business Administration, 1441 L Street, NW., Washington, DC 20416. Telephone No. (202) 653-6582.

**SUPPLEMENTARY INFORMATION:** Part 101 consists of rules relating to the Agency's organization and procedures; therefore, notice of proposed rulemaking, public participation and a regulatory flexibility review, 5 U.S.C. 501 et seq., are not required and this amendment is adopted without resort to those procedures. This amendment does not contain recordkeeping requirements subject to the Paperwork Reduction Act 44 U.S.C. Chapter 35 and is not a major rule for purposes of Executive Order 12291.

For the reasons set forth in the preamble Part 101, 13 CFR 101.3-2 is amended, following the index terms, as set forth below:

**List of Subjects in 13 CFR Part 101**

Authority delegations (Government agencies), Administrative practice and procedure, Organization and functions (Government agencies).

## PART 101—[AMENDED]

1. The authority citation for Part 101 continues to read as follows:

Authority: Secs. 4 and 5, Pub. L. 85-536, 72 Stat. 384 and 385 (15 U.S.C. 633 and 634, as amended); sec. 308, Pub. L. 85-699, 72 Stat. 694 (15 U.S.C. 687, as amended); sec. 5(b)(11), Pub. L. 93-386 (Aug. 23, 1974); and 5 U.S.C. 552, unless otherwise noted.

2. In § 101.3-2 Part VI, Section A is revised to read as follows:

**§ 101.3-2 Delegations of Authority to conduct program activities in field offices.**

* * * * *

**Part VI—Procurement Assistance Program (PA)**

*Section A—Certification of Competency Approval Authority*

1. To approve applications for a Certificate of Competency (COC) received from small business concerns located within the region's geographic jurisdiction, subject to the following monetary limitations:

| | |
|---|---|
| a. Regional Administrator | $5,000,000 |
| b. Deputy Regional Administrator | 2,000,000 |
| c. Assistant Regional Administrator/PA | 2,000,000 |
| d. COC Specialist | 250,000 |

2. To deny an application for a Certificate of Competency (COC) received from small business concerns located within the region's geographic jurisdiction, subject to the following monetary limitations:

| | |
|---|---|
| a. Regional Administrator | Unlimited |
| b. Deputy Regional Administrator | Unlimited |
| c. Assistant Regional Administrator/PA | Unlimited |
| d. COC Specialist | $250,000 |

* * * * *

Dated: December 11, 1985.

James C. Sanders,

*Administrator.*

[FR Doc. 85-30358 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

### 13 CFR Part 125

**[Revision 1, Amendment 5]**

### Certificate of Competency Program: Certificate of Competency Approval Authority

**AGENCY:** Small Business Administration (SBA).

**ACTION:** Final rule.

**SUMMARY:** This change transfers the monetary limit on the Regional Office's delegated COC authority from 13 CFR Part 125.5 to the more appropriate section of the regulation, 13 CFR Part 101.3. This is an administrative change and will not effect the COC process. An increase in the Regional Administrators delegated authority from the current $2,000,000 level to $5,000,000 is being processed simultaneously by amending Section 13 CFR 101.3.

**EFFECTIVE DATE:** December 24, 1985, for the period of one year.

**FOR FURTHER INFORMATION CONTACT:** John Whitmore, Director, Office of Industrial Assistance, Small Business Administration 1441 L Street, NW., Washington, DC 20416. Telephone No. (202) 653-6582.

**SUPPLEMENTARY INFORMATION:** Inasmuch as the amendment set forth below affects internal procedures only, notice of proposed rulemaking, public participation and a Regulatory Flexibility Review pursuant to 5 U.S.C. 601 et seq., are not required and this amendment is adopted without resort to those procedures. This amendment does not contain recordkeeping requirements subject to the Paperwork Reduction Act 44 U.S.C. Chapter 35 and is not a major rule for purposes of Executive Order 12291, since it relates solely to Agency organization.

The following topic index may be useful in determining interest in this regulation:

**List of Subjects in 13 CFR Part 125**

Government procurement, Small business, Technical assistance.

1. The authority citation for 13 CFR Part 125 continues to read as follows:

**Authority:** Secs. 8 and 15 of the Small Business Act, 72 Stat. 384, as amended (15 U.S.C. 631).

2. For the reasons set forth in the preamble 13 CFR Part 125, § 125.5(f) is revised as follows:

**§ 125.5 Certificate of competency program.**

* * * * *

(f) If the Regional Office's decision is negative, the COC is denied and both the firm and procuring agency are notified. If the Regional Office's decision is affirmative and the dollar value of the procurement is within the region's delegated authority, the Regional Office issues a Certificate. Contracting officers will be informed in advance of issuing. For procurements in excess of the region's delegated authority, if the Regional Office recommends issuance of the Certificate, the Associate Administrator for Procurement Assistance, SBA Central Office, causes a review to be made and either issues or denies the Certificate. If the Associate Administrator's decision is negative, the firm and procuring activity are so informed; if affirmative, a letter, certifying the responsibility of the firm as to the elements of responsibility referred (the COC) is sent to the procuring activity and the applicant informed of such issuance by the regional office.

* * * * *

Dated: December 11, 1985.

James C. Sanders,

*Administrator.*

[FR Doc. 85-30357 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

---

## DEPARTMENT OF TRANSPORTATION

### Federal Aviation Administration

### 14 CFR Part 39

[Docket No. 85-ASW-16, Amdt. 39-5186]

## Airworthiness Directives; Bell Helicopter Textron, Inc. (BHTI), Model 47B, 47B3, 47D, 47D1, 47E, 47G, 47H-1, and 47G-3; Hawkeye Rotor and Wing, U.S. Army Model OH-13E; and Texas Helicopter Corporation, U.S. Army Model OH-13E Helicopters

**AGENCY:** Federal Aviation Administration (FAA), DOT.

**ACTION:** Final rule.

**SUMMARY:** This action publishes in the **Federal Register** and makes effective as to all persons an amendment adopting a new airworthiness directive (AD) which was previously made effective as to all known U.S. owners and operators of certain Bell Helicopter Textron, Inc., Model 47B, 47B3, 47D, 47D1, 47E, 47G, 47H-1, and 47G-3; Hawkeye Rotor and Wing, U.S. Army Model OH-13E; and Texas Helicopter Corporation, U.S. Army Model OH-13E helicopters by individual priority letters. The AD requires removal of all Texas Helicopter Corporation tail rotor blade yokes. The AD is needed to prevent rotorcraft from flying with improperly heat treated tail rotor blade yokes which could fail prematurely resulting in probable loss of the helicopter.

**EFFECTIVE DATE:** January 8, 1986, as to all persons except those persons to whom it was made immediately effective by priority letter AD 85-15-04, issued July 23, 1985, which contained this amendment.

*Compliance:* Required within the next 10 hours' time in service after the effective date of this AD, unless already accomplished.

**FOR FURTHER INFORMATION CONTACT:** Gary B. Roach, Helicopter Certification Branch, ASW-170, Aircraft Certification Division, Southwest Region, Federal Aviation Administration, P.O. Box 1689, Fort Worth, Texas 76101, telephone number (817) 877-2593.

**SUPPLEMENTARY INFORMATION:** On July 23, 1985, priority letter AD 85-15-04 was issued and made effective as to all known U.S. owners and operators of certain BHTI Model 47B, 47B3, 47D, 47D1, 47E, 47G, 47H-1 and 47G-3; Hawkeye Rotor and Wing, U.S. Army Model OH-13E; and Texas Helicopter Corporation, U.S. Army Model OH-13E helicopters. The AD requires removal of all Texas Helicopter Corporation tail rotor blade yokes Part Number (P/N) 74-641-057-9.

This AD was prompted by the failure of a tail rotor blade yoke which resulted in loss of control and subsequent loss of the helicopter. During the postcrash investigation, it was discovered that spindle threads of the failed yoke had been nitrided which is not in accordance with the engineering drawing. This condition could cause premature failure of the yoke. A total of 90 tail rotor blade yokes (P/N 74-641-057-9) were manufactured by Texas Helicopter Corporation. Two other yokes randomly selected from the lot of 90 were examined and determined to have nitrided spindle threads. Thus, it was determined that AD action was necessary to prevent possible failure of the tail rotor blade yoke. Failure of the tail rotor blade yoke would probably result in loss of control of the helicopter.

Since it was found that immediate correction was required, notice and public procedure thereon were impracticable and contrary to public interest, and good cause existed to make the AD effective immediately by individual priority letter issued July 23, 1985, to all known U.S. owners and operators of certain BHTI Model 47B, 47B3, 47D, 47D1, 47E, 47G, 47H-1, and 47G-3; Hawkeye Rotor and Wing, U.S. Army Model OH-13E; and Texas Helicopter Corporation, U.S. Army Model OH-13E helicopters. These conditions still exist and the AD is hereby published in the **Federal Register** as an amendment to § 39.13 of the Federal Aviation Regulations to make it effective as to all persons.

The FAA has determined that this regulation is an emergency regulation that is not considered to be major under Executive Order 12291. It is impracticable for the agency to follow the procedures of Order 12291 with respect to this rule since the rule must be issued immediately to correct an unsafe condition in aircraft. It has been further determined that this action involves an emergency regulation under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979). If this action is subsequently determined to involve a significant/major regulation, a final regulatory evaluation or analysis, as appropriate, will be prepared and placed in the regulatory docket (otherwise, an evaluation or analysis is not required). A copy of it, when filed, may be obtained by contacting the person identified under the caption **"FOR FURTHER INFORMATION CONTACT."**

### List of Subjects 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Safety.

### Adoption of the Amendment

### PART 39—[AMENDED]

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends § 39.13 of Part 39 of the FAR as follows:

1. The authority citation for Part 39 continues to read as follows:

**Authority:** 49 U.S.C. 1354(a), 1421, and 1423; 49 U.S.C. 106(g) (Revised Pub. L. 97-449, January 12, 1983); and 14 CFR 11.89.

2. By adding the following new AD:

**Bell Helicopter Textron, Inc., Hawkeye Rotor and Wing, Texas Helicopter Corporation:** Applies to Model 47B, 47B3, 47D, 47D1, 47E, 47G, 47H-1, 47G-3, U.S. Army Model OH-13E helicopters certified in any category and other helicopters equipped with tail rotor blade yoke P/N 74-641-057-9.

Compliance is required as indicated, unless already accomplished.

To prevent the failure of the tail rotor blade yoke, accomplish the following:

(a) Within the next 10 hours' time in service after the effective date of this AD, remove from service Texas Helicopter Corporation tail rotor blade yoke P/N 74-641-057-9.

(b) Any equivalent method of compliance with this AD which provides an equivalent level of safety may be used when approved by the Manager, Helicopter Certification Branch, Federal Aviation Administration, 4400 Blue Mound Road, Fort Worth, Texas 76106.

(c) In accordance with FAR §§ 21.197 and 21.199, flight is permitted to a base where the replacement required by this AD may be accomplished.

This amendment becomes effective January 8, 1986, as to all persons except those to whom it was made immediately effective by priority letter AD 85-15-04, issued July 23, 1985, which contained this amendment.

Issued in Fort Worth, Texas, on December 10, 1985.

**C.R. Melugin, Jr.,**

*Director, Southwest Region.*

[FR Doc. 85-30308 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-13-M

---

**14 CFR Part 39**

**[Docket No. 85-ASW-30, Amdt. 39-5172]**

## Airworthiness Directives; Sikorsky Aircraft Model S-64E Helicopters

**AGENCY:** Federal Aviation Administration (FAA), DOT.

**ACTION:** Final rule.

**SUMMARY:** This amendment adopts a new airworthiness directive (AD) which requires (1) Repetitive visual inspections of the main rotor torque tube inner bracket assembly for cracks and corrosion; (2) replacement if cracked; and (3) replacement or rework, as necessary, if corroded on Sikorsky Aircraft Model S-64E helicopters. The AD is needed to prevent fatigue cracking in the main rotor head torque tube inner bracket which could lead to failure and possible loss of control of the helicopter.

**EFFECTIVE DATE:** December 30, 1985.

*Compliance:* As prescribed in the body of the AD.

The incorporation by reference of certain publications listed in the regulations is approved by the Director of the **Federal Register** as of December 30, 1985.

**ADDRESSES:** The applicable service information may be obtained from Sikorsky Aircraft Division, United Technologies Corporation, North Main Street, Stratford, Connecticut 06601.

A copy of the service bulletin is contained in the Rules Docket, Office of the Regional Counsel, FAA, Southwest Region, 4400 Blue Mound Road, Fort Worth, Texas 76106.

**FOR FURTHER INFORMATION CONTACT:** Cheryl McCabe, Boston Aircraft Certification Office, ANE-152, New England Region, FAA, 12 New England Executive Park, Burlington, Massachusetts 01803, telephone (617) 273-7112.

**SUPPLEMENTARY INFORMATION:** The U.S. Army reported an occurrence where a main rotor head torque tube inner bracket assembly experienced a fatigue crack in a military helicopter which uses an assembly similar to that used on the civilian version Model S-64E helicopter. The FAA has determined that a fatigue crack in the main rotor head torque tube inner bracket could lead to failure and possible loss of control of the helicopter. Since this condition is likely to exist or develop on other helicopters of the S-64E type design, an AD is being issued which requires: (1) Repetitive visual inspections of the main rotor torque tube inner bracket assembly for cracks and corrosion; (2) replacement if cracked; and (3) replacement or rework, as necessary, if corroded on Sikorsky Aircraft Model S-64E helicopters.

Since a situation exists that requires the immediate adoption of this regulation, it is found that notice and public procedure hereon are impracticable and good cause exists for making this amendment effective in less than 30 days.

The FAA has determined that this regulation is an emergency regulation that is not considered to be major under Executive Order 12291. It is impracticable for the agency to follow the procedures of Executive Order 12291 with respect to this rule since the rule must be issued immediately to correct an unsafe condition in aircraft. It has been further determined that this action involves an emergency regulation under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979). If this action is subsequently determined to involve a significant/major regulation, a final regulatory evaluation or analysis, as appropriate, will be prepared and placed in the regulatory docket (otherwise, an evaluation or analysis is not required). A copy of it, when filed, may be obtained by contacting the person identified under the caption **"FOR FURTHER INFORMATION CONTACT."**

**List of Subjects in 14 CFR Part 39**

Air transportation, Aircraft, Aviation safety, Safety, and Incorporation by reference.

**Adoption of the Amendment**

**PART 39—[AMENDED]**

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends § 39.13 of Part 39 of the FAR as follows:

1. The authority citation for Part 39 continues to read as follows:

**Authority:** 49 U.S.C. 1354(a), 1421, and 1423; 49 U.S.C. 106(g) (Revised Pub. L. 97-449, January 12, 1983); and 14 CFR 11.89.

2. By adding the following new AD:

**Sikorsky Aircraft: Applies to Model S-64E helicopters, certificated in any category.**

Compliance is required as indicated, unless already accomplished.

To prevent operation with a cracked main rotor head torque tube inner bracket, accomplish the following:

(a) Prior to the first flight of each day, after the effective date of this AD, visually inspect with a 10-power or higher magnifying glass the main rotor head torque tube inner bracket assembly, Part Number S1510-21332-0, for cracks and/or corrosion in accordance with Section 2, Paragraph A, of Sikorsky Alert Service Bulletin (ASB) No. 64B10-4A, dated July 17, 1985, or an FAA-approved equivalent.

(b) If the torque tube inner bracket assembly is cracked, replace with a serviceable torque tube inner bracket assembly prior to further flight in accordance with Section 2, Paragraph A, of Sikorsky ASB No. 64B10-4A, dated July 17, 1985, or an FAA-approved equivalent.

(c) If the torque tube inner bracket assembly is corroded, determine the extent and limits of the corrosion prior to further flight in accordance with Section 2, Paragraph B, of Sikorsky ASB No. 64B10-4A, dated July 17, 1985, or an FAA-approved equivalent. If the extent or limits of the corrosion are exceeded, replace with a serviceable torque tube inner bracket assembly prior to further flight in accordance with Section 2, Paragraph B, of Sikorsky ASB No. 64B10-4A, dated July 17, 1985, or an FAA-approved equivalent. Otherwise, rework the torque tube inner bracket assembly prior to further flight in accordance with Section 2, Paragraph A, of Sikorsky ASB No. 64B10-4A, dated July 17, 1985, or an FAA-approved equivalent.

(d) Aircraft may be ferried in accordance with the provisions of §§ 21.197 and 21.199 to a base where the AD can be accomplished.

(e) Upon request, an alternative means of

compliance with the requirements of this AD which provide an equivalent level of safety may be used when approved by the Manager, Boston Aircraft Certification Office, 12 New England Executive Park, Burlington, Massachusetts 01803, telephone (617) 273-7112.

Sikorsky ASB No. 64B10-4A, dated July 17, 1985, identified and described in this directive is incorporated herein and made a part hereof pursuant to 5 U.S.C. 552(a)(1). All persons affected by this directive who have not already received this document from the manufacturer may obtain copies upon request to Sikorsky Aircraft Division, United Technologies Corporation, North Main Street, Stratford, Connecticut 06601. These documents may also be examined at the Office of the Regional Counsel, FAA, Southwest Region, 4400 Blue Mound Road, Fort Worth, Texas 76106.

This amendment becomes effective December 30, 1985.

Issued in Fort Worth, Texas, on November 19, 1985.

F.E. Whitfield,

*Acting Director, Southwest Region.*

[FR Doc. 85-30307 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-13-M

---

## 14 CFR Part 71

**[Airspace Docket No. 85-AWA-2]**

### Establishment of Airport Radar Service Areas

*Correction*

In FR Doc. 85-29125, beginning on page 50254, in the issue of Monday, December 9, 1985, make the following corrections:

1. On page 50254, second column, in the sixth line under "ARSA Program Comments", "the" should read "that";

2. On page 50256, second column, in the fifth line from the bottom, "FCC" should read "FAA";

3. On page 50258, third column, in the fourth line of the fourth full paragraph, "ASA" should read "ARSA";

4. On page 50261, second column, under "Lubbock International Airport, TX [New]", the sixth and seventh lines should read "upward from 4,500 feet MSL to 7,300 feet MSL within a 10-mile radius of the";

5. On page 50262, under "Will Rogers World Airport, Oklahoma City, OK [New]", in the seventh line, "36°25'57"N" should read "36°26'57"N"; and

6. On page 50262, in the same paragraph, in the fourth line from the bottom, remove the "0" preceeding "lat.".

BILLING CODE: 1505-01-M

---

## 14 CFR Part 73

**[Airspace Docket No. ANM-26]**

### Establishment of Restricted Area R-6714E, Yakima, WA

*Correction*

In the issue of Wednesday, December 11, 1985, on page 50611 in the first column, a correction to FR Doc.85-27305 appeared. The last line should read: "46°33'00" N.".

BILLING CODE 1505-01-M

---

## 14 CFR Part 385

## Office of the Secretary

**[OST Docket No. 42745; Amendment, 385-1]**

### Assignment of Certain Aviation Economic Functions

**AGENCY:** Office of the Secretary, DOT.

**ACTION:** Final rule.

**SUMMARY:** This amendment reflects the redelegation of certain authorities related to consumer protection currently being carried out by to the Director, Office of Community and Consumer Affairs under 14 CFR 385.30 to the Assistant Secretary for Policy and International Affairs. The amendment also eliminates § 385.30(b), relating to approval or disapproval of air carrier statements explaining denied boarding compensation, and § 385.30(d), concerning applications for relief under § 250.11 of this chapter, since the Civil Aeronautics Board eliminated these underlying regulations prior to its sunset. The authority contained in § 385.30(c), relating to waivers and relief from baggage liability regulations, and § 385.30(e), relating to smoking regulation waivers, are delegated to the Assistant Secretary for Policy and International Affairs in a separate delegation document amending 49 CFR 1.56, which is contained in this edition of the **Federal Register**.

**DATE:** The effective date of this amendment is December 24, 1985.

**FOR FURTHER INFORMATION CONTACT:** Becky L. Bentson, Office of the General Counsel, U.S. Department of Transportation, Washington, DC (202) 472-5577.

**SUPPLEMENTARY INFORMATION:** Since this amendment relates to departmental management, procedures, and practice, notice and comment on it are unnecessary and it may be made effective fewer than thirty days after publication in the **Federal Register**.

On December 31, 1984, the Department of Transportation reissued the former Civil Aeronautics Board rules (14 CFR Part 385) dealing with the delegation of numerous items of discretionary authority needed to carry out Titles IV and X of the Federal Aviation Act of 1958, as amended, and related statutes (49 FR 50984, December 31, 1984.) Editorial corrections and a new subpart to Part 385 were issued later. (50 FR 7169, February 21, 1985.) Concurrently with the reissuance of Part 385, the Department issued amendments to 49 CFR Part 1 to delegate transferring CAB functions to Secretarial officers within DOT (49 FR 50994, December 31, 1984).

The Secretary has now determined that the authority to issue aviation consumer protection regulations, and waivers from those regulations (49 CFR 1.61(d)(4) and 14 CFR 385.30), should be carried out by the Assistant Secretary for Policy and International Affairs. This amendment, together with an amendment to 49 CFR Part 1, which is published in this edition of the **Federal Register**, accomplish that redelegation and deletes two obsolete provisions from 14 CFR 385.30.

### List of Subjects in 14 CFR Part 385

Organization and functions (government agencies).

### PART 385—[AMENDED]

Accordingly, 14 CFR Part 385 is amended as follows:

1. The authority citation for Part 385 continues to read as follows:

**Authority:** Federal Aviation Act of 1958, as amended (49 U.S.C. 1301 et seq.); Airline Deregulation Act of 1978 (Pub. L. 95-504, October 24, 1978); Civil Aeronautics Board Sunset Act of 1984 (Pub. L. 98-443, October 4, 1984); and 49 U.S.C. Subtitle I.

2. Section 385.30 is amended by revising paragraph (b) to read as follows, and removing paragraphs (c) through (f).

**§ 385.30 Authority of the Director, Office of Community and Consumer Affairs.**

* * * * *

(b) Recommend to the Deputy General Counsel the compromise of civil penalties in the resolution of informal consumer complaints.

Issued in Washington, DC, on December 14, 1985.

**Elizabeth Hanford Dole,**

*Secretary of Transportation.*

[FR Doc. 85-30388 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-62-M

## CONSUMER PRODUCT SAFETY COMMISSION

### 16 CFR Part 1000

### Commission Organization and Functions

**AGENCY:** Consumer Product Safety Commission.

**ACTION:** Final rule.

**SUMMARY:** The Commission is publishing revisions to its statement of organization and functions to reflect organizational changes made since the changes published December 31, 1984, 49 FR 50633. These include the creation of an Office of Media Relations and an Office of Information and Public Affairs, to assume functions formerly performed by the Office of Outreach Coordination and the Office of Information and Public Affairs.

**DATE:** December 24, 1985.

**ADDRESS:** Consumer Product Safety Commission, Office of the Secretary, Washington, DC 20207.

**FOR FURTHER INFORMATION CONTACT:** Joseph F. Rosenthal, Office of the General Counsel, Consumer Product Safety Commission, Washington, DC 20207, (301) 492-6980.

**SUPPLEMENTARY INFORMATION:** The Commission is revising its statement of organization and functions, 16 CFR Part 1000, to include organizational changes since the part was last revised on December 31, 1984, 49 FR 50633. The organizational changes are summarized below:

1. An Office of Media Relations was created and assumed responsibility for the Commission's relations with national print and broadcast media.

2. An Office of Information and Public Affairs was created and assumed responsibility for the Commission's national information and public affairs program.

Since this rule relates solely to internal agency management, pursuant to 5 U.S.C. 553(b), notice and other public procedures are not required and it is effective immediately upon publication in the Federal Register. Further, this action is not a rule as defined in the Regulatory Flexibility Act, 5 U.S.C. 601-612, and, thus, is exempt from the provisions of that Act.

**List of Subjects in 16 CFR Part 1000**

Organization and Functions (Government Agencies).

### PART 1000—[AMENDED]

Accordingly, Part 1000 of Chapter II of Title 16 of the Code of Federal Regulations is amended as shown.

1. The authority citation for Part 1000 continues to read as follows:

**Authority:** 5 U.S.C. 552(a).

2. Section 1000.12 is revised to read as follows:

**§ 1000.12 Organization structure.**

The Consumer Product Safety Commission is composed of the principal units listed in this section.

(a) The following units report directly to the Chairman of the Commission:

(1) Office of the General Counsel;

(2) Office of Congressional Relations;

(3) Office of Administrative Law Judge;

(4) Office of Media Relations;

(5) Office of the Secretary;

(6) Office of Internal Audit;

(7) Office of Equal Employment Opportunity and Minority Enterprise;

(8) Office of the Executive Director.

(b) The following units report directly to the Executive Director of the Commission:

(1) Office of Program Management;

(2) Office of Budget, Program Planning, and Evaluation;

(3) Office of Information and Public Affairs;

(4) Directorate for Epidemiology;

(5) Directorate for Economic Analysis;

(6) Directorate for Engineering Sciences;

(7) Directorate for Health Sciences;

(8) Directorate for Compliance and Administrative Litigation;

(9) Directorate for Administration;

(10) Directorate for Field Operations.

3. Section 1000.17 is revised to read as follows:

**§ 1000.17 Office of Media Relations.**

The Office of Media Relations is responsible for implementing the Commission's media relations program nationwide. The Office serves as the Commission's spokesperson to the national print and broadcast media, develops and disseminates the Commission's press releases, and organizes Commission press conferences.

4. Section 1000.21 is revised to read as follows:

**§ 1000.21 Office of the Executive Director.**

The Executive Director, under the broad direction of the Chairman and in accordance with Commission policy, acts as the chief operating manager of the agency, supporting the development of the agency's budget and operating plan before and after Commission approval and managing the execution of those plans. The Executive Director has direct line authority over seven operating directorates and three offices: Epidemiology, Economic Analysis, Engineering Sciences, Health Sciences, Compliance and Administrative Litigation, Administration, and Field Operations; the Office of Program Management; the Office of Budget, Program Planning, and Evaluation; and the Office of Information and Public Affairs.

5. Section 1000.24 is revised to read as follows:

**§ 1000.24 Office of Information and Public Affairs.**

The Office of Information and Public Affairs is responsible for the development, implementation, and evaluation of a comprehensive national information and public affairs program designed to promote product safety. This includes responsibility for developing and maintaining relations with a wide range of national groups such as consumer organizations; business groups; trade associations; state and local government entities; labor organizations; medical, legal, scientific and other professional associations; and other Federal health, safety and consumer agencies. The Office also manages the Commission's Hotline, described in § 1000.3.

Dated: December 18, 1985.

**Sadye E. Dunn,**

*Secretary, Consumer Product Safety Commission.*

[FR Doc. 85-30300 Filed 12-23-85; 8:45 am]

BILLING CODE 6355-01-M

## SECURITIES AND EXCHANGE COMMISSION

### 17 CFR Part 240

**[Release No. 34-22724; File No. S7-1000]**

### Securities; Broker-Dealers; Registration; Applicability to Banks; Requests for Exemptions

**AGENCY:** Securities and Exchange Commission.

**ACTION:** Availability of temporary exemptions from Rule 3b-9.

**SUMMARY:** The Securities and Exchange Commission is continuing to review requests from banks for temporary exemptions from Rule 3b-9 (17 CFR 240.3b-9) under the Securities Exchange

Act of 1934 ("Exchange Act"). Although many banks have already taken the steps necessary to comply with the provisions of Rule 3b–9 by its effective date, January 1, 1986, many others which are acting in good faith may not be able to take all steps necessary to comply with the Rule by that date. Banks that are making deligent, good faith efforts to satisfy the requirements of the Rule will be granted requests for temporary exemptions.

**DATES:** Requests for exemption from § 240.3b–9 will be considered until January 1, 1986.

**FOR FURTHER INFORMATION CONTACT:** Mary Chamberlin, Esq., Chief Counsel (202) 272–2848, Edward L. Pittman, Esq., Attorney (202) 272–2848. Requests for temporary exemptions from Rule 3b–9 should be addressed to Mary Chamberlin, Esq., Office of Chief Counsel, Division of Market Regulation, Securities and Exchange Commission, 450 5th Street, NW, Washington, DC. 20549.

**SUPPLEMENTARY INFORMATION:** On July 1, 1985, the Commission adopted Rule 3b–9 (17 CFR 240.3b–9) under the Exchange Act.[1] The Rule generally requires that a bank conduct certain securities activities through a broker-dealer registered under the Exchange Act. These activities are (1) public solicitation of brokerage business for transaction-related compensation, (2) receipt of transaction-related compensation for providing brokerage services for trust, managing agency or other accounts to which the bank provides advice, or (3) dealing in or underwriting securities. The Rule contains exceptions for banks that conduct only limited securities activities. The effective date of Rule 3b–9 is January 1, 1986.

A challenge to the Commission's legal authority to adopt Rule 3b–9 was brought in the United States District Court for the District of Columbia. The District Court has determined that Rule 3b–9 is a valid exercise of the Commission's rulemaking powers and the court refused to enjoin the rule.[2] Thus, absent an exemption from the Rule, banks that are not in compliance with the Rule by January 1, 1986 will be in violation of the federal securities laws.

In adopting Rule 3b–9, the Commission recognized that many banks would be required to take additional steps to comply with the Rule. Accordingly, it delayed the effective date of the Rule for approximately six months. In addition, the Commission's Division of Market Regulation subsequently announced that it would grant, on a case-by-case basis, written requests for temporary exemptions from the Rule by banks that could demonstrate good faith and diligent efforts to comply with the Rule.[3] Recently, it was brought to the Commission's attention by William Seidman, Chairman of the Federal Deposit Insurance Corporation, and others, that many banks may not fully understand the grounds on which the Commission's staff is willing to provide exemptive relief. Therefore, the Commission is issuing this release to set forth its willingness to grant temporary exemptions from Rule 3b–9 in order to allow banks to complete efforts to comply.

At the time the Commission adopted Rule 3b–9, it delegated authority to the Division of Market Regulation to grant exemptions where appropriate. Acting pursuant to delegated authority, the Division of Market Regulation has liberally granted requests for temporary exemptions from Rule 3b–9 to banks which have demonstrated a diligent and good faith effort to comply with the Rule.[4] The exemptions have been for periods of up to five months.

Although the Division will consider all relevant factors in determining whether to grant an exemption, among the common elements in each request for an exemption the Division has granted are the existence of one or more of the following: a broker-dealer registration application on file with the Commission, a membership application on file with the National Association of Securities Dealers, Inc., or personnel in the process of preparing for and taking the registered principal or registered representative examinations. Additional factors that the Division will consider in granting temporary exemptions include an application for approval to create a subsidiary to engage in brokerage activities on file with the appropriate banking regulator, the existence of a pending request for permanent exemptions under Rule 3b–9, and a representation that a broker-dealer application will be submitted to the Commission by a specific date before January 1, 1986. The Division will also consider granting temporary exemptions to banks that are involved in mergers that will ultimately result in the merging of brokerage operations into a single registered broker-dealer subsidiary or that are in the process of receiving internal corporate board approvals necessary for the creation of a new subsidiary or affiliate.[5]

It is the Division's intention to continue to consider requests for temporary exemptions from Rule 3b–9 up to the effective date of the Rule. Moreover, in the event that the Division is unable to respond to all requests received prior to the January 1, 1986 effective date, the staff will in all appropriate cases provide interim no-action relief pending issuance of the exemption letter. Requests for temporary exemptions from Rule 3b–9 should contain a brief narrative of the efforts taken by the bank which demonstrate a diligent and good faith effort to comply with Rule 3b–9.

By the Commission.

Dated: December 18, 1985.

**John Wheeler,**

*Secretary.*

[FR Doc. 30337 Filed 12–23–85; 8:45 am]

BILLING CODE 8010–01–M

[1] Securities Exchange Act Release No. 22205 (July 1, 1985), 50 FR 28385 (July 12, 1985).

[2] An appeal has been taken from the district court's decision. *American Bankers Association* v. *Securities and Exchange Commission*, No. 85–2482 (D.D.C. Oct. 30, 1985), *appeal docketed*, No. 85–6055 (D.C. Cir. Oct. 31, 1985).

[3] Letter dated August 28, 1984 from Richard Wessel, Esq., Associate Director, Division of Market Regulation, to James D. McLaughlin, Esq., Government Relations Counsel, American Bankers Association.

[4] *See, e.g.*, letters to David R. Sanders, Esq. (Suburban Bancorp) (October 25, 1985); Richard J. McCullen, (National Bank of Detroit) (November 27, 1985); Ralph F. MacDonald, III (Central Bank of the South) (December 9, 1985); William N. Stellin, (Union Bank and Trust Company) (December 13, 1985). Copies of exemptive requests and the Division's responses are available in the Commission's public files.

[5] Where banks themselves seek to register with the Commission as broker-dealers, rather than forming a subsidiary, the Commission indicated in the release adopting Rule 3b–9 that it would anticipate using its exemptive authority under the financial responsibility rules if any conflicts between bank and securities regulation result.

## DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

### Office of the Assistant Secretary for Fair Housing and Equal Opportunity

### 24 CFR Part 107

**[Docket No. R–85–1237; FR–2020]**

## Nondiscrimination and Equal Opportunity in Housing Under Executive Order 11063

**AGENCY:** Office of the Assistant Secretary for Fair Housing and Equal Opportunity, HUD.

**ACTION:** Final rule.

**SUMMARY:** This rule amends 24 CFR Part 107, "Nondiscrimination and Equal

Opportunity Under Executive Order 11063", to provide for the administrative data collection necessary to implement Executive Order 11063 which was revised by Executive Order 12259 to prohibit discrimination on the basis of sex and to clarify that the terms "religion" and "creed" are synonymous. This amendment is a conforming change inadvertently omitted from the final version of the implementing regulation published on August 2, 1985.

**EFFECTIVE DATE:** Upon expiration of the first period of 30 calendar days of continuous session of Congress after publication, but not before further notice of the effective date is published in the Federal Register.

**FOR FURTHER INFORMATION CONTACT:** Katrina Ross, Director, Fair Housing Enforcement Division, Room 5208, Department of Housing and Urban Development, 451 Seventh Street, SW., Washington, DC 20410, telephone (202) 755-5673. (This is not a toll-free number.)

**SUPPLEMENTARY INFORMATION:** Executive Order 11063, "Equal Opportunity in Housing" (November 20, 1962, 27 FR 11527), directs Federal departments and agencies to take all action necessary and appropriate to prevent discrimination because of race, color, creed, or national origin in (1) the sale, leasing, rental or other disposition of residential property and related facilities which are owned or operated by the Federal Government or provided with Federal assistance; and (2) the lending practices with respect to residential property and related facilities of lending institutions, insofar as such practices relate to loans insured or guaranteed by the Federal Government. Executive Order 12259, "Leadership and Coordination of Fair Housing in Federal Programs" (January 6, 1981, 46 FR 1253), revised Executive Order 11063 by adding a prohibition against discrimination based on sex, and by clarifying the reach of Executive Order 11063 with respect to "creed" by adding the word "religion".

On August 2, 1985, HUD published a final rule (50 FR 31359) which implemented Executive Order 12259 by amending 24 CFR Part 107, "Nondiscrimination and Equal Opportunity in Housing Under Executive Order 11063", to add the prohibition against discrimination based on sex and to clarify the reach of E.O. 11063 with respect to "creed" by adding the word "religion". The final version of the August 2, 1985 final rule inadvertently omitted a conforming change within Part 107. This final rule makes that change by revising §§ 107.30(a) and 107.30(b) to add sex and religion to the categories of data which should be maintained in order to carry out the mandate of Executive Order 12259.

The Department has concluded that, because this rule making is merely making a conforming change and is limited to the coverage of HUD's Executive Order 11063 implementation procedures in accordance with the policies reflected in Executive Order 12259, public comment on the rule is unnecessary. Accordingly, these amendments to Part 107 are being adopted as final rulemaking.

This rule does not constitute a "major rule" as the term is defined in section 1(b) of the Executive Order 12291 on Federal Regulation issued on February 17, 1981. Analysis of the rule indicates that it will not (1) have an annual effect on the economy of $100 million or more; (2) cause a major increase in costs or prices for consumers, individual industries, Federal, State or local government agencies, or geographic regions; or (3) have significant adverse effect on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises in domestic or export markets.

A Finding of No Significant Impact with respect to the environment has been made in accordance with HUD regulations in 24 CFR Part 50 that implement section 102(2)(C) of the National Environmental Policy Act of 1969, 42 U.S.C. 4332. The Finding of No Significant Impact is available for public inspection and copying during regular business hours in the Office of the Rules Docket Clerk, Room 10276, 451 Seventh Street, SW., Washington DC 20410.

Under 5 U.S.C. 605(b) (the Regulatory Flexibility Act), the Undersigned hereby certifies that this rule will not have a significant economic impact on a substantial number of small entities because the rule makes no substantive change in existing procedures associated with the Executive Order on Nondiscrimination and Equal Opportunity, but merely conforms its coverage to the revisions contained in Executive Order 12259.

This rule was listed as item number 943 in the Department's Semi-annual Agenda of Regulations published on October 29, 1985 (50 FR 44166, 44206) under Executive Order 12291 and the Regulatory Flexibility Act.

The Catalog of Federal Domestic Assistance Program number and titles are: 14.400, Equal Opportunity in Housing; and 14.401, Fair Housing Assistance Program.

**List of Subjects in 24 CFR Part 107**

Administrative practice and procedure, Fair housing, Loan programs—housing and community development.

Accordingly, 24 CFR Part 107 is amended as follows:

## PART 107—NONDISCRIMINATION AND EQUAL OPPORTUNITY IN HOUSING UNDER EXECUTIVE ORDER 11063

1. The authority citation for Part 107 continues to read as follows:

**Authority:** Sec. 7(d) of the Department of Housing and Urban Development Act, 42 U.S.C. 3535(d); Executive Order 11063, Equal Opportunity in Housing, issued November 20, 1962 (27 FR 11527); Executive Order 12259, Leadership and Coordination of Fair Housing in Federal Programs, January 6, 1981 (46 FR 1253).

2. Paragraphs (a) and (b) of § 107.30 are revised to read as follows:

**§ 107.30 Recordkeeping requirements.**

(a) All persons receiving assistance through any program or activity of the Department involving the provision of housing and related activities subject to Executive Order 11063 shall maintain racial, religious, national origin and sex data required by the Department in connection with its programs and activities.

(b) All lenders participating in Departmental mortgage insurance programs, home improvement loan programs, GNMA mortgage purchase programs, or special mortgage assistance programs, shall maintain data regarding the race, religion, national origin and sex of each applicant and joint applicant for assistance with regard to residential property and related facilities. Racial data shall be noted in the following categories: American Indian/Alaskan Native, Asian/Pacific Islander, Black, White, Hispanic. If an applicant or joint applicant refuses to voluntarily provide the information or any part of it, that fact shall be noted and the information shall be obtained, to the extent possible, through observation. Applications shall be retained for a period of at least twenty-five (25) months following the date the record was made.

* * * * *

Dated: December 17, 1985.

**Antonio Monroig,**

*Assistant Secretary for Fair Housing and Equal Opportunity.*

[FR Doc. 85-30378 Filed 12-23-85; 8:45 am]

BILLING CODE 4210-28-M

## DEPARTMENT OF THE TREASURY

### Internal Revenue Service

### 26 CFR Parts 1 and 602

[T.D. 8061]

### Fringe Benefits; Listed Property; Reporting and Recordkeeping Requirements; Temporary; Correction

**AGENCY:** Internal Revenue Service, Treasury.

**ACTION:** Correction to temporary rule.

**SUMMARY:** This document contains a correction to the **Federal Register** publication on Wednesday, November 6, 1985, beginning at 50 FR 46006 of the temporary regulations which were the subject of Treasury Decision 8061. T.D. 8061 relates to revised recordkeeping requirements with respect to listed property and taxation of fringe benefits.

**EFFECTIVE DATE:** The temporary regulations relating to the substantiation requirements of section 274(d) (§§ 1.274–5T and 1.274–6T) that are the subject of this correction are effective for taxable years beginning after December 31, 1985.

**FOR FURTHER INFORMATION CONTACT:** Carroll Yue of the Legislation and Regulations Division, Office of Chief Counsel, Internal Revenue Service, 1111 Constitution Avenue, NW., Washington, DC 20224. (Attention: CC:LR:T). Telephone 202–566–3935 (not a toll-free call).

**SUPPLEMENTARY INFORMATION:**

#### Background

On November 6, 1985, the Federal Register published temporary regulations (50 FR 46006) under section 274 of the Internal Revenue Code of 1954 (Code), relating to the substantiation requirements with respect to certain "listed property." Section 179 of the Tax Reform Act of 1984 (the 1984 Act) amended Code section 274 to provide that no deduction or credit shall be allowed with respect to "listed property" (as defined in Code section 280F(d)(4)), unless the taxpayer substantiated any deduction or credit with "adequate contemporaneous records." Temporary regulations were published in the **Federal Register** on October 24, 1984, and February 20, 1985 (49 FR 42701 and 50 FR 7038), providing guidance for taxpayers affected by the requirement to maintain adequate contemporaneous records for taxable years beginning after December 31, 1984. Section 1 of the Repeal of Contemporaneous Recordkeeping Requirements Act (the 1985 Act) amended Code section 274 to provide that any deduction or credit with respect to listed property must be substantiated by adequate records or sufficient corroborative evidence and repealed any regulations issued to carry out the amendments made to section 274 by the 1984 Act. T.D. 8061, in part, clarified the types of records that are generally necessary to substantiate any deduction or credit with respect to listed property.

Under the Explanation of Provisions section in the preamble to T.D. 8061, the discussion concerning the substantiation requirements for reimbursement arrangements and mileage allowances that begins at the top of the 2nd column of text on page 46009 advises employers and employees to consider the effect of the limitations on annual depreciation deductions imposed by section 280F of the Code on arrangements by which employers reimburse employees at the standard mileage rate for expenses incurred by employees who use their own automobiles in connection with their employers' businesses. This notice removes the last two paragraphs of that discussion.

If an employee who uses his own automobile in connection with his employer's business chooses to use the standard mileage rate to compute an allowable deduction for transportation expenses paid or incurred on behalf of his employer, the employee is deemed to have made an election to exclude his automobile from the Accelerated Cost Recovery System under section 168(e)(2) of the Code. (See Rev. Proc. 82–61, 1982–2 C.B. 849, as modified by Rev. Proc. 83–74, 1983–2 C.B. 593, Rev. Proc. 84–72, 1984–2 C.B. 735, and Rev. Proc. 85–49, 1985–40 I.R.B. 26.) If the automobile is not recovery property, it is not subject to the limitations imposed by section 280F. In determining the amount of a deduction at the standard mileage rate, the employee need not establish that use of the automobile was for the convenience of the employer and required as a condition of employment. If the employer reimburses the employee for transportation expenses at the standard mileage rate, the reimbursement would, therefore, not exceed the employee's deductible expenses and would not result in income to the employee.

#### Need for Correction

As published, Treasury Decision 8061 contained an error in the preamble to the temporary regulations in the discussion of reimbursement arrangements and mileage allowances that begins at the top of the 2nd column of text on page 46009.

#### Correction of Publication

Accordingly, in the publication of Treasury Decision 8061, which was the subject of FR Doc. 85–26358, (November 1, 1985), under the reimbursement arrangements and mileage allowances discussion that begins on page 46009, 2nd column, the 3rd and 4th paragraphs are removed.

**Peter K. Scott,**

*Director, Legislation and Regulations Division.*

[FR Doc. 85–30325 Filed 12–23–85; 8:45 am]

BILLING CODE 4830–01–M

## DEPARTMENT OF DEFENSE

### Office of the Secretary

### 32 CFR Part 166

### Defense Contracting; Reporting Procedures on Defense Related Employment

**AGENCY:** Office of the Secretary of Defense, DoD.

**ACTION:** Final rule.

**SUMMARY:** This rule is the fiscal year 1985 update of the section listing DoD contractors receiving negotiated contract awards of $10 million or more. The regulation is published to comply with the provisions of Section 1, Pub. L. 97–295, October 12, 1982; 10 U.S.C. 2397.

**EFFECTIVE DATE:** September 30, 1985.

**FOR FURTHER INFORMATION CONTACT:** Mr. J.R. Sungenis, Director for Information Operations and Reports, Washington Headquarters Services, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202–4302. Telephone (202) 746–0334.

**SUPPLEMENTARY INFORMATION:** In FR Doc. 70–15846 appearing in the **Federal Register** on November 25, 1970 (35 FR 18040), the Office of the Secretary of Defense published a final rule establishing criteria, prescribing procedures, and assigning responsibilities for monitoring contracting within the Department of Defense. Subsequently, paragraphs (a) and (d) of § 166.11, which constitute the list of DoD contractors receiving negotiated contract awards for $10 million or more, were updated for fiscal years 1971 (36 FR 18464); 1972 (37 FR 18727); 1973 (38 FR 25990); 1974 (39 FR 32985); 1975 (40 FR 44135); 1976 (41 FR 20466); 1977 (43 FR 1617); 1978 (44 FR 3049); 1979 (44 FR 75631); 1980 (45 FR 83486); 1981 (46 FR 60821); 1982 (47 FR 56847); 1983 (48 FR 55728); and 1984 (50 FR 77).

1. The authority citation for 32 CFR Part 166 continues to read as follows:

**Authority:** Sec. 410, 83 Stat. 210; 50 U.S.C. 1436.

2. Accordingly, § 166.11 is revised to read as follows:

**§ 166.11 Department of Defense contractors receiving negotiated contract awards of $10 million or more.**

Fiscal Year 1985:

3 A Industries, Inc.
A & S Tribal Industries
A A I Corp.
A C S Construction Co. of Miss.
A L M, Inc.
A M General Corp.
A R C Corp.
A T & T Information Systems
A T & T Technologies, Inc.
A V W Electronic Systems, Inc.
Abbott Products, Inc.
Abex Corp.
Accent General, Inc.
Accudyne Corp.
Action Mfg. Co.
Accurex Corp.
Addsco Industries, Inc.
Advance Computer Communications
Advanced Marine Enterprises
Advanced Technology, Inc.
Aero Corp.
Aerojet General Corp.
Aerojet Strategic Propulsion
Aerojet Tactical Systems
Aerojet Techsystems
Aeroquip Corp.
Aerospace Corp., The
Aerospace Technologies, Inc.
Alascom, Inc.
All Bann Enterprises, Inc.
Allen Corp. of America
Alliance Properties, Inc.
Allied Signal Corp.
Allis Chalmers Distribution Svc.
Altama Delta Corp.
Alvarado Construction, Inc.
Amber Refining, Inc.
Amerada Hess Corp.
American Airlines, Inc.
American Automar, Inc.
American Cyanamid Co., Inc.
American Development Corp.
American Electronic Laboratories, Inc.
American Express Co.
American Management Systems, Inc.
American President Lines, Ltd.
American Satellite Co.
American Systems Corp.
American Telephone & Telegraph Co.
American Trans Air, Inc.
Amertex Enterprises, Ltd.
Ametek, Inc.
Amex Systems, Inc.
Amoco Corp.
Ampex Corp.
Amron Corp.
Amstar Technical Products Co.
Analysis & Technology, Inc.
Analytic Sciences Corp., The
Analytic Services, Inc.
Analytical Systems Engnr. Corp.
Analytics, Inc.
Anderson, Arthur & Co.
Arcwel Corp
Argosystems, Inc.
Arinc Research Corp.
Arkla, Inc.
Arrow Airways, Inc.
Aryana Corp.
Ashland Oil, Inc.
Assurance Technology Corp.
Astronautics Corp. of America
Atlantic Dry Dock Corp.
Atlantic Marine, Inc.
Atlantic Research Corp.
Atlantic Richfield Co.
Atlas Processing Co.
Austin Co., The
Automated Data Management, Inc.
Automated Machine Products, Inc.
Automated Sciences Group, Inc.
Automation Industries, Inc.
Avco Corp.
Avondale Shipyards, Inc.
Aydin Corp.
Ayer N W, Inc.
B B N Communications Corp.
B D M Corp.
B D M International, Inc.
B E I Electronics, Inc.
B P North America Petroleum, Inc.
B S I Corp.
Ball Corp.
Baltimore Gas & Electric Co.
Barnes & Reinecke, Inc. (Del.)
Bataco Industries, Inc.
Bates, Ted Worldwide, Inc.
Bath Iron Works Corp.
Battelle Memorial Institute
Bay City Marine, Inc.
Bay Tankers, Inc.
Beacon Oil Co.
Beech Aerospace Services, Inc.
Beech Aircraft Corp.
Bell Aerospace Textron
Bell Helicopter—Boeing, JV
Bell Helicopter Textron, Inc.
Bell Telephone Labs, Inc.
Belleville Shoe Mfg. Co.
Bendix Corp., The
Bendix Field Engineering Corp.
Beretta USA Corp.
Beta Systems Velco Filter
Betac Corp.
Bethlehem Steel Corp.
Blue Cross & Blue Shield of RI
Blue Cross of Washington & Alaska, Inc.
Bodenhamer Building Corp.
Boeing Aerospace Co.
Boeing Co., The
Boeing Computer Services
Boeing Technical Operations
Bolt Beranek & Newman, Inc.
Booz Allen & Hamilton, Inc.
Borg Warner Corp.
Brunswick Corp.
Bulova Systems & Instruments Corp.
Bunker Ramo Corp.
Burnside Ott Aviation Training Center
Burroughs Corp.
Butler Associates, Inc.
Butt & Head, Inc.
C 3, Inc.
C A S, Inc.
C Construction Co., Inc.
C D I Marine Co.
C F M International, Inc.
C F S Air Cargo
CACI, Inc.
CACI, Inc. Federal
Caddell Construction Co., Inc.
Cadillac Gage Co.
Calcasieu Refining Co., Inc.
California Microwave, Inc.
California Pacific Associates
Calspan Corp.
Caltex Oil Products Co.
Caltex Petroleum Corp.
Campbell Soup Co.
Carbon Hill Mfg. Co.
Carnation Co.
Carnegie Mellon University
Carolina Power & Light Co.
Case, J I Co.
Caterpillar Tractor Co.
Cates Construction, Inc.
Central Gulf Lines, Inc.
Century Brass Products, Inc.
Cerberonics, Inc.
Cessna Aircraft Co., Inc.
Chamberlain Mfg. Corp.
Chaparral Industries, Inc.
Charles Stark Draper Laboratories, Inc.
Chevron USA, Inc.
Chromalloy American Corp.
Chrysler Corp.
Cincinnati Electronics Corp.
Cleveland Pneumatic Co.
Coastal Dry Dock & Repair Corp.
Coastal Industries, Inc.
Coastal Refining & Marketing
Cobro Corp.
Coca Cola Co.
Colt Industries, Inc.
Columbia Research Corp.
Comarco, Inc.
Command Control & Communications Corp.
Communication Mfg. Co.
Comptek Research, Inc.
Computer Sciences Corp.
Computervision Corp.
Comsat General Corp.
Conner Brothers Construction Co.
Conoco, Inc.
Container Research Corp.
Contel Page Systems, Inc.
Continental Maritime San Diego
Control Data Corp.
Cornell University
Coronado Technology, Inc.
Crane Co.
Cray Research, Inc.
Cubic Corp.
Cummins Engine Co., Inc.
Curtiss Wright Corp.
Dart & Kraft, Inc.
Dart Industries, Inc.
Dataproducts New England, Inc.
Dawson Construction Co., Inc.
Day & Zimmerman, Inc.
Day & Zimmerman, Inc. & Basil, FE JV
Dayron Corp.
Defense Research, Inc.
Del Mfg. Co., Inc.
Del Monte Corp.
Delta Industries, Inc.
Designers & Planners, Inc.
Developmental Sciences, Inc.
Devils Lake Sioux Mfg. Corp.
Dewey Electronics Corp.
Diagnostic Retrieval Systems, Inc.
Diamond Shamrock Chemicals Co.
Digital Equipment Corp.
Dresser Industries, Inc.
Dual Motors, Inc.

Dun & Bradstreet Corp.
Dynalectron Corp.
Dynamac Corp.
Dynamic Industries Corp.
Dynamic Systems, Inc.
Dynamics Corp. of America
Dynamics Research Corp.
E Systems, Inc.
E G & G Washington Analytical Services Center
E S L, Inc.
Eagle Technology, Inc.
Eastman Kodak Co.
Eaton Corp.
Edcar Industries, Inc.
Edo Corp.
Educational Computer Corp.
El Paso Electric Co.
Electro Methods, Inc.
Electronic Data Systems Corp.
Electrospace Systems, Inc.
Emco, Inc.
Emerson Electric Co.
Engineered Air Systems, Inc.
Engineering Research, Inc.
Enginetics Corp.
Environmental Elements Corp.
Environmental Research Institute, Michigan
Essex Corp.
Evaluation Research Corp.
Evergreen Intl. Airlines
Ex-Cell-O Corp.
Exxon Co. U.S.A.
Exxon Corp.
F M C Corp.
F N Mfg., Inc.
Fairchild Industries, Inc.
Fairchild Weston Systems, Inc.
Falcon Systems, Inc.
Farmers Union Central
Farrell Lines, Inc.
Federal Cartridge Corp.
Federal Data Corp.
Federal Data System Corp.
Federal Electric Corp.
Figgie International, Inc.
Flight Systems, Inc.
Florida Power & Light Co
Flow General, Inc.
Flying Tiger Line, Inc., The
Ford Aerospace & Communications
Four Phase Systems, Inc.
Freedom Industries, Inc.
G & M Oil Co., Inc.
G K S, Inc.
G T E Communications Systems Corp.
G T E Products Corp., Del.
G T E Service Corp.
G T E Sylvania, Inc.
Garrett Corp., The
Gary Refining Co.
Gates Learject Corp.
Gayston Corp.
General Defense Corp.
General Dynamics Corp.
General Dynamics Land Systems
General Electric Co.
General Foods Corp.
General Instrument Corp., Del.
General Motors Corp.
General Research Corp.
General Ship Corp.
General Signal Corp.
Gentex Corp.
Geodynamics Corp.
Georgia Technical Research Corp.
Getty Oil Co.
Giant Industries, Inc.
Gladieux Refinery, Inc.
Global Associates, A Joint Venture
Golden Mfg. Co., Inc.
Goodrich, B F Co., The
Goodyear Aerospace Corp.
Goodyear Tire & Rubber Co.
Goolsby Building Corp.
Gortons of Gloucester
Gould Defense Systems, Inc.
Gould, Inc.
Greenhut Construction Co., Inc.
Grey Advertising, Inc.
Grumman Aerospace Corp.
Gulf & Western Industries, Inc.
Gulf Refining & Marketing
Gulf Stream America Corp.
Gulf Tool Corp.
H & H Meat Products, Inc.
H L J Construction & Mgt. Group
H R B Singer, Inc.
H R Textron, Inc.
Halter Marine, Inc.
Hamilton Technology, Inc.
Harley Davidson Motor Co., Inc.
Harris Corp.
Harsco Corp.
Hawaiian Electric Co., Inc.
Hawaiian Independent Refinery
Hawaiian Telephone Co.
Hayes International Corp.
Hazeltine Corp.
Heckethorn Mfg. Co.
Hansel Phelps Construction Co.
Hercules, Inc.
Hess Oil Virgin Island Corp.
Hewlett Packard Co.
Hollingsworth, John R. Co.
Holmes & Narver, Inc.
Holmes & Narver Services Co., Inc.
Holston Defense Corp.
Honeycomb Co. of America
Honeywell, Inc.
Honeywell Information Systems
Horizons Technology, Inc.
Howell Corp.
Howmet Turbine Components Corp.
Hudson Institute, Inc.
Hughes Aircraft Co.
Hughes Communication Services
Hunt Oil Co.
Hycor, Inc.
Hydraulics International, Inc.
Hyster Co.
I C I Americas, Inc.
I I T Research Institute
I T T Avionics & Westinghouse JV
I T T Corp.
Inco, Inc.
Industrial Acoustics Co.
Informatics General Corp.
Information Spectrum, Inc.
Ingersoll Rand Co.
Institute for Defense Analyses
Integrated Systems Analysts
Intercontinental Mfg. Co., Inc.
Interlisearch
Intermetrics, Inc.
Intermountain Construction Co.
Intermouth International Oil, Inc.
International Business Machines
International Terminal Operating Co.
Interstate Electronics Corp.
Irvin Industries, Inc.
Israel Aircraft Industries
Itek Corp.
Jacksonville Shipyards, Inc.
Jaycor
Jersey Central Power & Light Co.
John Hopkins University
Jones Group, Inc., The
Jowett, Inc.
JR Son, Inc.
Jungclaus Campbell Co., Inc.
K D I Precision Products, Inc.
Kaiser Aerospace & Electronics Co.
Kaiser, Henry J., Co.
Kaman Aerospace Corp.
Kaman Sciences Corp.
Kansas Power & Light Co., Inc.
Keco Industries, Inc.
Kemenash, D. & Associates, Inc.
Kenco Refining Inc.
Kern Oil and Refining Co.
Key Airlines, Inc.
Kidde, Inc.
Kisco Co., Inc.
Koch Fuels, Inc.
Kollmorgen Corp.
Kvass Construction Co., Inc.
L S I Avionic Systems Corp.
L T V Aerospace & Defense Co.
L T V Corporation, The
Laguna Industries, Inc.
Laketon Refining Corp.
Landoll Corp.
Lanson Industries, Inc.
Lear Siegler, Inc.
Lewis Management Services Co.
Libby Corp.
Lite Industries, Inc.
Little, Arthur D., Inc.
Litton Industries, Inc.
Litton Systems, Inc.
Lockheed Corp.
Lockheed Electronics Co., Inc.
Lockheed Missiles & Space Co., Inc.
Lockheed Shipbuilding & Construction
Lockley Mfg. Co., Inc.
Loggins Meat Co.
Logicon, Inc.
Logistics Management Institute
Loral Electro Optical Sys.
Loral Electronics Corp.
Louis J. Sportswear, Inc.
Louisville Gas & Electric Co., Inc.
Lucas Industries, Inc.
Lundy Electronics & Systems, Inc.
Lykes Bros. Steamship Co., Inc.
M/A Com, Inc.
M/A Com Linkabit Corp.
Mac H B, Inc.
Magnavox Advance Products System Co.
Magnavox Government & Industrial Electronics Co.
Maitland Bros., Co.
Management & Technical Services Co.
Mantech International Corp.
Mapco, Inc.
Mapco Petroleum, Inc.
Mar, Inc.
Maremont Corp.
Marine Transport Lines, Inc.
Marinette Marine Corp.
Marquardt Co., Inc.
Martin Marietta Corp.
Martin Marietta, Diehl Co's., Thorn & Thomson, JV
Martin Marietta Ordnance System

Marvin Engineering Co., Inc.
Mason & Hanger Silas Mason Co., Inc.
Mason Chamberlain, Inc.
Massachusetts Institute of Technology
Maxima Corp., The
Maxwell Laboratories, Inc.
McCarty Corp., The
McDonnell Douglas Corp.
McDonnell Douglas Helicopter
McLaughlin Research Corp.
McMullen, John J. Associates, Inc.
McRae Industries, Inc.
Merck & Co., Inc.
Metal Trades, Inc.
Metro Machine Corp.
Michael Industries, Inc.
Michelson Organization
Microwave Laboratories, Inc.
Midland Ross Corp.
Milcom Systems Corp.
Miltope Corp.
Mine Safety Appliances Co.
Minnesota Mining & Mfg. Co.
Minowitz Mfg. Co., Inc.
Mission Research Corp.
Mit Con, Inc.
Mitre Corp., The
Mitsui & Co. USA, Inc.
Mobil Oil Corp.
Moog, Inc.
Morton Thiokol, Inc.
Moss Point Marine, Inc.
Motorola, Inc.
Murdock Engineering Co., Texas
N C R Corp.
N I Industries, Inc.
N I West, Inc.
N L Industries, Inc.
Nabisco Brands, Inc.
National Airlines, Inc., Del.
National Power Corp.
National Steel & Shipbuilding Co.
National Systems Management
Navajo Refining Co.
Needham, Inc.
Nero & Associates, Inc.
New Mexico State University
Newberg Brinderson, A Joint Venture
Newhall Refining Co., Inc.
Newport News Shipbuilding & Dry Dock Co.
Nichols Research Corp., Inc.
Nordam
Norden Systems, Inc.
Norfolk Shipbuilding & Dry Dock Corp.
North American Philips Corp.
North Atlantic Industries, Inc.
Northern Telecom, Inc., Del.
Northrop Corp.
Northrop Services, Inc.
Northrop Worldwide Aircraft Services, Inc.
Northwest Airlines, Inc.
Northwest Marine Iron Works
Nuclear Metals, Inc.
O A O Corp.
O R I, Inc.
Ocean Technology, Inc.
Ogden Bulk Transport, Inc.
Olin Corp.
Omni Spectra, Inc.
Optic Electronic Corp.
Oshkosh Truck Corp.
P P G Industries, Inc.
P R B Associates, Inc.
P S I Mobile Products, Inc.
Paccar, Inc.
Pacer Systems, Inc.
Pacific Construction
Pacific Refining Co.
Pacific Sierra Research Corp.
Pan American World Airways, Inc.
Pan American World Services, Inc.
Papago Chemicals, Inc.
Parker Hannifin Corp.
Parsons, Ralph M. Co., The
Pennsylvania Shipbuilding Co.
Pennsylvania State University
Perceptronics, Inc.
Percor, Inc.
Perkin Elmer Corp., The
Peterson Builders, Inc.
Phibro Salomon, Inc.
Philip Morris, Inc.
Philips Electronic Instruments
Phillips Petroleum Co.
Physics International Co.
Picker International, Inc.
Planning Research Corp.
Pneumo Corp.
Polorn Products-Bloomsberg, Inc.
Potomac Electric Power Co.
Power Conversion, Inc.
Presearch, Inc.
Pride Refining, Inc.
Proctor & Gamble Co., The
Propper International, Inc.
Prudential Lines, Inc.
Public Service Co. of New Mexico
Puerto Rico Sun Oil Company, Inc.
Purdy Corp.
Purvis Systems, Inc.
Q E D Systems, Inc.
Quality Apparel Co.
Questech, Inc.
Quintron Systems, Inc.
R & D Associates
RCA Corp.
RCA Global Communications
RF Products, Inc.
RGI, Inc.
RMI, Inc., Advance Marine
Radian Corp.
Rand Corp., The
Rantoul, Village of
Raymond Brown Root-Mowlin
Raymond Engineering, Inc.
Raytheon Co.
Raytheon Service Co.,
Refinery Associates, Inc.
Reflectone, Inc.
Remington Arms Co., Inc.
Resource Consultants, Inc.
Rexon Technology Corp.
Reynolds, R J Industries, Inc.
Reynolds, R J Tobacco Co.
Roberts, J R Corp.
Rockwell International Corp.
Roebbelen Engineering
Rohr Industries, Inc.
Rolls-Royce, Inc.
Rolm Corp.
Rosemount, Inc.
Rosenblatt, M & Son, Inc.
Ryan & Associates, Inc.
Ryan Walsh Stevedoring Co.
S Cubed
S C I Systems, Inc.
S K F Industries, Inc.
S M S Data Products Group, Inc.
S R I International
Saft America, Inc.
Sage Systems, Inc.
San Antonio, City of
Sanders Associates, Inc.
Santa Barbara Research Center
Sargent Fletcher Co.
Sargent Industries of Del., Inc.
Scallop Corp.
Scanoil International S A Inc.
Schafer, W J Associates, Inc.
Science Applications Intnl., Inc.
Scientific Atlanta, Inc.
Scientific Support Systems
Sea Land Service, Inc.
Sea Mobility, Inc.
Selma Apparel Corp.
Semcor Corp.
Serv Air, Inc.
Service Engineering Co.
Shell Oil Co.
Sheller Globe Corp.
Siemens Capital Corp.
Sierra Research Corp.
Simmonds Precision Products
Simplex Wire & Cable Co.
Sinclair Marketing, Inc.
Singer Co., The
Sippican, Inc.
Smith Industries
Softech, Inc.
Sohio Supply Co.
Solar Turbines, Inc.
Soltek of San Diego
Sonicraft, Inc.
Sooner Defense of Florida, Inc.
South Carolina Electric & Gas Co.
South Central Bell Telephone Co.
Southeast Machine Co.
Southern Air Transport, Inc.
Southern Dredging Co., Inc.
Southern Union Co.
Southwest Marine, Inc.
Southwest Research Institute
Southwestern Bell Telephone Co.
Space Communication Co.
Space Data Corp.
Sparta, Inc.
Sparton Corp.
Spears Associates, Inc.
Sperry Corp.
Standard Container Co.
Standard Mfg. Co.
Stanford, Leland Jr., University
Stanford Telephone, Inc.
Stearns, Roger, Inc.
Steuart Petroleum Co.
Stewart Warner Corp.
Sun Chemical Corp.
Sun Refining & Marketing Co.
Sundstrand Corp.
Sundland Refining Corp.
Superior Engineers Electronic Co.
Support Systems Associates, Inc.
Supreme Beef Processors, Inc.
Survival Technology, Inc.
Sverdrup Technology, Inc.
Swedlow, Inc.
Swift & Co.
Sygnetron Protection Systems
Syscon Corp.
Systems Development Corp.
Systematics General Corp.
Systems & Applied Sciences Corp.
Systems Management American, Inc.
Systems Research Laboratories, Inc.
T & G Construction Co., Inc.
T R W, Inc.

T S C Corp.
T W Oil (Houston), Inc.
Taurio Corp.
Techdyn Systems Corp.
Technology Applications, Inc.
Tektronix, Inc.
Teledyne, Inc.
Teledyne Industries, Inc.
Teledyne Microwave
Telephonics Corp.
Telos Computing, Inc.
Tempo, Inc.
Tetra Tech., Inc.
Texaco, Inc.
Texas Instruments, Inc.
Texas Power & Light Co.
Texas, State of
Therm, Inc.
Thompson, J. Walter Co.
Tilley Construction & Engineers
Todd Pacific Shipyards Corp.
Todd Shipyards Corp.
Tracor Aerospace Austin, Inc.
Tracor, Inc.
Tracor Marine, Inc.
Tracor MBA
Tradax Petroleum America, Inc.
Trans World Airlines, Inc.
Transamerica Airlines, Inc.
Transamerica Delaval, Inc.
Treadwell Corp.
Trepte Construction Co.
Tri-Ex Tower Corp
Triad Microsystems, Inc.
Triple A Machine Shop, Inc.
Turbo Compressor Technologies
Turtle Mountain Mfg. Co.
U S Oil & Refining Co.
U T L Corp.
Ultrasystems, Inc.
Unidynamics Corp.
Unified Industries, Inc.
Union Carbide Corp.
Union Oil Co. of California
Uniroyal, Inc.
United Airlines Aircrew Training
United Chem Con Corp.
United States Lines, Inc.
United Technologies Corp.
United Technologs Auto Holdings
United Telecontrol Elect., Inc.
Universal Energy System, Inc.
Universal Hydraulics, Inc.
Universal Maritime Service
University of California
University of Dayton
University of Illinois
University of Maryland, Inc.
University of New Mexico, The
University of Southern California
University of Texas System
Usibelli Coal Mine, Inc.
Utah Power & Light Co.
Utah State University
V S E Corp.
Valleydale Packers, Inc.
Valmac Industries, Inc.
Varian Associates, Inc.
Varo, Inc.
Veda, Inc.
Verac, Inc.
Vessel Charters, Inc.
Vickers, Inc.
Vitro Corp.
Voest Alpine Trading USA Corp.
W F Industries
Walters E & Co., Inc.
Wang Laboratories, Inc.
Wardoco, Inc.
Washington, University of
Watkins Johnson Co.
Wedtech Corp.
Wellco Enterprises, Inc.
West Systems
Western Gear Corp.
Western Research Corp.
Western Trading Co.
Western Union International
Western Union Telegraph Co.
Westinghouse Electric Corp.
White Engines, Inc.
Whittaker Corp.
Williams International Corp.
Williams Steel Industries, Inc.
Wilson Machine Co.
Winfield Mfg. Co., Inc.
Wisconsin Physicians Service Insurance
Wolf, L Co.
Woods Hole Oceanographic Institute
Woodward Governor Co.
World Airways, Inc.
Wyoming Refining Co.
Xerox Corp.
Zantop International Airlines, Inc.
Zenith Electronics Corp.

**Patricia H. Means,**

*OSD Federal Register Liaison Officer, Department of Defense.*

December 18, 1985.

[FR Doc. 85-30338 Filed 12-23-85; 8:45 am]

BILLING CODE 3810-01-M

## Department of the Army

## 32 CFR Part 584

**[Army Reg. 608-99]**

## Family Support, Child Custody, and Paternity

**AGENCY:** U.S. Army Community and Family Support Center, DoD.

**ACTION:** Final rule.

**SUMMARY:** This rule gives the Department of the Army's support, custody, and paternity policies and information on garnishment and involuntary allotments for payment of support under a court order. It includes guidance for processing complaints and claims, as well as requests regarding adoption proceedings of children of Army soldiers, and U.S. citizenship determinations. It provides a listing of administrative and punitive actions that may be taken against an Army soldier for failure to comply with the requirements of Army Regulation 608-99. Procedures for processing complaints and claims against nonactive duty or discharged Army personnel are also provided.

**DATE:** December 24, 1985.

**ADDRESS:** Commander, U.S. Army Community and Family Support Center (DACF-IS-PA), Room 468, Hoffman I, 2461 Eisenhower Avenue, Alexandria, VA 22331-0522.

**FOR FURTHER INFORMATION CONTACT:** LTC Milton J. Brokaw, (202) 325-8951.

**SUPPLEMENTARY INFORMATION:** 32 CFR Part 584 is added to show the Department of the Army's support, custody, and paternity policies. Army Regulation 608-99 applies to the Regular Army, the U.S. Army Reserve (USAR) on active duty, active duty for training, or official active duty for training (30 days or more duration), and the Army National Guard of the United States (ARNGUS) on active duty, active duty for training, or special active duty for training under title 10, U.S.C. (30 days or more duration). It does not apply to members of the USAR performing inactive duty training or to members of the ARNGUS performing duty in a State status under title 32, U.S.C. Penalties for violations of the minimum support requirements and child custody provisions include the full range of statutory and regulatory sanctions.

The U.S. Army Community and Family Support Center has certified that this regulation will not have a significant economic impact on a substantial number of small entities as they are defined in the Regulatory Flexibility Act (RFA), 5 U.S.C. 601-612.

Pursuant to 5 U.S.C. 605(b), the regulations, therefore, are exempt from the initial and final regulatory flexibility analyses requirements of sections 603 and 604.

This certification can be made because the regulation affects only individuals. It will have no significant economic impact on small entities, i.e., small businesses, small private and nonprofit organizations and small governmental jurisdictions.

**List of Subjects in 32 CFR Part 584**

Family support, Child custody, Paternity claims, Adoption proceedings, Citizenship and naturalization, Wages, Military personnel.

Accordingly, new Part 584 is added to Title 32 CFR to read as follows:

## PART 584—FAMILY SUPPORT, CHILD CUSTODY, AND PATERNITY

Sec.

584.1 General
584.2 Family support and child custody.
584.3 Paternity claims.
584.4 Adoption proceedings.
584.5 U.S. citizenship determinations on children born out of wedlock in a foreign country.
584.6 Procedures governing nonactive duty or discharged personnel.
584.7 Basic allowance for quarters.

Sec.
584.8 Garnishment.
584.9 Involuntary allotments.
Appendix A—References.
Glossary.

Authority: 10 U.S.C. 3012.

**§ 584.1 General.**

(a) *Purpose.*

This regulation sets forth the Department of the Army (DA) policy, responsibilities, and procedures on—

(1) Support and nonsupport of family members.

(2) Child custody.

(3) Paternity claims.

(4) Adoption proceedings involving the children of soldiers.

(b) *References.* Required and related publications and prescribed and referenced forms are listed in appendix A.

(c) *Explanation of abbreviations and terms.* Abbreviations and special terms used in this regulation are explained in the glossary.

(d) *Responsibilities.* (1) The Deputy Chief of Staff for Personnel will set policy for processing—

(i) Nonsupport complaints.

(ii) Child custody complaints.

(iii) Paternity claims.

(iv) Requests on adoption proceedings of children of soldiers.

(2) The Commanding General (CG), U.S. Army Community and Family Support Center (USACFSC) will—

(i) Set procedures for processing the following:

(A) Nonsupport complaints.

(B) Child custody complaints.

(C) Paternity claims.

(D) Requests regarding adoption proceedings of children of soldiers.

(ii) Process nonsupport complaints, child custody complaints, and paternity claims received at USACFSC regarding Army soldiers.

(iii) Carry out the objectives of this regulation to protect the rights of the soldier, the family, and the interests of the Army.

(iv) Advise and assist the heads of Headquarters, Department of the Army (HQDA) agencies, commanders of the major Army commands, and other commanders on matters pertaining to—

(A) Nonsupport.

(B) Child custody.

(C) Paternity

(D) Adoption proceedings of children of soldiers.

(3) Officers having general court-martial jurisdiction will give special emphasis to the support of family members in command information programs. This includes informing soldiers of Army policy and of their responsibility to provide adequate support for all family members and to comply with all court orders.

(4) First level field grade commanders will monitor all instances of soldiers' repeated failure to meet the requirements of this regulation that are brought to their attention. They will take action, when proper.

(5) Immediate commanders will—

(i) Ensure that soldiers are informed of the DA policy on support of family members and that they comply with court orders. They will also inform soldiers of the possible consequences of failing to fulfill financial obligations. This information will be included during inprocessing and outprocessing briefings, particularly during processing for mobilization and oversea movement.

(ii) Process nonsupport complaints, child custody complaints, and paternity claims per this regulation.

(iii) Counsel soldiers when complaints and claim are received. If the soldier is suspected of criminal conduct, self-incrimination protections (article 31, Uniform Code of Military Justice (UCMJ) and rights advisement) must be provided. (See § 584.2(g)(4).)

(iv) Answer all correspondence received from CG, USACFSC and other DA officials. In answering this correspondence, the commander will—

(A) Furnish complete details regarding nonsupport complaints, child custody complaints, and paternity claims.

(B) Reveal whether or not the soldier authorized the release outside the Department of Defense (DOD) of information obtained from a system of records. His or her decision should be recorded on DA Form 5459–R (Authorization to Release Information from Army Records on Nonsupport/Child Custody/Paternity Complaints).

(v) Answer all correspondence received directly from family members, legal assistance attorneys, and others. Normally, replies will not include information obtained from a system of records without the soldier's written consent. (See § 584.1(f).) Commanders may coordinate responses with the Staff Judge Advocate (SJA). Also, the commander will ask the SJA for guidance in unusual or difficult situations.

(vi) Inform the first level field grade commander of all instances of the soldier's repeated failure to meet the requirements of this regulation or to comply with court orders. Also, point out actions taken or contemplated to correct instances of nonsupport of family members or continuing violations of court orders.

(vii) Refer correspondence or queries received from news media organizations to the unit, installation, or command public affairs officer for response.

(viii) Take appropriate action against soldiers who fail to comply with this regulation. These actions include, but are not limited to, the actions in §§ 584.1(d)(5)(viii) (A) through (E). Failure to comply with the minimum support requirements (§ 584.2(d)) or the child custody provisions (§ 584.2(e)) of this regulation may be charged as violations of article 92, UCMJ. Article 132, UCMJ, prohibits the making of false claims. Article 133, UCMJ, covers conduct unbecoming an officer. Article 134, UCMJ, concerns dishonorable failure to pay debts and conduct of a nature to bring discredit upon the Armed Forces. Also, the criminal laws of some States prohibit the abduction of children by a parent or the nonsupport of family members in violation of existing court orders. These laws may also apply against soldiers under article 134, UCMJ, and Assimilative Crimes Act, section 13, title 18, United States Code (18 U.S.C. 13).

(A) Denial of reenlistment for enlisted members (AR 601–280).

(B) Letter of reprimand for filing in a soldier's Military Personnel Records Jacket or Official Military Personnel File (AR 600–37).

(C) Administrative separation from the service (AR 635–100 or AR 635–200).

(D) Nonjudicial punishment under article 15, UCMJ.

(E) Court-martial.

(ix) Urge soldiers to provide additional financial support beyond the required minimum whether the needs of the family so require.

(x) After coordination with the SJA and appropriate command representatives, and under applicable State, Federal, and host country laws, take remedial steps to assist in the following:

(A) Elimination of continuing violations of court orders and this regulation on child custody.

(B) Return of such children to the parent or guardian entitled to custody.

(6) The unit, installation, or command public affairs officer will—

(i) Answer correspondence and queries received from news media organizations.

(ii) Coordinate with the SJA before making any response.

(e) *Policy.* (1) Soldiers of the Army are required to manage their personal affairs satisfactorily. This responsibility includes—

(i) Providing adequate and continuous support to or for family members. (See § 584.2.)

(ii) Complying with all court orders.

(2) The Army has an interest in the welfare of both soldiers and their families. This is recognized by numerous laws and programs authorizing the following:

(i) Family housing.

(ii) Living and travel allowances.

(iii) Medical care.

(iv) Child care and development.

(v) Community support services.

(3) Because of military duty, soldiers and their families often live in States in which they have not established domicile. Frequently, they reside in foreign nations. This often places soldiers beyond the judicial process of State courts.

(4) The Army recognizes the transient nature of military duty. This regulation prohibits the use of a soldier's military status or assignment to deny financial support to family members or to evade court orders on child support or custody. Commanders have a responsibility to ensure that soldiers provide for the welfare of their families. Before recommending approval of requests for, or extensions of, oversea assignments, commanders should consider whether the soldier's oversea assignment will adversely affect the legal rights of family members in pending court actions against the soldier.

(5) The policy in this regulation regarding the financial support of family members is solely intended as an interim measure until the parties—

(i) Arrive at a mutually satisfactory agreement, or

(ii) Resolve their differences in court.

(6) Soldiers are entitled to the same legal rights and privileges in State courts as civilians. This includes determining the extent and amount of their support obligations to family members. This regulation is not intended to be used as a guide by courts in determining the following:

(i) The existence of support obligations.

(ii) The amount of past, present, or future support obligations.

(f) *Release of information.* (1) Soldiers will be provided the opportunity of completing DA Form 5459–R before being questioned about compliants or claims under this regulation. Information voluntarily provided by soldiers may be used by commanders to answer inquiries. Replies normally will not include information obtained from a system of records without the soldier's written consent.

(2) Some information may be released outside DOD from a system of records even without the soldier's written consent. Under the Privacy Act (5 U.S.C. 552a(b)(2) and AR 340–21, para 3–3), information may be released, if required, under the Freedom of Information Act. Under 5 U.S.C. 552(b)(6) and AR 340–17, chapter III, information from personnel and other similar files may be released if it does not constitute a "clearly unwarranted invasion of privacy." The information released must be in the public interest.

(3) The type of information that may be released from a system of records without the soldier's consent will vary from case to case. In each case, the public interest of having soldiers support their families and obey court orders must be balanced against the sensitivity of the privacy interests involved. Army policy favors permanent resolution of support and custody matters in court. The denial of information that hinders such resolution is not in the public interest.

(4) Before releasing information from a system of records without the soldier's consent, commanders may consult the SJA. Generally, the types of information shown below may be released to the complaining family member entitled to support or those authorized by the family member to act in his or her behalf (for example, legal assistance attorneys, Member of Congress, courts, Government welfare agencies).

(i) Present unit of assignment, including port calls and future duty assignments, permanent or temporary, if known.

(ii) Scheduled separation and retirement dates from the Service.

(iii) Rank and authorized pay and allowances for that grade.

(iv) Allotments authorized or being authorized for or in behalf of the family member entitled to support.

(v) The soldier's stated intentions, if any, regarding resolution of the complaint.

(vi) The general whereabouts of the soldier's children, if known.

(5) The SJA should be consulted for legal advice before the residential address of a soldier or family member is released.

(6) Any information released should be pertinent to the inquiry. The soldier's relationship, if any, to the person making the inquiry, should be considered. Consistent with the purpose of this regulation, information that unduly invades the privacy of the soldier or his or her family should not be released.

(g) *Penalties.* Compliance with the minimum support requirements § 584.2(d)) and child custody provisions (§ 584.2(e)) of this regulation will be enforced by administrative and criminal remedies as appropriate.

(h) *Basic allowance for quarters.* A summary of the rules regarding entitlements to basic allowance for quarters (BAQ) is in § 584.7. The minimum support requirements of this regulation are stated in amounts equal to a soldier's BAQ at the "with dependents" rate. However, a soldier's entitlement or lack of entitlement to such allowances has no relationship to the obligation under this regulation to support family members. Except for § 584.2(f)(2)(ii)(B), the actual receipt or nonreceipt of BAQ also has no relationship to that obligation.

(i) *Entitlement of variable housing allowance.* Soldiers entitled to BAQ at the "with" or "without dependents" rate may be entitled to variable housing allowance (VHA). Terms for receiving VHA are set forth in the Joint Travel Regulations, M4550 through M4557. Soldiers may use VHA to defray housing costs for family members.

(j) *Garnishment.* A summary of the rules regarding garnishment of Federal wages is in § 584.8.

(k) *Involuntary allotments.* A summary of the rules regarding involuntary allotments from pay and allowances is in § 584.9.

**§ 584.2 Family support and child custody.**

(a) *General.* (1) This chapter requires soldiers to provide financial support to family members and to obey court orders on child custody. It also provides guidance and policy to commanders to follow when resolving nonsupport and child custody issues. Consistent with specific provisions below, a soldier will—

(i) Furnish financial support to family members that meets at least the minimum support requirements of this regulation (§ 584.2(d)).

(ii) Provide such additional support within his or her financial ability to meet the financial needs of family members (§ 584.2(j)).

(iii) Comply with all court-imposed obligations (§ 584.2(c)(3)).

(iv) Obey court orders and this regulation on child custody and visitation rights (§ 584.2(e)).

(2) It is the responsibility of soldiers to resolve nonsupport issues with family members by one of the methods shown in § 584.2(a)(2)(i) through (iii). In all cases, Army support policy for family members should be considered temporary until either an agreement has been reached between the parties (including those acting on behalf of minor children) or court action has been taken.

(i) Oral agreements.

(ii) Written support agreements.

(iii) Court orders.

(3) Each complaint of nonsupport will be considered individually by the soldier's immediate commander. Alleged desertion or other marital misconduct on the part of a spouse has no effect on a soldier's obligation to provide financial support as required by § 584.2(d).

(b) *Separation from family due to military service.* Military service often requires soldiers to live separately from their families during oversea service or extended temporary duty. Soldiers must plan carefully for the support of their families during these periods. Commanders will educate soldiers and their families on the advantages of joint bank accounts. Such arrangements usually minimize the hardship and financial burden on family members that may occur during periods of such separation. If proper, commanders will urge soliders to start an allotment to or for their family to ensure continuous financial support. The amount of such a support allotment should be set up by agreement between the soldier and his or her family. In the absence of such an agreement or a court order, the provisions of §584.2(d)(2) apply. Each soldier is expected to keep reasonable contact with family members to minimize inquiries, claims, and compliants sent to Army officials.

(c) *Support by oral agreement, written support agreement, or court order.*—(1) *Oral agreement.* It is not the Army's policy to involve itself in disputes over the terms or enforcement of oral support agreements. Where an oral agreement exists and is being followed, the Army need not and will not interfere. When a dispute arises, the Army will require compliance only with the provisions of this regulation. Thus, if a family member complains that a soldier is not sending an agreed upon amount that is less or more than the minimum required by § 584.2(d), the commander will advise the soldier to either send the agreed upon amount or the minimum amount required by § 584.2(d). § 584.2(d) applies when the parties cannot reach an oral agreement or the amount agreed upon is in dispute. In appropriate cases, the commander can order additional support beyond the minimum amount required by § 584.2(d). (See §584.2(j).)

(2) *Written support agreement.* If the parties are separated and have a signed written agreement, the amount of support specified in such an agreement controls. A signed written agreement includes a separation agreement or a property settlement agreement. A written agreement on support also may be shown by letters exchanged between the parties in which the amount of support has been agreed to by the parties. If the agreement is silent on an amount of spousal and/or child support, the interim minimum financial support requirements of §584.2(d)(2) apply. The amount specified in the written agreement will be deemed adequate until modified by—

(i) Another agreement reduced to writing and signed by both parties.

(ii) Court order.

(3) Court order.

(i) Court orders often contain other financial obligations, such as provisions for property division, marital property awards, and payment of medical and other expenses. Commanders have a responsibility to ensure that soldiers comply with these provisions. Soldiers will comply with all court-imposed obligations. Failure to do so may result in costly and time-consuming litigation or court contempt proceedings. These actions often are to the detriment of the soldier and the unit's readiness mission. §584.2(d)(1)(i), however, only applies to court orders directing the soldier to provide financial support to family members on a periodic basis.

(ii) Court orders under this regulation include those orders issued by the courts of the Federal Republic of Germany (FRG). The courts must have acquired valid jurisdiction consistent with the provisions of articles 32 through 37 of the Supplementary Agreement concerning foreign forces stationed in the FRG. This agreement supplements the North Atlantic Treaty Organization Status of Forces Agreement. A soldier will comply with all other foreign nation court and administrative orders that are recognized by treaty or international agreement.

(iii) Commanders should be aware that conditions may have changed greatly from when a court order was issued. For example, a soldier may have gained other family responsibilies. Many outstanding and uncontested support orders against soldiers cause severe hardship. Such orders can only be modified by a court. If a soldier's income appears inadequate to satisfy an outstanding order and still maintain the soldier, the commander should urge the individual to consult a legal assistance attorney. However, the soldier will comply with the terms of a court order until relieved of this obligation by modification of the order by a court.

(d) *Minimum support requirements.* (1) Soldiers will not violate the following:

(i) Financial support provisions of a court order.

(ii) Financial support provisions of a written support agreement in the absence of a court order.

(iii) Interim minimum financial support requirements of § 584.2(d)(2) in the absence of a court order or written support agreement.

(2) In the absence of a court order or written support agreement, and until such an order or agreement is obtained, the following interim *minimum* financial support requirements apply:

(i) *Single family units.* (A) Family not living in Government family quarters. The soldier will provide support in an amount equal to the soldier's BAQ at the with-dependents rate. This amount of financial support will be provided for this family unit regardless of whether or not the soldier is—

(*1*) Receiving BAQ.

(*2*) Occupying Government family quarters.

(B) Family living in Government family quarters. While the supported family is occupying Government family quarters, the soldier will provide an amount equal to the difference between BAQ at the with- and without-dependents rate. When the supported family members move out of Government family quarters, support will be provided in an amount equal to BAQ at the with-dependents rate for the soldier's rank.

(ii) *Multiple-family units.* In multi-family unit support situations, each supported family member will receive a pro-rata share of the BAQ at the with-dependents rate. This share will be determined by dividing an amount equal to BAQ at the with-dependents rate for the soldier's rank by the total number of supported family members (excluding former spouses). The following modifications apply: First, any court ordered support will be paid as stated. Secondly, supported families living in Government family quarters will receive an amount equal to the difference between BAQ at the with- and without-dependents rate for the soldier's rank. Lastly, any remaining family members (excluding former spouses) will receive a pro-rata share of the BAQ amount. This will be provided regardless of the amount of support paid to other family members. Following are examples:

(A) *Example 1.* A soldier is divorced and has three children from that marriage. The soldier is required by a court order to pay $300 per month for the children and $100 per month for the former spouse. The soldier has remarried and has two more family members (spouse and child) living in private housing. The soldier now has a total of five family members that he or she must support under Army policy. (A former spouse does not qualify as a family member in pro-rata determinations.) The children by the previous marriage must receive $300 and the former spouse must receive $100 per the court order.

The present spouse and child should receive support equal to two-fifths of BAQ at the with-dependents rate for the soldier's rank.

(B) *Example 2.* A soldier has one child by a previous marriage. There is no court order for child support. The soldier is unable to show that the court granting the divorce had personal jurisdiction over the soldier so as to be able to order child support. The soldier has remarried and has a spouse and two children living in private housing. The soldier now has a total of four family members that he or she must support under Army policy. (These family members are the child by a previous marriage and the present spouse and two children.) Each family member should receive support equal to one-fourth of BAQ at the with-dependents rate for the soldier's rank.

(C) *Example 3.* A soldier has two children by a previous marriage. The soldier is required by court order to pay $200 per month for these children. Also, the soldier is required to pay $75 per month for support of a child per a court order that has declared him to be the father. He has remarried and has a spouse and three children living in Government family quarters. The soldier now has a total of seven family members that he must support under Army policy. The children by his previous marriage must receive $200 per the court order. His other child must receive $75 per the court order. The spouse and children of his present marriage should receive an amount equal to the difference between BAQ at the with- and without-dependents rate for the soldier's rank.

(iii) Military members married to one another. In the absence of a court order or written support agreement, an Army soldier is not required to provide support to a spouse on active duty in the Armed Forces.

(iv) Children of military member parents.

(A) *Single family units.* In the absence of a court order or written support agreement, the following interim support requirements apply:

(1) Single family units when the Army soldier does not have custody of any children of the marriage. The Army soldier will pay an amount equal to the difference between his or her own BAQ at the with- and without-dependents rate to the military member having custody of the child or children of the marriage. This amount of financial support will be provided regardless of which military member, if any, is receving BAQ or occupying Government family quarters.

(2) Single family units when the Army soldier has custody of the child or children of the marriage (for example, Army soldier has custody of one child and spouse has custody of two children). In this situation, the Army soldier is not required to provide a minimum amount of financial support for the children in the other military member's custody.

(B) *Multiple-family units.* The provisions of § 584.2(d)(2)(ii) apply. However, the amount in § 584.2(d)(2)(iv)(A) will not be diminished by proration because of the Army soldier's financial support obligations to other family members. For example: An Army soldier has an adopted child from a previous marriage. The soldier is required by court order to pay $150 per month for this child. The soldier presently is married to a spouse on active duty with the Air Force. They have two children from this marriage. The Air Force member and children reside in private housing. The Army soldier has a total of three family members that he or she must support. The Army soldier will pay $150 a month to the adopted child per the court order. The children from the present marriage will receive an amount equal to the difference between his or her BAQ at the with- and without-dependents rates for the Army soldier's rank.

(3) A commander has no authority to excuse a soldier from complying with the interim *minimum* support requirements of § 584.2(d)(2) when they are applicable.

(4) In the absence of a contrary provision in a written support agreement or court order, monthly financial support to family members will be sent before the last calendar day of the month for which the support is due. If the family members are not residing together, the soldier will ensure each family member receives his or her pro-rata share. (For example, spouse lives along and the children live with their grandparents.)

(e) *Child custody.* (1) A soldier relative, who is aware that another person is a lawful custodian of an unmarried child under the age of 14 years, will not—

(i) Abduct, taken, entice, or carry away the child from the lawful custodian.

(ii) Withhold, detain, or conceal the child away from the lawful custodian.

(2) A "lawful custodian" is a person authorized, either along or together with another person or persons, to have custody and exercise control over a child less than 14 years of age by order of a court. The fact that joint custody has been awarded to both parents by a court does not preclude a violation of this paragraph by the soldier parent. However, in the absence of a court order to the contrary, the mother of a child born out of wedlock who is not then, nor has ever been, married to the father of the child is deemed the "lawful custodian" of that child for the purpose of this regulation.

(3) A soldier relative is a soldier who is the parent, grandparent, brother, sister, uncle, aunt, or one who has at some time been the lawful custodian of the child.

(4) It is a defense to a violation of this paragraph that the soldier—

(i) At the time of the offense had custody of the child to the exclusion of others pursuant to a valid order of a court having jurisdiction over the child; or

(ii) Voluntarily returned the child to the lawful custodian within 96 hours after return was demanded by the lawful custodian.

(f) *Relief from the minimum support requirement.* (1) Court orders with financial support provisions.

(i) Court ordered financial support will be by the terms of the court order. Relief from a court order can only be obtained under the law. Nothing in this regulation affects or lessens a soldier's legal obligation to comply strictly with the terms of a court order.

(ii) A soldier who disobeys a court order may be held in contempt of the court that issued the order. Also, a soldier may be punished for violating this regulation. It is, however, a defense to any violation of § 584.2(d)(1)(i) that—

(A) The court issuing the order was without jurisdiction to do so, and

(B) The soldier at all times has been complying with any of the following:

(1) The financial support provisions of another court order.

(2) The financial support provisions of a written support agreement.

(3) The interim minimum financial support requirements of § 584.2(d)(2).

(2) Court orders without financial support provisions.

(i) A soldier will provide financial support to family members unless expressly relieved of this obligation by—

(A) Court order.

(B) Written support agreement.

(ii) A soldier will provide financial support under § 584.2(f)(2) to family members, which meets at least the minimum support requirements of this regulation. The financial support will be provided even when a court order contains no provision as to support except as follows:

(A) A soldier has no obligation to provide financial support to a former spouse except by order of court.

(B) A soldier has no obligation to provide financial support to minor children of the marriage if he or she can show the following:

(1) The court issuing the final order of divorce had personal jurisdiction over the soldier to order child support.

(2) The soldier is not receiving BAQ at the "with dependents" rate based solely

on the support of the minor children in question.

(3) *Written support agreements.* If a financial support obligation is evidenced by a written agreement between the parties, the soldier can only be relieved of this obligation by another written agreement or by court order.

(4) *Greater spousal income.* In the absence of a written support agreement or court order, a soldier has no obligation to support a civilian spouse who is receiving an annual income equal to or greater than the annual gross pay of the soldier. The income of the spouse does not affect the soldier's obligation to provide financial support to the children of that marriage in the physical custody of the spouse on a pro-rata basis. Example: A soldier is living in Government family quarters with one of their children. The soldier's spouse deserted the soldier and lives in private housing with their other child. The soldier's spouse earns $5,000 more in annual income from a civilian job than the soldier earns in annual gross pay. There is no court order or written support agreement. The soldier has a total of three family members. However, under Army support policy, the soldier does not have to provide a pro-rata share of financial support to the spouse because the spouse's income exceeds that of the soldier. (Note that under § 584.2(a)(3) marital misconduct is not a relevant consideration.) The soldier must support the child in Government family quarters. In addition, the soldier must provide an amount equal to one-third of BAQ (pro-rata share) at the "with dependents" rate to the spouse on behalf of the child living with the spouse.

(g) *Commander's inquiries.* (1) If a soldier denies he or she has a financial obligation to support a spouse or children for any reason, the soldier's commander will—

(i) Inquire into the matter.

(ii) Consult with the SJA prior to determining whether or not there is a support obligation. If there is no support obligation, BAQ at the "with dependents" rate should be stopped.

(2) If a soldier claims he or she has made support payments as required by this regulation, the soldier's commander will—

(i) Request the soldier to provide proof of payment in one of the following forms:

(A) Canceled personal checks.

(B) Leave and earnings statements showing allotments.

(C) Postal or money order receipts accompanied by a sworn statement from the soldier that the order was sent to the family member. If possible, evidence that the postal or money order was cashed by the complaining party should be provided.

(D) Other acceptable evidence of payment.

(ii) Consult with the SJA, if necessary, to determine whether the soldier has provided enough proof of payment.

(3) If a soldier is suspected of violating a child custody or visitation rights in a court order, the soldier's commander will—

(i) Inquire into the matter.

(ii) Consult with the SJA prior to taking action.

(4) In any case in which the soldier is suspected of violating this regulation (§ 584.2(d) or (e)), or of having committed other offenses, the commander, prior to questioning the soldier, will advise him or her of—

(i) The suspected offense.

(ii) The right to remain silent under article 31, UCMJ.

(iii) The right to counsel under the Fifth Amendment.

(h) *Form of support payment.* (1) Unless otherwise provided in the court order or by agreement, a financial support payment will be made in one of the following ways:

(i) In cash.

(ii) By check or money order.

(iii) By allotment.

(2) A soldier will receive credit for payments made to others on behalf of, and with the agreement of, the supported family members. Examples of support provided in kind include—

(i) Rent.

(ii) Utility services.

(iii) Interest and principal due on loans, mortgages, or charge accounts.

(iv) Insurance payments.

(i) Arrearages

(1) *General.* A soldier who falls into arrears without legal justification or excuse is in violation of § 584.2(d).

(2) Court orders and written support agreements.

(i) Amounts in arrears based on a past failure to comply with a court order or written support agreement will be paid at once in a lump sum amount. If an immediate lump sum payment is impractical, soldiers are expected to work out arrangements with the court or the affected family members to pay arrearages on a scheduled basis. If arrangements can not be worked out, commanders will intervene and order payment of arrearages on a scheduled basis based on the soldier's ability to pay.

(ii) When arrearages arise from noncompliance with court orders and written support agreements, this may result in—

(A) Garnishment of the soldier's pay account (§584.8).

(B) Initiation of an involuntary allotment against the soldier's pay account (§ 584.9).

(C) Contempt of court proceedings.

(D) Recoupment of BAQ received by the soldier.

(iii) Administrative or punitive action may be taken on a violation of this regulation for any month in which the soldier failed to provide the required financial support even if the amount in arrears eventually is paid.

(3) Interim minimum financial support requirements. A soldier should be encouraged to pay the amount in arrears based on past noncompliance with the interim minimum financial support requirements (§§ 584.2(d) (1)(iii) and (2)). However, a soldier cannot be ordered to pay such an amount. Nevertheless, administrative or punitive action may be taken on a violation of this regulation for any month in which the soldier failed to provide the required financial support even if the amount in arrears eventually is paid. Also, failure to provide required financial support in the past may be considered, together with other factors, in a commander's determination of the amount of additional support that may be ordered. (See § 584.2(j).)

(j) Additional support where there is no support agreement or court order.

(1) Ordinarily, a soldier should not be required to provide financial support beyond that required by § 584.2(d)(1)(iii). However, a soldier should provide additional support within his or her ability to meet the basic financial needs of family members when the interim support requirements of this regulation are shown to be inadequate.

(2) If there is a demonstrated need for immediate and temporary additional support because of unexpected and unforeseen circumstances and the parties are unable to agree on such additional support, a commander may order temporary additional support.

(3) Commanders will consider the following factors in determining the amount of additional support, if any, that a soldier should provide when a request for additional support is received:

(i) The pay, allowances, separate income, and other financial resources of both the soldier and the family member for whom additional support is requested.

(ii) The earning capacity of the family member on whose behalf support is requested.

(iii) The financial savings of the soldier and family member.

(iv) The separate and joint debts of the soldier and family member, by whom those debts were incurred, and the reasons behind them.

(v) The soldier's duty to provide financial support to other family members, including former spouses.

(vi) The financial needs of the soldier and the family member and whether these needs are temporary or permanent in nature.

(vii) The standard of living of the soldier and family member and whether such standard of living is reasonable under the circumstances.

(viii) With regard to spousal support, the duration of the marriage and the circumstances under which the parties separated.

(ix) The extent of the soldier's or family member's compliance with existing court orders and written support agreements. This includes those provisions dealing with child custody, visitation rights, property division, and marital property awards.

(x) The amount in arrears owed by the soldier based on past noncompliance with the minimum support requirements. (See §§ 584.2 (d) and (i).)

(xi) Any other fact which, in the judgment of the commander, has a logical bearing upon the amount of additional support the soldier reasonably should be expected to provide.

(k) *Procedure for making complaints.* (1) Complaints about nonsupport of family members and noncompliance with court orders on financial support and child custody should be sent through command channels. The complainant should be referred to the immediate commander of the soldier concerned.

(2) The Inspector General (IG) may assist in properly routing the complaint. The IG also may assist if the responsible commander has failed to respond in a satisfactory manner or as required by this regulation. (See AR 20-1, para 4-9.)

(3) The USACFSC (DACF-IS-PA) has set up an office to assist in these cases. USACFSC will provide policy interpretations and guidance on unresolved or complex cases, as needed. USACFSC normally will go through command channels to the immediate commander of the soldier concerned requesting that action be taken under this regulation.

(4) Family members who present complaints against a military member of another Service (Air Force, Marine Corps, Navy, or Coast Guard) should be referred to the appropriate Service.

(l) *Commander's actions.* (1) Upon receipt of a complaint of nonsupport or noncompliance with court orders, including provisions on child custody or visitation rights, the commander will review the complaint. He or she will do the following if the information is incomplete:

(i) Acknowledge receipt of the complaint.

(ii) Explain that the information or documentation sent is not enough to give proper help.

(iii) If appropriate, send the complainant DA Form 5460-R (Request for Help in Receiving Support and/or Identification Cards for Family Members).

(iv) Advise that help will be given with the complaint upon return of the completed form and other requested information and documents.

(v) If appropriate, advise that DA Form 5460-R alone is not enough documentation for issuance of a dependent identification card (ID card) (AR 640-3). Documentation (that is, court orders, birth certificates, marriage certificates, etc.) must be provided to support eligibility for benefits.

(vi) Answer any policy or procedural questions that have been asked.

(2) Upon receipt of DA Form 5460-R or a complaint that has enough information to properly respond, the commander will—

(i) Review soldier's legal financial obligations in light of the complaint and the facts presented by all parties concerned.

(ii) If necessary, ask the SJA if the complaint is valid, if the soldier must provide financial support or give up custody of children, and any other related questions.

(iii) Notify the soldier of the complaint of nonsupport or of a violation of a child custody court order.

(iv) Require the soldier to complete and sign DA Form 5459-R. Information obtained from a system of records ordinarily will not be released outside DOD without the soldier's consent. (See § 584.1(f).)

(v) If the soldier is suspected of violating this regulation or of having committed other offenses, the commander, prior to questioning the soldier, will also advise him or her of—

(A) The suspected offense.

(B) The right to remain silent under article 31, UCMJ.

(C) The right to counsel under the Fifth Amendment.

(vi) Explain the following to the soldier:

(A) The Army's policies regarding support of family members and compliance with court orders.

(B) That refusal to give required support per this regulation may result in administrative or punitive action.

(C) That a soldier is not entitled to BAQ at the "with dependents" rate when no part of the allowance is given to family members. Therefore, collection action may be initiated by the Army.

(vii) Explain what garnishment is (§ 584.8) and how it might affect the soldier's pay, allowances, and allotments. For example, explain that the amount garnisheed monthly might significantly exceed monthly support obligations previously agreed upon.

(viii) Tell the soldier of any court order for attachment or garnishment that has been received. Immediately send the court documents to the Commander, U.S. Army Finance and Accounting Center (USAFAC), ATTN: FINCL-G, Indianapolis, IN 46249-0260 for action. (See § 584.8(b).) Also, inform the soldier that if the document is in proper legal form, a portion of the soldier's pay and allowances will be garnisheed.

(ix) Explain involuntary allotments (§ 584.9) if appropriate.

(x) Coordinate with the soldier's servicing finance and accounting office (FAO) for problems of pay, allowances, and allotments.

(xi) Urge soldiers to provide continuous support to family members by allotment. The allotment should be for the mutually agreed amount, court order, or as computed under this regulation. An account may be set up in a financial institution by the recipient to receive the allotment. This action may preclude delays in receipt and other related problems in the future.

(xii) Help the soldier start an allotment to make the required support payments. Also, advise the soldier to let the commander know if there is a change or stoppage to the support allotment.

(xiii) Give the soldier a chance to consult with a legal assistance attorney if he or she desires. However, the commander should ensure that this is not used as a delaying tactic. Where appropriate, a support payment plan should be initiated without delay.

(xiv) Urge soldiers thinking about divorce to seek legal advice from a legal assistance attorney. Also, advise the soldier to ensure an amount of support is included in the court order for their children. This action may help to prevent future disputes.

(xv) Ensure that the soldier is not receiving BAQ at the "with dependents" rate when not entitled to it. (See § 584.7.)

(xvi) Ask the soldier about his or her intentions. Give the soldier the chance to furnish a voluntarily signed statement admitting or denying the complaint and stating his or her intentions.

(xvii) Send complaints received to the soldier's new duty station if he or she has been reassigned. Advise the complainant of the soldier's reporting date and the unit address to which correspondence should be sent. If proper, give the complainant a copy of DA Form 5460–R.

(3) Advise the complainant courteously and promptly—

(i) Of the Army policy in suitable areas of concern.

(ii) Of the soldier's intentions, if the soldier allows release of the information.

(iii) That personal problems outside the requirements of this regulation must be resolved in court if the parties cannot agree.

(4) If proper to the situation, remind complainant of other helping agencies on post, such as the chaplain and Army Community Service. These agencies can give timely, interim help to meet immediate needs pending a more permanent resolution of the problem.

(5) Retain the statements allowing or forbidding release of information to the complainant and the soldier's intentions with the case file for future reference. Documents/records will be filed per AR 600–37 and the Army Functional Files System (AR 340–2 and AR 340–18).

(6) Monitor actions closely to ensure promises of support or other actions by soldiers to complainants are being met.

(7) Consider administrative or punitive action if proper.

(8) Inform the first level field grade commander of the soldier's repeated failure to meet the requirements of this regulation. Also, point out actions taken or contemplated to correct instances of nonsupport of family members or violations of child custody court orders.

**§ 584.3 Paternity claims.**

(a) *General.* (1) This chapter sets policy and procedures to process paternity claims against male Army soldiers. These procedures apply to claims made in the continental United States and in foreign countries. They apply to claims made by the claimant or on behalf of the claimant by attorneys, court officials, and others.

(2) Soldiers will be informed of paternity claims against them. Commanders will ensure that soldiers are advised of their legal rights and will advise soldiers of their moral and legal obligations in the matter. Soldiers admitting paternity will be urged to provide the necessary financial support to the child. Also, they will take any other action proper under the circumstances.

(b) Procedures for questioning soldiers about paternity claims upon receipt of a claim of paternity against a soldier, the commander will take the following actions:

(1) If there is evidence that an offense (for example, rape, indecent acts with a minor) may have been committed—

(i) Inform law enforcement officials.

(ii) Inform the soldier of the suspected offense. Before questioning, advise the soldier of his right to remain silent under article, 31, UCMJ, and his right to counsel under the Fifth Amendment.

(iii) Coordinate further action under this regulation with the SJA and law enforcement officials if appropriate.

(2) If there is no evidence that an offense was committed—

(i) Allow the soldier a chance to talk with a legal assistance attorney about his legal rights and obligations.

(ii) Require the soldier to complete and sign DA Form 5459–R. Information obtained from a system of records normally will not be released outside DOD without the soldier's consent. (See § 584.1(f).)

(iii) Inform the soldier of Army policy on the support of family members contained in this regulation.

(iv) Advise the soldier that a court order against him on the paternity claim, followed by a refusal to support a child born out of wedlock, could result in—

(A) Administrative or punitive action for violating this regulation.

(B) Garnishment of the soldier's pay account (§ 584.8).

(C) Initiation of an involuntary allotment against the soldier's pay account (§ 584.9).

(D) Contempt of court proceedings.

(v) Ask the soldier about his intentions. Give the soldier the chance to furnish a voluntarily signed statement admitting or denying the claim and stating his intentions.

(c) *Procedures for processing paternity claims.* (1) When one of the conditions in § 584.3(c)(1)(i) applies, a claimant will be advised of the statement in § 584.3(c)(1)(ii).

(i) A soldier—

(A) Refuses to answer questions about the paternity claim.

(B) Denies paternity.

(C) Admits paternity, but refuses to provide financial support.

(ii) No action can be taken on the claim of paternity in the absence of a court order. The court order must identify the soldier in question as the father of the child. Also, the court order must direct that the soldier provide financial support to the child.

(2) The commander will reply directly to the claimant or the attorney or court official she has authorized to act in her behalf. Information obtained from a system of records ordinarily will not be released outside DOD without the soldier's consent. (See § 584.1(f).)

(3) If the soldier admits paternity and agrees to provide financial support, then the commander will—

(i) Ask the claimant to provide a copy of the birth certificate.

(ii) Help the soldier in filing for an allotment or providing other financial aid.

(iii) Advise the claimant of the amount, effective date, and means of payment.

(iv) Help the soldier apply for BAQ at the "with dependents" rate, if applicable. (A birth certificate may be required.)

(v) Ensure an ID card is issued for the child after the relationship is documented, if proper. (A birth certificate may be required.) (See AR 640–3, para 3–3, for dependency criteria for ID cards.)

(vi) Allow the soldier to take ordinary leave in order to marry the claimant, if leave is requested for this purpose. However, the leave may be delayed if it will interfere with military requirements. Travel in connection with leave (including travel to and from overseas commands) is the responsibility of the soldier. Travel will be at no expense to the Government. If the marriage is to take place overseas, the soldier must comply with AR 600–240 and AR 608–61 in applying for authorization to marry (DA Form 2029–R) (Application for Authorization to Marry Outside of the United States).

(d) *Court orders.* If a court order of paternity and support has been issued, the commander will—

(1) Advise the soldier of the policy regarding support of family members.

(2) Advise the soldier that refusal to support his child born out of wedlock could result in—

(i) Garnishment of the soldier's pay account (§ 584.8).

(ii) Initiation of an involuntary allotment against the soldier's pay account (§ 584.9).

(iii) Contempt of court proceedings.

(iv) Administrative or punitive action for violating this regulation.

(3) Refer the soldier to a legal assistance attorney for advice on his legal rights and obligations.

(4) Help the soldier file an attotment or give other financial aid.

(5) Advise the claimant of the amount, effective date, and means of payment.

(6) Help the soldier apply for BAQ at the "with dependents" rate, if applicable.

(7) Ensure an ID card is issued for the child.

(8) Consider administrative or punitive action if the soldier fails to obey the court order. (See § 584.1(d)(5)(viii.)

(9) Inform the first level field grade commander of the soldier's repeated failure to meet the requirements of this regulation. Also, point out actions taken or contemplated to correct instances of nonsupport of family members.

**§ 584.4 Adoption proceedings.**

(a) *General.* This chapter does not apply to those situations were a soldier is trying to adopt a child. It applies to those situations where another person is trying to adopt a legitimate or illegitimate child of a soldier. A child born in or out of wedlock normally may not be put up for adoption without the consent of the parents. Therefore, communications from a judge or court asking that a soldier appear at an adoption hearing must be answered.

(b) *Commander's actions.* The commander will—.

(1) Inform the soldier or the inquiry.

(2) Urge the soldier to see a legal assistance attorney.

(3) Advise the court or judge, as appropriate, that—.

(i) A request by the soldier for leave to attend an adoption hearing on (date) has been granted.

(ii) A request by the soldier for leave to attend an adoption hearing on (date), if made, would be approved..

(iii) Due to military requirements, the soldier cannot be granted leave to attend any court hearing until (date).

(iv) The soldier has stated that he or she is not the natural parent of the child.

(v) Since the soldier is not present because (give specific reasons), (for example, temporary duty or leave), a complete response cannot be made until (date).

(vi) The soldier is no longer in this command. The commander will provide the soldier's new military address to the court or judge. The commander then will send a copy of the inquiry to the soldier's new commander and advise the court or judge of this action.

(4) Furnish the soldier with a copy of the communication and the reply.

**§ 584.5 U.S. citizenship determinations on children born out of wedlock in a foreign country.**

(a) *General.* (1) A child born out of wedlock in a foreign country of an American citizen father and an alien mother does not automatically gain U.S. citizenship. The child must first be legally acknowledged by the father. Marriage to the mother may be required in order for the child to acquire U.S. citizenship. The father also must establish that he had at least 10 years of physical presence in the United States prior to the child's birth. Five of those years must have been spent in the United States after the father's 14th birthday. United States military service counts as physical presence in the United States. (See 8 U.S.C. 1101(c)(1), 1401(g), and 1409(c).) Whether the child gains the citizenship of its mother depends entirely upon the laws of the nation in which she is a citizen.

(2) A child born out of wedlock in a foreign country to an American citizen mother and an alien father or U.S. Citizen father gains U.S. citizenship at birth if the mother had been physically present in the United States for a continous period of 1 year prior to the child's birth. (See 8 U.S.C. 1409(c).) The child will gain the citizenship of the father only if the laws of the nation of which the father is a citizen so provide.

(b) *Procedures for claiming U.S. citizenship rights.* (1) A father desiring rights of U.S. citizenship for a foreign-born child must legally acknowledge the child as his own and prepare a case file. Each case is decided on its own merits. The Department of State, if the child is in a foreign nation, or the Immigration and Naturalization Service (INS), if the child is in the United States, will make the decision. Documents that may be important in supporting a citizenship determination are listed below:

(i) Proof of father's citizenship. This may consist of any of the following:

(A) A certified copy of his birth certificate (with a raised seal of the registrar of births).

(B) A report of birth abroad (FS Form 240 (Report of Birth Abroad of a Citizen of the United States)).

(C) A certificate of citizenship.

(D) A certificate of naturalization.

(E) A valid U.S. Passport.

(F) A certified copy of an approved U.S. passport application.

(G) Any secondary evidence acceptable by the State Department or INS.

(ii) Affidavit of paternity.

(iii) Proof of presence in the foreign country at time of conception. (This information can be extracted from the passport, DA Form 2–1 (Personnel Qualification Record—Part II), etc.).

(iv) Child's birth certificate.

(v) Proof of the father's physical presence in the United States for 10 years (5 after age 14).

(vi) Blood type tests of the mother, the father, and the child. (At the request of the examining officer.)

(vii) Two sworn affidavits (at the request of the examining officer) from individuals who personally knew the mother, father, and child at the time of birth and can identify the child.

(viii) A copy of a certified English translation of all needed legal documents that are in a foreign language.

(ix) An executed passport application with three signed pictures of the child.

(2) The soldier may consult a legal assistance attorney for help in preparing the case file. The case file should be taken to the nearest American Embassy, Consulate General, or Consulate in the country where he and his child live. If the father is not present in the country where the child lives, he will do one of the following—

(i) Take the necessary documents to the nearest American Embassy, Consulate General, or Consulate.

(ii) Mail the documents to the Department of State, ATTN: Office of Citizens Consular Service, WASH DC 20520. That office, in conjunction with the American Consul abroad, will decide if the child is a U.S. citizen.

(3) If both father and child are within the United States, a decision of citizenship status can be obtained from the INS. The soldier should file Form N–600 (Application for Certificate of Citizenship) at the nearest INS office. This form can be obtained from the INS. The appendix of AR 608–3 lists the location of INS offices.

(4) Any soldier who claims to be a U.S. citizen has the burden of proving that claim to the Department of State or INS, as applicable.

**§ 584.6 Procedures governing nonactive duty or discharged personnel.**

(a) *Procedures governing nonactive duty personnel.* (1) Nonsupport complaints and paternity claims against former soldiers or other not on active duty will be sent to the Commander, U.S. Army Reserve Components Personnel and Administration Center (RCPAC), ATTN: DARC–PSE–VS, 9700 Page Boulevard, St. Louis, MO 63132–5200.

(2) After RCPAC verifies the status, the following officials will act as prescribed below:

(i) Chief, National Guard Bureau, WASH DC 20310–2500, for members of the Army National Guard.

(ii) The area commander concerned for Ready Reservists assigned to troop program units under his or her control. (See AR 140–1, para 1–6.)

(iii) Commander, RCPAC for nonunit members assigned to Control Groups of the Ready Reserve, Standby Reserve, and Retired Reserve.

(3) The officials cited above will ensure that correspondence claiming

nonsupport or paternity is delvered to the person concerned, using military channels. When the correspondence cannot be delviered through military channels, it will be sent to the last known mailing address of the person by certified mail (PS Form 3811 (Return Receipt, Registered, Insured and Certified Mail)). It should be marked "Return Receipt Requested—Deliver to Addressee Only." This form is available at U.S. post offices.

(4) After delivery of correspondence, the responsible official will advise the complainant or claimant—

(i) Of the date and method of delivery.

(ii) That the military department does not control the personal affairs of nonactive duty personnel. These personnel usually are in a civilian status and are not subject to military discipline. Therefore, the matter has been left to the person's discretion.

(iii) Of the person's mailing address only if the conditions in § 584.6(c) are met.

(b) *Procedures governing discharged personnel.* Nonsupport complaints or paternity claims against persons who have been discharged from the Service will be sent to RCPAC. These persons do not hold any military status whatsoever. Commander, RCPAC will return the correspondence and all accompanying documentation and advise the complainant or claimant—

(1) That the person is no longer a member of the Army or the Reserve Components.

(2) Of the date of discharge.

(3) That the Army no longer has control or authorty over the discharged member. Therefore, the Army can take no further action in the matter.

(4) Of the person's mailing address only if the conditions in § 584.6(c) are met.

(c) *Conditions for disclosing mailing address.* Nonactive duty and discharged personnel's mailing addresses will not be disclosed except for one of the following reasons:

(1) The person consents in writing to the release of his or her address.

(2) The complainant or claimant sends a court order directing the release of the address.

(3) Any other reason that does not constitute a violation of the Privacy Act of 1974.

(d) *Retired personnel.* (1) Court orders for garnishment or attachment of pay of retired persons will be sent to USAFAC.

(2) The complainant or claimant will be advised that correspondence may be sent to the retired member as follows:

(i) Place correspondence in a stamped envelope with retired member's name typed or printed on the envelope.

(ii) Place stamped envelope in a second envelope and send to the Commander, RCPAC, ATTN: DARC-PSE-VS, 9700 Page Boulevard, St. Louis, MO 63132-5200.

(3) Commander, RCPAC will send the correspondence to the retired member but cannot release the address under the provisions of the Privacy Act of 1974.

**§ 584.7 Basic allowance for quarters.**

(a) *Eligibility.* (1) Soldiers entitled to basic pay, who have family members, are entitled to BAQ at the rates prescribed for soldiers "with dependents" under certain conditions. The Department of Defense Military Pay and Allowances Entitlements Manual (DODPM) governs entitlements. (See DODPM, part 3, chap 2.)

(2) Soldiers may receive BAQ at the "with dependents" rate as long as they pay at least the difference between BAQ at the with- and without-dependents rate each month in support of their families. (See DODPM, part 3.) This is so even if a divorce decree or court order is silent on support or releases the soldier from the responsibility of supporting the family. (See § 584.2(f)(2).) Normally, a soldier is not entitled to BAQ on behalf of a former spouse or stepchildren after the divorce. BAQ at the "with dependents" rate is not authorized when the soldier or the supported family is residing in Government family quarters. Also, if two soldier member-parents are supporting the same child, only one soldier member is entitled to BAQ at the "with dependents" rate.

(b) *False claims.* BAQ at the "with dependents" rate is not payable to soldier who are not supporting their families. Cases involving alleged failure or refusal of soldiers to pay at least the difference between BAQ at the with- and without-dependents rate for the support of family members will be referred to the proper FAO after investigation. Nonsupport of family members for whom BAQ is claimed may result in—

(1) Collection of BAQ received but not given to the family members.

(2) Stoppage of BAQ at the "with dependents" rate.

(3) Punitive or administrative action against a soldier for—

(i) Violating the minimum support requirements of this regulation.

(ii) Submitting a fraudulent claim for BAQ based on false information.

(c) *Forfeiture of BAQ.* Forfeiture of the "with dependents" portion of BAQ does not relieve the soldier of the obligation to support family members as set up in this regulation.

(d) BAQ entitlements versus Army minimum support requirements Terms for entitlements to BAQ are set forth in DODPM, part 3, chapter 2. Except as provided in this regulation, BAQ entitlements have no relationship to Army minimum support requirements.

**§ 584.8 Garnishment.**

(a) *General.* (1) Pub. L. 93-647 (42 U.S.C. 659) permits garnishment, attachment, or assignment of Federal wages and retirement payments to enforce court-ordered child support and alimony obligations that are in arrears. It includes foreign court orders when—

(i) Required by treaty or international agreement. (A soldier is subject to garnishment for child support issued by the FRG only while physically stationed in Germany.)

(ii) Recognized by a court of competent jurisdiction. Applicable State laws govern legal procedures to be used by complainants. Jurisdictional or procedural challenges to garnishment actions remain the responsibility of individual members.

(2) In the absence of State law more favorable to the soldier, 15 U.S.C. 1673 limits the amount of pay that can be garnisheed as follows:

(i) Fifty percent of disposable pay when a soldier is supporting a spouse or dependent child who is not the subject of the support order. (See § 584.8(a)(3) for an explanation of disposable pay.)

(ii) Sixty percent of disposable pay when a soldier is not supporting such spouse or dependent child.

(iii) An additional 5 percent in each of the above cases if payments are more than 12 weeks overdue.

(3) The items of pay listed in § 584.8(a)(3)(i) are subject to garnishment except for amounts deducted for the items listed in § 584.8(a)(3)(ii).

(i) Items of pay and bonus subject to garnishment.

(A) Basic pay.

(B) Special pay (including enlistment and reenlistment bonuses).

(C) Incentive pay.

(D) Inactive duty training pay.

(E) Academy officials pay (except personal money allowances).

(F) Accrued leave payments (basic pay portion only).

(G) Retired and retainer pay.

(H) Lump-sum Reserve bonus.

(I) Separation payments (readjustment pay and severance pay).

(ii) Deductions not subject to garnishment.

(A) Federal income tax withholding

(B) State income tax withholding.

(C) Servicemen's Group Life Insurance.

(D) Social Security taxes (Federal Insurance Contributions Act).

(E) United States Soldier's and Airmen's Home.

(F) Survivor Benefit Plan.

(G) Retired Servicemen's Family Protection Plan.

(H) Indebtedness to the United States and delinquent Federal taxes.

(I) Fines and forfeitures ordered by a court-martial or commander.

(b) *USAFAC procedures.* The USAFAC will process most garnishment orders. Unless the order is contrary to Federal law or the laws of the jurisdiction from which it was issued, the soldier's pay will be garnished per the court order. Garnishment orders will be sent by certified or registered mail to the Commander, USAFAC, ATTN: FINCL–G, Indianapolis, IN 46249–0160. However, all legal process issued by German courts will be processed under DODPM, section 70710, when the soldier is stationed in the FRG. The documents must expressly state they pertain to child support or alimony. Also, the name and social security number (SSN) of the soldier must be included. The submission of a divorce decree or support order alone is not enough, as a garnishment order is required.

**§ 584.9 Involuntary allotments.**

(a) *General.* Pub. L. 97–248 (42 U.S.C. 665) permits involuntary allotments from pay and allowances of soldiers on active duty as child, or child and spousal, support payments when—

(1) The soldier has failed to make payments under a court order for 2 months or in a total amount equal to or in excess of the support obligations for 2 months.

(2) Failure to make such payments is established by notice from an authorized person to the Commander, USAFAC, ATTN: FINCL–G, Indianapolis, IN 46249–0160. An authorized person is—

(i) Any agent or attorney of any State having in effect a plan approved under part D of title IV of the Social Security Act (42 U.S.C. 651–664), who has the duty or authority under the plan to seek recovery of any amounts owed as child or child and spousal support (including, when authorized under a State plan, any official of a political subdivision).

(ii) A court or agent of the court that has authority to issue an order against the soldier for the support and maintenance of a child.

(3) Such notice must give the soldier's full name and SSN. Also, it must list the name and address of the person to whom the allotment is payable. The amount of the allotment will be the amount needed to comply with the support order. The allotment may include arrearages as well as amounts for current support if provided for in the support order. A copy of this must be included with the notice. If proper, a statement must be included that the support allotment qualifies for the additional 5 percent in excess of the maximum percentage limitations. These limitations are prescribed in 15 U.S.C. 1673.

Also, a copy of the underlying support order must be included with the notice. An allotment under this provision will be adjusted or discontinued only upon notice from an authorized person.

(b) *Procedures.* No action will be taken to set up an allotment until the soldier has the chance to consult a legal assistance attorney. The purpose of the meeting is to discuss the legal and other factors involved with respect to the soldier's support obligation and failure to make payments. If the soldier has not consulted with legal counsel, the allotment will start the first end-of-month payday after 30 days have elapsed since notice was given to the affected soldier.

**Appendix A—Reference**

*Section I—Required Publications*

AR 340–17
Release of Information and Records from Army Files. (Cited in § 584.1(f)(2).)

AR 340–21
The Army Privacy Program. (Cited in § 584.1(f)(2).)

AR 600–37
Unfavorable Information. (Cited in §§ 584.1(d)(5)(viii)(B) and 584.2(l)(5).)

AR 640–3
Identification Cards, Tags, and Badges. (Cited in §§ 584.2(l)(1)(v) and 584.3(c)(3)(v).)

Misc Pub 13–1
DOD Military Pay and Allowances Entitlements Manual. (Cited In §§ 584.7a, 584.7(d) and 584.8(b).)

Uniform Code of Military Justice
(Cited In §§ 584.1(d)(5), 584.2(g)(4)(ii), 584.2(l)(2)(v)(B), and 584.3(b)(1)(ii).)

*Section II—Related Publications*

A related publication is merely a source of additional information. The user does not have to read it to understand this regulation.

AR 11–2
Internal Control Systems

AR 20–1
Inspector General Activities and Procedures

AR 140–1
Mission, Organization, and Training

AR 340–2
Maintenance and Disposition of Records for TOE Units and Certain Other Units of the Army.

AR 340–18
The Army Functional Files System

AR 600–240
Marriage in Oversea Commands

AR 601–280
Army Reenlistment Program

AR 608–3
Naturalization and Citizenship of Military Personnel and Dependents

AR 608–61
Application for Authorization to Marry Outside of the United States

AR 635–100
Officer Personnel (Separations)

AR 635–200
Enlisted Personnel (Separations)

Misc Pub 8–1
Joint Travel Regulations, Volume 1: Members of the Uniformed Services

*Section III—Prescribed Forms*

DA Form 5459–R
Authorization to Release Information from Army Records on Nonsupport/Child Custody/Paternity Complaints. (Cited in §§ 584.1(d)(5)(iv)(B), 584.1(f)(1), 584.2(1)(2)(iv), and 584.3(b)(2)(ii).)

DA Form 5460–R
Request for Help in Receiving Support and/or Identification Cards for Family Members. (Cited in § 584.2(1).)

*Section IV—Referenced Forms*

DA Form 2–1
Personnel Qualification Record-Part II

DA Form 2029–R
Application for Authorization to Marry Outside of the United States

FS Form 240
Report of Birth Abroad of a Citizen of the United States

Form N–600
Application for Certificate of Citizenship

PS Form 3811
Return Receipt, Registered, Insured, and Certified Mail

**Glossary**

*Section I—Abbreviations*

ARNGUS
Army National Guard of the United States

BAQ
Basic allowance for quarters

DA
Department of the Army

DOD
Department of Defense

DODPM
Department of Defense Military Pay and Allowances Entitlements Manual

FAO
Finance and accounting office

FRG
Federal Republic of Germany

HQDA
Headquarters, Department of the Army

ID cards
Identification cards

IG
Inspector general

INS
Immigration and Naturalization Service

RCPAC
U.S. Army Reserve Components Personnel and Administration Center

SJA
Staff Judge Advocate

SSN
Social Security Number

UCMJ
Uniform Code of Military Justice
USACFSC
U.S. Army Community and Family Support Center
USAFAC
U.S. Army Finance and Accounting Center
USAR
U.S. Army Reserve
VHA
Variable Housing Allowance

*Section II—Terms*

Arrearage

The total amount of money a soldier owes a family member for prior months in which the soldier failed to comply with the minimum support requirements of this regulation.

*Basic Allowance for Quarters*

An amount of money prescribed and limited by law that a soldier receives to pay for quarters not provided by the Government.

*Child Custody Complaint*

A written or oral complaint by a family member, or a third party acting on behalf of a family member, that alleges that the soldier is violating a court order granting custody of minor children to someone other than the soldier. It also includes a complaint by a mother of a child born out of wedlock against a soldier father who has abducted or detained the child.

*Court Order*

As used in this regulation, court order includes all judicial and administrative orders and decrees, permanent and temporary, granting child custody, directing financial support, and executing paternity findings. It also includes any foreign nation court or administrative order recognized by treaty or international agreement. Court orders are presumed valid in the absence of evidence to the contrary.

*Family Member*

For the purpose of this regulation only, a family member includes—

a. A soldier's present spouse. (A former spouse is not a family member. However, except as otherwise indicated, the term "family member" includes any former spouse for whom the soldier is required by any court order to provide financial support.)

b. A soldier's minor children from present and former marriages, including children legally adopted by the soldier. (A family member does not include the child of a soldier who has been legally adopted by another person.)

c. Minor children born out of wedlock to—

(1) A woman soldier.

(2) A male soldier if evidenced by a decree of paternity identifying the soldier as the father and ordering the soldier to provide support.

d. Any other person (for example, parent, stepchild, etc.) for whom the soldier has an obligation to provide financial support under the law of the domicile of either the soldier or the supported person.

*Financial Support Provision*

The provision in a court order or separation agreement directing the soldier to provide financial support to a family member on a periodic basis.

*Government Family Quarters*

Any sleeping accommodations or family-type housing owned or leased by the U.S. Government.

*Gross Pay*

For support purposes, gross pay includes basic pay and allowances to include special, incentive, and other pay when received on a monthly basis. Gross pay does not include funds not received on a monthly basis (that is, enlistment and reenlistment bonuses and accrued leave payments). Gross pay does not include wages from off-duty employment.

*Legal Assistance Attorney*

Army lawyers designated to advise and assist soldiers and their families on family law matters. Such matters include marriage, divorce, adoption, paternity, child custody problems, and support obligations. In the context of this regulation, a legal assistance attorney also includes a lawyer retained by a soldier at his or her own expense.

*Minor Children*

Unmarried children under 18 years of age who are not on active duty with the Armed Forces.

*Nonsupport Complaint*

A written or oral complaint by a family member, or a third party acting on behalf of a family member, that alleges one of the following:

a. Soldier is providing no financial support.

b. Soldier is providing insufficient financial support.

c. Soldier is failing to comply with—

(1) An oral agreement,

(2) A written support agreement, or

(3) A court order that sets up a financial support requirement.

*Soldier*

As used in this regulation, the term soldier includes commissioned officers, warrant officers, and enlisted personnel.

*Staff Judge Advocate*

The chief legal officer and his or her staff who advise commanders on laws and regulations affecting the command. Includes command judge advocates and post judge advocates, but not legal assistance attorneys or attorneys assigned to the Trial Defense Service.

*System of Records*

Any record under DA control from which information is retrieved by the name of the individual or by his or her SSN.

*Variable Housing Allowance*

An amount of money prescribed by law that a soldier receives to defray high housing costs in the continental United States.

*Written Support Agreement*

Any written agreement between husband and wife in which the amount of periodic financial support to be provided by the soldier spouse has been agreed to by the parties. A written support agreement may be contained in a separation agreement or property settlement agreement. Also, the support agreement may be shown by letters exchanged between the parties in which the amount of support has been agreed to by the parties.

John O. Roach, II,

*Army Liaison Officer with the Federal Register.*

[FR Doc. 85-30311 Filed 12-23-85; 8:45 am]

BILLING CODE 3710-08-M

## LIBRARY OF CONGRESS

## Copyright Office

## 37 CFR Part 201

[Docket No. RM 85-6]

## Recordation and Certification of Coin-Operated Phonorecord Players

**AGENCY:** Library of Congress, Copyright Office.

**ACTION:** Final Regulations.

**SUMMARY:** The Copyright Office of the Library of Congress is issuing final regulations amending portions of 37 CFR 201.16 concerning deletion of certain information from the jukebox certificate. The change facilitates the private administration of an agreement reached between the performing rights societies and the Amusement & Music Operators Association regarding civil enforcement of the jukebox complusory license of 17 U.S.C. 116.

**EFFECTIVE DATE:** December 24, 1985.

**FOR FURTHER INFORMATION CONTACT:** Dorothy Schrader, General Counsel, U.S. Copyright Office, Library of Congress, Washington, DC 20559 (202) 287-8380.

**SUPPLEMENTARY INFORMATION:** The Copyright Act, title 17 U.S.C. 116 establishes conditions under which operators of coin-operated phonorecord players—commonly referred to as "jukeboxes"—may obtain a complusory license for the performance of nondramatic musical works.

A complusory license permits the use of a copyrighted work without the consent of the copyright owner, if certain conditions are met and royalties paid. Section 116 establishes general rules governing the conditions of the complusory license for coin-operated phonorecord players, and requires the Register of Copyrights to prescribe regulations governing complusory license applications and certificates to be affixed to licensed phonorecord players.

The administration and civil enforcement of the compulsory licensing system has caused friction between copyright owners and jukebox operators.[1] The royalty fee initially established in the 1976 Copyright Act was $8 annually per coin-operated phonorecord player. In 1981, the Copyright Royalty Tribunal, under its statutory authority, raised the royalty fee. 46 FR 884 (1981). In 1982 and 1983 the fee became $25 per jukebox, and, thereafter, $50 per jukebox, subject to a cost of living adjustment on January 1, 1987. Jukebox operators argued this increase was too high, but the rate adjustment was upheld by the courts. *Amusement and Music Operators Ass'n. v. Copyright Royalty Tribunal*, 676 F.2d 1144 (7th Cir. 1982), *cert. denied*, 459 U.S. 907 (1982). The Copyright Office implemented the rate adjustment by publishing final regulations at 47 FR 25004 (June 9, 1982).

The AMOA then sought legislative reform of the jukebox compulsory license, particularly with respect to the copyright royalties payable. Several bills were introduced in the 98th Congress (e.g., S. 1734, H.R. 3858, and H.R. 4010), which would have established a one-time royalty fee per jukebox for its entire useful life, in lieu of the current annual licensing fee.

The performing rights societies opposed these bills on the ground of fairness and argued that voluntary compliance with the compulsory licensing scheme by operators was low. While significant penalties in the copyright law existed for performance by coin-operated phonorecord players of musical compositions without a license, enforcement of those remedies was expensive. As a result of perceived noncompliance with the licensing scheme, copyright owners lost a significant portion of the royalties to which they were entitled under the existing law.

In order to reach a mutually acceptable solution, Congressional leaders urged the interested parties to enter into private negotiations.[2] Following this advice, the performing rights societies and AMOA succeeded in reaching an agreement to be in effect until 1990, which resolves several points of controversy.

One part of the agreement would allow jukebox operators to transfer certificates from jukeboxes not in service to those which are publicly performing musical compositions. The parties to the agreement believes such a policy is both equitable and consistent with the statute.

In order to facilitate the private administration of this agreement the Copyright Office issued a proposed regulation on October 23, 1985, making two minor changes. 50 FR 42965. Under the existing regulation, the certificate was required to contain the name of the manufacturer of the coin-operated phonorecord player and the player's serial number. In addition, subsection 201.16(c)(2) provided that the certificate consisted of two parts. Under the proposed regulation, information relating specifically to the coin-operated phonorecord player would be deleted from the certificate and subsection 201.16(c)(2) would be modified to reflect the fact that the certificate would no longer consist of two parts.

The Copyright Office received two comments on the proposed regulation,—one from the AMOA, and another from a jukebox operator. Both comments urged adoption of the proposed regulation.

Under section 116 of the copyright law, the Copyright Office is authorized to determine the content of the certificate. The resolution of disputes through private negotiation is clearly a laudable goal. All interested parties appear to agree that the change would facilitate a more equitable administration of the compulsory license. The Copyright Office received no comments opposing the modification. For these reasons the Copyright Office has decided to adopt the proposed regulation as final, without change.

With respect to the Regulatory Flexibility Act, the Copyright Office takes the position that this Act does not apply to Copyright Office rulemaking. The Copyright Office is a department of the Library of Congress, which is part of the legislative branch. Neither the Library of Congress nor the Copyright Office is an "agency" within the meaning of the Administrative Procedure Act of June 11, 1946, as amended (title 5, Chapter 5 of the U.S. Code, Subchapter II and Chapter 7). The Regulatory Flexibility Act consequently does not apply to the Copyright Office since that Act affects only those entities of the Federal Government that are agencies as defined in the Administrative Procedure Act.[3]

**List of Subjects in 37 CFR Part 201**

Copyrights Copyrights Office Jukeboxes.

**PART 201—[AMENDED]**

In consideration of the foregoing, Part 201 of 37 CFR, Chapter II is amended as follows:

1. The authority citation for Part 201 is revised to read as follows:

**Authority.** Sec. 702, 90 Stat. 2541, 17 U.S.C. 702; § 201.16 is also issued under 17 U.S.C. 116.

2. Section 201.16 (c)(1) and (c)(2) is revised to read as follows:

**§ 201.16 Recordation and certification of coin-operated phonorecord players.**

* * * * *

(c) *Certificate.* (1) After receipt of the prescribed form and fee, the Copyright Office will issue a certificate containing the information set forth in paragraphs (b)(1) (i) and (ii) of this section, together with a unique licensing number, the date of issuance of the certificate and the date of expiration of the license. The date of expiration of the license will be December 31st of the year in which the certificate is issued. Certificates issued upon payment of a half-year fee will be valid only after July 1 of the year in which they are issued and will be so identified.

(2) The certificate may be affixed in the record selection (title strip) panel of a player or in another position on the player where it can be readily examined by the public, but in any case it must be clearly visible.

* * * * *

Dated: December 13, 1985.

**Ralph Oman,**

*Register of Copyrights.*

Approved:

**Daniel J. Boorstin,**

*The Librarian of Congress.*

[FR Doc. 85-30369 Filed 12-23-85; 8:45 am]

BILLING CODE 1410-01-M

[1] In general, the licensing of performance rights of musical compositions are handled by the performing rights societies. Section 116(e) of the copyright law identifies the performing rights societies as the American Society of Composers, Authors, and Publishers (ASCAP), Broadcast Music Inc. (BMI), and SESAC, Inc. In copyright matters, jukebox operators have been represented by their trade association, Amusement & Music Operators Ass'n. (AMOA).

[2] Billboard, May 25, 1985, at 1.

[3] The Copyright Office was not subject to the Administrative Procedure Act before 1978, and it is now subject to it only in areas specified by section 701(d) of the Copyright Act (i.e. "all actions taken by the Register of Copyrights under this title (17)," except with respect to the making of copies of copyright deposits) (17 U.S.C. 706(b)). The Copyright Act does not make the Office an "agency" as defined in the Administrative Procedure Act. For example, personnel actions taken by the Office are not subject to APA-FOIA requirements.

**ENVIRONMENTAL PROTECTION AGENCY**

**40 CFR Part 52**

**[FL-014; A-4-FRL-2942-3]**

## Approval and Promulgation of Implementation Plans; Florida; Elemental Sulfur Storage and Handling Rule

**AGENCY:** Environmental Protection Agency.

**ACTION:** Final rule.

**SUMMARY:** EPA today approves the Florida elemental sulfur storage and handling rule. This rule sets up specific regulations for the storage and handling of sulfur, both in the solid and molten form. This rule conforms to all EPA guidelines on particulate matter.

**EFFECTIVE DATE:** This action will be effective on February 24, 1986 unless notice is received within 30 days that someone wishes to submit adverse or critical comments.

**ADDRESSES:** Written comments should be addressed to Kelly McCarty of EPA Region IV's Air Management Branch (see second address below). Copies of the State's submittal are available for review during normal business hours at the following locations:

Bureau of Air Quality Management, Florida Department of Environmental Regulation, Twin Towers Office Building, 2600 Blair Stone Road, Tallahassee, Florida 32301

Environmental Protection Agency, Region IV, Air Management Branch, 345 Courtland Street, NE., Atlanta, Georgia 30365

Public Information Reference Unit, Library Systems Branch, Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460

**FOR FURTHER INFORMATION CONTACT:** Kelly McCarty, EPA Region IV, Air Management Branch, at the above address, and phone 404/881-3286, or FTS 257-3286.

**SUPPLEMENTARY INFORMATION:** The Florida Department of Environmental Regulation (FDER) submitted the elemental sulfur storage and handling rule to EPA on May 31, 1985. The only existing sources are located in the Tampa Bay area, which is nonattainment for the secondary standard for Total Suspended Particulates (TSP). The Part D plan for attainment of the secondary TSP standard was submitted, and approved by the EPA on May 2, 1982. This plan contained measures for implementing Reasonably Available Control Technology (RACT' for certain sources, plus a commitment to study certain other non-traditional sources to ascertain their impact. The only part of this Part D plan which would apply to sulfur storage and handling facilities is a generic rule applying to materials handling, sizing, screening, crushing, and grinding operations. This current rule supplements that previous RACT rule with additional requirements for sulfur storage and handling facilities. This sulfur storage and handling rule will not interfere with the current EPA-approved SIP, including the New Source Review (NSR) requirements, because it does not create any additional exemptions, only additional requirements, for these facilities.[1]

### Scope

The rule includes revisions to the following sections of the Florida Administrative Code:

- 17-2.100 Definitions: Adds definitions as needed for the rule.
- 17-2.215 Emission Estimates: This section establishes standards for making emission estimates of the sulfur particulates generated during handling for all regulatory purposes including permitting and reporting. The equations used are the same as those used for particulate matter.
- 17-2.540 Source Specific New Source Review Requirements: The requirements of this section apply to specific categories of new and modified sources and/or facilities, and includes a preconstruction sulfur deposition analysis and postconstruction monitoring. All facilities that produce less than 5000 tons per year are exempt from the requirements of this section. This section does not exempt any source from existing new source review requirements (including prevention of significant deterioration requirements).
- 17-2.600 Specific Source Emission Limiting Standards: This section outlines specific work practices that must be followed when transporting, storing, and handling elemental sulfur in the pelletized or molten form. It includes unloading from marine vessels, railcars, and trucks. The section also prohibits the handling, storage or transporting of any form other than pelletized or molten sulfur, except for transferral within the boundaries of a single facility. This section also allows sources to utilize alternate methods or control technologies to control sulfur particulate emissions, provided that they result in emissions that are less than or equal to those achieved by the equivalent methods or technologies stated in the rule, and that prior Department approval is obtained.
- 17-2.700 Stationary Point Source Emissions Test Procedures: This change adds several new subsections of testing procedures by reference, including several Sulfur Development Institute of Canada (SUDIC) test methods, and reformants the Particulate Emissions section.
- 17-2.753 DER Ambient Test Methods: This change adds subsection: (2) DER Reference Method for Monitoring the Deposition of Sulfur Particulate.

The FDER also deleted part of Section 17-2.630 Best Available Control Technology (BACT). This deletion consists of the references to Lowest Reasonably Available Control Technology, since that rule has been replaced by BACT.

EPA's review was based upon particulate matter regulations and guidelines, since EPA has no elemental sulfur emission limitations or guidelines, only sulfur dioxide emission limitations. Since the rule strengthens rather than relaxes the EPA-approved SIP, EPA believes that approval of the rule is consistent with the applicable requirements of the Clean Air Act.

Action. EPA has reviewed the submitted material and is approving it as submitted. This action is taken without prior proposal because the changes are non-controversial and EPA anticipates no comments on them. The public should be advised that this action will be effective 60 days from the date of this **Federal Register** notice. However, if notice is received within 30 days that someone wishes to submit adverse or critical comments, this action will be withdrawn, and two subsequent notices will be published before the effective date. One notice will withdraw the final action, and the other will begin a new rulemaking by announcing a proposal of the action and establishing a comment period.

Under section 307(b)(1) of the Clean Air Act, petitions for judicial review of this action must be filed in the United States Court of Appeals for the appropriate circuit by February 24, 1986. This action may not be challenged later in proceedings to enforce its requirements (see 307(b)(2)).

Pursuant to the provisions of 5 U.S.C. 605(b), I hereby certify that the attached rule will not have a significant economic impact on a substantial number of small entities. (See 46 FR 8709.)

Incorporation by reference of the Florida State Implementation Plan was

[1] Prior to this rule, sulfur in the pelletized form was not allowed to be handled in the state, but this prohibition was not part of the EPA-approved SIP.

approved by the Director of the Federal Register on July 1, 1982.

The Office of Management and Budget has exempted this rule from the requirements of section 3 of Executive order 12291.

**List of Subjects in 40 CFR Part 52**

Air pollution control, Intergovernmental relations, Sulfur oxides, Particulate matter, Incorporation by reference.

Dated: December 16, 1985.

**Lee M. Thomas,**

*Administrator.*

**PART 52—[AMENDED]**

Part 52 of Chapter I, Title 40 Code of Federal Regulations, is amended as follows:

**Subpart K—Florida**

1. The authority citation for Part 52 continues to read as follows:

**Authority:** 42 U.S.C. 7401–7642.

2. Section 52.520 is amended by adding paragraph (c)(57) as follows:

**§ 52.520 Identification of plan.**

* * * * *

(c) The plan revisions listed below were submitted on the dates specified.

* * * * *

(57) Changes to Florida Administrative Code (FAC) Chapter 17–2, submitted on May 31, 1985, by the Florida Department of Environmental Regulation (FDER).

(i) Incorporation by reference.

(A) May 31, 1985 letter from the Florida DER, and Amendments to FAC Chapters 17–2.100, 17–2.215, 17–2.540, 17–2.600, 17–2.700 and 17–2.753 which were adopted by the FDER on April 11, 1985. Allow sulfur in the pelletized form to be shipped and handled in the State. Also establish new source review requirements, emission estimating procedures, emission limiting standards, and test procedures for elemental sulfur storage and handling facilities.

(ii) Additional Information.

(A) None.

[FR Doc. 85–30348 Filed 12–23–85; 8:45 am]

BILLING CODE 6560–50–M

**40 CFR Part 52**

**[A–1–FRL–2943–5]**

## Approval and Promulgation of Implementation Plans; Rhode Island; Correction

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final rule; correction.

**SUMMARY:** This document corrects (1) the table codified at 40 CFR 52.2076 which summarizes the dates for attainment of the National Ambient Air Quality Standards (NAAQS) for the State of Rhode Island; (2) the section codified at 40 CFR 52.2084 which lists the elements of Rhode Island's revisions for which EPA has taken no action; and (3) the section codified at 40 CFR 52.2085 which granted an extension for submission of Rhode Island's plan for attainment and maintenance of the primary standard for suspended particulate matter (TSP) in the Providence primary standard nonattainment area.

**FOR FURTHER INFORMATION CONTACT:** David B. Conroy, (617) 223–4869, FTS 223–4869.

**SUPPLEMENTARY INFORMATION:** On July 6, 1983 (48 FR 31026) EPA approved the Rhode Island State Implementation Plan for attainment of the primary NAAQS for ozone. On this date the attainment date for ozone was changed from December 31, 1987 to December 31, 1982. The table codified at 40 CFR 52.2076 which lists the dates for attainment of the NAAQS for the State of Rhode Island was not revised to reflect this change on this approval date. This notice corrects the statewide attainment date for ozone listed in the table codified at 40 CFR 52.2076.

On July 12, 1982 (47 FR 30065) EPA approved a request from the Rhode Island Department of Environmental Management to change the attainment status of Providence, Rhode Island from nonattainment for the primary TSP standard to nonattainment for the secondary TSP standard. On this approval date, neither the table codified at 40 CFR 52.2076 which lists the dates for attainment of the NAAQS for the State of Rhode Island nor the section codified at 40 CFR 52.2085 which granted an extension for submission of Rhode Island's primary TSP plan for Providence was revised to reflect the change in the attainment status for TSP in Providence. Since Rhode Island has shown that the primary TSP standard has been attained in Providence, the extension to submit a primary TSP attainment plan in Providence granted by § 52.2085 is no longer relevant. This notice removes § 52.2085 and corrects the attainment status for the primary TSP standard in Providence in the table codified at 40 CFR 52.2076.

On July 6, 1984 (49 FR 27750) EPA approved Rhode Island's Prevention of Significant Deterioration (PSD) plan. On this approval date, the section codified at 40 CFR 52.2084 which lists PSD as one of the elements of Rhode Island's plan on which EPA has taken no action, was not revised. Since EPA has fully approved Rhode Island's PSD plan, this is no longer an element of Rhode Island's plan for which EPA has taken no action. This notice deletes this item.

Dated: December 10, 1985.

**Michael R. Deland,**

*Regional Administrator, Region I.*

**PART 52—[AMENDED]**

Accordingly, Part 52 of Chapter I, Title 40 of the Code of Federal Regulations is corrected as follows:

**Subpart 00—Rhode Island**

1. Section 52.2076 is corrected to read as follows:

**§ 52.2076 Attainment of dates for national standards.**

The following table presents the latest dates by which the national standards are to be attained. These dates reflect the information presented in Rhode Island's plan, except where noted.

| Air quality control region [1] | Pollutant | | | | | | |
|---|---|---|---|---|---|---|---|
| | TSP | | $SO_2$ | | $NO_2$ | CO | $O_3$ |
| | Primary | Secondary | Primary | Secondary | | | |
| Providence | a | d | a | b | a | c | c |
| E. Providence | a | b | a | b | a | a | c |
| Cranston | a | b | a | b | a | a | c |
| Warwick | a | b | a | b | a | a | c |
| N. Providence | a | b | a | b | a | a | c |
| Pawtucket | a | b | a | b | a | a | c |
| Central Falls | a | b | a | b | a | a | c |
| Remainder of Rhode Island portion of AQCR 120. | a | b | a | b | a | a | c |

a. Air quality levels presently better than primary standards or area is unclassifiable.
b. Air quality levels presently better than secondary standards or area is unclassifiable.
c. December 31, 1982.
d. Attainment date not established.

[1] Sources subject to plan requirements and attainment dates established under section 110(a)(2)(A) prior to the 1977 Clean Air Act Amendments remain obligated to comply with those requirements by the earlier deadlines. The earlier attainment dates are set out at 40 CFR 52.2076 (1978).

**§ 52.2084 [Amended]**

2. Section 52.2084 is corrected by removing and reserving paragraph (b)(i).

**§ 52.3085 [Reserved]**

3. Section 52.2085 is removed and reserved.

[FR Doc. 85-30350 Filed 12-23-85; 8:45 am]
BILLING CODE 6560-50-M

## FEDERAL COMMUNICATIONS COMMISSION

### 47 CFR Part 2

### Deletion of Footnotes US249 and US293 From the Commission's Rules

**AGENCY:** Federal Communications Commission.

**ACTION:** Final rule.

**SUMMARY:** The Federal Communications Commission amends Part 2 of its Rules to delete footnotes US249 and US293 from the Table of Frequency Allocations. Footnote US293 provided an allocation in the 21850–21870 kHz band to the radio astronomy service until January 1, 1985 and US249 provided an allocation in the 25550–25600 kHz band to the fixed and mobile, except aeronautical mobile, services until January 1, 1985. This action will bring the Commission's Rules into conformance with current and projected uses of these bands.

**EFFECTIVE DATE:** January 23, 1986.

**ADDRESS:** Federal Communications Commission, Washington, DC 20554.

**FOR FURTHER INFORMATION CONTACT:** Mr. Fred Thomas, Office of Science and Technology, 2025 M Street NW, 20554, (202) 653–8162.

**SUPPLEMENTARY INFORMATION:**

**List of Subjects in 47 CFR Part 2**

Radio.

**Order**

In the matter of amendment of Part 2 to delete footnotes US249 and US293 from the Table of Frequency Allocations.

Adopted: December 16, 1985.
Released: December 17, 1985.

By the Managing Director.

1. To accommodate the HF spectrum requirements of the radio astronomy service, the 1979 World Administrative Radio Conference changed an allocation for the radio astronomy service from the 21850–21870 kHz band to the 25550–25600 kHz band. In implementing this reallocation domestically, the Commission provided two footnotes to the Table of Frequency Allocations, Section 2.106 of the Commission's Rules, to allow for the transition.[1] Footnote US249 provided an allocation in the 25550–25600 kHz band to the fixed and mobile services, except the aeronautical mobile service, until January 1, 1985. Footnote US293 provided an allocation in the 21850–21870 kHz band to the radio astronomy service until January 1, 1985. Since that date has passed, the footnotes are obsolete. Therefore, footnotes US249 and US293 are being removed from the Table of Frequency Allocations, Section 2.106, as shown in the Appendix.

2. This action is considered to be editorial in nature. Accordingly, it is ordered, That pursuant to authority found in Sections 4(i), 302, and 303 of the Communications Act of 1934, as amended, 47 U.S.C. Sections 154(i), 302, and 303, and pursuant to Section 0.231(d) of the Commission's Rules, Part 2 of the Commission's Rules and Regulations is amended as specified in the Appendix. This amendment becomes effective January 23, 1986.

3. Point of contact on this matter is Fred Thomas, (202) 653–8162.

Federal Communications Commission.

Edward J. Minkel,

*Managing Director.*

**Appendix**

### PART 2—FREQUENCY ALLOCATIONS AND RADIO TREATY MATTERS; GENERAL RULES AND REGULATIONS

Part 2 of Chapter I of Title 47 of the Code of Federal Regulations is amended as follows:

The authority citation in 47 CFR Part 2 continues to read:

**Authority:** Secs. 4, 303, 48 Stat. 1066, 1082 as amended; 47 U.S.C. 154, 303.

**§ 2.106 [Amended]**

Section 2.106 is amended by removing footnote designator US249 at columns 4 and 5 in the 25550–25670 kHz band, by deleting footnote designator US293 at columns 4 and 5 in the 21850–21924 kHz band and by deleting the text of footnotes US249 and US293 from the list of footnotes following the Table of Frequency Allocations.

[FR Doc. 85-30200 Filed 12-23-85; 8:45 am]
BILLING CODE 6712-01-M

[1] See Second Report and Order in General Docket No. 80-739, FCC 83-511, 49 FR 2357 (adopted November 8, 1983).

### 47 CFR Part 76

**[MM Docket No. 85-38; FCC 85-587]**

### Technical and Operational Requirements of Part 76 Cable Television

**AGENCY:** Federal Communications Commission.

**ACTION:** Final rule.

**SUMMARY:** This action revises technical signal quality standards for cable television. These standards were established in 1972, when the cable industry was in its early stages of development. Since that time, the industry has matured, and competition has grown. In view of that fact, the purpose of this action is to relax and to better relate these quality standards to marketplace development.

**EFFECTIVE DATE:** January 23, 1986.

**ADDRESS:** Federal Communications Commission, Washington, DC 20554.

**FOR FURTHER INFORMATION CONTACT:** Bernard Gorden, Mass Media Bureau, (202) 632–9660.

**SUPPLEMENTARY INFORMATION:**

**List of Subjects in 47 CFR Part 76**

Cable television.

**Report and Order**

In the matter of review of the technical and operational requirements of Part 76, Cable Television; MM Docket No. 85–38.

Adopted: October 31, 1985.
Released: December 17, 1985.

By the Commission: Chairman Fowler concurring and issuing a statement.

**Introduction**

1. By this *Report and Order*, the Commission is amending its rules concerning technical and operating requirements for cable television systems. We hereby change the existing rules into standards. These standards may be applied but not exceeded by franchise authorities in the regulation of the technical quality of Class I (broadcast) channels by cable television systems. Enforcement of all such standards by the Commission is eliminated. The decision as to whether such standards should be used and how they should be administered is left to local and state regulatory authorities. This decision reflects the Commission's belief that in an increasingly competitive marketplace there is a reduced need for detailed regulation of technical quality specifications. The decision, however, leaves local regulatory authorities discretion, in

accordance with the provisions of section 624(e) of the Cable Communications Policy Act of 1984 (1984 Cable Act), to address technical quality issues. Authority of municipal and state regulators to establish requirements for "facilities and equipment" in accordance with section 624(b) of the Cable Act is unaffected by this decision. Certain changes in the cable television signal leakage rules that were proposed in the *Notice* in this proceeding have not been adopted but will be addressed separately at a later date.

**Background**

2. The present cable technical rules are set forth in Subpart K of Part 76 of the Commission's rules. These rules were adopted in the *Cable Television Report and Order*.[1] The rules specify numerous technical performance criteria and requirements for annual performance tests. The technical standards contained in § 76.605 include: (1) The frequency boundaries of cable television channels delivered to subscriber terminals; (2) the frequency tolerance of CATV visual carriers; (3) the frequency tolerance of CATV aural carriers; (4) the minimum visual carrier levels at subscriber terminals; (5) the allowable tolerance for visual carrier level variations within 24 hours; (6) the maximum and minimum aural carrier specifications with respect to visual carrier levels; (7) the maximum allowable level of visual low frequency distortion; (8) the frequency response of each channel; (9) the allowable visual signal-to-system noise level and to any undesired co-channel signal; (10) the allowable level of intermodulation distortion; (11) the minimum amount of isolation between subscriber terminals; and (12) requirements regarding signal leakage.[2]

3. In adopting the 1972 rules, the Commission was explicit that its standards were not intended to place any barrier in the way of franchising authorities adopting "more stringent technical standards." *Reconsideration of Cable Television Report and Order*, 36 FCC 2d 326, 359–60 (1972). This policy did not succeed, however, and in 1974, the Commission adopted the current preemption policy.[3] This policy prohibits state and local technical regulations for Class I signals that are inconsistent with those adopted by the Commission.[4] In addition, our preemption policy bars any state and local technical regulation for non-Class I signals. This policy was instituted to ensure the growth of cable services and cable-related technology and to avoid the detrimental impact on cable service and technical innovation in the cable industry that would have resulted from the necessity for system operators and equipment manufacturers having to design and comply with numerous different and potentially conflicting standards.

4. On February 12, 1985, the Commission adopted the *Notice of Proposed Rule Making* in this proceeding.[5] The *Notice* proposed revision of certain rules in Subpart K of Part 76 of the Commission's Rules and Regulations. The *Notice* requested comments on the need for cable television subscriber signal quality standards and on the appropriate level of cable signal leakage limits.

5. In response to the *Notice*, the Commission received comments from 50 parties and reply comments from 20 parties. In addition, approximately 70 individual letters were received from cable TV subscribers, amateur radio groups and operators.[6] The vast majority of the letters received were concerned with cable signal leakage requirements.

**Discussion**

*Technical Quality Performance Standards*

6. *Federally Enforced Standards.* In the *Notice*, we indicated our belief that competitive forces are sufficient to ensure adequate signal quality for the provision of cable service. Accordingly, we proposed to delete the technical standards for Class I signals from the rules and, alternatively, publish them as guidelines in an Office of Science and Technology bulletin. We indicated in the *Notice* that francise authorities could use these guidelines in their franchise agreements with the cable operator. We also stated that the imposition of technical quality standards more stringent than those in the guidelines would be considered inconsistent with our national policy and would not be permitted.

7. The National Cable Television Association (NCTA), Capital Cities Cable, Inc., and other cable system operators generally support the proposed elimination of the present signal quality standards for Class I signals. They agree with the Commission that competition from alternative video sources now provide cable operators with sufficient incentives to maintain technical signal quality.

8. Other commenters assert that the market forces do not provide sufficient incentives for cable systems to deliver quality signals. In particular, commenters representing State and local governments argue that cable systems generally have monoply-like powers, and therefore, cannot be relied upon to ensure satisfactory cable signal performance. The State of Hawaii, for example, expresses concern that cable systems will not maintain acceptable technical quality and reliability unless required to do so. In addition, some commenters, such as the National Association of the State Cable Agencies (NASCA), make reference to the recent Commission proceeding that implemented the Cable Communications Policy Act of 1984.[7] That proceeding, among other matters, defined effective competition for the purpose of rate regulation of basic cable service.

---

[1] 36 FCC 2d 143 1972.

[2] At the time of their adoption in 1972 these standards were referred to as "minimum" standards which caused some confusion at that time and some of that confusion has continued to the present. *See* 49 FCC 2d 470, para 5 (1974). The standards are minimum in that they describe a level of servicethat must be delivered to subscribers at even the worst locations on a system. This necessarily means that most subscribers, including in particular those closer to the system headend, will receive service that is superior to this minimum. It has also been noted that the standards have been referred to by the Commission itself as incomplete. It was for this reason that the Commission created the Cable Television Technical Advisory Committee in 1972 to provide advice on possible changes to the standards. The work of this Committee led to some changes in the standards. Other changes were not made, however, as it was becoming increasingly clear that the technical interrelationships between the standards involved were extremely complex and that commercial incentives were driving the industry in the same direction as the recommended standards but with both greater force and greater flexibility than could be acccomplished with more detailed regulatory requirements. The standards, however, remained valid as a means of defining an acceptable quality of service at the worst subscriber location and thus a better quality of service to the average subscriber. Suggestions that new standards be adopted were received informally in this proceeding. Specific recommendations were not included, however, and this was not, in any case, the focus of this proceeding.

[3] *See Report and Order in Docket 20018*, 49 FCC 2d 470 (October 22, 1974).

[4] Class I channels are television channels received off-the-air or obtained by the cable operator via microwave or direct connection to the television broadcast station. Class II to IV channels are other types of signals that may be provided by a cable system. For example, signals that require an auxiliary decoder, such as most pay cable services, are defined as Class III channels. The Commission's technical performance standards and requirements have traditionally applied only to Class I cable television channels. *See* 47 CFR 76.5(t), (u), (v), and (w).

[5] 50 FR 7801 (February 26, 1985).

[6] A list of commenters appears in Appendix B.

[7] *See Report and Order in Docket 84-1298*, 50 Fed. Reg. 18637 (May 2, 1985); *See also* Cable Communications Policy Act of 1984, Pub. L. No. 98-549, Sec. 1 *et seq.*, 98 Stat. 2779 (1984).

NASCA assets that the Commission's decision on effective competition should be taken into account in determining whether to deregulate technical standards. Other commenters note that performance would most likely deteriorate in areas where over-the-air reception is already poor.

9. The process of governmental standards setting, in highly complex and evolving fields, carries with it significant risks. Extremely sophisticated economic and technical tradeoffs in a changing environment must be made in order to satisfy consumer demands in an economically sustainable fashion. Standards setting organizations are necessarily removed from this function and react to change in a manner and through processes that invite delay. Nevertheless, there are many areas in which the standard setting function cannot be avoided. In adopting standards in the cable field, the historical record reflects little discussion of whether and in what situations standards could effectively advance the interests of consumers.[8] Recently the Commission recognized that a more rigorous analysis of the areas in which it can play a positive role in standard setting is desirable. In addressing this broad general issue in Docket 83-114, the Commission found it useful to focus on four rationales relating to technical standards regulation: (1) Interference, (2) spectrum efficiency, (3) interoperability, and (4) technical quality. Interference and spectrum efficiency considerations were judged to warrant the highest priority as to the need for regulatory action. Interoperability was also found to be of high priority, varying, however, depending on the particular service involved. In contrast, technical quality matters were generally found not to require regulation in those services that were considered to be sufficiently competitive.[9]

10. Having reviewed the cable television technical standards against this background and in light of the comments in this proceeding, it is our view that the primary determinants of the quality of service that will be provided are the technical state of the art, the underlying economics of the industry, and the market incentives and competitiveness of the markets involved. The state of the art has clearly advanced to the point where a very high level of service can be provided. The economic situation varies greatly depending on local circumstances, but, if not unduly burdened, an economic base for high quality service appears to exist in all but the more rural areas of the country. And, as we have discussed in other contexts,[10] and as Congress has recognized through passage of the 1984 Cable Communications Policy Act of 1984, cable television systems operate in an increasingly competitive environment. Given these factors we are persuaded that in the vast majority of situations the severe penalties that will be imposed in the marketplace for those operations that do not perform satisfactorily far exceed and can safely be used to replace FCC penalties that might be imposed through the regulatory process. Given the authority, described below, that will remain in state and local regulatory authorities to adopt technical standards, we conclude that federally enforced standards are no longer necessary or desirable.

11. *State and Local Standards.* Notwithstanding this decision we continue to believe that there is an important role for the Commission to play in this area. Technical standards that vary from community to community create potentially serious negative consequences for cable system operators and cable consumers in terms of the cost of service and the ability of the industry to respond to technological changes. To address this problem, we proposed in the *Notice* to retain technical standards guidelines at the federal level which could be used, but could not be exceeded, in state and local technical quality regulations.

12. In their comments, cable interests assert that the franchising authorities are primed to reinstitute excessive technical standards if the Commission abandons its preemption policy. They note the comments from some franchising authorities which challenged the adequacy of the Commission's current technical standards. The cable operators suggest that such comments are indicative of an inappropriate and excessive regulatory attitude that is prevalent at the local level.

13. Comments filed by local government interest groups oppose Federal preemption of signal quality standards, stating that under the Cable Act, the Commission lacks authority to preempt non-Federal technical regulation. These groups argue that section 632 of the 1984 Cable Act which authorizes franchising authorities to adopt and enforce customer service provisions and construction-related requirements implicitly authorizes local authorities to adopt non-Federal technical quality standards for cable television.

14. After a review of the record in this proceeding, we continue to believe that the policy adopted in 1974 was effective, should remain in force, and is entirely consistent with both the specific provisions and the general policy objectives underlying the 1984 Cable Act. This preemption policy has constrained state and local regulation of cable technical performance to Class I channels and has prohibited performance standards more restrictive than those contained in the Commission's rules. The reasons that caused the adoption of this policy appear to be as valid today as they were when the policy was first adopted.

15. The video products that cable systems sell and the processing and transmission equipment used in the construction of cable systems are overwhelmingly associated with national markets that can be severely burdened by disparate and conflicting local regulations and standards. Cable systems now operate in more than 18,500 different communities. There can be no doubt that suppliers of cable service and equipment, in the absence of national standards, face a wide array of different operating requirements. The cost of keeping track of and complying with numerous different requirements is undeniably significant and there appear to be few if any countervailing benefits

[8] In the middle 1960s broadcast interests sought the adoption of such standards for a cable industry which, at the time, still operated on a tube rather than transistor technology. See *Notice of Inquiry and Notice of Proposed Rule Making in Docket 15971*, 1 FCC 2d 453, para. 62 (1965). The Commission later declined to adopt specific quality standards. *First Report and Order in Dockets 14895 et al.*, 38 FCC 683, para. 130 (1965), and then in 1968 raised the issue again stating only that such standards should be considered "to further high quality service to the public" and to promote "compatibility among systems for purposes of interconnection." *Notice of Proposed Rule Making in Docket 18397*, 15 FCC 2d 417, para 29 (1968). More specific proposals were made in 1970, again with the statement that the standards would further the quality of service received by the public. *Notice of Proposed Rule Making in Docket 18894*, 25 FCC 2d 38, para 13 (1970). The standards proposed were adopted in 1972 with the sole discussion of their need consisting of a statement that the standards would "provide much needed uniformity on a nationwide basis yet still allow sufficient flexibility for technical change." *Cable Television Report and Order*, 36 FCC 2d 143, para. 149 (1972).

[9] *Report and Order in Gen. Docket 83-114*, 99 FCC 2d 903 (1984). The *Report and Order* stated that "the pressure of competition and consumer choice have brought about a generally higher level of technical quality than required by our rules." (footnote omitted). It is worth noting in this context that detailed governmental standard setting efforts in complex technical areas have generally been eschewed even in areas where franchised monopolies are involved. In the telephone industry, for example, the function of setting detailed quality of service specifications has been principally performed by the carriers themselves rather than by governmental agencies.

[10] See e.g., *Report and Order in MM Docket 84-1296*, 50 F. R. 18637 (1985) (Implementation of Cable Act).

associated with such disparate requirements.

16. More important, however, is the potential detrimental impact of such standards on technological innovation in the industry. The problem is not hypothetical. One relatively recent example of the potential problems involved, from our own experience, involved the development of "baseband" cable converters (see note 16 below). Cable systems distribute NTSC picture format video. This format involves a complex interlinking of the various components of the video signal, including the sound, picture, and color components. The baseband technology, which makes possible increased flexibility and security in the delivery of cable services, involves unassembling and reassembling these components in a way that potentially conflicts with traditional standards designed to assure reception of a quality video picture service. The service delivered, however, is of good quality and baseband converters are now being used in connection with many modern high capacity cable systems, notwithstanding that such devices were not developed until the early 1980s. The obstacles that would be created to such innovation were it necessary to win the approval of numerous franchise authorities before use was possible would be most formidable, even if local authorities were equipped to respond to the sophisticated technical issues involved. The possibilities are evident of similar problems being created as efforts are made to improve the quality and fidelity of television through high definition or quasi-high definition techniques, to add greater communications capacity through greater use of subcarriers and the vertical blanking interval, or to develop other innovations. Such obstacles burden the delivery of interstate communications service, are not necessary to the fundamental objectives of local cable franchising, and are inconsistent with the congressional intent that competition in cable communications be promoted and that "unnecessary regulation that would impose an undue economic burden on cable systems" be minimized.[11]

17. Section 624(e) of the 1984 Cable Act appears to specifically anticipate the continuation of our existing policy. It specifies that the "Commission may establish technical standards relating to the facilities and equipment of cable systems which a franchising authority may require in a franchise." Contrary to the opinions of some commenters, we find nothing in the legislative history that suggests Congress did not approve of the existing policy or that it intended to limit our ability to continue it.[12] The policy is fact wholly consistent with the Cable Act's intent to establish a national policy that encourages the growth and development of cable television services.[13] The legislative history indicates that franchising authorities are limited to establishing only those standards "which are not inconsistent with standards established by the FCC." On this basis, we believe that Congress intended for the Commission to have authority to oversee technical policy. Further, Congress specifically prohibited local governments from enforcing technical regulations that are inconsistent with Federal policy.[14]

18. In summary, we find our existing preemption policy has furthered the growth and development of cable television service and should be continued, that nothing in the Cable Act limits our authority with regard to technical regulation of cable systems, and that nothing in the statute or its legislative history indicates that Congress intended to alter our 1974 preemption policy in this area.[15]

*Review of Standards*

19. Two issues regarding the modified approach to technical deregulation deserve more specific attention. First, a few franchise authorities were exempt from our 1974 preemption policy. That grandfathering provision will continue. Second, for those franchise authories that want to enforce the Commission's rules and do not have the rules in current franchise agreements, the rules may be enforced at franchise renewal time in accordance with the provisions of the Cable Act. Subsequent agreements will have to contain the rules or the rules will not apply. In the interim, the Commission's rule provisions remain a standard that is available to judge the implicit franchise obligation to provide service to the cable consumer that is of acceptable quality. A number of commenters suggested changes to the current technical requirements. After review of the record, we concur that some adjustments to our technical rules is appropriate for Class I signals.

20. The General Electric Co. (GE) and Zenith Electronics Corp. (Zenith), in their comments, suggest a relaxation of the aural center frequency requirement contained in § 76.605 (a)(3) of the rules. They suggest that the requirement that the aural carrier be 4.5 MHz ±1 kHz above the frequency of the visual carrier should be changed to 4.5 MHz ±5 kHz. GE and Zenith contend that many commercially available baseband converters create potential problems under the existing aural carrier specifications and that such a change would not degrade signal quality at the subscriber's televisions set. We agree with the commenters that this variance could be changed without affecting signal quality. Therefore, we are relaxing the tolerance of the aural center frequency of ±15 kHz.[16]

21. A further review of the current rules focused on the requirement that the aural signal voltage be maintained between 13 and 17 dB below the associated visual signal level, or between 7 and 17 below if there are no immediate first adjacent channel signals. Because the technical standards only apply to Class I, or television broadcast stations, and the Commission, in Dociet 83.117,[17] eliminated the minimum aural power level requirements for television broadcast stations, the deletion of this provision is appropriate in order to align the cable rules with the broadcast rules on this

[11] Communications Act of 1934, as amended, section 601(6).

[12] Some commenters asserted that because Section 632 of the Cable Act authorized franchising authorities to adopt and enforce customer service provisions and construction-related requirements, it would implicitly authorize the adoption of non-Federal technical quality standards for cable television. We find nothing in the Cable Act or in its legislative history supporting that assertion. Furthermore, in Docket 20018, the Commission made it clear that the preemptive policy applied only to objective technical standards, i.e., standards that dealt only with shaping amplification, purity, etc., of signals carried in cable systems. We have never preempted in such areas of local concern, as studio capacities, electrical safety codes, or construction requirements.

[13] *See* H.R. Report 98-934, 98th Con., 2d sess. 70 (1984).

[14] It is well established that a clearly articulated policy of deregulation provides a clear basis for federal preemption of inconsistent state regulation. *See, e.g., New York State Commission on Cable Television v. FCC*, 749 F. 2d 804 (D.C. Cir. 1984); *Brookhaven Cable TV, Inc. v. Kelly*, 573 F. 2d 765 (2d Cir. 1978), *cert. denied*, 441 U.S. 904 (1978); *Earth Satellite Communications, Inc.* 95 FCC 2d 1223 (1983), *recons. denied*, FCC 84-206 (May 14, 1984), *aff'd sub nom New York State Commission on Cable Television v. FCC*, 749 F. 2d 804 (D.C. Cir. 1984). See generally *Fidelity Federal Savings & Loan Association v. de la Cuesta*, 458 U.S. 141 (1982).

[15] *See* 46 FCC 2d 175.

[16] *See Viacom Cable Television of Wisconsin, Inc.*, 50 RR 2d 1558 (1982). In that order the Commission permitted Viacom to use, under certain conditions, decoders in its cable systems which did not meet the standard aural frequency specifications set forth in § 76.605 (a)(3) of the Rules. This action was taken under § 76.605(b) of the rules which makes special provision for cable systems "using multiple cable techniques or specialized receiving devices."

[17] 49 FR 22089 (May 25, 1984).

point. All changes mentioned in the review of standards are reflected in the attached Appendix A.

22. We are also eliminating the measurement and recordkeeping requirements. For example, § 76.601 sets forth the responsibility of the cable system operator to perform such tests and measurements as necessary to offer reasonable assurance that the system performance is continuously satisfactory. While the information required by Section 76.601 may be considered minimal at the start-up of a system, the periodic measurement requirements and bookkeeping, however, can become costly and unnecessary. Therefore, we are deleting these signal quality measurements as federal requirements. However, § 76.601 also contains requirements for signal leakage tests which, for reasons stated below, we will retain.

*Signal Leakage Limitations*

23. In the *Notice*, the Commission proposed to relax the signal leakage limits to 50 uV/m at 3 meters in the frequency band 54 to 216 MHz. Response to the *Notice* varied dramatically. Cable operators want further relaxation to 100 uV/m at 3 meters based on the findings of the Final Report of the Advisory Committee on Cable Signal Leakage (NTIS Pub. PB80-119605). Comments from over-the-air frequency users refute our Part 15 analogy and request no leakage relaxation, stating that there are numerous instances of interference to terrestrial radio facilities at the present levels. Review of the comments does not produce sufficient supportive and conclusive engineering data from either side. Therefore, we will retain the periodic measurement tests for signal leakage and plan to issue a *Further Notice of Proposed Rule Making*, requesting additional engineering monitoring and study.

**Regulatory Flexibility Final Analysis**

24. Pursuant to the Regulatory Flexibility Act of 1980, the Commission's final analysis is as follows:

I. *Need and purpose of this action:*

The regulations affected by this decision were drafted in 1972, when the cable industry was in its early stage of development. Since then, the industry has matured and competition has grown for cable. In view of that maturity and competition, this action is appropriate to update the Commission's standards policy and reflect the competition.

II. *Summary of issues raised by the public comments in response to the Initial Regulatory Flexibility Analysis:*

The Initial Regulatory Flexibility Analysis estimated that adoption of the *Notice* in its entirety would save over 51,200 work hours. Although one commenter disagreed with that figure, upon careful review of the information before us we still believe that these savings are an accurate estimate.

III. *Significant alternatives considered and rejected:*

The Commission considered all of the alternatives raised in this proceeding, including the deletion of all standards, the retention of the existing standards, and the retention of standards only in certain defined circumstances, and it considered all the timely filed comments directed to the various issues in the *Notice*. After carefully weighing all aspects of this proceeding, the Commission has adopted the course of action under the mandate of the Communications Act of 1934, as amended that appears best calculated to eliminate unnecessary regulatory requirements, preserve the appropriate role of federal, state, and local regulatory authorities, and promote rapid and efficient communications to the public.

**Paperwork Reduction Act Statement**

25. The proposal contained herein has been analyzed with respect to the Paperwork Reduction Act of 1980 and found to impose no new or modified requirements or burden upon the public.

**Actions**

26. The Secretary shall cause a copy of this *Report and Order*, including the Final Regulatory Flexibility Analysis, to be sent to the Chief Counsel for Advocacy of the Small Business Administration, in accordance with Paragraph 603(a) of the Regulatory Flexibility Act (Pub. L. No. 96-354, 94 Stat. 1164, 5 U.S.C. 601 *et seq.*, (1981).

27. Accordingly, it is ordered that under the authority contained in Section 4(i) and 303(r) of the Communications Act of 1934, as amended, and the Cable Communications Policy Act of 1984, Part 76 of the Commissions's Rules is amended as set forth in Appendix A, effective January 23, 1986.

28. Further information on this proceeding may be obtained from Bernard Gorden or John Wong at 202-632-9660.

Federal Communications Commission.

**William J. Tricarico,**

*Secretary.*

**Appendix A**

**PART 76—[AMENDED]**

47 CFR Part 76 is amended as follows:

1. The authority citation for Part 76 continues to read as follows:

Authority: 47 U.S.C. 154, 303, and 601

2. 47 CFR 76.601 is amended by revising paragraph (b) and removing paragraphs (c), (d), (e), and (f).

**§ 76.601 Signal leakage measurements.**

* * * * *

(b) All cable television systems serving 1,000 or more subscribers, and all cable television systems serving less than 1,000 subscribers that use any frequency spectrum other than that allocated to over-the-air broadcasting (as described in §§ 73.603 and 73.210), shall conduct all tests, measurements and monitoring of radiation and signal leakage to demonstrate compliance with the radiation limits set forth in § 76.605(a)(11) as follows:

(1) The Cable system operator shall conduct signal leakage measurements in accordance with §76.609(h) at least once each calendar year (at intervals not to exceed 14 months) and shall maintain the resulting test data on file at the operator's local business office for at least five (5) years. It shall be made available for inspection by the Commission on request. This data shall include a description of instruments and procedure and a statement of the qualification of the person performing the tests.

(2) Successful completion of the performance tests does not relieve the system of the obligation to comply with all other pertinent technical standards set forth in this subpart. Additional or repeat tests may be required by the Commission in order to secure compliance with these standards.

3. 47 CFR 76.605 is amended by revising paragraph (a)(3), by removing paragraph (a)(6), by redesignating current paragraphs (a)(7) through (a)(12) as new paragraphs (a)(6) through (a)(11) and by adding a note at the end of the section to read as follows:.

**§ 76.605 Technical standards.**

(a) * * *

(3) The aural center frequency of the aural carrier must be 4.5 MHz ± kHz above the frequency of the visual carrier

* * * * *

**Note.**—The requirements of §§ 76.605(a)(1) through 76.605(a)(10) do not apply directly to cable systems. These rule sections or less stringent versions of them may be used as standards by state or local regulatory authorities. No technical parameter in excess of the above rule sections may be required.

**Appendix B—List of Commenters**

*Initial Comments*

1. Adelphia Communications Corporation

2. Addison, Illinois
3. American Radio Relay League, Inc. (ARRL)
4. Association of Maximum Service Telecasters (MST)
5. Atlantic Research Corporation
6. Austin, Texas
7. Cable Television Information Center
8. California Department of Forestry
9. Capital Cities Cable, Inc. (Capital Cities)
10. CBS, Inc.
11. Communications General Corporation
12. Connecticut Department of Public Utility Control
13. County of San Diego (California) Cable Television Review Comm.
14. Forestry, Conservation Communications Association, Inc. (FCCA)
15. General Electric Company (GE)
16. Gill Industries
17. Joseph S. Gans, Inc.; Mid-Coast Cable Television, Inc.; and Service Electric Cable TV, Inc.
18. Hawaii Dept. of Commerce and Consumer Affairs (State of Hawaii)
19. Iowa City, Iowa
20. City of Los Angeles, California
21. Monroe City-County (Michigan) Office of Civil Preparedness
22. Motorola, Inc. (Motorola)
23. Naperville, Illinois
24. National Academy of Sciences (NAS)
25. National Association of Broadcasters (NAB)
26. National Association of State Cable Agencies (NASCA)
27. National Cable Television Association, Inc. (NCTA)
28. National League of Cities
29. National Telephone Cooperative Association
30. New York Citizens' Committee for Responsible Media
31. City of New York
32. New York State Commission on Cable Television
33. Raystay Company
34. Sacramento County, Calif.; California Metro; Montgomery County, Md.; Cincinnati, Ohio; Scottsdale, Ariz.; and East Saint Louis, Mo.
35. Scientific Atlanta
36. State of California, Telecommunications Division
37. State of New York Department of Environmental Conservation
38. State of New York Department of State
39. Suburban Cablevision
40. Telecable Corporation
41. Tele-Communications Inc.
42. Viacom International Inc.
43. Victor Gates
44. Village of Addison, Illinois
45. Village of Brookfield, Illinois
46. Villiage of Lisle, Illinois
47. Village of Mayville, and Town of Chautauqua (New York) Cable TV Advisory Committee
48. Village of Woodridge, Illinois
49. Wheaton, Illinois
50. Zenith Electronics Corporation (Zenith)

*Reply Comments*

1. ARRL
2. Cable Television Information Center
3. Capital Cities
4. Dallas, Texas
5. Department of Defense
6. Joseph S. Gans, Inc.; Mid Coast Cable Television, Inc.; and Service Electric Cable TV, Inc.
7. Gaylord Broadcasting Company
8. J. Steven Grantham
9. Group W Cable, Inc.
10. Harron Communications Corp., Telecable Corporation, and Tribune Cable Communications, Inc.
11. MST
12. NAB
13. NCTA
14. New York Citizens' Committee for Responsible Media
15. City of New York
16. New York State Sheriffs' Association
17. Riverview, Michigan
18. David Alkire Smith
19. Storer Communications, Inc.
20. Viacom International, Inc.

**Concurring Statement of Chairman Mark S. Fowler**

Re: Signal Quality Rules for Cable Television

The Commission today correctly decided to continue its 1974 preemption of state and local cable signal quality regulations. The possibility of hundreds or even thousands of different standards being adopted by the more than 18,000 cable franchise authorities creates a clear and present danger both to the provision of economically sound interstate cable communications services and to technical progress and innovation from the equipment manufacturing sector. Particularly in times of great technological change and innovation, technical standards may impede such forces. It is also our responsibility at the federal level to ensure that interstate communications is not substantially burdened by a patchwork of different local regulations. This applies both to cable software and hardware.

As to the local standard setting process, even within federal guidelines, I think the fundamental questions still need to be asked. Where is the compelling government interest? Where is the need for signal quality regulation? Where is the record which shows that the marketplace forces will not accomplish the goal at which signal quality regulation is aimed?

Cable operators, like all providers of video services, depend centrally on signal quality to operate successfully. Cable subscribers have direct access, through their monthly subscription payment, to marketplace mechanisms which control cable operators decisions on matters such as signal quality. I am unable to understand how anyone could think government standard setters—with their lack of practical experience in cable construction and maintenance, and inability to react rapidly and flexibly to technological innovations—can or should be setting quality standards, regulating signal quality, or otherwise second-guessing cable subscribers' decisions as to the signal they receive.

Even if such practical expertise existed, there remains unanswered the justification or governmental intervention. That was my view when we eliminated signal quality standards for broadcast signals; we have not observed any deterioration in that instance. That also was my view when we considered mandating cable carriage of stereo sound. The observations in my separate statement in that stereo must-carry case are relevant here as well: this too is "a situation where marketplace forces will accomplish the goals that a prior Commission—with a proregulatory philosophy and less understanding of the value of unregulation in fostering the development of telecommunications—would have tried to accomplish by imposing rules." That view does not change just because there are intervening parties—the cities—who don't agree with the marketplace approach to communications regulation being implemented by this Commission and who wish for some reason to reverse the basic proposition that proof of need should precede government regulation of the people's lives and commerce.

[FR Doc. 85-30196 Filed 12-23-85; 8:45 am]
BILING CODE 6712-01-M

## DEPARTMENT OF TRANSPORTATION

### Office of the Secretary

### 49 CFR Part 1

**[OST Docket No. 1; Amdt. 1-205]**

### Organization and Delegation of Powers and Duties

**AGENCY:** Office of the Secretary DOT.

**ACTION:** Final rule.

**SUMMARY:** This amendment delegates to the Assistant Secretary for Policy and International Affairs authority to issue aviation consumer protection regulations and waivers from these regulations. This authority had been delegated to the Assistant Secretary for Governmental Affairs. By an amendment to 14 CFR Part 385, a portion of that authority was delegated to the Director, Office of Community and Consumer Affairs.

**DATE:** The effective date of this amendment is December 24, 1985.

**FOR FURTHER INFORMATION CONTACT:** Becky L. Bentson, Office of the General Counsel, U.S. Department of

Transportation, Washington, DC. (202) 472-5577.

**SUPPLEMENTARY INFORMATION:** Since this amendment relates to Departmental management, procedures, and practice, notice and comment on it are unnecessary and it may be made effective fewer than thirty days after publication in the **Federal Register.**

On December 31, 1984, the Department of Transportation reissued the former Civil Aeronautics Board rules (14 CFR Part 385) dealing with the delegation of numerous items of discretionary authority needed to carry out Titles IV and X of the Federal Aviation Act of 1958, as amended, and related statutes (49 FR 50984, December 31, 1984.) Concurrently with the reissuance of Part 385, the Department issued amendments to 49 CFR Part 1 to delegate transferring CAB functions to Secretarial officers within DOT (49 FR 50994, December 31, 1984). Editorial corrections and a new subpart to 14 CFR Part 385 were issued later. (50 FR 7169, February 21, 1985.)

The Secretary has now determined that the authority to issue aviation consumer protection regulations, and waivers from those regulations, should be carried out by the Assistant Secretary for Policy and International Affairs rather than the Assistant Secretary for Governmental Affairs. This amendment redelegates that authority to the Assistant Secretary for Policy and International Affairs. A separate amendment to 14 CFR Part 385 appearing in this issue of the **Federal Register** makes a conforming change to 14 CFR Part 385.

**List of Subjects in 49 CFR Part 1**

Authority delegations (government agencies), Organization and functions (government agencies), Transportation Department.

Accordingly, 49 CFR Part 1 is amended as follows:

## PART 1—[AMENDED]

1. The authority citation for Part 1 continues to read as follows:

Authority: 49 U.S.C. 322.

**§ 1.56 Delegations to Assistant Secretary for Policy and International Affairs.**

2. Section 1.56 is amended by adding at the end thereof a new paragraph (j) to read as follows:

* * * * *

(j) Carry out the following consumer protection functions:

(1) Issue consumer protection regulations, and waivers and exemptions therefrom;

(2) Carry out the following statutory provisions relating to consumer protection:

(i) Section 4(a)(5) of the Civil Aeronautics Board Sunset Act of 1984 (October 4, 1984; Pub. L. 98-443), relating to enforcement of the Consumer Credit Protection Act;

(ii) Sections 101(3) (relating to relieving certain carriers from provisions of the Federal Aviation Act), 204 (relating to taking such actions and issuing such regulations as may be necessary to carry out responsibilities under the Act), 404 (relating to enforcing the duty of carriers to provide safe and adequate service), 407(a) (relating to requiring the production of information, entering carrier property, and inspecting records), 411 (relating to determining whether any carrier or ticket agent is engaged in unfair or deceptive practices or unfair methods of competition), and 416 (relating to establishing just and reasonable classifications of carriers and rules to be followed by each) of the Federal Aviation Act of 1958, as amended, (49 U.S.C. 1301(3), 1324, 1374, 1377(a) and (e), 1381, and 1386) as appropriate to the consumer protection functions in this paragraph.

**§ 1.61 Delegations to Assistant Secretary for Governmental Affairs. [Amended]**

3. Section 1.61(d)(4) is removed and marked "[Reserved]".

4. Section 1.61(d)(5) is revised to read as follows:

* * * * *

(d) * * *

(5) Carry out the following statutory provisions:

(i) Section 4(a)(5) of the Civil Aeronautics Board Sunset Act of 1984 (October 4, 1984; Pub. L. 98-443), relating to enforcement of the Consumer Credit Protection Act;

(ii) Sections 204 (a) and (b) (relating to taking such actions as may be necessary to carry out responsibilities under the Federal Aviation Act), 407 (a) and (e) (relating to requiring the production of information, entering carrier property, and inspecting records), and 411 (relating to determining whether any carrier or ticket agent is engaged in unfair or deceptive practices or unfair methods of competition), of the Federal Aviation Act of 1958, as amended, (49 U.S.C. 1324 (a) and (b), 1377(a) and (e), and 1381) as appropriate to the consumer information and assistance functions in this paragraph.

Issued in Washington, DC, on December 14, 1985

**Elizabeth Hanford Dole,**

*Secretary of Transportation.*

[FR Doc. 85-30387 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-62-M

# Proposed Rules

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

## DEPARTMENT OF AGRICULTURE

### Federal Grain Inspection Service

### 7 CFR Part 68

### Regulations and Standards for Inspection and Certification of Certain Agricultural Commodities and Their Products

**AGENCY:** Federal Grain Inspection Service, USDA.[1]

**ACTION:** Proposed rule.

**SUMMARY:** In compliance with requirements for periodic review, the Federal Grain Inspection Service (FGIS or Service) reviewed and proposes to revise Subpart A of the Part 68 regulations under the Agricultural Marketing Act of 1946, as amended (Act), by completely rewriting and reorganizing these regulations. The proposed changes would combine and consolidate compatible requirements, incorporate many procedures currently found in instructions, simplify the overall language, conform certain provisions to present marketing practices, and facilitate the use of the regulations. This proposal would remove the requirement that all factor information determined during the course of an inspection be reported on an official certificate. It would also remove certain definitions that are no longer required and certain provisions that are no longer necessary. The proposal would establish provisions for providing a service on nongraded commodities, permitting appeal inspection services to be performed on a new sample when insect fragments are present, and for applications, terminations, and surrender of licenses issued by the Services.

[1] The authority to exercise the functions of the Secretary of Agriculture contained in the Agricultural Marketing Act of 1964, as amended (7 U.S.C. 1621–1627) concerning inspection and standardization activities related to grain and similar commodities and products thereof has been delegated to the Administrator, Federal Grain Inspection Service (7 U.S.C. 75a; 7 CFR 68.2(e)).

**DATE:** Comments must be submitted on or before February 24, 1986.

**ADDRESS:** Comments must be submitted in writing to Lewis Lebakken, Jr., Information Resources Staff, RM, USDA, FGIS, Room 0667 South Building, 1400 Independence Avenue SW., Washington, DC 20250, telephone (202) 382–1738. All comments received will be made available for public inspection at the above address during regular business hours (7 CFR 1.27(b)). A summary of comments received on this proposal will be published with the final rule.

**FOR FURTHER INFORMATION CONTACT:** Lewis Lebakken, Jr., (address above), telephone (202) 382–1738.

**SUPPLEMENTARY INFORMATION:**

#### Executive Order 12291

This proposed rule has been issued in conformance with Executive Order 12291 and Departmental Regulation 1512–1. This action has been classified as nonmajor because it does not meet the criteria for a major regulation established in the Order.

#### Regulatory Flexibility Act Certification

Dr. Kenneth A. Gilles, Administrator, FGIS, has determined that this proposed rule will not have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*) because most users of the official inspection and weighing services and those entities that perform these services do not meet the requirement for small entities, and this action poses no new or additional duties or obligations to business entities involved in the loading, weighing, handling, or sampling of commodities.

#### Information Collection and Recordkeeping Requirements

In compliance with the Office of Management and Budget (OMB) regulations (5 CFR Part 1320) which implement the Paperwork Reduction Act of 1980 (Pub. L. 96–511) and section 3504(h) of this Act, the information collection and recordkeeping requirements contained in this proposed rule have been submitted to OMB for review.

#### Regulatory Review

The review of the regulations concerning Part 68, Subpart A—Regulations included a determination of continued need for and consequences of the regulations. The objective of the review was to ensure that the regulations are serving their intended purpose, the language is clear, and the regulations are consistent with FGIS policy and authority. FGIS has determined that, in general, these regulations are serving their intended purpose, are consistent with FGIS policy and authority, and should remain in effect. FGIS, however, proposes to revise Part 68, Subpart A—Regulations in its entirety. This proposed action would consolidate compatible provisions, organize them into a more logical order, clarify and remove unnecessary language, and remove provisions that are no longer needed. The proposed revisions will facilitate the use of these regulations. These revisions, if adopted, would remove the regulatory requirements currently found in § 68.40, *Samples to be identified;* § 68.48, *Refunds,* § 68.52, *Political activity;* and § 68.54, *Loaning of samples.* In addition, four definitions in the current § 68.2, *Terms defined* would be removed. They are § 68.2(f), *Division;* § 68.2(g), *Director;* § 68.2(1), *Supervising inspector;* and § 68.2(o), *Office of inspection.* These proposed deletions would eliminate unnecessary, outdated, or duplicative provisions in the regulations. All other provisions in the current Part 68, Subpart A—Regulations have been retained in the proposed revision.

These regulations have not been extensively changed since 1954. In the interim, marketing and inspection practices and procedures have changed; and, when appropriate, such changes have been addressed in the instructions. This proposed revision has incorporated many of these changes. The inclusion of these provisions would update them to current inspection practices and procedures. This proposed incorporation of inspection procedures covered by instructions would not adversely impact on users of inspection services, since they are already following the procedures.

Specifically, the following changes are proposed:

1. The proposed § 68.1, headed as, *Definitions,* would be revised by combining the current §§ 68.1, 68.2, and 68.36, plus consolidating definitions from other sections of the current regulations. Some new definitions would also be added. The definitions in current

§ 68.2(f), (g), (l), and (o) would be removed because they are no longer applicable or necessary. The remaining and new definitions would be placed in alphabetical order for easy reference.

2. The proposed §§ 68.5–68.13, headed as, *Administration*, would include provisions of an administrative nature, such as nondiscrimination policy, procedures for establishing regulations, complaints, provisions for hearings, and public information. These proposed sections reflect, in part, the applicable portions of §§ 68.3, 68.5, 68.49, 68.51, and 68.53 of the current regulations.

3. The proposed §§ 68.20–68.26, headed as, *Conditions for Obtaining or Withholding Service*, would include provisions for obtaining or withdrawing requests for service, dismissing requests for service, conditional withholding of service, denial of service, and payment of expenses incurred by the cooperator or the Service. Current provisions relating to these proposed sections are contained in §§ 68.4, 68.9–68.11, 68.21, 68.22, 68.24, 68.30, 68.32, 68.34, 68.35, 68.43, and 68.50.

4. The proposed §§ 68.30–68.36, headed as, *Inspection Methods and Procedures*, would include the methods and order for performing inspection service, sample requirements, partial inspection, and sampling provisions by level of service. These sections reflect appropriate portions of § 68.6, 68.12–68.14, 68.21, 68.23, 68.33, 68.34, 68.37, and 68.39 of the current regulations. In addition, a section covering loss of identify would delineate situations when the identify of a commodity lot and the identity of a commodity sample would be considered lost.

5. The proposed §§ 68.40–68.44, headed as, *Original Inspection Service*, would provide for who may request inspection service, contract service, how to request original service, certificating original inspection results, and new original inspection service. Current provisions relating to these proposed sections are contained in §§ 68.4, 68.7, 68.8, 68.12, 68.13, 68.29, 68.30, and 68.43. The proposed section on new original inspection service would clarify when an applicant may request a new original inspection. A better guideline is needed for clarity as to when and on what basis a new original inspection can be requested. The proposed clarification would permit new original inspection on previously-inspected commodity lots only when circumstances are such as to prevent a retest, appeal, or Board appeal inspection; and all new original inspections would be performed on new samples drawn from the lot.

6. The proposed §§ 68.50–68.52, headed as, *Retest Inspection Service*, would provide a new level of inspection service for nongraded commodities. The proposed sections would include provisions covering who may request service, how to request retest inspection service, and certificating retest results. The proposed retest service would allow applicants to request additional testing on the file sample for one or more factors when they are dissatisfied with that results of an original inspection. Currently, if an applicant is dissatisfied with the result of one or more factors, the applicant must request an appeal inspection service whereby all factors are retested. The current procedure for retesting all factors as part of an appeal inspection service for nongraded commodities is costly and may not meet the needs of the industry. Many factors are included in contract specifications for nongraded commodities that require tests using specialized laboratory equipment. This results in laboratory charges that average approximately $111 for flour, $127 for corn meal (Export), $145 for soy-fortified corn meal, $145 for corn-soy blend, $116 for rolled oats, and $105 for corn-soya milk. Since each test result is individually compared to contract specifications, it may be costly to retest all factors when the applicant is dissatisfied with the results of one or more factors. To provide inspection services that meet industry needs while at the same time minimizing costs to applicants for service, FGIS is proposing a retest service for nongraded commodities. Under the proposed retest inspection service, certificates issued for retest services will supersede the original inspection certificate. If an applicant for inspection is not satisfied with the retest results, an appeal inspection service may be requested. Under this proposal, all fators that were determined during the original inspection would be tested as part of the appeal inspection service. This proposal would also provide applicants for inspection of nongraded commodities with three levels of service which are consistent with the current provisions for graded commodities. The three levels of service are also consistent with other commodities inspected under the Agricultural Marketing Act of 1946 which provides retest service on one or more factors when laboratory testing services have been performed.

7. The proposed §§ 68.60–68.63, headed as, *Appeal Inspection Service*, would include provisions setting out who may request appeal inspection service, how to request appeal inspection service, who shall perform appeal inspection service, and certificating appeal results. These proposed sections reflect appropriate portions of current §§68.21, 68.22, 68.25, 68.26, 68.28, and 68.28a. In addition, these proposed revisions would permit an appeal inspection for insect fragments found in nongraded processed products to be peformed on a new sample. Currently, the regulations limit appeal inspections to a review of the sampling procedure and an analysis of the file sample when, as a result of the original inspection, the commodity was found to be contaminated with filth or to contain a deleterious substance. In all other cases, an appeal inspection may be based on a new sample or a file sample. Various industry groups have requested that FGIS consider permitting the analysis of new samples under appeal inspections when the insect fragment and rodent hair levels exceed the Food and Drug Administration's Defect Action Levels or contract specifications. Based on day-to-day testing experience, FGIC has determined that rodent hair contamination, like glass, metal, or a toxic substance, may not be homogeneously distributed throughout commodity lots. However, FGIS has determined based upon program test results that insect fragment contamination is usually homogeneous in nongraded processed products. Consequently, FGIS proposes to permit an analysis of new samples for insect fragments in nongraded processed products but not for rodent hairs.

8. The proposed §§ 68.70–68.75, headed as, *Official Certificates*, would include provisions for official certificate issuance and distribution, certificate requirements, certification of results, corrected certificates, divided-lot certificates, and duplicate certificates. The current provisions relating to these proposed sections are in §§ 68.14–68.16a, 68.27, and 68.31. In addition, these proposed sections would remove the requirement that any factor on graded commodities for which an official determination is made during the course of the inspection be shown on the inspection certificate. Various industry groups have indicated that the requirement to report factor information not requested by the buyer is not needed and confuses both the buyer and financial institutions. After reviewing industry concerns that reporting factor information not requested by the buyer may cause confusion in the marketplace, it is proposed that the requirement be removed. However, the requirement to show grade determining factors on all certificates would be retained since the information is generally desired by the industry. This proposal would not prohibit applicants from obtaining

specific factor information, when requested.

9. The proposed §§ 68.80–68.84, headed as, *Licensed Inspectors, Technicians, and Samplers*, would provide for who may be licensed, licensing procedures, and suspension or revocation of licenses. The current regulations provide for licensing in §§ 68.37, 68.38, 68.41, and 68.50.

10. The proposed §§ 68.90,92, headed as, *Fees*, would provide for FGIS fee schedules. These fees have already been reviewed and published as a final rule on June 28, 1984, in the **Federal Register** (49 FR 26547). The specific fees and charges in current §§ 68.42a and 68.42b pertaining to commodity and rice inspection services would not be changed. If this proposal is adopted, the current § § 68.42a, 68.42b, and 68.43 would be redesignated §§ 68.90, 68.91, and 68.92, respectively. In addition, the current provisions in § 68.43(a) would be moved to § 68.1 and paragraphs (b) through (i) would be redesignated (a) through (h).

**List of Subjects in 7 CFR Part 68**

Administrative practice and procedure.

Accordingly, it is proposed that 7 CFR Part 68, be amended as follows:

1. The authority citation for Part 68 revised to read as follows:

**Authority:** Secs. 202–208, 60 Stat. 1087, as amended (7 U.S.C. 1621 *et seq.*)

2. Subpart A is revised to read as follows:

## PART 68—REGULATIONS AND STANDARDS FOR INSPECTION AND CERTIFICATION OF CERTAIN AGRICULTURAL COMMODITIES AND THEIR PRODUCTS

**Subpart A—Regulations**

Sec.


Definitions

68.1 Meaning of terms.

Administration

68.5 Administrator.
68.6 Nondiscrimination—policy and provisions.
68.7 Procedures for establishing regulations and standards.
68.8 Complaints and reports of alleged violations.
68.9 Provisions for hearings.
68.10 Information about the Service, Act, and regulations.
68.11 Public information.
68.12 Identification.
68.13 Regulations not applicable for certain purposes.

Conditions for Obtaining or Withholding Service

68.20 Availability of services.
68.21 Requirements for obtaining service.
68.22 Withdrawal of request for inspection service by applicant.
68.23 Dismissal of request for inspection service.
68.24 Conditional withholding of service.
68.25 Denial or withdrawal of service.
68.26 Expenses of the cooperator or the Service.

Inspection Methods and Procedures

68.30 Methods and order of performing inspection service.
68.31 Kinds of inspection services.
68.32 Who shall inspect commodities.
68.33 Sample requirements; general.
68.34 Partial inspection.
68.35 Sampling provisions by level of service.
68.36 Loss of identity.

Original Inspection Service

68.40 Who may request original inspection service.
68.41 Contract service.
68.42 How to request original inspection service.
68.43 Certificating original inspection results.
68.44 New original inspection.

Retest Inspection Service

68.50 Who may request retest inspection service.
68.51 How to request retest inspection service.
68.52 Certificating retest results.

Appeal Inspection Service

68.60 Who may request appeal inspection service.
68.61 How to request appeal inspection service.
68.62 Who shall perform appeal inspection service.
68.63 Certificating appeal results.

Official Certificates

68.70 Official certificates, issuance and distribution.
68.71 Official certificate requirements.
68.72 Certification of results.
68.73 Corrected certificates.
68.74 Divided-lot certificates.
68.75 Duplicate certificates.

Licensed Inspectors, Technicians, and Samplers

68.80 Who may be licensed.
68.81 Licensing procedures.
68.82 Voluntary cancellation or suspension of license.
68.83 Automatic suspension of license by change in employment.
68.84 Suspension or revocation of license.

Fees

68.90 Fees for certain Federal inspection services.
68.91 Fees for certain Federal rice inspection services.

Sec.

68.92 Explanation of service fees and additional fees.


* * * * *

**Subpart A—Regulations**

**Definitions**

**§ 68.1 Meaning of terms.**

(a) *Construction.* Words used in the singular form are considered to imply the plural and vice versa, as appropriate.

(b) *Definitions.* For the purpose of these regulations, unless the context requires otherwise, the following terms have the meanings given for them below.

(1) *Act.* The Agricultural Marketing Act of 1946, as amended (60 Stat. 1087 *et seq.*, as amended, 7 U.S.C. 1621 *et seq.*).

(2) *Administrator.* The Administrator of the Federal Grain Inspection Service or any person to whom authority has been delegated.

(3) *Appeal inspection service.* A review by the Service of the results of an original inspection or retest inspection service.

(4) *Applicant.* An interested person who requests any inspection service with respect to a commodity.

(5) *Authorized inspector.* The Administrator may authorize a Departmental employee to inspect a commodity after the employee has demonstrated a thorough knowledge of a commodity and the Act, regulations, standards, instructions, and procedures under which it is inspected.

(6) *Board appeal inspection service.* A review by the Board of Appeals and Review of the results of an original inspection or appeal inspection service on graded commodities.

(7) *Board of Appeals and Review or Board.* The Board of Appeals and Review of the Service.

(8) *Business day.* The established field office working hours, any Monday through Friday that is not a holiday, or the working hours and days established by a cooperator.

(9) *Carrier.* A truck, trailer, truck/trailer(s) combination, railroad car, barge, ship, or other container used to transport bulk, sacked, or packaged commodity.

(10) *Commodity.* Agricultural commodities and products that the Secretary has assigned to the Service for inspection under the Act, including but not limited to, dry beans, grain, hay, hops, lentils, oilseeds, dry peas, split peas, rice, and straw.

(11) *Continuous inspection.* The conduct of inspection services in an

approved plant where one or more official inspection personnel are present during the processing of a commodity to make in-process examinations of the preparation, processing, packing, and warehousing of the commodity and to determine compliance with applicable sanitation requirements.

(12) *Contract service.* Any service performed under a contract between an applicant and the Service.

(13) *Contractor.* Any person who enters into a contract with the Service to perform specified inspection services.

(14) *Cooperator.* An agency or department of the Federal Government which has an interagency agreement or State agency which has a reimbursable agreement with the Service.

(15) *Cooperator inspection service.* The inspection service provided by a cooperator under the regulations. Under this service, inspection certificates are issued by the cooperator and all fees and charges are collected by the cooperator, except as provided in the agreement.

(16) *Department.* The United States Department of Agriculture.

(17) *Factor.* A quantified physical or chemical property identified in official standards, specifications, abstracts, contracts, or other documents whose measurement describes a specific quality of a commodity.

(18) *Field office.* An office of the Service designated to perform, monitor, or supervise inspection services.

(19) *Grade.* A grade designating a level of quality as defined in the commodity standards promulgated by the Administrator.

(20) *Holiday.* The legal public holidays specified in paragraph (a) of section 6103, Title 5, of the United States Code (5 U.S.C. 6103(a)) and any other day declared to be a holiday by Federal Statute or Executive Order. Under section 6103 and Executive Order 10357, as amended, if the specified legal public holiday falls on a Saturday, the preceding Friday shall be considered to be the holiday, or if the specified legal public holiday falls on a Sunday, the following Monday shall be considered to be the holiday.

(21) *Inspection certificate.* A written printed official document which is approved and which shows the results of an inspection service performed under the Act.

(22) *Inspection service.* (i) Applying such tests and making examinations of a commodity and records by official personnel as may be necessary to determine the kind, class, grade, other quality designation, the quantity, or condition of commodity; (ii) performing condition of container, carrier stowage examinations, and any other services as related to commodities, as necessary; and (iii) issuing an inspection certificate.

(23) *Instructions.* The Notices, Instructions, Handbooks, and other directives issued by the Service.

(24) *Interagency agreement.* An agreement between the Service and other branches of the Federal Government to conduct commodity inspection services as authorized in the Act.

(25) *Interested person.* Any person having a contract or other financial interest in a commodity as the owner, seller, purchaser, warehouseman, carrier, or as otherwise.

(26) *Licensee.* Any person licensed by the Service.

(27) *Nonregular workday.* Any Sunday or holiday.

(28) *Official inspector.* Any official personnel who performs, monitors, or supervises the performance of inspection service and certifies the results of the commodity.

(29) *Official personnel.* Any authorized Departmental employee or person licensed by the Administrator to perform all or specified functions under the Act.

(30) *Official sampler.* Any official personnel who performs, monitors, or supervises the performance of sampling of a commodity.

(31) *Official technician.* Any official personnel who performs, monitors, or supervises the performance of specified inspection services and certifies the results thereof, other than certifying the grade of a commodity.

(32) *Origin.* The geographical area or place where the commodity is grown.

(33) *Original inspection service.* An initial inspection of a commodity.

(34) *Person.* Any individual, partnership, association, corporation, or other business entity.

(35) *Plant.* The premises, buildings, structure, and equipment (including but not limited to machines, utensils, vehicles, and fixtures located in or about the premises) used or employed in the preparation, processing, handling, transporting, and storage of commodities.

(36) *Regular workday.* Any Monday through Saturday that is not a holiday.

(37) *Regulations.* The regulations in this Part.

(38) *Reimbursable agreement.* An agreement between the Service and State agencies to conduct commodity inspection services authorized by the Act.

(39) *Retest inspection service.* To test again a factor(s) of nongraded commodities previously tested using the same laboratory procedures.

(40) *Secretary.* The Secretary of Agriculture of the United States or any person to whom authority has been delegated.

(41) *Service.* The Federal Grain Inspection Service of the United States Department of Agriculture (FGIS).

(42) *Serviced representative.* An employee authorized by the Service or a person licensed by the Administrator.

(43) *Specification.* A document which clearly and accurately describes the essential and technical requirements for items, materials, or services including the inspection procedures.

(44) *Standards.* The commodity standards in this Part that describe the physical and biological condition of a commodity at the time of inspection.

(45) *Submitted sample.* A sample submitted by or for an interested person for inspection.

(46) *Test.* A procedure to measure a factor using specialized laboratory equipment involving the application of established scientific principles and laboratory procedures.

## Administration

### § 68.5 Administrator.

The Administrator, under the authority delegated by the Secretary, is charged with administering the regulations and those parts of the Act that relate to the regulations.

### § 68.6 Nondiscrimination—policy and provisions.

In implementing, administering, and enforcing the Act and the regulations, standards, and instructions, it is the policy of the Service to promote adherence to the provisions of the Civil Rights Act of 1964 (42 U.S.C. 2000a et seq.).

### § 68.7 Procedures for establishing regulations and standards.

Notice of proposals to prescribe, amend, or revoke regulations and standards shall be published in accordance with applicable provisions of the Administrative Procedures Act (5 U.S.C. 551, *et seq.*). Any interested person desiring to file a petition for the issuance, amendment, or revocation of regulations or standards may do so in accordance with 7 CFR 1.28 of the regulations of the Office of the Secretary of Agriculture.

### § 68.8 Complaints and reports of alleged violations.

(a) *General.* Except as provided in paragraph (b) of this section, complaints and reports of violations involving the Act or the regulations, standards, and instructions issued under the Act should

be filed with the Service in accordance with 7 CFR 1.133 of the regulations of the Office of the Secretary of Agriculture and these regulations and instructions issued pursuant to the Act.

(b) *Retest inspection and appeal inspection services.* Complaints involving the results of inspection services shall, to the extent practicable, be submitted as requests for retest inspection, appeal inspection, or Board appeal inspection services as set forth in these regulations.

**§ 68.9 Provisions for hearings.**

Opportunities shall be provided for hearings either in accordance with the Rules of Practice Governing Formal Adjudicatory Proceedings Instituted by the Secretary under Various Statutes (7 CFR, Part 1, Subpart H) or in accordance with FGIS procedures, as would be appropriate.

**§ 68.10 Information about the Service, Act, and regulations.**

Information about the Service, Act, regulations, standards, rules of practice, instructions, and other matters related to the inspection of commodities may be obtained by telephoning or writing the U.S. Department of Agriculture, Federal Grain Inspection Service, 1400 Independence Avenue SW., Washington, DC 20250, or any field office or cooperator.

**§ 68.11 Public information.**

(a) *General.* This section is issued in accordance with §§ 1.1–1.16 of the regulations of the Secretary in Part 1, Subpart A, of Subtitle A of Title 7 (7 CFR 1.1–1.16), and Appendix A thereto, implementing the Freedom of Information Act (5 U.S.C. 552). The Secretary's regulations, as implemented by this section, govern the availability of records of the Service to the public.

(b) *Public inspection and copying.* Materials maintained by the Service, including those described in 7 CFR 1.2(a), will be made available, upon a request which has not been denied, for public inspection and copying at the U.S. Department of Agriculture, Federal Grain Inspection Service, 1400 Independence Avenue, SW., Washington, DC 20250. The public may request access to these materials 8:00 a.m.–4:30 p.m. during regular workdays.

(c) *Indexes.* The Service shall maintain an index of all material required to be made available in 7 CFR 1.2(a). Copies of these indexes will be maintained at the location given in paragraph (b) of this section. Notice is hereby given that quarterly publication of these indexes is unnecessary and impracticable because the material is voluminous and does not change often enough to justify the expense of quarterly publication. However, upon specific request, copies of any index will be provided at a cost not to exceed the direct cost of duplication.

(d) *Requests for records.* Requests for records under 5 U.S.C. 552(a)(3) shall be made in accordance with 7 CFR 1.3(a) and shall be addressed as follows: Office of the Administrator, Federal Grain Inspection Service, FOIA Request, U.S. Department of Agriculture, 1400 Independence Avenue SW., Washington, DC 20250.

(e) *FOIA Appeals.* Any person whose request, under paragraph (d) of this section, is denied shall have the right to appeal such denial in accordance with 7 CFR 1.3(e). Appeals shall be addressed to the Administrator, Federal Grain Inspection Service, FOIA Appeal, U.S. Department of Agriculture, Washington, DC 20250.

(f) *Disclosure of information.* FGIS employees or persons acting for FGIS under the Act shall not, without the consent of the applicant, divulge or make known in any manner any facts or information acquired pursuant to the Act and regulations except as authorized by the Administrator, by a court of competent jurisduction, or otherwise by law.

**§ 68.12 Identification.**

All official personnel shall have in their possession and present upon request, while on duty, the means of identification furnished to them by the Department.

**§ 68.13 Regulations not applicable for certain purposes.**

These regulations do not apply to the inspection of grain under the United States Grain Standards Act, as amended (7 U.S.C. 71 *et seq.*) or the inspection of commodities under the United States Warehouse Act, as amended (7 U.S.C. 241 *et seq.*).

**Conditions for Obtaining or Withholding Service**

**§ 68.20 Availability of services.**

(a) *Original inspection service.* Original inspection services are available according to this section and §§ 68.40–.45.

(b) *Retest inspection and appeal inspection services.* Retest inspection, appeal inspection, and Board appeal inspection services are available according to §§ 68.50–.52 and §§ 68.60–.63.

(c) *Proof of authorization.* A cooperator or the Service may request satisfactory proof that an applicant is an interested person or their authorized agent.

**§ 68.21 Requirements for obtaining service.**

(a) *Consent and agreement by applicant.* In submitting a request for inspection service, the applicant and the owner of the commodity consent to the special and general requirements specified in paragraphs (b) through (j) of this section.

(b) *Written confirmation.* Verbal requests for inspection service shall be confirmed in writing upon request. Each written request shall be made in English and shall include (1) the date filed; (2) the identification, quantity, and location of the commodity; (3) the type of service(s) requested; (4) the name and mailing address of the applicant and, if made by an authorized agent, the agent's name and mailing address; and (5) any other relevant information that the official with whom the application is filed may request. A written request or a written confirmation of a verbal request shall be signed by the applicant or a duly authorized agent.

(c) *Names and addresses of interested persons.* When requested, each applicant for inspection service shall show on the application form the name and mailing address of each known interested person.

(d) *Surrender of superseded certificates.* Superseded certificates must be promptly surrendered.

(e) *Accessibility.* (1) *Commodities.* Each commodity lot inspected shall be arranged so the entire lot may be examined or, if necessary, a representative sample can be obtained. If the entire lot is not accessible for examination or a representative sample cannot be obtained, the inspection shall be restricted to an examination or sampling of the accessible portion and the results certified as stated in § 68.34.

(2) *Origin records.* When an applicant requests origin inspection, the records indicating the origin of the commodity to be inspected shall be made accessible for examination and verification by official personnel.

(f) *Plant examination.* Plant surveys shall be performed when required by contract or upon request. Survey results shall be reported in writing to a designated plant official. If the plant is approved as a result of the survey, inspection service may begin or continue at a time agreed upon by the plant management and the cooperator or Service. If the plant is not approved as a result of the survey, inspection service shall be conditionally withheld according to the procedures in § 68.24.

(g) *Working space.* Applicant must provide adequate and separate space when inspection service is performed at a plant.

(h) *Loading and unloading conditions.* Each applicant for inspection service shall provide or arrange for suitable conditions in the (1) loading and unloading areas and the truck and railroad holding areas; (2) pier or dock areas; (3) deck and stowage areas in the carrier; (4) other service areas; and (5) equipment used in loading or unloading, processing, and handling the commodity. Suitable conditions are those which will facilitate accurate inspection, maintain the quantity and the quality of the commodity that is to be inspected, and not be hazardous to the health and safety of official pesonnel as prescribed in the instructions.

(i) *Timely arrangements.* Requests for inspection service shall be made in timely manner; otherwise, official personnel may not be available to provide the requested service. For the purpose of this paragraph, "timely manner" shall mean not later than 2 p.m., local time, of the preceding business day.

(j) *Payment of bills.* Each applicant for inspection service shall pay bills for the service according to §§ 68.90–68.92.

(Approved by the Office of Management and Budget under control number 0580–0012)

**§ 68.22 Withdrawal of request for inspection service by applicant.**

An applicant may withdraw a request for inspection service any time before official personnel release results, either verbally or in writing. Reimbursement of expenses, if any, shall be made according to § 68.26.

**§ 68.23 Dismissal of request for inspection service.**

(a) *Conditions for dismissal.*—(1) *General.* A cooperator or the Service shall dismiss requests for inspection service when:

(i) Performing the requested service is not practicable.

(ii) The cooperator or the Service lacks authority under the Act or regulations.

(iii) Sufficient information is not available to make an accurate determination.

(2) *New original inspection service.* A request for new original inspection service shall be dismissed if a retest inspection, appeal inspection, or Board appeal inspection may be performed on the same lot.

(3) *Retest inspection service.* A request for a retest inspection service shall be dismissed by official personnel when (i) the factor requested was not tested during the original inspection; (ii) the condition of the commodity has undergone a material change; (iii) a representative file sample is not available; (iv) the applicant requests that a new sample be obtained; (v) the request is for a graded commodity; or (vi) the reasons for the retest inspection are frivolous.

(4) *Appeal inspection service.* A request for an appeal inspection service shall be dismissed by official personnel when (i) the scope is different from the scope of the original inspection service; (ii) the condition of the commodity has undergone a material change; (iii) the request specifies a file sample and a representative file sample is not available; (iv) the applicant requests that a new sample be obtained and a new sample cannot be obtained; or (v) the reasons for the appeal inspection are frivolous.

(5) *Board appeal inspection service.* A request for a Board appeal inspection service shall be dismissed by official personnel when (i) the scope is different from the scope of the original inspection service; (ii) the condition of the commodity has undergone a material change; (iii) a representative file sample is not available; (iv) the applicant requests that a new sample be obtained; or (v) the reasons for the Board appeal inspection are frivolous.

(b) *Procedure for dismissal.* The cooperator or the Service shall notify the applicant of the proposed dismissal of service. The applicant will then be afforded reasonable time to take corrective action or to demonstrate there is no basis for the dismissal. If corrective action has not been adequate, the applicant will be notified of the decision to dismiss the request for service, and any results of service shall not be released.

**§ 68.24 Conditional withholding of service.**

(a) *Conditional withholding.* A cooperator or the Service shall conditionally withhold requests for service when an applicant fails to meet any requirement prescribed in § 68.21.

(b) *Procedure for withholding.* The cooperator or the Service shall notify the applicant of the reason for the proposal to conditionally withhold service. The applicant will then be afforded reasonable time to take corrective action or to demonstrate that there is no basis for withholding service. If corrective action has not been adequate, the applicant will be notified of the decision to withhold service; and any results of service shall not be released.

**§ 68.25 Denial or withdrawal of service.**

(a) *General.* Service may be denied or withdrawn because of (1) any willful violation of the Act, regulations, standards, or instructions or (2) any interference with or obstruction of any official personnel in the performance of their duties by intimidation, threat, assualt, or any other improper means.

(b) The Rules of Practice Governing Formal Adjudicatory Proceedings Instituted by the Secretary under Various Statues (7 CFR Part 1, Subpart H) shall be followed in the denial or withdrawal of service.

**§ 68.26 Expenses of the cooperator or the Service.**

For any request that has been withdrawn, dismissed or withheld under §§ 68.22, 68.23, or 68.24, respectively, each applicant shall pay expenses incurred by the cooperator or the Service.

**Inspection Methods and Procedures**

**§ 68.30 Methods and order of performing inspection service.**

(a) *Methods.*—(1) *General.* All sampling and inspection services performed by official personnel shall be made in accordance with standards and instructions authorized by the Administrator.

(2) *Lot inspection service.* A lot inspection service shall be based on official personal obtaining representative samples, examining the commodity in the entire lot, and making an accurate analysis of the commodity on the basis of the samples.

(3) *Submitted sample inspection service.* A submitted sample inspection service shall be based on a submitted sample of sufficient size to enable official personnel to perform an accurate, complete analysis. The sample size will be prescribed in the instructions. If an accurate analysis cannot be made because of an inadequate sample size or other conditions, the request shall be dismissed or a factor only inspection certificate issued for factors that can be determined.

(b) *Order of service.* Inspection service shall be performed, to the extent practicable, in the order in which requests for service are received.

(c) *Recording receipt for documents.* Each document submitted by or on behalf of an applicant for inspection service shall be promptly stamped or similary marked by official personnel to show the date of receipt.

(d) *Conflicts of interest.* (1) Official personnel shall not perform or participate in performing an inspection

service on a commodity or a carrier or container in which they have a direct or indirect financial interest.

(2) Official personnel shall not perform, participate in performing, or issue a certificate if they participated in a previous inspection or certification of the lot unless there is only one authorized person available at the time and place of the requestd inspection service.

**§ 68.31 Kinds of inspection services.**

(a) *General.* The inspection of commodities shall be (1) according to the (i) standards of class, grade, other quality designation quantity, or condition for such commodities promulgated by the Administrator; or (ii) specifications prescribed by Federal agencies; or (iii) specifications of trade associations or organizations approved by the Administrator; or (iv) instructions authorized by the Administrator or (2) for one or more factors of class, grade, other quality designations, quantity, or condition, as defined in such standards, specifications, or instructions and procedures, or otherwise as approved by the Administrator. The kinds of services provided and the basis for performing them are shown in paragraphs (b) through (m) of this section. Some or all of these kinds of services are provided when performing a complete inspection service.

(b) *Lot inspection service.* This service consists of official personnel (1) obtaining representative sample(s) of an identified commodity lot; (2) examining, grading, or testing the sample(s); (3) examining relevant records for the lot; (4) performing other requested services; and (5) certifying results.

(c) *Submitted sample inspection.* This service consists of an applicant submitting a commodity sample; and official personnel grading, or testing the sample or performing other requested services, and certifying results.

(d) *Examination.* This service consists of official personnel examining supplies without the use of special laboratory equipment or procedures to determine conformance ot contract requirements and certifying results.

(e) *Checkweighing service (container).* This service consists of official personnel (1) physically weighing a selected number of containers from a commodity lot; (2) determining the estimated total gross, tare, and net weights, or the estimated average gross or net weight per filled container; and (3) certifying results.

(f) *Bulk weighing.* This service consists of official personnel (1) completely supervising the loading or the unloading of an identified lot of bulk or containerized commodity, (2) physically weighing or completely supervising the weighing of the commodity, and (3) certifying results.

(g) *Checkloading service.* This service consists of official personnel (1) performing a stowage examination; (2) computing the number of filled commodity containers loaded aboard a carrier; (3) permitting only undamaged commodity containers to be loaded into the carrier; (4) if practicable, sealing the carrier for security; and (5) certifying results.

(h) *Checkcounting.* This service consists of official personnel determining the total number of filled outer containers in a lot to verify that the number of containers shown by the applicant is correct and cerifying results.

(i) *Condition inspection.* This service consists of official personnel determining the present physical condition of the commodity by determining whether an identifiable commodity lot has water damage, fire damage, rodent or bird contamination, insect infestation, or any other deteriorating condition and certifying results.

(j) *Condition of food containers.* This service consists of official personnel determining the degree of acceptability of the containers with respect to absence of defects which affect the serviceability, including appearance as well as usability, of the container for its intended purpose and certifying results.

(k) *Observation of loading.* This service consists of official personnel verifying that an identified lot is moved from a warehouse or carrier and loaded into another warehouse or carrier and certifying results.

(l) *Plant approval.*[1] This service consists of official personnel performing a plant survey to determine if the plant premises, facilities, sanitary conditions, and operatring methods are suitable to begin or continue inspection service.

(m) *Stowage examination service.* This service consists of official personnel visually determining if an identified carrier or container is clean; dry; free of infestation, rodents, toxic substances, and foreign odor; and suitable to store or carry commodities and certifying results.

**§ 68.32 Who shall inspect commodities.**

Commodity inspections shall be performed only by official personnel.

[1] Compliance with the requirements in this paragraph does not excuse failure to comply with all applicable sanitation rules and regulations of city, county, State, Federal, or other agencies having jurisdiction over such plants and operations.

**§ 68.33 Sample requirements; general.**

(a) *Samples for lot inspection service.*—(1) *Original lot inspection service.* The sample(s) on which the original inspection is determined shall be (i) Obtained by official personnel; (ii) representative of the commodity in the lot; (iii) protected from manipulation, substitution, and improper or careless handling; and (iv) obtained within prescribed geographical boundaries of the cooperator or field office performing the inspection service.

(2) *Retest lot inspection service.* The sample(s) on which the retest is determined shall (i) be obtained by official personnel and (ii) otherwise meet the requirements of pargraph (a)(1) of this section. The retest inspection shall be prformed on the basis of a file sample(s), and the samples must meet the requirements prescribed in § 68.35(e).

(3) *Appeal lot inspection service.* For an appeal lot inspection service, the sample(s) on which the appeal is determined shall (i) be obtained by official personnel and (ii) otherwise meet the requirements of paragraph (a)(1) of this section. If the appeal inspection is performed on the basis of a file sample(s), the samples shall meet the requirements prescribed in § 68.35(e). An applicant may request that a new sample be obtained and examined as part of the appeal inspection service in accordance with § 68.61(b)(2) and (3). The provision for obtaining a new sample shall not apply if obtaining the new sample involves a change in the method of sampling.

(4) *Board appeal lot inspection service.* A Board appeal lot inspection service shall be performed on the basis of a file sample.

(b) *Sampler requirement.* A licensed sampler may be requested to sample commodities and forward the samples to the appropriate field office or other location as specified. A sampling report signed by the licensed sampler shall accompany each sample. The report shall provide the identify, quantity, and location of the commodity sampled; and the name and mailing address of the applicant; and all other information regarding the lot as may be required.

(c) *Representative sample.* A sample shall not be considered representative of a commodity lot unless the sample (1) has been obtained by official personnel; (2) is of the size prescribed in the instructions; and (3) has been obtained, handled, and submitted in accordance with the instructions.

(d) *Protecting samples.* Official personnel shall protect samples from manipulation, substitution, and improper

and careless handling which might deprive the samples of their representativeness or which may change the physicial and chemical properties of the commodity from the time of sampling until inspection services are completed and file samples have been discarded.

**§ 68.34 Partial inspection.**

When the entire lot is not accessible for examination or a representative sample cannot be obtained from the entire lot, the certificate shall state the estimated quantity of the commodity in the accessible portion and the quantity of the entire lot. The inspection shall be restricted to the accessible portion. Furthermore, the words "Partial Inspection" shall be printed or stamped on the certificate.

**§ 68.35 Sampling provisions by level of service.**

(a) *Original inspection service.*—(1) *Lot inspection service.* Each original lot ispection service shall be made on the basis of one or more representative samples obtained by official personnel from the commodity in the lot and forwarded to the appropriate location.

(2) *Submitted sample service.* Each original submitted sample inspection service shall be performed on the basis of the sample as submitted.

(b) *Retest inspection service.* Each retest inspection service performed on a commodity lot or a submitted sample shall be based on an analysis of the file sample.

(c) *Appeal inspection service.*—(1) Lot inspection service. Each appeal inspection service on a commodity lot shall be made on the basis of the most representative samples available, including file samples, at the time of the appeal inspection service.

(2) *Submitted sample service.* Each appeal inspection service on the commodity in a submitted sample shall be based on an analysis of the file sample.

(d) *Board appeal inspection service.* Each Board appeal inspection service performed on a commodity lot or submitted sample shall be based on an analysis of the file sample.

(e) *Use of file samples.*—(1) *Requirements for use.* A file sample that is retained by official personnel in accordance with the procedures prescribed in the instructions may be considered representative for retest inspection, appeal inspection, and Board appeal inspection service if (i) the file sample have remained at all times in the custody and control of the official personnel that performed the inspection service in question and (ii) the official personnel who performed the inspection service in question and those who are to perform the retest inspection, the appeal inspection, or the Board appeal inspection service determines that the samples were representative of the commodity at the time the inspection service in question was performed and that the qualify or condition of the commodity in the samples has not since changed.

(2) *Certificate statement.* The certificate for a retest inspection, appeal inspection, or Board appeal inspection service which is based on a file sample shall show the statement "Results based on file sample."

**§ 68.36 Loss of identity.**

(a) *Lots.* The identity of a packaged lot, bulk lot, or sublot of a commodity shall be considered lost if:

(1) A portion of the commodity is unloaded, transferred, or otherwise removed from the carrier or location after the time of original inspection, unless the identity is preserved; or

(2) More commodity or other material, including a fumigant or insecticide, is added to the lot after the original inspection was performed, unless the addition of the fumigant or insecticide was performed according to instructions; or

(3) At the option of official personnel performing an appeal inspection or Board appeal inspection service, the identity of a commodity is a closed carrier or container may be considered lost if the carrier or container is not sealed or the seal record is incomplete.

(b) *Carriers and containers.* The identity of a carrier or container shall be considered lost if (1) the stowage area is cleaned, treated, fumigated, or fitted after the original inspection was performed or (2) the identification has been changed since the original inspection.

(c) *Submitted sample.* The identity of a submitted sample of a commodity shall be considered lost if:

(1) The identifying number, mark, or symbol for the sample is lost or destroyed; or

(2) The sample has not been retained and protected by official personnel as prescribed in the instructions.

**Original Inspection Service**

**§ 68.40 Who may request original inspection service.**

Any interested person may apply for inspection service.

**§ 68.41 Contract service.**

Any interested person may enter into a contract with a cooperator or the Service whereby the cooperator or Service will provide original inspection services for a specified period, and the applicant will pay a specific fee.

**§ 68.42 How to request original inspection service.**

(a) *General.* Requests may be made verbally or in writing. All verbal requests shall be confirmed in writing when requested by official personnel. All written requests shall include the information specified in § 68.21. Copies of request forms may be requested from the cooperator or the Service. If all required documentation is not available when the request is made, it shall be provided as soon as it is available. At their discretion, official personnel may withhold inspection service pending receipt of the required documentation.

(b) *Request requirements.* Requests for original inspection service, other than submitted sample inspections, must be made with the cooperator or the Service responsible for the area in which the service will be provided. Requests for submitted sample inspections may be made with any cooperator or any field office that provides original inspection service. Requests for inspection of commodities during loading, unloading, handling, or processing shall be received for enough in advance so official personnel can be present.

**§ 68.43 Certificating original inspection results.**

Official certificates shall be issued in accordance with § 68.70 and the instructions.

**§ 68.44 New original inspection.**

When circumstances prevent a retest inspection, appeal inspection, or Board appeal inspection, an applicant may request a new original inspection on any previously inspected lot; except that a new original inspection may not be performed on an identifiable commodity lot which, as a result of a previous inspection, was found to be contaminated with filth, other than insect fragments in nongraded processed products, or to contain a deleterious substance. A new original inspection shall be based on a new sample and shall not be restricted to the scope of any previous inspection. The applicant may request subsequently any or all of the inspection services provided for by the regulations. A new original inspection certificate shall not supersede any previously issued certificate.

Retest Inspection Service

**§ 68.50 Who may request retest inspection service.**

(a) *General.* Any interested person may request a retest inspection service on nongraded commodities. When more than one interested person requests a retest inspection service, the first interested person to file is the applicant of record. Only one retest inspection service may be performed on any original inspection service.

(b) *Scope of request.* A retest inspection service may be requested for any or all quality factors tested but shall be limited to analysis of the file sample.

**§ 68.51 How to request retest inspection service.**

(a) *General.* Requests shall be made with the field office responsible for the area in which the original inspection service was performed. Verbal requests shall be confirmed in writing as specified in § 68.21. Copies of request forms may be obtained from the field office upon request. If at the time the request is filed and the documentation required by § 68.21 is not available, official personnel may, at their discretion, withhold service pending the receipt of the required documentation.

(b) *Request requirements.* Requests will be considered filed on the date they are received by official personnel.

**§ 68.52 Certificating retest results.**

(a) *General.* Retest inspection certificates shall be issued according to § 68.70 and instructions. The certificate shall show the results of the factor(s) retested and the original results for all other factors and/or service not included in the retest service.

(b) *Required statements on retest certificates.* Each retest inspection certificate shall show the statements required by this section, § 68.71, and the instructions.

(1) Each retest inspection certificate shall clearly show the term "Retest" and a statement identifying the superseded certificate. The superseded certificate shall be considered null and void as of the date of the retest certificate. When applicable, the certificate shall also show a statement as to which factor(s) result is based on the retest inspection service and that all other results are those of the original inspection service.

(2) If the superseded certificate is in the custody of the Service, the superseded certificate shall be marked "Void." If the superseded certificate is not in the custody of the Service at the time the retest certificate is issued, a statement indicating that the superseded certificate has not been surrended shall be shown on the retest certificate.

Appeal Inspection Service

**§ 68.60 Who may request appeal inspection service.**

(a) *General.* Any interested person may request appeal inspection or Board appeal inspection service. When more than one interested person requests an appeal inspection or Board appeal inspection service, the first interested person to file is the applicant of record. Only one appeal inspection may be obtained from any original inspection or retest inspection service. Only one Board appeal inspection may be obtained from any original or appeal inspection service. Board appeal inspection shall be performed on the basis of the file sample.

(b) *Kind and scope of request.* When the results for more than one kind of service are reported on a certificate, an appeal inspection or Board appeal inspection service, as applicable, may be requested on any or all kinds of services reported on the certificate. The scope of an appeal inspection service will be limied to the scope of the original inspection or, in the case of a Board appeal inspection service, the original or appeal inspection service. If the request specifies a different scope, the request shall be dismissed. An appeal inspection for grade shall include a review of all factors that (1) may determine the grade; or (2) are reported on the original or, in the case of a Board appeal inspection, the original or appeal inspection certificate; and (3) are required to be shown on a certificate for grade.

**§ 68.61 How to request appeal inspection service.**

(a) *General.* Requests shall be made with the field office responsible for the area in which the original service was performed. Requests for Board appeal inspections may be made with the Board of Appeals and Review or the field office that performed the appeal inspection. Verbal requests must be confirmed in writing as specified in § 68.21. Copies of request forms may be obtained from the field office upon request. If at the time the request is mad the documentation required by § 68.21 is not available, official personnel may, at their discretion, withhold service pending the receipt of the required documentation.

(b) *Request requirements.* (1) This paragraph is applicable to rice inspection only. Except as may be agreed upon by the interested persons, the application shall be made (i) before the rice has left the place where the inspection being appealed was performed and (ii) no later than the close of business on the second day following the date of the inspection being appealed. However, the Administrator may extend the time requirement.

(2) Subject to the limitations of paragraph (b)(3) of this section, the applicant may request that an appeal inspection be based on (i) the file sample or (ii) a new sample. However, an appeal inspection shall be based on a new sample only if the lot can positively be identified by official personnel as the one that was previously inspected and the entire lot is available and accessible for sampling and inspection. Board appeals shall be on the basis of the file sample.

(3) An appeal inspection shall be limited to a review of the sampling procedure and an analysis of the file sample when, as a result of a previous inspection, the commodity was found to be contaminated with filth (other than insect fragments in nongraded processed products) or to contain a deleterious substance. If it is determined that the sampling procedures were improper, a new sample shall be obtained if the lot can be positively identified as the lot which was previously inspected and the entire lot is available and accessible for sampling and inspection.

**§ 68.62 Who shall perform appeal inspection service.**

(a) *Appeal.* Appeal inspection service shall be performed by the field office responsible for the area in which the original inspection was performed.

(b) *Board appeal.* Board appeal inspection service shall be perfomed only by the Board of Appeals and Review. The field office will act as a liaison between the Board of Appeals and Review and the applicant.

**§ 68.63 Certificating appeal results.**

(a) *General.* Appeal inspection certificate shall be issued according to § 68.70 and instructions. Except as provided in paragraph (b)(2) of this section, only the results of the appeal inspection or Board appeal inspection service shall be shown on the appeal inspection certificate.

(b) *Required statements.* Each appeal inspection certificate shall show the statements required by this section, § 68.71, and instructions.

(1) Each appeal inspection certificate shall clearly show (i) the term "Appeal," or "Board Appeal" and (ii) a statement identifying the superseded certificate. The superseded certificate shall be considered null and void as of the date

of the appeal inspection or Board appeal inspection certificate.

(2) When the results for more than one kind of service are reported on a certificate, the appeal or Board appeal inspection certificate shall show a statement of which kind of service(s) results are based on the appeal or Board appeal inspection service; and that all other results are those of the original inspection, retest, or appeal inspection service.

(3) If the superseded certificate is in the custody of the Service, the superseded certificate shall be marked "Void." If the superseded original inspected, retest inspection, or appeal inspection certificate is not in the custody of the Service at the time the appeal certificate is issued, a statement indicating that the superseded certificate has not been surrendered shall be shown on the appeal certificate.

(c) *Finality of Board appeal inspection.* A Board appeal inspection shall be the final appeal inspection service.

**Official Certificates**

**§ 68.70 Official certificates; issuance and distribution.**

(a) *Required issuance.* An inspection certificate shall be issued to show the results of each kind and each level of inspection service.

(b) *Distribution.*—(1) *Original.* The original and one copy of each inspection certificate shall be distributed to the applicant or the applicant's order. In addition, one copy of each inspection certificate shall be filed with the office providing the inspection; and, if the inspection is performed by a cooperator, one copy shall be forwarded to the appropriate field office. If requested by the applicant prior to issuance of the inspection certificate, additional copies not to exceed a total of three copies will be furnished at no extra charge.

(2) *Retest and appeal inspection service.* In addition to the distribution requirements in subparagrah(b)(1) of this section, one copy of each retest or appeal inspection certificate will be distributed to each interested person of record or the interested person's order and to the cooperator or field office that issued the superseded certificate.

(3) *Additional copies.* Additional copies of certificates will be furnished to the applicant or interested person upon request. Fees for extra copies may be assessed according to the fee schedules established by the cooperator or the Service.

(c) *Prompt issuance.* An inspection certificate shall be issued before the close of business on the business day following the date the inspection is completed.

(d) *Who may issue a certificte.*—(1) *Authority.* Certificates for inspection services may be issued only by official personnel who are specifically authorized or licensed to perform and certify the results reported on the certificate.

(2) *Exception.* The person in the best position to know whether the service was performed in an approved manner and that the determinations are accurate and true should issue the certificate. If the inspection is performed by one person, the certificate should be issued by that person. If an inspection is performed by two or more persons, the certificate should be issued by the person who makes the majority of the determinations or the person who makes the final determination. Supervisory personnel may issue a certificate when the individual is licensed or authorized to perform the inspection being certificated.

(e) *Name requirement.* The name and the signature of the person who issued the inspection certificate shall be shown on the original and all copies of the certificate.

(f) *Authorization to affix names.*—(1) *Requirements.* The names and the signatures of official personnel may be affixed to official certificates which are prepared from work records signed or initialed by the person whose name will be shown. The agent affixing the name and signature shall (i) be employed by a cooperating agency or the Service, (ii) have been designated to affix names and signatures, and (iii) hold a power of attorney from the person whose name and signature will be affixed. The power of attorney shall be on file with the employing cooperating agency or the Service, as appropriate.

(2) *Initialing.* When a name and signature is affixed by an authorized agent, the initials of the agent shall appear directly below or following the signature of the person.

(g) *Advance information.* Upon request, the contents of an official certificate may be furnished in advance to the applicant and any other interested person, or to their order, and any additional expense shall be borne by the requesting party.

(h) *Certification; when prohibited.* An official certificate shall not be issued for service after the request for an inspection service has been withdrawn or dismissed.

(Approved by the Office of Management and Budget under control number 0580-0011).

**§ 68.71 Official certificate requirements.**

Official certificates shall (1) be on standard printed forms prescribed in the instructions; (2) be in English; (3) be typewritten or handwritten in ink and be clearly legible; (4) show the results of inspection services in a uniform, accurate, and concise manner; (5) show the information required by §§ 68.70–.75; and (6) show only such other information and statements of fact as are provided in the instructions authorized by the Administrator.

**§ 68.72 Certification of results.**

(a) *General.* Each official certificate shall show the results of the inspection services.

(b) *Graded commodities.* Each official certificate for graded commodities shall show (1) the class, grade, and any other quality designation according to the official grade standards; (2) all factor information requested by the applicant; and (3) all grade determining factors for commodities graded below the highest quality grade.

**§ 68.73 Corrected certificates.**

(a) *General.* The accuracy of the statements and information shown on official certificates must be verified by the individual whose name and signature is shown on the official certificate or by the authorized agent who affixed the name and signature. Errors found during this process shall be corrected according to this section.

(b) *Who may correct.* Only official personnel or their authorized agents may make corrections, erasures, additions, or other changes to official certificates.

(c) *Corrections prior to issuance.* No corrections, erasures, additions, or other changes can be made which involve identification, quantity, or quality. If errors are found, a new official certificate shall be prepared and issued and the incorrect certificate marked "Void." Otherwise, errors may be corrected provided that (1) the corrections are neat and legible, (2) each correction is initialed by the individual who corrects the certificate, and (3) the corrections and initials are shown on the original and all copies.

(d) *Corrections after issuance.*—(1) *General.* If errors are found on an official certificate at any time up to a maximum of 1 year after issuance, the errors shall be corrected by obtaining the incorrect certificate and replacing it with a corrected certificate. When the incorrect certificate cannot be obtained, a corrected certificate can be issued superseding the incorrect one.

(2) *Certification requirements.* The same statements and information, including permissive statements, that were shown on the incorrect certificate, along with the correct statement or information, shall be shown on the corrected certificate. According to this section and the instructions, corrected certificates shall show (i) the terms "Corrected-Original" and "Corrected-Copy;" (ii) a statement identifying the superseded certificate and the corrections; (iii) a statement indicating the superseded certificate was not surrendered when the incorrect certificate was not submitted; and (iv) a new serial number. In addition, the incorrect certificate shall be marked "Void" when submitted.

(e) *Limitations.* Corrected certificates cannot be issued for a certificate that has been superseded by another certificate or on the basis of a subsequent analysis for quality.

**§ 68.74 Divided-lot certificates.**

(a) *General.* When commodities are offered for inspection and are certificated as a single lot, the applicant may exchange the inspection certificate for two or more divided-lot certificates.

(b) *Application.* Requests for divided-lot certificates shall be made (1) in writing, (2) by the applicant who made the initial request, (3) to the office that issued the outstanding certificate, (4) within 5 business days of the outstanding certificate date, and (5) before the identity of the commodity has been lost.

(c) *Quantity restrictions.* Divided-lot certificates shall not show an aggregate quantity different than the total quantity shown on the superseded certificate.

(d) *Surrender of certificate.* The certificate that will be superseded shall (1) be in the custody of the cooperator or the Service, (2) be marked "Void," and (3) show the identification of the divided-lot certificates.

(e) *Certification requirements.* The same information and statements, including permissive statements, that were shown on the superseded certificate shall be shown on each divided-lot certificate. Divided-lot certificates shall show (1) a statement indicating the commodity was inspected as an undivided lot; (2) the terms "Divided Lot-Original," and the copies shall show "Divided Lot-Copy;" (3) the same serial number with numbered suffix (for example, 1764–1, 1764–2, 1764–3, and so forth); and (4) the quantity specified by the request.

(f) *Issuance and distribution.* Divided-lot certificates shall be issued no later than the close of business on the next business day after the request and the distributed according to § 68.70(b).

(g) *Limitations.* After divided-lot certificates have been issued, further dividing or combining is prohibited except with the approval of the Service.

**§ 68.75 Duplicate certificates.**

Upon request, a duplicate certificate may be issued for a lost or destroyed official certificate.

(a) *Application.* Requests for duplicate certificates shall be filed (1) in writing, (2) by the applicant who requested the service covered by the lost or destroyed certificate, and (3) with the office that issued the initial certificate.

(b) *Certification requirements.* The same information and statements, including permissive statements, that were shown on the lost or destroyed certificate shall be shown on the duplicate certificate. Duplicate certificates shall show (1) the terms "Duplicate-Original," and the copies shall show "Duplicate-Copy" and (2) a statement that the certificate was issued in lieu of a lost or destroyed certificate.

(c) *Issuance.* Duplicate certificates shall be issued as promptly as possible and distributed according to § 68.70(b).

(d) *Limitations.* Duplicate certificates shall not be issued for certificates that have been superseded.

**Licensed Inspectors, Technicians, and Samplers**

**§ 68.80 Who may be licensed.**

(a) *Inspectors.* The Administrator may license any person to inspect commodities and to perform related services if the individual (1) is employed by a cooperator; (2) possesses the qualifications prescribed in the instructions; and (3) has no interest, financial or otherwise, direct or indirect in merchandising, handling, storing, or processing the kind of commodities or related products to be inspected. The Administrator may require applicants to be examined for competency at a specific time and place and in a prescribed manner.

(b) *Technicians or samplers.* The Administrator may license any person as a technician to perform official specified laboratory functions, including sampling duties and related services or as a sampler to draw samples of commodities and perform related services if the individual (1) possesses proper qualifications and (2) has no interest, direct or indirect in merchandising, handling, storing, or processing the commodities or related products to be chemically analyzed, mechanically tested, sampled, and so forth. The Administrator may require applicants to be examined for competency at a specific time and place and in a prescribed manner.

(The information collection requirements contained in paragraph (b) have been approved by the Office of Management and Budget under contol number 0580–0011.)

**§ 68.81 Licensing procedures.**

(a) *Application.* An application for a license, the renewal of a license, or the return of a suspended license shall be submitted to the Service on forms furnished by the Service. Each application shall be in English, be typewritten or legibly written in ink, show all information prescribed by the application form, and be signed by the applicant.

(b) *Examinations and reexaminations.* Applicants for a license and individuals who are licensed to perform any or all inspection services shall, at the discretion of the Service, submit to examinations or reexaminations to determine their competency to perform the inspection functions for which they desire to be or are licensed.

(c) *Termination.*—(1) *Procedure.* Each license shall terminate according to the termination date shown on the license and as specified by the schedule in this paragraph. The termination date for a license shall be no less than 3 years or more than 4 years after the issuance date for the initial license; thereafter, every 3 years. Upon request of a licensee and for good cause shown, the termination date may be advanced or delayed by the Administrator for a period not to exceed 60 days.

TERMINATION SCHEDULE

| Last name beginning with | Termination date |
|---|---|
| A | January. |
| B | February. |
| C, D | March. |
| E, F, G | April. |
| H, I, J | May. |
| K, L | June. |
| M | July. |
| N, O, P, Q | August. |
| R | September. |
| S, T, U, V | October. |
| W | November. |
| X, Y, Z | December. |

The Service shall issue a termination notice 60 days before the termination date. The notice shall give detailed instruction for requesting renewal of license, state whether a reexamination is required, and, if a reexamination is required, give the scope of the examination. Failure to receive a notice from the Service shall not exempt a licensee from the responsibility of having the license renewed by the termination date.

(2) *Exception.* The license of an individual under contract with the Service shall terminate upon termination of the contract.

(d) *Surrender of license.* Each license that is terminated or which is suspended or cancelled under § 68.84 shall be promptly surrendered to the Administrator or other official of the Service designated by the Administrator.

**§ 68.82 Voluntary cancellation or suspension of license.**

Upon request by a licensee, the Service may cancel a license or suspend a license for a period of time not to exceed 1 year. A license that has been voluntarily suspended shall be returned by the Service upon request by the licensee within 1 year, subject to the provisions of § 68.81(a); a license that has been cancelled shall be considered void and shall not be subject to return or renewal.

**§ 68.83 Automatic suspension of license by change in employment.**

A license issued to an individual shall be automatically suspended when the individual ceases to be employed by the cooperator. If the individual is reemployed by the cooperator or employed by another cooperator within 1 year of the suspension date and the license has not terminated in the interim, upon request of the licensee, the license will be reinstated subject to the provisions of § 68.81(a) and (b).

**§ 68.84 Suspension or revocation of license.**

(a) *General.* An inspector's, technician's, or sampler's license may be suspended or revoked if the licensee (1) through willfulness, carelessness, or incompetence fails to perform the duties specified in the regulations and in the instructions and procedures prescribed by the Administrator or (2) becomes incapable of performing required duties.

(b) *In cases of willfulness or those in which the pubic health, interest, or safety are involved.* The Administrator may summarily suspend an inspector's, technician's or sampler's license without hearing pending investigation. However, the licensee shall be advised of the facts which appear to warrant suspension or revocation of the license. The licensee shall also be accorded an opportunity for a hearing before an official in the Department before the license is finally suspended or revoked.

(c) *In cases not involving willfulness or cases which the public health, interest, or safety are not involved.* The Administrator, before instituting proceedings for the suspension or revocation of a license, shall have served upon the licensee, in person or by registered mail, a statement of the facts which appear to warrant such suspension or revocation. The statement shall also specify a reasonable time, depending upon the circumstances, within which the licensee may demonstrate or achieve compliance with the Act, regulations, standards, instructions, and procedures prescribed by the Administrator. A licensee may demonstrate compliance by the presentation of evidence in writing or, at the discretion of the Administrator, at an oral hearing. If, at the end of the time allowed for demonstration or achievement of compliance, the Administrator finds the licensee in compliance, proceeding for the suspension or revocation of the licensee shall not be instituted. If the licensee is not in compliance, the Administrator may institute proceedings. However, a licensee may not be suspended or revoked until the individual (1) has been served notice, in person or by registered mail, that suspension or revocation of the license is under consideration for reasons set out in the previously served statement and (2) has been given an opportunity for a hearings before a proper Departmental official.

## Fees

**§ 68.90 Fees for certain Federal inspection services.**

The following fees apply to the Federal inspection services specified below.

### Fees for Inspection of Hops, Pulses, Hay, Straw and Miscellaneous Processed Commodities

TABLE 1—HOURLY RATES

| Service[1] | Regular workday (Monday-Saturday) | Nonregular workday (Sunday and Holiday) |
|---|---|---|
| Contract (per hour per Service representative) | $18.40 | $21.00 |
| Noncontract (per hour per Service representative) | 22.40 | 25.40 |

[1] Original and appeal inspection services include: grading, sampling, factor analysis, checkweighing, checkloading, condition examination, demonstration of grading, and other services requested by the applicant when performed at the point of service.

TABLE 2—UNIT RATES

| Service[1] | Bean, Pea and Lentil | Hay and Straw | Hops | Nongraded, nonprocessed commodities |
|---|---|---|---|---|
| Lot or sample (per lot or sample) | | $15.00 | $22.40 | |
| Field run (per lot or sample) | $15.00 | | | |
| Other than field run (per lot or sample) | 11.20 | | | |
| Factor analysis (per factor) | 3.75 | 3.75 | | $3.75 |
| Extra copies of certificates (per copy) | 3.00 | 3.00 | 3.00 | 3.00 |

[1] Fees apply to determinations (original or appeal) for kind, class, grade, factor analysis, and any other quality designation as defined in the official U.S. Standards or applicable instructions when performed at other than the point of service.

TABLE 3—LABORATORY FEES [1]

| | Fees |
|---|---|
| Laboratory report | $3.00 |
| Laboratory testing: | |
| (a) In addition to the fees if any, for sampling or other requested service a fee will be assessed for each laboratory test as follows: | |
| (1) Acidity Greek | 6.30 |
| (2) Acid value-oil | 6.30 |
| (3) Aflatoxin (Minicolumn method) | 18.90 |
| (4) Aflatoxin (TLC) | 44.00 |
| (5) Appearance, flavor and odor-oils | 3.15 |
| (6) Arachidic acid | 12.10 |
| (7) Ash | 7.60 |
| (8) Bacteria count | 7.90 |
| (9) Baking test-bread | 18.90 |
| (10) Baking test-cake | 26.50 |
| (11) Baking test-cookies | 23.60 |

TABLE 3—LABORATORY FEES [1]—Continued

| | Fees |
|---|---|
| (12) Baume | 6.30 |
| (13) Bostwick (cooked) | 12.60 |
| (14) Bostwick (uncooked) | 6.30 |
| (15) Calcium (AOAC) | 7.90 |
| (16) Calcium enrichment | 7.90 |
| (17) Carotenoid color | 9.45 |
| (18) Checked and broken macaroni units | 6.30 |
| (19) Clarity of oil involving heating | 6.30 |
| (20) Cold test-oil | 6.30 |
| (21) Coliform | 18.90 |
| (22) Color-bleached | 9.45 |
| (23) Color-gardner | 3.15 |
| (24) Color-lovibond | 3.15 |
| (25) Color-oil and shortening | 3.15 |
| (26) Congeal point | 15.10 |
| (27) Cooking test | 6.30 |
| (28) Crude fat | 6.30 |
| (29) Crude fiber | 10.10 |
| (30) Density | 6.30 |
| (31) Dextrose equivalent | 18.00 |
| (32) Diastatic activity of flour | 18.90 |
| (33) Enrichment-quick test | 3.15 |
| (34) Falling number | 6.30 |
| (35) Farinograph characteristics | 23.60 |
| (36) Fat-acid hydrolysis | 12.60 |
| (37) Fat acidity | 9.45 |
| (38) Fat stability-AOM | 12.60 |
| (39) Filth-heavy | 15.60 |
| (40) Filth-light | 18.90 |
| (41) Flash point-open and close cup | 9.45 |
| (42) Foam test | 18.90 |
| (43) Foots-heated and/or chilled | 6.30 |
| (44) Foreign material-processed grain products | 9.45 |
| (45) Free fatty acids | 6.30 |
| (46) Heating test-oil and shortening | 6.30 |
| (47) Hydrogen ion activity pH | 9.45 |
| (48) Insoluble bromides | 6.30 |
| (49) Insoluble impurities-oil and shortening | 6.30 |
| (50) Iodine number or value | 9.45 |
| (51) Iron enrichment | 12.60 |
| (52) Linolenic acid (fatty acid profile) | 12.10 |
| (53) Lipid phosphorous | 47.00 |
| (54) Loaf volume | 18.90 |
| (55) Lysine from fortification | 23.10 |

TABLE 3—LABORATORY FEES [1]—Continued

| | Fees |
|---|---|
| (56) Lysine form hydrolysis of protein | 12.10 |
| (57) Maltose value-flour | 18.90 |
| (58) Marine oil in vegetable oil-qualitative | 6.30 |
| (59) Melting point-Wiley | 12.60 |
| (60) Moisture-distillation | 9.45 |
| (61) Moisture-oven | 4.40 |
| (62) Moisture and volatile matter-oil and shortening | 6.30 |
| (63) Neutral oil loss | 18.90 |
| (64) Nitrogen solubility index | 15.70 |
| (65) Oven leak test-oil can | 9.45 |
| (66) Oil content-oilseed | 9.45 |
| (67) Particle size-flour | 14.90 |
| (68) Performance test-prepared bakery mix | 21.70 |
| (69) Peroxide value | 6.30 |
| (70) Phosphorous | 12.60 |
| (71) Popping value-popcorn | 18.90 |
| (72) Potassium bromate-qualitative | 3.15 |
| (73) Potassium bromate-quantitative | 9.45 |
| (74) Protein dispersibility index | 15.70 |
| (75) Protein, Kjeldahl | 7.30 |
| (76) Purity-Monosodium glutamate | 24.20 |
| (77) Reducing sugars | 18.90 |
| (78) Refractive index | 9.45 |
| (79) Riboflavin | 25.20 |
| (80) Rope spore count | 31.50 |
| (81) Salmonella | 37.00 |
| (82) Salt content | 9.45 |
| (83) Saponification number | 9.45 |
| (84) Sedimentation | 15.70 |
| (85) Sieve test | 4.40 |
| (86) Smoke point | 9.45 |
| (87) Softening point | 12.60 |
| (88) Solid fat index | 21.80 |

TABLE 3—LABORATORY FEES [1]—Continued

| | Fees |
|---|---|
| (89) Specific baking volume-cake mix | 21.80 |
| (90) Specific gravity-oils | 12.60 |
| (91) Starch damage-flour | 14.90 |
| (92) Staphylococcus aureas | 24.50 |
| (93) Sucrose | 18.90 |
| (94) Test weight per bushel-other than grain | 2.60 |
| (95) Tilletia controversa Kuhn (TCK) | 25.20 |
| (96) Unsaponifiable matter | 12.60 |
| (97) Urease activity | 9.45 |
| (98) Viscosity | 12.60 |
| (99) Water soluble protein | 15.70 |
| (100) Xanthydrol test for rodent urine | 12.60 |
| (101) Other laboratory tests | [2] |
| (b) If a requested test is to be reported on a specified moisture basis, a fee for moisture test will also be assessed. | |

[1] When laboratory testing service is provided for FGIS by a private laboratory, the applicant will be assessed a fee which, as nearly as practicable, covers the costs to FGIS for the service provided.

[2] Fees for other laboratory tests not referenced above will be based on the noncontract hourly rate listed in Table 1.

### § 68.91 Fees for certain Federal rice inspection services.

The fees shown in tables 4 and 5 apply to Federal rice inspection services.

Fees for Federal Rice Inspection Services.

TABLE 4—HOURLY RATES

| Service [1] | Regular workday (Monday-Saturday) | Nonregular workday (Sunday and Holiday) |
|---|---|---|
| Contract (per hour per Service representative) | $28.40 | $39.40 |
| Noncontract (per hour per Service representative) | 34.40 | 48.00 |

[1] The hourly rate includes sampling, grading, weighing and other services requested by the applicant when performed at the point of service.

TABLE 5—UNIT RATES

| Service [1] | Rough Rice | Brown Rice for processing | Milled Rice |
|---|---|---|---|
| Inspection for quality (per lot, sublot, or sample inspection) | $23.00 | $20.00 | $14.30 |
| Factor analysis for any single factor (per factor) | 8.60 | 8.60 | 8.60 |
| Interpretive line samples: [2] | | | |
| (a) Milling degree (per set) | | | 60.00 |
| (b) Parboiled light (per sample) | | | 15.00 |
| Extra copies of certificates (per copy) | 3.00 | 3.00 | 3.00 |

[1] Fees apply to determinations (original or appeals) for kind, class, grade, factor analysis, equal to type, milling yield, or any other quality designation as defined in the U.S. Standards for Rice or applicable instructions, whether performed singly or combined at other than the point of service.

[2] Interpretive line samples may be purchased from the U.S. Department of Agriculture, Federal Grain Inspection Service, Field Management Division, Board of Appeals and Review, Richards-Gebaur AFB, Building #221, Grandview, MO 64030. Interpretive line samples also are available for examination at selected FGIS field offices. A list of field office may be obtained from the Deputy Director, Field Management Division, USDA, FGIS, Washington, DC 20250.

The interpretive line samples illustrate the lower limit for milling degrees only and the color limit for the factor "Parboiled Light" rice.

### § 68.92 Explanation of service fees and additional fees.

(a) *Costs included in the fees.* Fees for official services in §§ 68.90 and 68.91 include (1) the cost of performing the service and related supervision and administrative costs; (2) the cost of per diem, subsistence, mileage, or commercial transportation to perform the service; (3) the cost of first-class mail service; (4) the cost of overtime and premium pay; and (5) the cost of certification except as provided in § 68.92)(c).

(b) *Computing hourly rates.* Hourly fees will be assessed in quarter hour increments for (1) travel from the FGIS field office or assigned duty location to the service point and return and (2) the performance of the requested service, less mealtime.

(c) *Additional fees.* Fees in addition to the applicable hourly or unit fee will be assessed when (1) an applicant requests more than the original and three copies of a certificate, (2) an applicant requests onsite typing of certificates or typing of certificates at the FGIS field office during other than normal working hours, and (3) an applicant requests the use of express-type mail or courier service.

(d) *Application of fees when service is delayed by the applicant.* Hourly fees will be assessed when (1) service has been requested at a specified location, (2) a Service representative is on duty and ready to provide service but is unable to do so because of a delay not caused by the Service, and (3) FGIS officials determine that the Service representative(s) cannot be utilized elsewhere or cannot be released without cost to the Service.

(e) *Application of fees when an application for service is withdrawn or dismissed.* Hourly fees will be assessed to the applicant for the scheduled service if the request is withdrawn or dismissed after the Service representative departs for the service point or if the request for service is not withdrawn or dismissed by 2 p.m. of the business day preceding the date of scheduled service. However, hourly fees will not be assessed to the applicant if FGIS officials determine that the Service representative can be utilized elsewhere or if the Service represenative can be released without cost to the Service.

(f) *To whom fees are assessed.* Fees for official services including additional fees as provided in § 68.92(c) shall be assessed to and paid by the applicant for the service.

(g) *Advance payment.* As necessary, the Administrator may require that fees shall be paid in advance of the performance of the requested service. Any fees paid in excess of the amount due shall be used to offset future billings, unless a request for a refund is made by the applicant.

(h) *Time and form of payment.* (1) *Fees for Federal inspection service.* Bills for fees assessed under the regulations for official services performed by FGIS shall be paid by check, draft, or money order, payable to U.S. Department of Agriculture, Federal Grain Inspection Service.

(2) *Fees for cooperator inspection service.* Fees for inspection services provided by a cooperator shall be paid by the applicant to the cooperator in accordance with the cooperator's fee schedule.

Dated: December 2, 1985.

**D.R. Galliart,**

*Acting Administrator.*

[FR Doc. 85-30277 Filed 12-23-85; 8:45 am]

BILLING CODE 3410-EN-M

## FEDERAL HOME LOAN BANK BOARD

## 12 CFR Parts 543 and 544

[No. 85-1068]

## Corporate Governance II

Dated: November 22, 1985.

**AGENCY:** Federal Home Loan Bank Board.

**ACTION:** Proposed rule.

**SUMMARY:** The Federal Home Loan Bank Board is proposing extensive revisions to its regulations regarding the corporate governance of Federal associations, in order to update and clarify its rules in this important area. Due to the magnitude of the revisions, the Board intends to present the proposal in four parts which will be issued separately for public comment. The proposed regulations would reorganize portions of Subchapter C (the regulations for federally chartered associations), and amend and add sections to provide a more cohesive and complete body of rules for the corporate governance of Federal associations. Part I would provide proposed definitions and set forth rules for the organization and incorporation of Federal associations. Part II would contain provisions regarding Federal stock associations and Federal mutual associations. Part III would propose revisions to the rules governing operations of charter coversion to Federal associations. Part IV would contain provisions regarding conservators, receivers, trust powers, miscellaneous provisions, Board rulings and statements of policy. Part I was proposed on September 13, 1985, (50 FR 38832, September 25, 1985.)

**DATE:** Comments on the proposal should be received by February 24, 1986.

**ADDRESS:** Send comments to the Director, Public Information Services Section, Office of the Secretariat, Federal Home Loan Bank Board, 1700 G Street, NW., Washington, DC, 20552. Comments will be available for public inspection at the above address.

**FOR FURTHER INFORMATION CONTACT:** David A. Permut, Senior Attorney, (202-377-6962); V. Gerard Comizio, Attorney, (202-377-6457); Patricia D. Neidecker, Paralegal, (202-377-6410); Laura Patriarca, Deputy Director, (202-377-6411) or Julie L. Williams, Associate General Counsel and Director, (202-377-6459); Corporate and Securities Division, Office of General Counsel, at the above address.

**SUPPLEMENTARY INFORMATION:**

### I. Overview

On October 15, 1982, the Garn-St Germain Depository Institutions Act of 1982 ("Act"), Pub. L. 97-320, was enacted. The Act greatly broadened the types of charters and organizational options open to Federal associations. Previously, Federal associations could be organized on a *de novo* basis only as Federal mutual institutions with accounts insured by the Federal Savings and Loan Insurance Corporation, and only as a direct consequence of a conversion from a state-chartered mutual savings bank. The Act substantially expanded the Board's authority in this area, permitting not only *de novo* organization of Federal savings banks but also allowing any current or future Federal associations to be chartered either as a Federal savings and loan association or Federal savings bank. Further, the Act enabled Federal charters, whether in the stock or mutual form, to be obtained by state-chartered savings banks without the requirement that they surrender their Federal Deposit Insurance Corporation insurance in favor of Federal Savings and Loan Insurance Corporation insurance of accounts.

In recognition of the fact that multiple options exist for the organization of *de novo* Federal associations and the conversion of various corporate entities, the Board directed the staff to study whether the existing regulations adequately covered the multiplicity of structural options for Federal associations. As a result, the Board has concluded preliminarily that the existing regulations cover many of the options, but in a piecemeal fashion, and that a number of important matters relating to the corporate governance of Federal associations either have not been adequately covered or have not been addressed in codified form. Consequently, the Board has preliminarily determined to propose a substantial updating of its regulations for corporate governance of Federal associations. The following proposed amendments to the Federal regulations were developed, following an extensive review of the Model Business Corporation Act ("MBCA"), the corporate codes of Delaware, California, New York and Florida, and the Board's experience with the specific statutory requirements involved in chartering or converting Federal associations, set forth under the Home Owners' Loan Act of 1933, as amended ("HOLA") 12 U.S.C. 1464 *et seq. See* Corporate Governance, Part I (50 FR 38832).

### II. Reorganization

The Board believes that the existing organization of the Federal Regulations could be improved, in order to present a more logical and cohesive structure, so that the public would not be required to hunt for the various rules governing Federal associations. The following chart was developed to reorganize the Federal Regulations:

**Regulations for the Federal Savings and Loan System**

| Present | Proposed |
|---|---|
| **Part I** | |
| Part 541—Definitions | Part 541—Definitions |
| Part 542—[removed 6/3/79] | Part 542—Organization and Incorporation of Federal Associations |
| **Part II** | |
| Part 543—Incorporation, Organization and Conversion of Federal Mutual Associations | Part 543—Federal Stock Associations |
| Part 544—Charter and Bylaws | Part 544—Federal Mutual Associations |
| **Part III** | |
| Part 545—Operations | Part 545—Operations |
| Part 546—Merger, Dissolution, Reorganization and Conversion | Part 546—Conversion of and to Federal Associations |
| **Part IV** | |
| Part 547—Appointment of Conservators and Receivers | Part 547—Appointment of Conservators and Receivers |
| Part 548—Powers of Conservator and Conduct of Conservatorship | Part 548—Powers of Conservator and Conduct of Conservatorship |
| Part 549—Powers of Receiver and Conduct of Receivership | Part 549—Powers of Receiver and Conduct of Receivership |
| Part 550—Trust Powers of Federal Associations | Part 550—Trust Powers of Federal Associations |
| Part 551—Service of Process Upon Board | Part 551—Miscellaneous |
| Part 552—Stock Associations | Part 552—Reserved |
| Part 553— | Part 553—Reserved |
| Part 554— | Part 554—Reserved |
| Part 555—Board Rulings | Part 555—Board Rulings |
| Part 556—Statements of Policy | Part 556—Statements of Policy |

### III. Description of the Proposed Amendments in Part II

#### *A. Part 543—Federal Stock Associations*

1. Sections of existing Parts 543, 545, 546 and 552, and a number of new proposed sections have been put into this Part to cover the areas of final organization, charters and bylaws, combinations, bulk purchases or sale of assets, reorganization and dissolution of Federal stock associations.

2. The following 60 sections, appendix and reserved sections are proposed:

Sec.

543.1 Procurement for organization of Federal stock association; intitial sale of capital stock; organizational meeting.
543.2 Powers of Federal stock associations.
543.3 Charter for Federal stock associations.
543.4 Preapproved charter amendments.
543.4-1 Additional charter provisions.

Sec.
543.5 Procedures for obtaining Board approval of charter amendments.
543.6 Reissuance of charter.
543.7 Bylaws.
543.8 Effect of subsequent charter or bylaw change amendment.
543.9 Stockholder meetings.
543.9-1 Stockholder voting.
543.9-2 Voting trusts among stockholders.
543.9-3 Books and records; stockholder access.
543.9-4 Annual reports to stockholders.
543.9-5 Stockholder derivative actions.
543.10 Board of directors.
543.10-1 Director's meetings.
543.10-2 Director's conflicts of interest.
543.10-3 Liability of directors for improper distributions.
543.10-4 Officers.
543.10-5 Indemnification of directors, officers and employees.
543.11 Certificates for stock and their transfer.
543.11-1 Consideration for stock.
543.11-2 Stock rights and options.
543.11-3 Fractional shares of stock.
543.11-4 Liability of stockholders.
543.12 Authority to acquire own stock.
543.12-1 Authority to pay dividends to stockholders.
543.12-2 Limitations on distributions to stockholders.
543.12-3 Reduction of paid-in capital.
543.13 Fiscal year; annual audit.
543.14 Corporate procedures.
543.15-543.19 [Reserved].
543.20 Combinations involving Federal stock associations.
543.21 Merger or consolidation.
543.22 Short-form merger.
543.23 Approval by stockholders for merger or consolidation.
543.24 Articles of combination for merger or consolidation.
543.25 Effective date; date of consummation for merger or consolidation.
543.26 Continuity of corporate existence after merger or consolidation.
543.27 Dissenters' appraisal rights in merger or consolidation.
543.28 Supervisory combinations.
543.29 [Reserved]
543.30 Bulk purchase or sale of assets.
543.31 Approval by stockholders.
543.32 Articles of combination.
543.33 Effective date; date of consummation.
543.34 Continuity of corporate existence after bulk purchase or sale of assets.
543.35 Dissenters' appraisal rights in bulk purchase or sale of assets.
543.36 Partial purchase or sale of assets.
543.37-543.39 [Reserved]
543.40 Reorganization.
543.41-543.49 [Reserved]
543.50 Dissolution.
543.51 Voluntary dissolution.
543.52 Approval by stockholders for dissolution.
543.53 Notice of dissolution.
543.54 Procedure for dissolution after Board and stockholder approval.
543.55 Temination of corporate existence.
543.56 Involuntary dissolution.
543.57-543.59 [Reserved].
543.60 Supervisory waiver.

**Appendix A to Part 543—Model Bylaws for Stock Associations**

3. *Section 543.1 Procedure for organization of Federal stock association; initial sale of capital stock; organizational meeting*—contains many parts of current § 552.2-1, the outline of information to obtain insurance of accounts, and articulates several longstanding Board policies concerning escrow of funds and bonding of officers. The section also clarifies the circumstances under which organizers may collect organizaitonal expenses from subscribers and the procedures of refunding of subscription and expense funds in the event organization is not completed.

Paragraph (a)—*General*—indicates that the provisions of Part 542 apply to applications for permission to organize a Federal stock association.

Paragraph (b)—*Initial sale of capital stock*—sets forth the requirements for selling the capital stock of the association and includes conditional approval, bonding of officers, directors, employees and agents, compliance with Part 568g, escrow and return of money collected for the offering of stock, necessity for uniform price and terms of the initial offering, Board policy on options and warrants, and par value of stock.

Paragraph (c)—*Organizational meeting*—revises current § 552.2-1(f) to allow an organizational meeting within six months of receiving a certificate of authority to commence business, rather than the current delayed method of opening for business only after a stockholders' meeting with proper notice.

4. *Section 543.2 Powers of Federal stock associations*—is a revised § 552.9 referencing other sections that deal with investments and other activities of Federal associations.

5. *Section 543.3 Charter for Federal stock associations*—is essentially current § 552.3 with clearer directions and certain modifications to the current Federal stock charter.

Paragraph (a)—*Initial charter*—sets out that the initial charter must be in the form specified in paragraph (d) but may contain preapproved optional provisions.

Paragraph (b)—*Converted associations*—contains information from current § 552.3(a).

Paragraph (c)—*Federal savings bank charter*—outlines the additional charter language converting associations must use.

Paragraph (d)—*Federal stock charter*—contains the wording for the standard form of charter from current § 552.3, with the following revisions:

(1) Use of the terms "retained earnings" and "paid-in capital" instead of "surplus" and "stated capital" in section 5 dealing with consideration for stock issued as dividends, to reflect current terminology;

(2) Application of the charter restriction on direct issuance of stock to insiders in section 5 rephrased to apply to beneficial owners of more than 10 percent of an association's stock, rather than to "controlling persons," to make the applicability of the restriction more easily ascertainable; and

(3) A reduction in the minimum size of the board of directors in section 7 to five members rather than seven in recognition of the large number of closely-held associations and to conform to the required number of organizers of a Federal association.

Signature page—A date line has been added to the charter so the effective date of the charter may be specified.

6. *Section 543.4 Preapproved charter amendments*—is essentially current § 552.4(b), which provides for preapproved charter amendments which are deemed to have received preliminary Board approval and therefore can be presented to stockholders without a prior filing with the Board.

Paragraph (a)—*Title change*—sets out the current rule at § 552.4(b)(1) and adds the current § 543.1(b) language regarding prior submission to the Supervisory Agent.

Paragraph (b)—*Change of location*—is essentially current § 552.4(b)(3).

Paragraph (c)—*Number of shares of stock and par value*—is essentially current § 552.4(b)(4).

Paragraph (e)—*Preferred stock*—is essentially current § 552.4(b)(5) with the same changes to section 5 of the charter as noted above in reference to proposed § 543.3(d).

Paragraph (f)—*Limitations on subsequent issuances*—retains the ability of a Federal stock association to amend its charter to require stockholder approval for the issuance of common stock when such approval would be required under the rules of the New York or American stock exchanges, currently 18.5 percent and 20 percent, respectively, of the shares of stock then outstanding, as is now available under § 552.4(b)(6); in addition, allows an association to amend its charter to require stockholder approval for issuance of common stock in excess of 15 percent of the shares of stock then outstanding, to enable institutions to avoid the more complicated

requirements of the stock exchange limitations, a provision that used to be authorized for Charter S-type associations.

Paragraph (g)—*Anti-takeover provisions following conversion*—is essentially current § 552.4(b)(6) which is available for Federal associations which have converted to stock form within the past 5 years. These provisions are available only to institutions that have converted from mutual to stock form within the preceding five years.

Paragraph (h)—*Cumulative voting*—is a new section which allows an association to eliminate cumulative voting on a permanent basis. There appears to be no compelling basis to require cumulative voting and therefore cumulative voting would be made optional. This treatment also reflects current trends in state codes and the Model Business Corporation Act. Any existing Federal stock association with a cumulative voting provision in its charter that wanted to remove the requirement would be required to persent the matter to stockholders for repeal.

Paragraph (i)—*Preemptive rights*—is a new section which allows an association to provide for preemptive rights as an optional charter provision.

7. *Section 543.4–1 Additional charter provisions*—is a section which expands current § 552.4(c) in providing for non-pre-approved charter amendments, which include, but are not limited to, anti-takeover amendments. In a change from current rules, however, the Board would not be governed by any state law in assessing the permissibility of anti-takeover charter provisions. Instead, the Board would look to its own statutes, rules and policies, and also look to Delaware law for guidance in interpreting the permissibility of particular antitakeover provisions. The Board notes that any amendments, including anti-takeover amendments, not consistent with law, regulations or policy of the Board, would not be approved by the Board or its delegate, regardless of their purported permissibility under state law. In addition, any provision requiring greater than majority stockholder votes for certain transactions, or supermajority provisions, could only be adopted if approved by at least the same supermajority of stockholders being proposed. The Board specifically requests public comments on this section of the proposal, and in particular, whether the Board should more specifically describe the type of anti-takeover provisions that will be considered acceptable.

8. *Section 543.5 Procedures for obtaining Board approval of charter amendments*—outlines the procedures for preliminary and final approval now found in §552.4(a).

Paragraph (a)—*Procedure for obtaining preliminary approval of charter amendments*—clarifies that if a proposed amendment's effect would be render more difficult a change in control of the institution, an opinion of counsel independent of the association must accompany the proposal and must express a reasoned opinion that such an amendment is consistent with applicable statutes, regulations and Boards policies and indicate whether such a provison would be permissible for a corporation incorporated under the laws of Delaware.

Paragraph (b)—*Procedure for obtaining final approval of amendments*—restates the filing requirement and the date of effectiveness of amendments now found at § 552.4(a).

9. *Section 543.6 Reissuance of charter*—is essentially current § 552.4(d) with a description of required supporting documents.

10. *Section 543.7 Bylaws*—is essentially current § 552.5, with language requiring an opinion of independent counsel if a proposed bylaw would render more difficult a change of control of the institution, in the same manner as required for charter amendments. The Board wishes to stress that bylaws would not be approved if they were inconsistent with the Board's rules of corporate governance, or with provisions in a association's charter.

Paragraph (a)—*General*—is essentially current § 552.5(a) except for requiring bylaws consistent with the proposed rules governing bylaws.

Paragraph (b)—*Permissible bylaws*—is essentially current § 552.5(b).

Paragraph (b)—*Effectiveness*—establishes when bylaws are effective and the requirement of an opinion of independent counsel in certain circumstances.

Paragraph (d)—*Procedure*—sets forth the procedures for filing bylaws and amendments thereto.

11. *Section 543.8 Effect of subsequent charter or bylaw change amendment*—is essentially current § 552.16.

12. *Section 543.9 Stockholder meetings*—incorporates much of current § 552.6 but separates various stockholder voting paragraphs into a new section.

Paragraph (a)—*Stockholder meetings*—is essentially current § 552.6(a) except (1) annual meetings may now be held within 150 days after the end of an association's fiscal year instead of the current 120 days to allow institutions registered under the Securities Exchange Act to employ materials filed in connection requirements of the rules of the Board and the Securities and Exchange Commission under the Securities Exchange Act of 1934; (2) special meetings can be called by holders of up to 25 percent of the stock, as specified in the bylaws, rather than the existing "10 percent or more" requirement; and (3) meetings of stockholders may now be held in the state where the association has its principal place of business *or* where it maintains branches, in recognition of the growing number of interstate associations.

Paragraph (b)—*Notice of stockholder meetings*—is essentially current § 552.6(b) except that this section will clarify that the method of mailing notice must be calculated to ensure delivery within a reasonable period of time and also that the notice requirement is not necessary for associations wholly owned by a holding company. In addition, the Board invites comments on whether the time limits on notice should be modified; they are currently 20 to 50 days, which times were also applied to the fixing of record dates and availability of the voting list. The Board is aware that a number of state corporate codes call for 10- to 60-day requirements.

Paragraph (c)—*Fixing of record dates*—is essentially current § 552.6(c) except for modification of the time period as discussed above.

Paragraph (d)—*Voting lists*—modifies current § 552.6(d) by providing that a voting list will be made available for inspection for a period beginning 20 days prior to the meeting and at the meeting, only for a purpose germane to the meeting. The Board specifically requests comments concerning the sanction that should be applied in the case of a refusal of directors to provide a voting list.

Paragraph (e)—*Stockholder quorum*—is essentially current § 552.6(e) with the addition of language indicating that the affirmative vote of a majority of shares of stock represented at a meeting is the act of the stockholders when a quorum is present unless a greater number is required by law or the association's charter.

Paragraph (f)—*Nominations*—is a more detailed codification than current § 552.6(g) of the language in the current model bylaws regarding the selection of management nominees and the procedures for stockholder nominations

either prior to the meeting or at the meeting if the nominating committee has failed to act at least 20 days prior to the meeting. It is noted that nonstandard bylaw amendments calling for cumbersome procedural barriers or unreasonable information requirements in connection with stockholder nominations would not be permitted. The same caution should be noted for more cumbersome requirements for the introduction of new business at an annual meeting. The new language also clarifies that the stockholder nomination and new business procedures are available only for stockholders of record.

Paragraph (g)—*New business*—is a more detailed codification than current § 552.6(g) of the language in the current model bylaws regarding the introduction of new business at an annual meeting.

Paragraph (h)—*Informal action by stockholders*—is a new section added from the current model bylaws which the Board felt should be expressed in the regulations. The Board solicits comment on whether actions which can be taken without a meeting should require unanimous consent as provided in this proposal, or only the consent of the number of shares of stock needed to approve the action if such shares of stock had been present at a legal meeting.

13. *Section 543.9–1 Stockholder voting*—expands the current § 552.6(f) pertaining to proxies, treasury shares and cumulative voting, to discuss stock controlled by others and by fiduciaries, receivers or pledgees.

Paragraph (a)—*Proxies*—expands current § 552.6(f)(1) to allow telephonic or electronic proxies and to allow proxies to designate corporations, partnerships or companies as holders. The Board notes in this regard that under certain circumstances, as set forth in the Board's Acquisition of Control regulations, 12 CFR Part 574, the holding of proxies may constitute an acquisition of control requiring prior Board approval.

Paragraph (b)—*Stock controlled by association and others*—encompasses current 552.6(f)(2) and adds rules for listing stock held in the name of another corporation, held by an administrator, executor, guardian or conservator, stock transferred into a trustee's name, stock standing in the name of receiver or under the control of a receiver and stock which is pledged.

Paragraph (c)—*Cumulative voting*—is essentially current § 552.6(f)(3).

14. *Section 543.9–2 Voting trusts among stockholders*—is a new section based on Model Business Corporation Act which clarifies that stockholders may enter into written voting trusts by depositing their stock with a trustee and delivering a copy of the trust agreement to the association, subject to inspection by other stockholders, and for a term not to exceed 10 years. The trustee is directed to maintain a list of the beneficial owners, which must also be delivered to the association.

15. *Section 543.9–3 Books and records; stockholder access*—is essentially current § 552.11 but expands the description of "proper purpose", incorporates certain language modelled upon section 13(b) of the rules under the Securities Exchange Act with regard to maintenance of books and records, and specifies procedures regarding access to stockholder lists for associations subject to such rules, and adds a remedy to compel inspection.

Paragraph (a)—*General*—has modified current § 552.11(a) to include more specific requirements with respect to maintenance of books and records in compliance with generally accepted accounting principles.

Paragraph (b)—*Right to examine*—is essentially current § 552.11(b) with the expanded description of proper purpose and the language concerning stockholder lists noted above.

Paragraph (c)—*Denial of right to examine*—is essentially current § 552.11(c).

Paragraph (d)—*Confidentiality of records*—is essentially curent § 552.11(d) which codifies the Board's longstanding policy on the right to privacy of depositors of a Federal association.

Paragraph (e)—*Compelling inspection*—is a new section which codifies the common law right of a stockholder to pursue a remedy in court if a demand for inspection is refused.

16. *Section 543.9–4 Annual reports to stockholders*—is essentially current § 552.10, with certain clarifications regarding the content of financial statements reflecting the requirements of the Board's rules.

17. *Section 543.9–5 Stockholder derivative actions*—is a new, clarifying section derived primarily from the Model Business Corporation Act and Rule 23.1 of the Federal Rules of Civil Procedure.

Paragraph (a)—*Right to bring an action*—essentially restates Rule 23.1 of the Federal Rules of Civil Procedure providing that derivative actions may only be brought if the plaintiff was a stockholder of record at the time of the transactions of which he complains. In addition, a stockholder is required to obtain approval from the Principal Supervisory Agent for the institution before bringing an action. This latter provision is derived from features of California law. The Board specifically solicits comments on this requirement and on the need to include more specific procedures for obtaining Principal Supervisory Agent approval.

Paragraph (b)—*Payment of expenses*—directs plaintiffs in a derivative action to pay the defendant reasonable expenses, including attorney's fees, if final judgment brings a finding that the action was brought without reasonable cause.

Paragraph (c)—*Security for expenses*—includes a requirement for security for expenses to avoid frivolous suits.

18. *Section 543.10 Board of directors*—includes a number of the provisions currently found in § 552.6–1 with an expanded section describing the duties of a director, a reduction in the size of a board to five members and a new definition of "cause" with regard to director removals. With respect to this definition of "cause," the Board specifically requests comments as to whether the definition should be exclusive.

Paragraph (a)—*General*—expands current § 552.6–1(a) to include the authority to fix compensation and authorize reimbursement for expenses and to allow for non-stockholder directors unless the bylaws so require. In addition, the section would require a majority of directors be independent as defined in § 543.10–1(c). The Board also requests comment on this requirement for independent directors, which is similar to the requirement already imposed on all insured institutions pursuant to § 563.33.

Paragraph (b)—*Performance of duties*—is a new section which defines the director's duty to act in good faith in a manner he reasonably believes to be in the best interests of the association, and with such care as an ordinary prudent person in a like position would use under similar circumstances.

Paragraph (c)—*Number and term*—is essentially current § 552.6–1(b) except for the reduction to five in the allowable size of a board.

Paragraph (d)—*Vacancies*—is essentially current § 552.6–1(e).

Paragraph (e)—*Resignation or removal of directors*—is essentially current §552.6–1(f) and the existing Model Bylaws, with the addition of a definition of the term "cause" and a procedure for a defense to be presented by a director in a removal action. This section also provides that directors may only be removed for cause. The Board specifically requests comments as to

whether stockholders should be able to remove directors other than for "cause."

Paragraph (f)—*Age limitation on directors*—is essentially current § 552.6-1(k).

19. *Section 543.10-1 Directors' meetings*—expands a number of provisions currently found in § 552.6-1 with additional provisions for conference telephone meetings and a new requirement that associations establish an audit committee and an investment committee, at least a majority of the members of which are independent directors.

Paragraph (a)—*Meetings*—includes the language of current § 552.6-1(c) and adds provisions from the current model bylaws for determination of place, frequency, time and procedures for notice for regular meetings of at least 24 hours, unless waived, and provision for telephonic meetings which, unlike the current model bylaws, will be deemed to constitute presence in person for all purposes.

Paragraph (b)—*Quorum*—is essentially current § 552.6-1(d).

Paragraph (c)—*Executive and other committees*—is essentially current § 552.6-1(g) with several important additions. Section 2 of that paragraph requires the appointment of an audit committee of at least three directors the majority of whom shall be independent and who shall not be the same directors as the independent. Section 3 requires the appointment of an investment committee of at least three directors the majority of whom shall be independent directors of the audit committee. The provision also defines independence and sets forth the duties of the audit committee and the investment committee. The Board specifically requests comments on the requirements of an audit committee and investment committee and the further requirement concerning independent directors of both committees.

Paragraph (d)—*Notice of special meetings*—is essentially current § 552.6-1(h).

Paragraph (e)—*Action without a meeting*—is essentially current § 552.6-1(i).

Paragraph (f)—*Presumption of assent*—is essentially current § 552.6-1(j).

20. *Section 543.10-2 Director's conflicts of interest*—is a new section derived from the Board's conflict-of-interest regulations.

Paragraph (a)—*General*—details when contracts or other transactions are not void or voidable even though a director may have a material financial interest in the transaction.

Paragraph (b)—*Presence of interested directors at meeting*—details when contracts or other transactions are not void or voidable even if a director may be an "interested director," if there has been adequate disclosure of his interest and approval by disinterested directors.

Paragraph (c)—*Determining a quorum*—allows interested directors to be counted in determining the presence of a quorum at a meeting that ratifies a contract or transaction discussed above.

Paragraph (d)—*Transactions with affiliates*—preserves the Board's right to object to a contract in conjunction with its regulations on transactions with affiliates.

21. *Section 543.10-3 Liability of directors for improper distributions*—is a new section that sets forth a director's liability for distributions to stockholders in contravention of the Board's rules or the association's charter.

Paragraph (a)—*Director liability*—sets out the circumstances under which a director might be liable, jointly or severally, for certain distributions.

Paragraph (b)—*Right to contribution from stockholders*—sets out the right to receive contributions from stockholders who knowingly receive certain impermissible distributions.

Paragraph (c)—*Right to contribution from directors*—sets out the right of directors to contribution from other directors who assented to certain impermissible distributions in certain circumstances.

Paragraph (d)—*Distribution*—defines the term "distribution."

22. *Section 543.10-4 Officers*—is based upon current § 552.6-3 with the addition of a paragraph on employment contracts.

Paragraph (a)—*Positions*—is essentially current § 552.6-2(a).

Paragraph (b)—*Removal*—is essentially current § 552.6-2(b), with the addition of a new definition of "cause" which is the same as used in the new definition of "cause" applicable in the case of removal of directors.

Paragraph (c)—*Employment contracts*—specifically authorizes employment contracts in conformance with Insurance Regulation § 563.39. The Board specifically requests comments in this regard as to whether it should adopt additional regulations governing so-called "golden parachute" or "silver wheelchair" types of employment contracts.

Paragraph (d)—*Age limitation on officers*—is essentialy current § 552.6-2(a).

23. *Section 543.10-5 Indemnification of directors, officers, and employees*—is a new section derived from current Federal Regulation 545.121. Indemnification is extended for officers directors and employees of the association and specifically permitted for officers, directors and employees of wholly-owned service corporation subsidiaries. The Board specifically requests comments on the extension of indemnification to wholly-owned service corporations, as well as the limitation of persons eligible to be indemnified to officers, directors and employees.

Paragraph (a)—*General*—is essentially current § 545.121(b) with the inclusion of service performed for subsidiaries discussed above.

Paragraph (b)—*Conditions*—is essentially current § 545.121(c) with the retention of the 60-day notice to the Board and the expansion of delegated authority to the Office of Examinations and Supervision with the concurrence of the Office of General Counsel to object to the indemnification. The new section also allows for the stockholders to determine to permit indemnification if a quorum of disinterested directors is not obtainable. The Board is aware that some state codes allow a disinterested attorney to make the determination and the Board specifically solicits comments as to the use of such disinterested counsel, particularly where a quorum of disinterested directors is not available and the question of indemnification would therefore be required to be put to the stockholders in what could be relatively costly proxy solicitation. The Board also solicits comments in this regard on the standard to be used in determining whether a counsel is "disinterested." In addition, this section adds a provision for action to be brought in the right of the association.

Paragraph (c)—*Insurance*—is essentially current § 545.121(d).

Paragraph (d)—*Advance payment of expenses*—is essentially current § 545.121(e) with the addition of disinterested stockholders being allowed to authorize payments.

Paragraph (e)—*Prohibited indemnification*—is a new section prohibiting indemnification if in contravention of public policy, which would include, without limitation, violation of statutes and regulations administered by the Board.

Paragraph (f)—*Exclusiveness of provisions*—is essentially current § 545.121(f) which clarifies the grandfathering of bylaws in effect as of October 1, 1969.

Paragraph (g)—*Definitions and rules of construction*—is essentially current § 545.121(a) with an additional definition of the term "disinterested."

The Board specifically invites comments on the scope of this term.

24. *Section 543.11 Certificates for stock and their transfer*—is essentially paragraphs (a) and (b) of current § 552.6–3.

25. *Section 543.11–1 Consideration for stock*—is a new section derived from the Model Business Corporation Act and several state codes. It includes a discussion of permissible consideration for stock, treasury stock, stock dividends and stock issued in an exchange of indebtedness or for stock.

Paragraph (a)—*General*—sets forth the ability of the board of directors to set consideration for stock as cash or other consideration, or both, on certain terms.

Paragraph (b)—*Treasury stock*—sets forth the method of disposing of such stock.

Paragraph (c)—*Stock dividends*—describes that the consideration for stock dividends is derived from retained earnings.

Paragraph (d)—*Stock issued in exchange*—sets forth the derivation of the consideration for stock issued an exchange of indebtness or for stock.

26. *Section 543.11–2 Stock rights and options*—is a new section setting forth Board policy on stock rights and options, including the conditions under which stock options or rights can be granted to non-employee directors.

Paragraph (a)—*Creation and issuance*—describes the requirements for creation and issuance of stock rights and options.

Paragraph (b)—*Restriction on grants to non-employee directors*—sets forth the conditions under which such stock options or rights could be granted to non-employee directors", including a definition of that term.

Paragraph (c)—*Payments for stock rights or options*—sets forth the right of the association to adopt a plan to redeem or repurchase shares of stock of the association as payment for stock options or rights, as long as the association's net-worth requirement would still be met.

27. *Section 543.11–3 Fractional shares of stock*—is a new section derived from the Model Business Corporation Act and other state corporation codes allowing for the issuance of fractional shares, cash or scrip in lieu of fractional shares.

28. *Section 543.11–4 Liability of stockholders*—is a new section defining a stockholder's obligation to pay full consideration for his shares of stocks.

29. *Section 543.12 Authority to acquire own stock*—is a new section which clarifies the right of a Federal stock association to acquire its own stock.

30. *Section 543.12–1 Authority to pay dividends to stockholders*—is a new section setting forth the association's ability to pay dividends out of retained earnings.

31. *Section 543.12–2 Limitations on distributions to stockholders*—is a new section which defines what constitutes a distribution, sets out the limitations on distributions and describes measurement dates.

Paragraph (a)—*Distributions*—defines the term to mean a direct or indirect transfer of money, other property or indebtedness to or for the benefit of any of the association's stockholders.

Paragraph (b)—*Limitation on distributions*—prohibits distributions such as dividends or repurchases of stock, that would reduce an association's net worth below that required by §563.13 of the Insurance Regulations.

Paragraph (c)—*Measurement date*—sets forth a date to measure when the distribution occurs.

32. *Section 543.12–3 Reduction of paid-in capital*—is a new section setting forth the manner in which an association could reduce its paid-in capital and the restrictions applicable to such a reduction.

33. *Section 543.13 Fiscal year; annual audit*—is essentially current §552.6–4.

34. *Section 543.14 Corporate procedures*—is a new section containing several permissible bylaw provisions found in the current mutual association model bylaws, including provisions concerning execution of instruments, corporate seal and miscellaneous provisions.

Paragraph (a)—*Execution of instruments generally*—is essentially current §544.5(b)(12).

Paragraph (b)—*Seal*—is essentially current §544.5(b)(15).

Paragraph (c)—*Miscellaneous*—is essentially current §544.5(b)(17).

35. *Appendix A to Part 543 Model Bylaws for Stock Associations*—is a set of 12 Articles derived from the current model bylaws for Federal stock associations but containing revisions based upon proposed §§ 543.8 through 543.14, discussed above.

36. Sections 543.15–543.19 are reserved sections to maintain the numbering order for stock and mutual sections and to allow for any necessary additional rules. Other sections described herein are reserved for similar reasons.

37. *Section 543.20 Combinations involving Federal stock associations*—is a section largely derived from current section § 552.13 (1985) with modifications to the merger rules, additions to the required contents of a combination agreement, revised notice requirements and separation of the "bulk purchase of assets" section into a distinct section. In addition, the Board has added a new short-form merger section, based upon state corporate codes, and specifically invites comments on that addition.

38. *Section 543.21 Merger of consolidation*—the first two types of permissible combinations; tracks current § 552.13.

Paragraph (a)—*Permissible merger or consolidation*—lists the two conditions under which a Federal stock association may merge or consolidate with other associations, now found at § 552.13(c), and adds a third condition now found at § 546.2 requiring that mergers with state-chartered institutions be in accordance wih state law. Current § 552.13(b) definitions have been moved to the definitional section of newly proposed Part 541. (*See* Corporate Governance, Part I.)

Paragrpah (b)—*Board approval*—is essentially current § 552.13(d).

Paragraph (c)—*Approval by the Board's Principal Supervisory Agent*—is essentially current § 552.13(e), incorporating recently amended § 563.22 which expands the authority of the Principal Supervisory Agents and the Board's Washington staff to act on many applications pursuant to delegated authority. The section also is expanded to include the delegated authority in current § 546.2 to approve maintenance of branch offices and temporary increases in the size of boards of directors.

Paragraph (d)—*Approval of board of directors*—is essentially current § 552.13(f).

Paragraph (e)—*Conservator or receiver action*—brings the current §546.2(f) provision to the rules for Federal stock associations.

Paragraph (f)—*Combination agreement*—is essentially current § 552.13(g) describing the required contents of the combination agreement, with several additional provisions.

Paragraph (g)—*Corporate title; change of location*—specifies that the charter must be amended in certain instances and is derived from current § 546.2(g).

Paragraph (h)—*Application for Board approval*—is essentially current § 552.13(h) regarding filing requirements, with an additional reminder to applicants that any required Hart-Scott-Rodino antitrust filings must also be made.

Paragraph (i)—*Notice*—is a modified version of current § 552.13(i). The modifications include the following: The requirement that public notice appear in the communities in which the home offices of all constituent associations are located; deletion of the current "double notice" requirement to stockholders so that notice is required for stockholders only if the combination agreement is not subject to stockholder approval; and revision of contents of the notice to narrow the time when coments will be accepted to expedite processing, and to appraise each stockholder, where applicable, of his dissenters' appraisal rights.

39. *Section 543.22 Short-form merger*—is a new section derived from various state corporation codes. The section sets forth procedures for merging associations that are at least 90-percent owned by another association without the requirement of stockholder approval. Appraisal rights are provided in certain circumstances.

Paragraph (a)—*General*—sets forth the types of transactions where short-form mergers are available and the procedures for effecting such transactions. The Board specifically requests public comment as to whether the short-form merger process should be expanded to allow a short-form merger of a service corporation into its parent association.

Paragraph (b)—*Subsidiary resulting association*—sets forth the requirement that, if the parent insured institution is not the resuling association, evidence must be submitted to the Supervisory Agent that the merger was approved by the affirmative vote of the stockholders of the parent.

Paragraph (c)—*Corporate title*—details what to do to change a corporate title in a short-form merger.

Paragraph (d)—*Processing; delegation*—sets out the processing requirements and delegates approval authority to the Principal Supervisory Agent in many circumstances.

Paragraph (e)—*Appraisal rights*—gives appraisal rights as provided under § 543.27 to stockholders in a short-form merger if the disappearing association is a Federal association.

40. *Section 543.23 Approval by stockholders for merger or consolidation*—is essentially current § 552.13(j).

Paragraph (a)—*General rule*—is essentially current § 552.13(j)(1).

Paragraph (b)—*General exception*—is essentially current § 552.13(j)(2), setting forth the situations where approval of the stockholders of a Federal association is not required to approve a merger or consolidation.

Paragraph (c)—*Exception for certain combinations involving an interim*—is essentially current § 552.13(j)(3).

Paragraph (d)—*Disclosure*—is essentially current § 552.13(k)

41. *Section 543.24 Articles of combination for merger or consolidation*—is essentially current § 552.13(*l*) paragraphs 1 and 2.

42. *Section 543.25 Effective date; date of consummation for merger or consolidation*—is partially derived from current § 552.13(m) and various state codes provisions allowing for a later effective date for a combination if requested. The section on date of consummation of a merger or consolidation was proposed to clarify an ongoing procedural problem that the effective date and date of consummation are often not the same.

Paragraph (a)—*Effective date*—tracks the language of current § 552.13(m) but allows a later effective date of a merger or consolidation if requested. In addition, delegated authority to approve combinations is recognized by this section.

Paragraph (b)—*Date of consummation*—specifies that combinations cannot be concluded until all necessary compliance materials are submitted to the Supervisor Agent's satisfaction, and explicitly provides that the Board or its delegate may suspend, alter or withdraw its approval if such action is warranted on the basis of a material change in circumstances, prior to the date of consummation.

43. *Section 543.26 Continuity of corporate existence after merger or consolidation*—is essentially current § 552.13(n).

44. *Section 543.27 Dissenters' appraisal rights in merger or consolidation*—is largely derived from current § 552.14. The right to apply for the payment of the fair value of stock is limited. Dissenters' appraisal rights would not exist where stock is listed on a national securities exchange or quoted on the NASDAQ or where stockholder action is not required. The section also now defines the term "fair value."

Paragraph (a)—*Right to demand payment of fair value*—is essentially current § 552.14(a).

Paragraph (b)—*Exceptions*—is essentially current § 552.14(b) modified to include NASDAQ quoted stocks within the category where dissenters' appraisal rights are not present.

Paragraph (c)—*Procedure*—is essentially current § 552.14(c) with minor modifications. Stockholders must now receive notice of their appraisal rights, if any, in their proxy materials or in any substitute stockholder notice. The petition to the Board to review an association's offer to dissenting stockholders if an offer is not accepted is now filed with the Office of General Counsel.

Paragraph (d)—*Valuation by the Board or its delegate*—is essentially current § 552.14(c—) (8) and (9).

Paragraph (e)—*Reorganization using interims*—is a new section to recognize that interim associations would have little or no assets, so that in the case of an association recognizing into a holding company form using an interim, where the interim technically is the resulting association, the Board would view the holding company in such a reorganization as the resulting association for purposes of satisfying dissenters' appraisal rights. This provision clarifies and formalizes this treatment, which the Board believes has always been implicit in the structure of a reorganization into a holding company structure using an interim association.

Paragraph (f)—*Definitions*—is a new section to define the terms "fair value," NASDAQ," "National securities exchange" and "Qualified consideration", the latter taken from current § 552.14(b). The Board specifically requests comments on its definition of "fair value" for appraisal purposes.

45. *Section 543.28 Supervisory combinations*—is esentially current § 552.15 with additional language dervied from section 5(o)(2)(F) of the HOLA regarding cases where severe financial conditions exist which threaten the stability of an association.

46. *Section 543.29* is reserved.

47. *Section 543.30 Bulk purchase or sale of assets*—is derived from current § 552.13. The definition of bulk purchase of assets has been expanded.

Paragraph (a)—*Permissible bulk purchase of assets*—is derived from current § 552.13(c)(3) with clarifying language to better address bulk transfers to interim associations as well as to operating associations.

Paragraph (b)—*Permissible bulk sale of assets*—restates the Board's current policy that bulk *sales* of assets by Federal associations are only permissible in supervisory cases. The Board invites comments from the public on this policy.

Paragraph (c)—*Bulk purchase or sale of assets defined*—expands the current definitional § 552.13(b)(2), now appearing in the definitions section of Corporate Governance, Part I, new proposal Part 541, to include a percentage-of-assets test to determine whether substantially all of the assets of an association are involved such that a transaction would constitute a bulk

purchase or sale. The Board invites comments on the choice of 50 percent of total assets of the association prior to the acquisition as the appropriate percentage.

Paragraph (d)—*Board approval*—tracks the language of current § 552.13(d).

Paragraph (e)—*Approval by the Board's Principal Supervisory Agent*—is essentially current § 552.13(e), incorporating recently amended 563.22 which expands the authority of the Principal Supervisory Agent and the Board's Washington staff to act on many applications pursuant to delegated authority.

Paragraph (f)—*Approved by board of directors*—is essentially current § 552.13(f).

Paragraph (g)—*Combination agreement*—refers the applicant to new § 543.21(f)(2).

Paragraph (h)—*Application for Board approval*—refers the applicant to new § 543.21(h).

Paragraph (i)—*Notice*—refers the applicant to new § 543.21(i).

48. *Section 543.31 Approval by stockholders*—refers the applicant to new § 543.23.

49. *Section 543.32 Articles of combination*—refers the applicant to new § 543.24.

50. *Section 543.33 Effective date; date of consummation*—refers the applicant to new § 543.25.

51. *Section 543.34 Continuity of corporate existence after bulk purchase or sale of assets*—makes clear that a bulk purchase or sale of assets does not effect the corporate existence of the transferee or transferor Federal stock association.

52. *Section 543.35 Dissenters' appraisal rights in bulk purchase or sale of assets*—refers the applicant to new § 543.27.

53. *Section 543.36 Partial purchase or sale of assets*—is a new section differentiate between a bulk purchase or sale and a partial purchase or sale. The same percentage-of-assets test is used in this section as was used in new § 543.30, and the Board specifically requests public comments on this aspect of the proposal. In addition, the section refers applicants to § 563.22 of the Insurance Regulations for the rules governing procedures for obtaining required approval of partial purchases or sales of assets.

54. *Sections 543.37–543.39* are reserved.

55. *Section 543.40 Reorganization*—is also reserved.

56. *Sections 543.41–543.49* are reserved.

57. *Section 543.50 Dissolution*—is derived primarily from current § 546.4, the Model Business Corporation Act and the Delaware and California codes.

58. *Section 543.51 Voluntary dissolution*—is derived from current § 546.4.

Paragraph (a)—*Plan for dissolution*—sets forth the requirements for a board of directors to propose a dissolution and the criteria for an approval.

Paragraph (b)—*Board approval*—sets forth the necessity for Board approval of such a plan of dissolution and the criteria for an approval.

59. *Section 543.52 Approval by stockholders for dissolution*—is derived from current § 546.4.

Paragraph (a)—*Stockholder vote*—requires a two-thirds vote of the stockholders to approve a dissolution instead of merely a majority vote.

Paragraph (b)—*Dissenters' appraisal rights*—explains that there will not be such rights in a dissolution.

60. *Section 543.53 Notice of dissolution*—is a new section on notice of dissolution generally derived from the Model Business Corporation Act.

Paragraph (a)—*Notice to creditors*—is a new requirement to notify all known creditors of the intention to dissolve upon filing a plan of dissolution with the Board.

Paragraph (b)—*Notice to accountholders*—sets forth the affirmative duty of the association to notify affected accountholders of the approval of the stockholders to dissolve in accordance with the Board's existing notice requirements for termination of insurance at § 565.5 of the Insurance Regulations.

61. *Section 543.54 Procedure for dissolution after Board and stockholder approval*—is a new section directing the association to do what acts are necessary to liquidate its business and affairs.

62. *Section 543.55 Termination of corporate existence*—is derived from current § 546.4 and the Model Business Corporation Act.

Paragraph (a)—*Completion of dissolution*—is essentially the last two sentences of current § 546.4.

Paragraph (b)—*Continuation of corporate existence after dissolution*—is a new section derived from the Model Business Corporation Act which continues the corporate existence for three years of a dissolving association solely for the purpose of defending or prosecuting legal actions, settling and closing the business, conveying property, discharging liabilities and distributing the remaining assets.

63. *Section 543.56 Involuntary Dissolution*—is a new section which allows the Board to waive any provision of the dissolution section if instituted for supervisory reasons or pursuant to Part 547.

64. *Sections 543.57–543.59* are reserved.

65. *Section 543.60 Supervisory waiver*—is a new section which allows the Board to waive any provision of Part 543 if necessary in specified supervisory circumstances.

## B. PART 544—FEDERAL MUTUAL ASSOCIATIONS

66. Sections of existing Parts 543, 544, 545 and 546, and a number of new proposed sections modeled on the proposed sections in new Part 543, have been put into this new Part to cover the areas of final organization, charters and bylaws, combinations, bulk purchases or sale of assets, reorganization and dissolution of Federal mutual associations.

67. The following 60 sections, appendix and reserved sections are proposed:

544.1 Procedures for organization of Federal mutual associations; initial collection of pledged capital; organizational meeting
544.2 Powers of Federal mutual associations
544.3 Charters for Federal mutual associations
544.4 Preapproved charter amendments
544.4–1 Additional charter provisions [Reserved]
544.5 Procedures for obtaining Board approval of charter amendments
544.6 Reissuance of charter
544.7 Bylaws
544.8 Effect of subsequent charter or bylaw amendment
544.9 Members' meetings
544.9–1 Voting by proxy
544.9–2 Communications between members
544.9–3 Annual reports to members
544.10 Board of directors
544.10–1 Directors' meetings
544.10–2 Director's conflicts of interest
544.10–3 [Reserved]
544.10–4 Officers
544.10–5 Indemnification of directors, officers and employees
544.11–544.12 [Reserved]
544.13 Fiscal year; annual audit
544.14 Corporate procedures
544.15–544.19 [Reserved]
544.20 Combinations involving Federal mutual associations
544.21 Merger or consolidation
544.22–544.23 [Reserved]
544.24 Articles of combination for merger or consolidation
544.25 Effective date; date of consummation for merger or consolidation
544.26 Continuity of corporate existence after merger or consolidation
544.27 [Reserved]
544.28 Supervisory combinations
544.29 [Reserved]
544.30 Bulk purchase or sale of assets

544.31 [Reserved]
544.32 Articles of combination for bulk purchase or sale of assets
544.33 Effective date; date of consummation for bulk purchase or sale of assets
544.34 Continuity of corporate existence after bulk purchase or sale of assets
544.35 [Reserved]
544.36 Partial purchase or sale of assets
544.37–544.39 [Reserved]
544.40 Reorganization [Reserved]
544.41–544.49 [Reserved]
544.50 Dissolution
544.51 Voluntary dissolution
544.52 Approval by members of dissolution
544.53 Notice of dissolution
544.54 Procedure for dissolution after Board and member approval
544.55 Termination of corporate existence
544.56 Involuntary dissolution
544.57–544.59 [Reserved]
544.60 Supervisory waiver

**APPENDIX A TO PART 544—MODEL BYLAWS FOR MUTUAL ASSOCIATIONS**

68. *Section 544.1 Procedures for organization of Federal mutual association; initial collection of pledged capital; organizational meeting*—contains many parts of current § 543.6, the outline of information to obtain insurance of accounts, and codifies several longstanding Board policies on escrow of funds and bonding of officers. The section also clarifies the circumstances under which organizers may collect organizational expenses from subscribers and the procedures for refunding of subscription and expense funds in the event organization is not completed.

Paragraph (a)—*General*—indicates the provisions of Part 542 apply to applications for permission to organize a Federal mutual association.

Paragraph (b)—*Initial collection of pledged capital*—is derived from current § 543.6 and sets forth the requirements for collecting subscription pledges only after receiving conditional approval, the bonding of officers, directors, employees and agents, the escrow and return of pledged capital and the composition of the consideration for the initial minimum capitalization.

Paragraph (c)—*Organizational meeting*—revises current § 543.6(a)(2) to allow an organizational meeting within six months of receiving a certificate of authority to commence business, rather than the current delayed method of opening for business only after a subscribers' meeting with proper notice.

69. *Section 544.2 Powers of Federal mutual associations*—is a revised § 552.9, applicable now to mutual associations, that references other sections that deal with investments and other activities of Federal associations.

70. *Section 544.3 Charters for Federal mutual associations*—is essentially current § 544.1 with clearer directions and certain modifications to the current Federal mutual charter.

Paragraph (a)—*Initial charter*—establishes that the initial charter must be in the form specified in paragraph (c) but may contain preapproved optional provisions.

Paragraph (b)—*Federal savings bank charter*—sets out the additional charter language converting associations must include in their charters.

Paragraph (c)—*Federal mutual charter*—contains the wording for the standard form of charter; derived from current § 544.1 with the following revisions:

(1) The section 6 voting requirements, proxy requirements and quorum requirements have been moved to the bylaws; and

(2) In section 7 directions on vacancies and the election of directors have been moved to the bylaws.

Signature Page—A date line has been added to the charter so the effective date of the charter may be specified.

71. *Section 544.4 Preapproved charter amendments*—is essentially current § 544.2(b) which provides for preapproved charter amendments which are deemed to have received Board approval and therefore can be presented to the members without a prior filing with the Board.

Paragraph (a)—*Purposes and powers*—retains the optional paragraph two in section 4 of the Federal mutual charter now found at 544.2(b)(1).

Paragraph (b)—*Title change*—sets out the current rule of § 544.2(b)(2) and adds the current § 543.1(b) language regarding prior submission to the Supervisory Agent

Paragraph (c)—*Change of location*—is essentially current § 544.2(b)(3).

Paragraph (d)—*Savings bank charter*—is essentially current § 544.3.

Paragraph (e)—*Mutual capital certificates*—is essentially current § 544.2(b)(4).

Paragraph (f)—*Maximum number of votes for members*—is a new section designed to allow existing Federal mutual associations the option of amending their current charter to allow up to 1000 votes per member, a frequently requested amendment in conjunction with mutual to stock conversions.

72. *Section 544.4–1 Additional charter provisions*—is reserved.

73. *Section 544.5 Procedures for obtaining Board approval of charter amendments*—outlines the procedures for preliminary and final approval now found in §§ 552.4(a) and 544.2(a).

Paragraph (a)—*Procedure for obtaining preliminary approval of amendments*—establishes that if a proposed amendment's effect would be to render more difficult a change in control of the institution, an opinion of counsel independent of the association must accompany the proposal and must express a reasoned opinion that such an amendment is consistent with applicable statutes, regulations and board policies, and indicate whether such a provision would be permissible for a corporation incorporated under the laws of Delaware.

Paragraph (b)—*Procedure for obtaining final approval of amendments*—reiterates the filing requirement and the date of effectiveness of amendments now found at § 544.2(a).

74. *Section 544.6—Reissuance of charter*—is essentially current §544.2(c), with a description of required supporting documentation.

75. *Section 544.7—Bylaws*—for mutual associations have been extensively revised with language requiring an opinion of independent counsel if a proposed bylaw would render more difficult a change of control of the institution, in the same manner as required for charter amendments. The Board wishes to stress that bylaws would not be approved if they were inconsistent with the Board's rules of corporate governance or with provisions in an association's charter.

Paragraph (a)—*General*—is essentially current § 552.5(a) now applied to mutual associations, except for requiring bylaws consistent with the proposed rules governing bylaws.

Paragraph (b)—*Permissible bylaws*—is essentially current § 544.5(a).

Paragraph (c)—*Effectiveness*—sets forth when bylaws are effective and the requirement of an opinion of independent counsel in certain circumstances.

Paragraph (d)—*Procedure*—sets forth the procedures for filing bylaws and amendments thereto.

76. *Section 544.8 Effect of subsequent charter or bylaw amendment*—is essentially current § 544.6.

77. *Section 544.9 Members' meetings*—incorporates much of current § 544.5(b) (1), (2), (3), (4), (13) and (14).

Paragraph (a)—*Annual meetings of members*—is essentially current § 544.5(b)(1) except that annual meetings could now be held within 150 days after the end of an association's fiscal year instead of the current 120 days, and meetings could now be held in the state where the association has its principal

place of business or where it maintains branches, in recognition of the growing number of interstate associations.

Paragraph (b)—*Special meetings of members*—is essentially current § 544.5(b)(2).

Paragraph (c)—*Notice of meetings of members*—is essentially current § 544.5(b)(3), except that this section would clarify that the method of publication of notice must be calculated to ensure that notice will be conspicious. In addition, the Board invites comments on whether the time limits on notice should be modified to 20 to 50 days, as has been done in the proposal with respect to stock associations, which times were also applied to the fixing of record dates. The Board is aware that a number of state corporate codes call for 10-to-60 day requirements.

Paragraph (d)—*Fixing of record date*—is essentially current § 544.5(b)(4) except for modification of the time period as discussed above in paragraph (c).

Paragraph (e)—*Member quorum*—is essentially the language taken out of current charter section 6, indicating that the affirmative vote of a majority of votes cast at any properly convened meeting of the association's members is the act of the members when a quorum is present.

Paragraph (f)—*Nominations for directors*—is a more detailed codification than current § 544.5(b)(13) of the language in the current model bylaws regarding the selection of management nominees and the procedures for member nominations either prior to the meeting or at the meeting. It is noted again that non-standard bylaw amendments calling for cumbersome procedural barriers or unreasonable information requirements in connection with member nominations would not be permitted. The same will be true for the introduction of new business at an annual meeting which is discussed below.

Paragraph (g)—*New business*—is a more detailed codification than current § 544.5(b)(14) of the language in the current model bylaws regarding the introduction of new business at an annual meeting. It also provides for the introduction of new business at least 10 days prior to the meeting, rather than the current 30-day requirement.

78. *Section 544.9–1 Voting by proxy*—expands the current § 544.5(b)(5) and will now cover proxies, and other accounts controlled by parties such as fiduciaries, receivers and pledgees, and joint accounts.

Paragraph (a)—*General*—expands the notice requirements of current § 544.5(b)(5) to allow telephonic or electronic proxies and to allow proxies to designate corporations, partnerships or companies as holders.

Paragraph (b)—*Other voting arrangements*—is a new section which encompasses current § 544.5(f)(2), applies it to mutual associations, and adds rules for voting accounts held by an administrator, executor, guardian or conservator, accounts transferred into a trustees' name, accounts standing in the name of a receiver or under the control of a receiver, and accounts which are pledged.

Paragraph (c)—*Joint accounts*—is a new section setting forth rules derived from the opinions of the Office of General Counsel. The section sets out rules for voting joint accounts, splitting votes if agreed to in writing, and the treatment of situations where joint owners cannot agree on how to vote.

79. *Section 544.9–2 Communication between members*—is essentially current § 544.5(b)(6) and also incorporates a Board policy, now found at § 552.11(d), on the right to privacy of depositors of any Federal association.

80. *Section 544.9–3 Annual reports to members*—is a new section referencing § 544.115 which now governs this area.

81. *Section 544.10 Board of directors*—is a new section for mutual associations which partially encompasses current § 544.5(b), (7), (8), (10) and (11) but more closely resembles current § 552.6–1, with a greatly expanded section on the performance of duties of a director and a new definition of "cause" with regard to director removals. With respect to this definition of "cause" the Board specifically requests comments as to whether the definition should be exclusive.

Paragraph (a)—*General*—expands current § 544.5(b)(11) to include the authority to fix compensation and authorize reimbursement for expenses. In addition, the section would require a majority of directors be independent as defined in § 544.10–1(c). The Board also requests comment on this requirement for independent directors, which is similar to the requirement already imposed on all insured institutions pursuant to § 563.33.

Paragraph (b)—*Performance of duties*—is a new section which defines the director's duty to act in good faith, in a manner he reasonably believes to be in the best interests of the association, and with such care as an ordinary prudent person in a like position would use under similar circumstances.

Paragraph (c)—*Number and term*—is essentially current § 544.5(b)(7) and 552.6–1(b).

Paragraph (d)—*Vacancies*—is essentially current § 552.6–1(e) as it applies to mutual associations and is derived from old charter section 7.

Paragraph (e)—*Resignation or removal of directors*—is essentially current §§ 552.4(b)(10) and 552.6–1(f) with the addition of a definition of the term "cause" and a procedure for a defense to be presented by a director in a removal action. This section provides that directors may only be removed for cause. The Board specifically requests comments as to whether the members should be able to remove directors other than for "cause."

Paragraph (f)—*Age limitation on directors*—is essentially current § 552.6–1(k) as applied to mutual associations.

82. *Section 544.10–1 Directors' meetings*—expands a number of provisions currently found in §§ 544.5(b)(8) and 552.6–1 with additional provisions for conference telephone meetings and a new requirement for the establishment of an audit committee and an investment committee.

Paragraph (a)—*Meetings*—includes the language of current § 544.5(b)(8) for determination of place, frequency, time and procedures for notice for regular meetings of at least 24 hours, unless waived, and adds provision for telephonic meetings which will now constitute presence in person the for all purposes.

Paragraph (b)—*Quorum*—is essentially the last two sentences of current § 544.5(b)(8).

Paragraph (c)—*Executive and other committees*—is essentially current §§ 544.5(b)(11)(a) and 552.6–1(g) with several important additions. Section 2 of that paragraph requires the appointment of an audit committee of at least three directors the majority of whom shall be independent. Section 3 requires the appointment of an investment committee of at least three directors, the majority of whom shall be independent directors of the audit committee. The provisions also define independence and sets forth the duties of the audit committee and investment committee. The Board specifically requests comments on the requirement of an audit committee and an investment committee and the further requirement concerning independent directors of both committees.

Paragraph (d)—*Notice of special meetings*—is essentially current § 552.6–1(h) adapted for a Federal mutual association.

Paragraph (e)—*Action without a meeting*—is essentially current § 552.6–1(i) adapted for a Federal mutual association.

Paragraph (f)—*Presumption of assent*—is essentially current § 552.6–1(j) adapted for a Federal mutual association.

83. *Section 544.10–2 Director conflicts of interest*—is a new section

derived from the Board's conflicts-of-interest regulations.

Paragraph (a)—*General*—details when contracts or other transactions are not void or voidable even though a director may have a material financial interest in the transaction.

Paragraph (b)—*Presence of interested directors at meeting*—details when contracts or other transactions are not void or voidable even if a director may be an "interested director," if there is adequate disclosure of his interest and approval by the disinterested directors.

Paragraph (c)—*Determining a quorum*—allows interested directors to be counted in determining the presence of a quorum at a meeting that ratifies a contract or transaction discussed above.

Paragraph (d)—*Transactions with affiliates*—preserves the Board's right to object to a contract or transaction discussed above in conjunction with its regulations on transactions with affiliates.

84. *Section 544.10-3* is reserved.

85. *Section 544.10-4 Officers*—is based upon current §§ 544.5(b)(9) and 552.6-2 with the addition of a paragraph on employment contracts.

Paragraph (a)—*Positions*—is essentially current §§ 544.5(b)(9) and 552.6-2(a).

Paragraph (b)—*Removal*—is essentially current § 552.6-2(b) adapted for Federal mutual associations, with the addition of a new definition of "cause" which is the same as used in the new definition of "cause" applicable to removal of directors.

Paragraph (c)—*Employment contracts*—specifically authorizes employment contracts in conformance with Insurance Regulation § 563.39. The Board specifically requests comments in this regard as to whether it should adopt additional regulations governing so-called "golden parachute" or "silver wheelchair" types of employment contracts.

Paragraph (d)—*Age limitation on officers*—is essentially current § 552.6-2(c).

86. *Section 544.10-5 Indemnification of directors, officers, and employees*—is a new section derived from current § 545.121. Indemnification is extended for officers, directors, and employees of the association and specifically permitted for officers, directors, and employees of wholly-owned service corporation subsidiaries. The Board specifically requests comments on the extension of indemnification to wholly-owned service corporations as well as the limitation of persons eligible to be indemnified to officers, directors, and employees.

Paragraph (a)—*General*—is essentially current § 545.121(b) with the inclusion of service performed for wholly-owned subsidiaries discussed above.

Paragraph (b)—*Conditions*—is essentially current § 545.121(c) with the retention of the 60-day notice to the Board and the expansion of delegated authority to the Office of Examinations and Supervision with the concurrence of the Office of General Counsel to object to the indemnification. In addition, this section adds a provision for action to be brought in the right of the association. The Board is aware some state codes allow a disinterested attorney to make the determination and the Board specifically solicits comments as to the use of such disinterested counsel, particularly where a quorum of disinterested directors is not available. The Board also solicits comments in this regard on the standard to be used in determining whether a counsel is "disinterested."

Paragraph (c)—*Insurance*—is essentially current § 545.121(d).

Paragraph (d)—*Advance payment of expenses*—is essentially current § 545.121(e).

Paragraph (e)—*Prohibited indemnification*—is a new section prohibiting indemnification if in contravention of public policy.

Paragraph (f)—*Exclusiveness of provisions*—is essentially current § 545.121(f) which clarifies the grandfathering of bylaws in effect as of a certain date.

Paragraph (g)—*Definitions and rules of construction*—is essentially current § 545.121(a) with an additional definition of the term "disinterested." The Board specifically invites comments on the scope of this term.

87. *Section 544.11-544.12* are reserved.

88. *Section 544.13 Fiscal year; annual audit*—is essentially current § 552.6-4 adapted for Federal mutual associations.

89. *Section 544.14 Corporate procedures*—is a new section containing several permissible bylaws in the current mutual association model bylaws which include execution of instruments, corporate seal and miscellaneous provisions.

Paragraph (a)—*Execution of instruments generally*—is essentially current § 544.5(b)(12).

Paragraph (b)—*Seal*—is essentially current § 544.5(b)(15).

Paragraph (c)—*Miscellaneous*—is essentially current § 544.5(b)(17).

90. *Appendix A to Part 544—Model Bylaws for Mutual Association*—is a set of 12 Articles derived from the current model bylaws for Federal mutual associations and formatted to look like the current model bylaws for Federal stock associations but containing significant revisions based upon §§ 544.8 through 544.14, discussed above.

91. *Section 544.15-544.19* are reserved sections.

92. *Section 544.20 Combinations involving Federal mutual associations*—is a section largely derived from current §§ 552.13 (1985) and 546.2 with modifications to the merger rules, additions to the combination agreement, revised notice requirements and a severing of the bulk purchase of assets section into a separate section.

93. *Section 544.21 Merger or consolidation*—as the first two types of permissible combinations tracks current §552.13.

Paragraph (a)—*Permissible merger or consolidation*—lists the two conditions under which a Federal mutual association may merge or consolidate with other associations now found at §552.13(c) and adds a third condition now found at § 546.2 requiring that mergers with state-chartered institutions be in accordance with state law. Current § 552.13(b) definitions have been moved to the definitional section of Corporate Governance, Part I, new proposed Part 541.

Paragraph (b)—*Board approval*—is essentially current §552.13(d).

Paragraph (c)—*Approval by the Board's Supervisory Agent*—is essentially current § 552.13(e) expanded to include the delegated authority in current § 546.2 to approve maintenance of branch offices and temporary increases in the size of the board of directors.

Paragraph (d)—*Approval of board of directors*—is essentially current § 552.13(f).

Paragraph (e)—*Approval by members*—is essentially current § 546.2(e).

Paragraph (f)—*Conservator or receiver action*—is essentially current § 546.2(f).

Paragraph (g)—*Combination agreement*—is essentially current §552.13(g).

Paragraph (h)—*Corporate title; change of location*—specifies that the charter must be amended in certain instances and is derived from current § 546.2(g).

Paragraph (i)—*Application for Board approval*—is essentially current § 552.13(h) with an additional reminder to applicants that any required Hart-Scott-Rodino antitrust filing must also be made.

Paragraph (j)—*Notice*—is a modified version of current § 552.13(i). The modifications include the requirement that public notice must appear in the communities in which the home offices of all constituent associations are located.

94. *Section 544.22–544.23* are reserved.

95. *Section 544.24 Articles of combination for merger or consolidation*—is essentially current § 552.13(1) paragraphs 1 and 2.

96. *Section 544.25 Effective date; date of consummation for merger or consolidation*—is partially derived from current § 552.13(m) and various state code provisions allowing for a later effective date if requested. The section on date of consummation of a merger or consolidation was proposed to clarify an ongoing procedural problem that the effective date and date of consummation are often not the same.

Paragraph (a)—*Effective date*—tracks the language of current § 552.13 (m) but allows the possibility of a later effective date of a merger or combination if requested. In addition delegated authority to approve combinations is recognized by this section.

Paragraph (b)—*Date of consummation*—specifies that combinations cannot be concluded until necessary compliance materials are submitted to the Supervisory Agent's satisfaction and adds that the Board or its delegate may suspend, alter or withdraw its approval if such action is warranted on the basis of a material change in circumstances, prior to the date of consummation.

97. *Section 544.26 Continuity of corporate existence after merger or consolidation*—is essentially current § 546.3.

98. *Section 544.27* is reserved.

99. *Section 544.28 Supervisory combinations*—is essentially current § 552.15 with additional language derived from section 5(o)(2)(F) of the HOLA regarding cases where severe financial conditions exist which threaten the stability of an association.

100. *Section 544.29* is reserved.

101. *Section 544.30 Bulk purchase of sale of assests*—is derived from current § 552.13. The definition of "bulk purchase of assets" has been expanded.

Paragraph (a)—*Permissible bulk purchase of assets*—is essentially current § 552.13(c)(3) with clarifying language to better address bulk transfers to interim associations as well as to operating associations.

Paragraph (b)—*Permissible bulk sale of assets*—restates the Board's current policy that bulk sales of assets are only permissible in supervisory cases. The Board invites comments from the public on this policy.

Paragraph (c)—*Bulk purchase or sale of assets defined*—expands the current definitional § 552.13(b)(2), now appearing in the definitions section of Corporate Governance, Part I, new proposed Part 541, to include a percentage-of-assets test to determine whether substantially all of the assets of an association are involved such that a transaction would constitute a bulk purchase or sale. The Board invites comments on the choice of 50 percent of total assets of the association prior to the acquisition as the appropriate percentage.

Paragraph (d)—*Board approval*—tracks the language of current § 552.13(d).

Paragraph (e)—*Approval by the Board's Principal Supervisory Agent*—is essentially current § 552.13(e). incorporating recently amended § 563.22 which expands the authority of the Principal Supervisory Agent and the Board's Washington staff to act on many applications pursuant to delegated authority.

Paragraph (f)—*Approval by board of directors*—is essentially current § 552.13(f).

Paragraph (g)—*Combination agreement*—refers the applicant to new § 544.21(g)(2).

Paragraph (h)—*Application for Board approval*—refers the applicant to new § 544.21(i).

Paragraph (i)—*Notice*—refers the applicant to new § 544.21(j).

102. *Section 544.31* is reserved

103. *Section 544.32 Articles of combination for bulk purchase or sale of assets*—refers the applicant to new § 544.24.

104. *Section 544.33 Effective date; date of consummation for bulk purchase or sale of assets*—refers the applicant to new § 544.25.

105. *Section 544.34 Continuity of corporate existence after bulk purchase or sale of assets*—makes clear that a bulk purchase or sale of assets does not affect the corporate existence of the transferee or transferor Federal mutual association.

106. *Section 544.35* is reserved

107. *Section 544.36 Partial purchase or sale of assets*—is a new section to differentiate between a bulk purchase or sale and a partial purchase or sale. The same percentage-of-asset test is used in this section as was used in new § 544.30, and the Board specifically requests public comments on this aspect of the proposal. In addition, the section refers applicants to § 563.22 of the Insurance Regulations for the rules governing procedures for obtaining approval of partial purchases or sales of assets.

108. *Section 544.37–544.39* are reserved.

109. *Section 544.40 Reoganization*—is also reserved.

110. *Sections 544.41–544.49* are reserved.

111. *Section 544.50 Dissolution*—is derived from current § 546.4, the Model Business Corporation Act and the Delaware and California Codes.

112. *Section 544.51 Voluntary dissolution*—is derived from current § 546.4.

Paragraph (a)—*Plan for dissolution*—set forth the requirements for a board of directors to propose a dissolution.

Paragraph (b)—*Board approval*—sets forth the necessity for Board approval of such a plan of dissolution and the criteria for an approval.

113. *Section 544.52 Approval by members for dissolution*—is derived from current § 546.4.

114. *Section 544.53 Notice of dissolution*—is a new section derived from the Model Business Corporation Act.

Paragraph (a)—*Notice to creditors*—is a new requirement to notify all known creditors of the intention to dissolve upon filing a plan of dissolution with the Board.

Paragraph (b)—*Notice to accountholders*—sets forth the affirmative duty of the association to notify affected accountholders of the approval of the members to dissolve in accordance with the Board's existing notice requirements for termination of insurance of § 565.5 of the Insurance Regulations.

115. *Section 544.54 Procedure for dissolution after Board and member approval*—is a new section directing the association to do what acts are necessary to liquidate its business and affairs.

116. *Section 544.55 Termination of corporate existence*—is derived from current § 546.4 and the Model Business Corporation Act.

Paragraph (a)—*Completion of dissolution*—is essentially the last two sentences of current § 546.4.

Paragraph (b)—*Continuation of corporate existence after dissolution*—is a new section derived from the Model Business Corporation Act which continues the corporate existence for three years of a dissolving association solely for the purpose of defending or prosecuting legal actions, settling and closing the business, conveying property, discharging liabilities and distributing the remaining assets.

117. *Section 544.56 Involuntary Dissolution*—is a new section which allows the Board to waive any provision of the dissolution section if the dissolution is instituted for supervisory reasons or pursuant to Part 547.

118. *Sections 544.57–544.59* are reserved.

119. *Section 544.60 Supervisory waiver*—is a new section which allows the Board to waive any provision of Part 544 if necessary in specified supervisory circumstances.

*C. Comment Period and Effective Date*

The Board is soliciting comments on Part II of the proposal for a period of 60 days, but will also accept comments after the 60-day period if made in conjunction with comments regarding later Parts of the proposal. Comments on Part I of the Board's Corporate Governance proposal also may be submitted during the current period for this Part II. The Board specifically requests public comment on procedures for implementing these proposed rules at such time as they become effective. The Board is considering requiring compliance with the proposed regulations by the next annual meeting which occurs 120 days after the effective date of the final regulations.

*Initial Regulatory Flexibility Analysis*

Pursuant to section 3 of the Regulatory Flexibility Act, 5 U.S.C. 603 (1982), the Board is providing the following initial regulatory flexibility analysis:

1. *Reasons, objectives, and legal bases underlying the proposed rules.* These elements have been discussed elsewhere in the supplementary information regarding the proposal.

2. *Small entities to which the proposed rules would apply.* The rules would apply to all federally chartered savings and loan associations and savings banks ("Federal associations").

3. *Impact of the proposed rules on small institutions.* The policies will affect all Federal associations equally and will not have an adverse impact on small institutions.

4. *Overlapping or conflicting Federal rules.* There are no known Federal rules which duplicate, overlap, or conflict with the proposed rules.

5. *Alternatives to the proposed rule.* There are no alternatives that would be less burdensome than the proposal in addressing the concerns expressed in the supplementary information set forth above.

**List of Subjects in 12 CFR Parts 543 and 544**

Savings and Loan Associations, Savings banks.

Accordingly, the Federal Home Loan Bank Board hereby proposes to revise Parts 543 and 544, Subchapter C, Chapter V of Title 12, Code of Federal Regulations, as set forth below.

**SUBCHAPTER C—FEDERAL SAVINGS AND LOAN SYSTEM**

## PART 543—FEDERAL STOCK ASSOCIATIONS

1. Revise Part 543 as follows:

## PART 543—FEDERAL STOCK ASSOCIATIONS

Sec.


543.1 Procedure for organization of Federal stock association; Initial sale of capital stock; organizational meeting.
543.2 Powers of Federal stock associations.
543.3 charter for Federal stock associations.
543.4 Preapproved charter amendments.
543.4–1 Additional charter provisions.
543.5 Procedures for obtaining Board approval of charter amendments.
543.6 Reissuance of charter.
543.7 Bylaws.
543.8 Effect of subsequent charter or bylaw change amendment.
543.9 Stockholder meetings.
543.9–1 Stockholder voting.
543.9–2 Voting trusts among stockholders.
543.9–3 Books and records: stockholder access.
543.9–4 Annual reports to stockholders.
543.9–5 Stockholder derivative actions.
543.10 Board of directors.
543.10–1 Directors' meetings.
543.10–2 Director's conflicts of interest.
543.10–3 Liability of directors for improper distributions.
543.10–4 Officers.
543.10–5 Indemnification of directors, officers and employees.
543.11 Certificates for stock and their transfer.
543.11–1 Consideration for stock.
543.11–2 Stock rights and options.
543.11–3 Fractional shares of stock.
543.11–4 Liability of stockholders.
543.12 Authority to acquire own stock.
543.12–1 Authority to pay dividends to stockholders.
543.12–2 Limitations on distributions to stockholders.
543.12–3 Reduction of paid-in capital.
543.13 Fiscal year; annual audit.
543.14 Corporate procedures.
543.15–543.19 [Reserved]
543.20 Combinations involving Federal stock associations.
543.21 Merger or consolidation.
543.22 Short-form merger.
543.23 Approval by stockholders for merger or consolidation.
543.24 Articles of combination for merger or consolidation.
543.25 Effective date; date of consummation for merger or consolidation.
543.26 Continuity of corporate existence after merger or consolidation.
543.27 Dissenters' appraisal rights in merger or consolidation.
543.28 Supervisory combinations.
543.29 [Reserved]
543.30 Bulk purchase or sale of assets.
543.31 Approval by stockholders.
543.32 Articles of combination.
543.33 Effective date; date of consummation.
543.34 Continuity of corporate existence after bulk purchase or sale of assets.
543.35 Dissenters' appraisal rights in bulk purchase or sale of assets.
543.36 Partial purchase or sale of assets.
543.37–543.39 [Reserved]
543.40 Reorganization [Reserved]
543.41–543.49 [Reserved]
543.50 Dissolution.
543.51 Voluntary dissolutions.
543.52 Approval by stockholders for dissolution.
543.53 Notice of dissolution.
543.54 Procedure for dissolution after Board and stockholder approval.
543.55 Termination of corporate existence.
543.56 Involuntary dissolution.
543.57–543.59 [Reserved]
543.60 Supervisory waiver.
Appendix A to Part 543–Model Bylaws for Stock Associations


**Authority:** 12 U.S.C. 1464; Reorg. Plan No. 3 of 1947, 3 CFR, 1943–1948 Comp., p. 1071.

**§ 543.1 Procedure for organization of Federal stock association; initial sale of capital stock; organizational meeting.**

(a) *General.* Applications for permission to organize a Federal stock association shall be subject to the provisions of §§542.1 through 542.12 of this Subchapter.

(b) *Initial sale of capital stock.* No stock may be offered or sold until the organizers have received conditional approval of the application for permission to organize. Upon the conditional approval of an application for permission to organize a Federal stock association and after the interim officers, directors, employees and agents have been bonded to the extent required by §563.19 of this chapter, the association may proceed to offer and sell its shares of stock and to make all required related filings in accordance with the following:

(1) No shares of stock shall be offered or sold except pursuant to Part 563g of this Chapter, in such final form as adopted by the Board; [Proposed Part 563g is set forth at 50 FR 38839, September 25, 1985.]

(2) Any funds received in an offering of securities in connection with organization and any interest earned thereon shall be held in an escrow, trust account, or similar separate account (which includes an underwriter's or broker-dealer's account), for the association, until (a) the association has received the certificate of authority to do business specified in §542.7 and the securities are issued or (b) the offering is

terminated. The escrow or trust account is required to be with an independent financial institution insured by the Federal Savings and Loan Insurance Corporation or the Federal Deposit Insurance Corporation and shall not be reachable by personal creditors of an organizer. The association shall not collect any funds from the escrow, trust account or similar separate account until the offering has been completed pursuant to the terms of the offering, all conditions of the Board's approval of the application for Permission to Organize are satisfied and the Principal Supervisory Agent approves the release of the funds. While organizers may make contributions to a separate expense fund, subscribers shall not make such contributions. If an offering is not completed within the term of the proposed offering period, any funds collected shall be promptly refunded in full with any interest earned thereon, less a deduction from any interest earned, *Provided*, that: (i) Such deduction is for reasonable organizational or offering expenses and (ii) the terms of the offering provide for such a deduction from interest;

(3) All shares of stock sold in the initial capitalization shall be offered to all purchasers on the same basis and sold at a uniform price and on uniform terms and conditions, and unless approved specifically by the Board, consideration for the initial minimum capitalization shall consist of cash or tangible property to the extent investment in such property would be permitted to the association. Further all stock sold shall be paid in full and shall be nonassessable. Stock options and warrants granted at or before the completion of organization shall be granted subject to stockholder approval and shall have an exercise price at least equal to the initial offering price of the stock;

(4) The par value of stock, if any, shall be as specified in the charter and if no par value is specified then each share of stock shall have a stated value equal to the purchase price of each share.

(c) *Organizational meeting.* Within six months of receiving the certificate of authority to commence business, the association shall provide notice, pursuant to § 543.9 of this Part, of a meeting of its stockholders to elect a board of directors. Until such time, the interim board of direcors shall be governed by the Model Bylaws. Immediately following such election the directors shall meet to adopt permanent bylaws, elect the officers of the association and undertake any other action necessary to complete corporate organization.

**§ 543.2 Powers of Federal stock associations.**

In addition to the authority contained in this Part and in its charter, a Federal stock association may make any loan or investment or engage in any activity authorized for a Federal association in Part 545, 550, 555, or 556 of this Chapter and in section 5(c) of the Home Owners' Loan Act of 1933, as amended, or the successor provisions of any of the foregoing.

**§ 543.3 Charter for Federal stock associations.**

(a) *Initial charter.* The initial charter of a *de novo* Federal stock association shall be in the form specified in paragraph (d) of this section and may also include any preapproved optional provision contained in §543.4 of this Part. Initial federal stock charters of institutions converting from the state stock form may also include additional charter provisions carried over from the association's former charter, provided that such provisions must be approved by the Board in accordance with §543.5 and be separately submitted to the association's stockholders for approval.

(b) *Converted associations.* An association that has converted from the mutual form pursuant to Part 563b of this Chapter shall include in its charter (1) a section establishing a liquidation account as required by § 563b.3(c)(13) of this Chapter and (2) the bracketed clause in the third paragraph of section 5.

(c) *Federal savings bank charter.* A charter for a Federal stock savings bank shall substitute the term "savings bank" for "association" and, for savings banks converting pursuant to §546.10 of this Subchapter shall include the following sentence at the end of section 4 of the Charter set forth at paragraph (d) of this section: "In addition, the savings bank may make any investment and engage in any activity as may be specifically authorized by action of the Board, including authorization by delegated authority, in connection with action approving the issuance of the charter."

(d) *Federal stock charter.* The following is the standard form of Federal stock charter. Associations may vary the wording of charters only in accordance with bracketed instructions.

**Federal Stock Charter**

Section 1. *Corporate title.* The full corporate title of the association is ———.

Section 2. *Office.* The home office shall be located at ———.

Section 3. *Duration.* The duration of the association is perpetual.

Section 4. *Purpose and powers.* The purpose of the association is to pursue any or all of the lawful objectives of a Federal association chartered under section 5 of the Home Owners' Loan Act and to exercise all of the express, implied, and incidental powers conferred thereby and by all acts amendatory thereof and supplemental thereto, subject to the Constitution and laws of the United States as they are now in effect, or as they may hereafter be amended, and subject to all lawful and applicable rules, regulations, and orders of the Federal Home Loan Bank Board ("Board").

Section 5. *Capital stock.* The total number of shares of all classes of the capital stock which the association has the authority to issue is ———, all of which shall be common stock of par [or if no par is specified then shares shall have a stated] value of ——— per share. The shares may be issued from time to time as authorized by the board of directors without the approval of its stockholders, except as otherwise provided in this Section 5 or to the extent that such approval is required by governing law, rule, or regulation. The consideration for the issuance of the stock shall be paid in full before its issuance and shall not be less than the par [or stated] value. Neither promissory notes nor future services shall constitute payment or part payment for the issuance of stock of the association. The consideration for the stock shall be cash, tangible property (to the extent direct investment in such property would be permitted to the association), labor, or services actually performed for the association, or any combination of the foregoing. In the absence of fraud, the value of such property, labor, or services, as determined in good faith by the board of directors of the association, shall be conclusive. Upon payment of such consideration, such stock shall be deemed to be fully paid and nonassessable. In the case of a stock dividend, that part of the retained earnings of the association which is transferred to common stock or paid-in capital accounts upon the issuance of stock as a stock dividend shall be deemed to be the consideration for their issuance.

Except for stock issued in the initial organization of the association or in the conversion of the association from the mutual to stock form, no shares of capital stock (including shares issuable upon conversion, exchange, or exercise of other securities) shall be issued, directly or indirectly, to officers, directors, or beneficial owners of ten percent or more of any class of capital stock of the association other than as part of a general public offering or as qualifying stock to a director, unless the issuance or the plan under which they would be issued has been approved by a majority of the total votes eligible to be cast at legal meeting.

The holders of the common stock shall exclusively possess all voting power. Each holder of shares of common stock shall be entitled to one vote for each share held by such holder, except as to the cumulation of votes for the election of directors, unless the charter otherwise provides that there shall be no such cumulative voting. In the event of any liquidation, dissolution, or winding up of

the association [and subject to any provision for a liquidation account], the holders of the common stock shall be entitled, after payment or provision for payment of all debts and liabilities of the association, to receive the remaining assets of the association available for distribution, in cash or in kind. Each share of common stock shall have the same relative rights as and be identical in all respect with all the other shares of common stock.

Section 6. *Preemptive rights.* Holders of the capital stock of the association shall not be entitled to preemptive rights with respect to any stock of the association which may be issued.

Section 7. *Directors.* The association shall be under the direction of a board of directors. The authorized number of directors, as stated in the association's bylaws, shall not be fewer than five nor more than fifteen except when a greater number is approved by the Board or its delegate.

Section 8. *Amendment of charter.* Except as provided in Section 5, no amendment, addition, alteration, change, deletion to or repeal of this charter shall be made, unless such is first proposed by the board of directors of the association, then preliminarily approved by the Board, which preliminary approval may be granted by the Board pursuant to regulations specifying preapproved charter amendments, and thereafter approved by the stockholders by a majority of the total votes eligible to be cast at a legal meeting, unless a higher vote is otherwise required. Any amendment, addition, alteration, change, deletion to or repeal so acted upon shall be effective upon filing with the Board in accordance with regulatory procedures or on such other date as the Board may specify in its preliminary approval.

Attest: ———,

*Secretary of the Association.*

By: ———,

*President or Chief Executive Officer of the Association.*

Attest: ———,

*Secretary to the Board.*

By: Federal Home Loan Bank Board.

———,

———,

Effective date: ———.

**§ 543.4 Preapproved charter amendments.**

This section constitutes preliminary approval by the Board of proposals to stockholders by the board of directors of any Federal stock association, for the adoption or deletion of any of the following amendments to such association's charter, including the adoption of the Federal stock charter as set forth in § 543.3(d) of this Part: *Provided,* that the association follows the requirements of its charter in adopting the amendments, and *Provided further,* that where a paragraph specifies wording for an amendment, such amendment uses the exact wording as specified in that paragraph. Citations to charter sections refer to the charter set forth at § 543.3(d) of this Part.

(a) *Title change.* A Federal stock association may amend its charter by substituting a new corporate title upon satisfaction of the requirements of this paragraph. Prior to submitting the proposed amendment to its stockholders, the association must file with the Supervisory Agent a written notice setting forth the proposed title. The Supervisory Agent shall provide to the association a timely written acknowledgement of receipt. If, within 30 days of receipt of notice, the Supervisory Agent does not notify the association of his objection on the grounds set forth in § 542.2 of this Subchapter, the association may change its title by amending its charter in accordance with § 543.5(b) of this Part and the amendment provisions of its charter, except that an association may change its title to indicate that it is a Federal savings bank, and an association chartered as a Federal savings bank may change its title to indicate that it is a Federal savings and loan association, only pursuant to paragraph (c) of this section.

(b) *Change of location.* A Federal stock association that has complied with § 545.95 of this Subchapter may amend its charter by substituting a new home office in section 2.

(c) *Savings bank charter.* A Federal stock savings and loan association may amend its charter to read in the form of a Federal stock savings bank charter as specified in § 543.3(c) of this Part and a Federal stock saving bank may amend its charter to read in the form of a Federal stock savings and loan association charter: *Provided,* that such association complies with the requirements of § 546.10 of this Subchapter.

(d) *Number of shares of stock and par value.* A Federal association may amend section 5 of its charter to change the number of authorized shares of stock, the number of shares within each class of stock, and the par or stated value of such stock.

(e) *Preferred stock.* A Federal stock association may amend its charter by revising Section 5 to read as follows:

Section 5. *Captial stock.* The total number of shares of stock of all classes of the capital stock which the association has the authority to issue is ———, of which ——— shall be common stock of par [or if no par value is specified, the stated] value of ——— per share and of which [list the number of each class of preferred and the par or stated value per stock of each such class]. The stock may be issued from time to time as authorized by the board of directors without further approval of stockholders, except as otherwise provided in this Section 5 or to the extent that such approval is required by governing law, rule, or regulation. The consideration for the issuance of the stock shall be paid in full before its issuance and shall not be less than the par [or stated] value. Neither promissory notes nor future services shall constitute payment or part payment for the issuance of stock of the association. The consideration for the stock shall be cash, tangible property (to the extent direct investment in such property would be permitted to the association), labor, or services actually performed for the association, or any combination of the foregoing. In the absence of fraud, the value of such property, labor, or services, as determined in good faith by the board of directors of the association, shall be deemed to be fully paid and non-assessable. In the case of stock a dividend, that part of the retained earnings of the association which is transferred to paid-in capital upon the issuance of stock as a stock dividend shall be deemed to be the consideration for its issuance.

Except for stock issued in the initial organization of the association or in the conversion of the association from the mutual to the stock form, no shares of capital (including stock issuable upon conversion, exchange, or exercise, or other securities) shall be issued, directly or indirectly, to officers, directors, or beneficial owners of ten percent or more of any class of capital stock of the association other than as part of a general public offering or as qualifying stock to a director, unless the issuance of such stock or the plan under which it would be issued has been approved by a majority of the total votes eligible to be cast at a legal meeting.

Nothing contained in this Section 5 (or in any supplementary section hereto) shall entitle the holders of any class of or series of capital stock to vote as a separate class or series or to more than one vote per share, except as to the cumulation of votes for the election of directors, unless the charter otherwise provides that there shall be no such cumulative voting: *Provided,* that this restriction on voting separately by class or series shall not apply:

(i) To any provison which would authorize the holders of preferred stock, voting as a class or series, to elect members of the board of directors constituting fewer than a majority thereof, in the event of default in the payment of dividends on any class or series of preferred stock;

(ii) To any provision which would require the holders of preferred stock, voting as a class or series, to approve the merger or consolidation of the association with another corporation or the sale, lease, or conveyance (other than by mortgage or pledge) of properties or business exchange for securities of a corporation other than the association if the preferred stock is exchanged or securities of such other corporation: *Provided,* that no provision may require such approval for transactions undertaken with the assistance or pursuant to the direction of the Federal Savings and Loan Insurance Corporation;

(iii) To any amendment which would adversely change the specific terms of any

class or series of capital stock as set forth in this section 5 (or in any supplementary sections thereto), including any amendments which would create or enlarge any class or series ranking prior thereto in rights and preferences. An amendment which increases the number of authorized shares of any class or series of capital stock, or substitutes the surviving association in a merger or consolidation for the association, shall not be considered to be such an adverse change.

A description of the different classes and series (if any) of the associaiton's capital stock and a statement of the designation, and the relative rights, preferences and limitations of the shares of each class of and series (if any) of capital stock are as follows:

A. *Common stock.* Except as provided in this Section 5 (or in any supplmentary sections thereto), the holders of the common stock shall exclusively possess all voting power. Each holder of shares of common stock shall be entitled to one vote for each share held by such holder, except as to the cumulation of votes for the election of directors; unless the charter otherwise provides that there shall be no such cumulative voting.

Whenever there shall have been paid, or declared and set aside for payment, to the holders of the outstanding shares of any class of stock having preference over the common stock as to the payment of dividends, the full amount of dividends and of sinking fund, retirement fund, or the retirement payments, if any, to which such holders are respectively entitled in preference to the common stock, then dividends may be paid on the common stock and on any class or series of stock entitled to participate therewith and to dividends out of any assets legally available for the payment of dividends.

In the event of any liquidation, dissolution, or winding up of the association, the holders of the common stock (and the holders of any class or series of stock entitled to participate with the common stock in the distribution of assets) shall be entitled to receive, in cash or in kind, the assets of the association available for distribution remaining after: (i) Payment or provision for payment of the association's debts and liabilities; (ii) distributions or provision for distributions to holders of any class or series of stock having preference over the common stock in the liquidation, dissolution, or winding up of the association. Each share of common stock shall have the same relative rights as and be identical in all respects with all the other shares of common stock.

B. *Preferred Stock.* The association may provide in supplementary sections to its charter for one or more classes of preferred stock, which shall be separately designated so as to distinguish the stock thereof from the stock of all other series and classes. The terms of each series shall be set forth in a supplementary section to the charter. All shares of stock of the same class shall be identical except as to the following relative rights and preferences, as to which there may be variations between different series:

(a) The distinctive serial designation and the number of shares of stock constituting such series;

(b) The dividend rate or the amount of dividends to be paid on the shares of stock of such series, whether dividends shall be cumulative and, if so, from which date(s), the payment date(s) for dividends, and the participating or other special rights, if any, with respect to dividends;

(c) The voting powers, full or limited, if any, of shares of stock of such series;

(d) Whether the shares of stock of such series shall be redeemable and, if so, the price(s) at which, and the terms and conditions on which, such stock may be redeemed;

(e) The amount(s) payable upon the shares of stock of such series in the event of voluntary or involuntary liquidation, dissolution, or winding up of the association;

(f) Whether the shares of stock of such series shall be entitled to the benefit of a sinking or retirement fund to be applied to the purchase or redemption of such stock, and if so entitled, the amount of such fund and the manner of its application, including the price(s) at which such stock may be redeemed or purchased through the application of such fund;

(g) Whether the shares of stock of such series shall be convertible into, or exchangeable for, shares of stock of any other class or classes of stock of the association and, if so, the conversion price(s) or the rate(s) of exchange, and the adjustments thereof, if any, at which such conversion or exchange may be made, and any other terms and conditions of such conversion or exchange;

(h) The price or other consideration for which the shares of stock of such series shall be issued; and

(i) Whether the shares of stock of such series which are redeemed or converted shall have the status of authorized but unissued shares of serial preferred stock and whether such shares of stock may be reissued as shares of the same or any other series of serial preferred stock.

Each share of stock of each series of serial preferred stock shall have the same relative rights and be identical in all respect with all the other shares of stock of the same series.

Except as otherwise provided in this Section 5, the board of directors shall have authority by resolution or resolutions from time to time adopted to divide, by the adoption of supplementary charter sections, any authorized class of preferred stock into series, and, within the limitations set forth in this section and the articles of incorporation, fix and determine the relative rights and preferences of the shares of any series so established.

Prior to the issuance of any preferred stock of a series established by a supplementary charter section adopted by the board of directors, the association shall file with the Supervisory Agent, the Office of General Counsel and with the Secretary to the Board a dated copy of that supplementary section of this charter establishing and designating the series and fixing and determining the relative rights and preferences thereof.

(f) *Limitations on subsequent issuances.* A Federal stock association may amend its charter to require stockholder approval of the issuance or reservation of common stock or securities convertible into common stock under circumstances which would require stockholder approval under the rules of the New York Stock Exchange or the American Stock Exchange if the stock were then listed on the New York or American Stock Exchanges, or to insert in the second paragraph of section 5 before the word "unless" the following: "or shares of common stock exceeding fifteen percent of the total number of stock than outstanding,".

(g) *Anti-takeover provisions following conversion.* A Federal stock association that has converted to the stock from pursuant to Part 563b may amend its charter by renumbering existing sections as appropriate and adding a new section 8 as follows:

Section 8. *Certain Provision Applicable for Five Years.* Notwithstanding anything contained in the association's charter or bylaws to the contrary, for a period of [specify period up to five years from the date of completion of the conversion of the association from mutual to stock form], the following provisions shall apply:

(A) *Beneficial Ownership Limitation.* No person shall directly or indirectly offer to acquire or acquire the beneficial ownership of more than ten percent of any class of an equity security of the association. This limitation shall not apply to a transaction in which the association forms a holding company without change in the respective beneficial ownership interests of its stockholders other than pursuant to the exercise of any dissenters' appraisal rights, or to the purchase of stock by underwriters in connection with an offering of the association's equity securities.

In the event stock is acquired in violation of this section 8, all stock beneficially owned by any person in excess of ten percent shall be considered "excess stock" and shall not be counted as stock entitled to vote and shall not be voted by any person or counted as voting shares in connection with any matters submitted to the stockholders for a vote.

For purposes of this section 8, the following definitions apply:

(a) The term "person" includes an individual, a group acting in concert, or any "company" as defined in § 574.2(e).

(b) The term "offer" includes every offer to buy or otherwise acquire, solicitation of an offer to sell, tender offer for, or request for invitation for tenders of, a security or interest in a security for value.

(c) The term "acquire" includes every type of acquisition, whether effected by purchase, exchange, operation or law or otherwise.

(d) The term "acting in concert" means (a) knowing participation in a joint activity or conscious interdependent parallel action towards a common goal whether or not pursuant to an express agreement, or (b) a combination or pooling of voting or other interests in the securities of an issuer for a common purpose pursuant to any contract, understanding, relationship, agreement or other arrangement, whether written or otherwise.

(B) *Cumulative Voting Limitation.* Stockholders shall not be permitted to cumulate their votes for election of directors.

(C) *Call for Special Meetings.* Special meetings of stockholders relating to changes in control of the association or amendments to its charter shall be called only upon direction of the board of directors.

(h) *Cumulative voting.* A Federal stock association may amend its charter by substituting the following sentence for the second sentence in the third paragraph of Section 5: "Each holder of shares of common stock shall be entitled to one vote for each share held by such holder and there shall be no right to cumulate votes in an election of directors."

(i) *Preemptive rights.* A Federal stock association may amend its charter by substituting the following language as a new Section 6: "Each holder of the capital stock of the association shall be entitled to preemptive rights with respect to any stock of the association which may be issued."

**§ 543.4–1 Additional charter provisions.**

After a Federal stock charter is issued, the board of directors of a Federal stock association may request perliminary approval of additional charter provisions not listed in § 543.3 or § 543.4; *Provided*, that any such provision must be consistent with applicable statutes, regulations and Board policies; and *Provided further* that any such provision having the effect of rendering more difficult a change in control of the association which requires for any corporate actions (other than the election or removal of directors), the affirmative vote of a larger percentage of stockholders than is required by this Part, including approval of the transactions involving certain stockholders, shall not be effective unless adopted by a percentage of stockholder vote at least equal to the highest percentage that would be required to take any action under such provision.

**§ 543.5 Procedures for obtaining Board approval of charter amendments.**

(a) *Procedure for obtaining preliminary approval of charter amendments.* Preliminary approval is the approval required before submitting charter amendments to a vote of the stockholders. Adoption or deletion of any of the provisions set forth at § 543.3 or § 543.4 of this Part are granted preliminary approval. The board of directors of a Federal stock association may request preliminary approval of amendments to the association's Federal stock charter not listed in § 543.3 or 543.4 by filing with the Office of General Counsel, with a copy to the Supervisory Agent, a certified resolution of the board of directors of the association proposing the amendment and setting forth the text of the amendment. Any such provision must be consistent with applicable statutes, regulations and Board policies. In addition, if the effect of the proposed amendment would be to render more difficult a change in control of the institution, the filing shall include an opinion, acceptable to the Board, of counsel independence from the association, demonstrating that the proposed charter provision is consistent with applicable statutes, regulations and Board policies and indicating whether such a provision would be permissible for a corporation incorporated under the laws of Delaware. Any amendment not consistent with statutes, regulations or policies of the Board need not be approved by the Board or its delegate, regardless of their purported permissibility under state law. The Board's General Counsel or his designee has delegated authority to make determinations under this section and grant or deny the preliminary approval of the Board for amendments to Federal stock of the Board for amendments to Federal stock charters or to Charles S or T. Upon making any such determination, the General Counsel shall notify the Supervisory Agent who shall forward a copy of that determination to the association.

(b) *Procedures for obtaining final approval of amendments.* Whenever a Federal stock association whose charter specifies that amendments shall be effective upon filing completes the procedures necessary to amend its charter, or adds supplementary sections thereto, the association shall submit three signed copies of such amendment, along with a certification by the secretary of the association that the amendment has been validly authorized and approved, to the Supervisory Agent, who shall return to the association a signed copy of the charter amendment stamped to demonstrate its filing and forward one copy to the Board's Office of District Banks. Such filing shall constitute filing with the Board for purposes of determining the effectiveness of the amendment. A Federal stock association whose charter provides that any amendment shall be effective on the date it receives final approval of the Board shall be deemed to have obtained such final approval on the date it files a copy of the properly adopted amendment with the Supervisory Agent in the manner specified in the first sentence of this paragraph (b).

**§ 543.6 Reissuance of charter.**

A Federal stock association that has amended its charter may apply to have its charter, including any amendments thereto, reissued by the Board by filing three executed copies, with the signatures required under § 543.3 of this Part, with the Board's Office of District Banks, with such supporting documents as are needed to demonstrate that the amendments were properly adopted. Supporting documents shall include copies of the letters granting preliminary approval of the amendments and certifications regarding the vote of stockholders. The Board delegates to the General Counsel or his designee authority to sign on its behalf charters submitted for reissuance pursuant to this paragraph. Following attestation by the Secretary to the Board or his designee, a copy shall be returned to the association with copies forwarded to the Supervisory Agent and Office of District Banks.

**§ 543.7 Bylaws.**

(a) *General.* At its first meeting following election by the stockholders, the board of directors of a Federal stock association shall adopt a set of bylaws for the administration and regulation of its affairs. Except as otherwise provided in this section or in the charter, bylaws may be adopted, amended, or repealed by either a majority of the votes cast by the stockholders at a legal meeting or a majority of the board of directors. The bylaws shall contain sufficient provisions to govern the association in accordance with the requirements of §§ 543.8 through 543.13 of this Part.

(b) *Permissible bylaws.* The bylaws and all amendments thereto shall not contain any provision that is inconsistent with §§ 543.8 through 543.14 of this Part or with other applicable laws, rules, regulations, or the policies underlying such rules, or with the charter of the association. Bylaw provisions that adopt the language of the Model Bylaws set out in the Appendix to this Part shall be deemed to comply with the requirements of this section.

(c) *Effectiveness.* Bylaws and amendments thereto that adopt the wording of the Model Bylaws in the Appendix shall be effective upon filing with the Supervisory Agent along with a statement that such provisions conform to the Model Bylaws. Bylaws and amendments that do not adopt the wording of the Model Bylaws shall not be effective unless approved by the Supervisory Agent. Approval by the Supervisory Agent shall constitute the approval of the Board for associations

whose bylaws require such approval for amendment. The Supervisory Agent shall not accept any bylaws or amendments thereto for filing not conforming to the Model Bylaws unless accompanied by an opinion of counsel independent from the association that such bylaws or amendments conform to the requirements of paragraph (b) of this section. Notwithstanding anything in this section, however, no bylaw provision whose effect would be to render more difficult a change in control of the institution or which adversely affects the ability of stockholders to participate in the governance of the institution shall be effective unless such bylaw or amendment has been approved by the General Counsel or his designee. Any such provision must be filed with the Office of General Counsel together with an opinion, acceptable to the Board, of counsel independent from the association, demonstrating that the proposed provision is consistent with applicable statutes, regulations and Board policies and indicating whether such provision would be permissible for a corporation incorporated under the laws of Delaware. The General Counsel may condition approval on the favorable vote of the stockholders or such other conditions as he may deem appropriate.

(d) *Procedure.* Three copies of all bylaws and amendments thereto shall be filed with the Supervisory Agent with a copy of any required legal opinion and a certification from the secretary of the association stating such bylaws or amendments thereto were adopted by resolution of the board of directors or stockholders by the requisite vote. Upon approval the Supervisory Agent shall return one copy to the association, and forward one copy to the Board's Office of District Banks, except that with respect to bylaws requiring the approval of the General Counsel, the association shall file two copies with the General Counsel and one copy with the Supervisory Agent and upon approval the General Counsel shall return one copy to the Supervisory Agent who shall notify the association.

**§ 543.8 Effect of subsequent charter or bylaw change amendment.**

Notwithstanding any subsequent change to its charter or bylaws, the authority of a Federal stock association to engage in any transaction shall be determined only by the association's charter or bylaws then in effect, unless otherwise provided by federal law or regulation.

**§ 543.9 Stockholder meetings.**

(a) *Stockholder meetings.* An annual meeting of the stockholders of the association for the election of directors and for the transaction of any other business of the association shall be held annually within 150 days after the end of the association's fiscal year. Special meetings of the stockholders may be called by the board of directors or as set forth in the charter or in the bylaws, on the request of the holders of a percentage of the total shares of stock entitled to vote at the meeting, provided that such percentage shall not exceed 25 percent, or by such other persons as may be specified in the bylaws of the association as entitled to call special meetings. All annual and special meetings of stockholders shall be held at such places as the board of directors may determine in the state in which the association has its principal place of business or in which the association maintains branches.

(b) *Notice of stockholder meetings.* A Federal association shall provide written notice of each stockholders' meeting setting forth the place, day, and hour of the meeting and the purpose or purposes for which the meeting is called. Such notice shall be delivered not fewer than 20 nor more than 50 days before the date of the meeting, either personally or by mail, by or at the direction of the chairman of the board, president, secretary, or directors, or other persons calling the meeting, to each stockholder of record entitled to vote at such meeting. If mailed, such notice shall be deemed to be delivered when deposited in the United States mail, proper postage prepaid, and addressed to the stockholder at the address appearing on the stock transfer books or records of the association as of the record date prescribed in paragraph (c) of this section. *Provided,* that such mailing is conducted in a manner designed to ensure delivery within a resonable time. When any stockholders' meeting, either annual or special, is adjourned for 30 days or more, notice of the adjourned meeting shall be given as in the case of an original meeting. Notwithstanding anyting in this section, however, a Federal stock association wholly owned by a holding company, (disregarding any required qualifying shares of directors), shall not be subject to the stockholder notice requirement.

(c) *Fixing of record dates.* For the purpose of determining stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or stockholders entitled to receive payment of any dividend, or in order to make a determination of stockholders for any other proper purpose, the board of directors shall fix in advance a date as the record date for any such determination of stockholders. Such date in any case shall not be more than 50 days and, in case of a meeting of stockholders, no fewer than 20 days prior to the date on which the particular action, reguiring such determination of stockholders, is to be taken. When a determination of stockholders entitled to vote at any meeting or stockholders has been made as provided in this section, such determination shall apply to any adjournment thereof.

(d) *Voting lists.* (1) A Federal stock association, at least 20 days before each meeting of the stockholders, shall direct the officer or agent having charge of the stock transfer books for stock of the association to make available a complete list of the record stockholders entitled to vote at such meeting or any adjournment thereof, and including the names of any beneficial owners furnished to the association pursuant to rules of the Securities and Exchange Commission, arranged in alphabetical order, with the address and the number of shares of stock held by each. This list of stockholders shall be kept on file at the home office of the association and shall be subject to inspection, for any purpose germane to the meeting, by any stockholder of record or such stockholder's agent, at any time during usual business hours, for a period of 20 days prior to such meeting. Such list shall also be produced and kept open at the time and place of the meeting and shall be subject to the inspection of any stockholder of record or the stockholder's agent during the entire time of the meeting. The original stock transfer book shall constitute *prima facie* evidence of the stockholders entitled to examine such list or transfer books or to vote at any meeting of stockholders. Notwithstanding anything in this section, however, a Federal stock association wholly owned by a holding company (disregarding any required qualifying shares of directors), shall not be subject to the voting list disclosure requirements.

(2) In lieu of making the stockholder list available for inspection by any stockholder as provided in this section, the board of directors may perform such acts as required by paragraphs (a) and (b) of Rule 14a-7 of the General Rules and Regulations under the Securities Exchange Act of 1934 as may be duly requested in writing, with respect to any matter which may be properly considered at a meeting of stockholders, by any stockholder who is entitled to vote on such matter and who shall defray the reasonable expenses to be incurred by the association in performance of the act or acts required.

(e) *Stockholder quorum.* A majority of the outstanding stock of the association

entitled to vote, represented in person or by proxy, shall constitute a quorum at a meeting of stockhodlers. The stockholders present at a legal meeting may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. If a quorum is present, the affirmative vote of the majority of the shares of stock represented at the meeting and entitled to vote on the subject matter shall be the act of the stockholders, unless the vote of a greater number of stockholders voting together or voting by classes is required by law of the charter.

(f) *Nominations.* The board of directors or a committee of directors appointed by a majority of directors shall act as a nominating committee for selecting the management nominees for election as directors. Except in the case of a nominee substituted as a result of the death or other incapacity of a management nominee, the nominating committee shall deliver written nominations to the secretary at least 20 days prior to the date of the annual meeting. No nominations for directors except those made by the nominating committee shall be voted upon at the annual meeting unless other nominations by stockholders of record are made in writing and delivered to the secretary of the association. Such nominations by stockholders may be submitted until the later of (1) 10 days before the date of the annual meeting; (2) 10 days after a notice of the annual meeting and related proxy statement or information statement containing the names of management nominees is sent to stockholders; or (3) 10 days after management nominations are submitted to the secretary of the association. Ballots bearing the names of all persons nominated by the nominating committee and by stockholders shall be provided for use at the annual meeting. However, if the nominating committee shall fail or refuse to act at least 20 days prior to the annual meeting, nominations for directors may be made at the annual meeting by any stockholder of record and shall be voted upon.

(g) *New business.* Any new business to be taken up at the annual meeting must be stated in writing by a stockholder of record and filed with the secretary of the association at least ten days before the date of the annual meeting, and all business so stated, proposed, and filed shall be considered at the annual meeting; and no other proposal shall be acted upon at the annual meeting. Any stockholder of record may make any other proposal at the annual meeting and the same may, but need not, be discussed and considered, but unless stated in writing and filed with the secretary at least ten days before the meeting, such proposal shall be laid over for action at an adjourned, special, or next annual meeting of the stockholders taking place 30 days or more thereafter. This provision shall not prevent the consideration and approval or disapproval at the annual meeting of reports of officers, directors, and committees; but in connection with such reports, no new business shall be acted upon at such annual meeting unless stated and filed as provided in this section.

(h) *Informal action by stockholders.* If the bylaws of the association so provide, any action required to be taken at a meeting of the stockholders, or any other action which may be taken at a meeting of stockholders, may be taken without a meeting if consent in writing, setting forth the action so taken, shall be given by all of the stockholders entitled to vote with respect to the subject matter. The record date for determining stockholders entitled to consent to such action without a meeting shall be the date on which the first written consent is given.

**§ 543.9–1 Stockholder voting.**

(a) *Proxies.* At all meetings of stockholders, a stockholder may vote in person or by a duly authorized attorney in fact. Proxies may be given telephonically or electronically as long as the holder uses a reasonable procedures, determined to be acceptable by the General Counsel or his designee, for identifying the stockholder. Notwithstanding § 569.3(b) of this Subchapter, a proxy may designate as holder a corporation, partnership, company as defined in Part 574 or other person. Proxies solicited on behalf of the management shall be voted as directed by the stockholder or, in the absence of such direction, as determined by a majority of the board of directors. No proxy shall be valid more than eleven months from the date of its execution except for a proxy coupled with an interest.

(b) *Stock controlled by association and others.* (1) Neither treasury shares of its own stock held by the association nor stock held by another company, if such other company is controlled by the association as defined in Part 574 of this Chapter, shall be voted at any meeting or counted in determining the total number of outstanding shares at any given time for purposes of any meeting.

(2) Stock standing in the name of another corporation, domestic or foreign, may be voted by such officer, agent or proxy as the bylaws of such other corporation may prescribe, or, in the absence of such provision, as the board of directors of such other corporation may determine.

(3) Stock held by an administrator, executor, guardian or conservator may be voted by him, either in person or by proxy, without a transfer of such stock into his name. Stock standing in the name of a trustee may be voted by him, either in person or by proxy, in accordance with the terms of the trust agreement, but no trustee shall be entitled to vote stock held by him without a transfer of such stock into his name.

(4) Stock standing in the name of a receiver may be voted by such receiver, and shares held by or under the control of a receiver may be voted by such receiver without the transfer thereof into the receiver's name if authority to do so is contained in an appropriate order by which receiver was appointed.

(5) A stockholder whose stock is pledged shall be entitled to vote such stock until the stock has been transferred into the name of the pledgee, and thereafter the pledgee shall be entitled to vote the stock go transferred.

(c) *Cumulative voting.* Unless otherwise provided in the association's charter, every stockholder entitled to vote at an election for directors shall have the right to vote, in person by proxy, the number of shares of stock owned by the stockholder for as many persons as there are directors to be elected and for whose election the stockholder has a right to vote, or to cumulate the votes by giving one candidate as many votes as the number of such directors to be elected multipled by the number of shares of stock shall equal, or by distributing such votes on the same principle among any number of candidates.

**§ 543.9–2 Voting trusts among stockholders.**

Any number of stockholders of an association may create a voting trust for the purpose of conferring upon a trustee or trustees the right to vote or otherwise represent their stock, for a period not to exceed ten years, by entering into a written voting-trust agreement specifying the terms and conditions of the voting trust, by depositing a counterpart of the agreement with the association at its home office, and by transferring their stock to such trustee or trustees for the purposes of the agreement. Such trustee or trustees shall keep a record of the holders of voting-trust certificates evidencing a beneficial interest in the voting-trust, giving the

names and addresses of all such holders and the number and claim of the stock in respect of which the voting-trust certificates held by each are issued, and shall deposit a copy of such record with the association's secretary. The counterpart of the voting-trust agreement and the copy of such record so deposited with the association shall be subject to the same right of examination by a stockholder of the association, in person or by agent, as are the books and records of the association, and such counterpart and such copy of such record shall be subject to examination by any holder of record of voting-trust certificates, either in person or by agent at any reasonable time for any proper purpose.

**§ 543.9–3 Books and records; stockholder access.**

*(a) General.* Books, records and minutes may be in written from or in any other form capable of being converted into written form within a reasonable time. Each Federal stock association shall: (1) keep correct and complete books and records of accounts which, in reasonable detail, accurately reflect the transactions and dispositions of assets of the association; (2) devise and maintain a system of internal accounting controls sufficient to provide reasonable assurance that:

(i) Transactions are executed in accordance with management's general or specific authorization;

(ii) Transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles or any other criteria applicable to such statements, and to maintain accountability for assets;

(iii) Access to assets is permitted only in accordance with management's general or specific authorization; and

(iv) The recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences;

(3) Keep minutes of proceedings of its stockholders, board of directors, and committees of directors; and (4) keep at its home office, or at the office of its transfer agent or registrar, a record of its stockholders, giving the names and addresses of all stockholders, and the number, class and series, if any, of the shares of stock held by each.

(b) *Right to examine.* Any stockholder or group of stockholders of a Federal stock association holding of record the number of voting stock of such association specified in this section, upon making written demand to the secretary of the association under oath and stating the purpose thereof, shall have the right to examine for any proper purpose, in person or by agent, at any reasonable time or times, non-confidential portions of its books and records of accounts, minutes, voting trust agreements filed with the association, and record of stockholders, and to make extracts therefrom. A "proper purpose" shall mean a purpose reasonably related to such person's interest as a stockholder. Such right to examination is limited to a stockholder or group of stockholders holding of record (1) voting stock having a cost of not less than $100,000 or constituting not less than one percent of the total outstanding voting stock, provided in either case that such stockholder or group of stockholders have held of record such voting stock for a period of at least six months before making such written demand, or (2) not less than five percent of the total outstanding voting stock. No stockholder or group of stockholders of a Federal stock association shall have any other right under this section or common law to examine its books and records of account, minutes and record of stockholders, except as provided in § 543.9(d) of this Part with respect to inspection of a list of stockholders, or in rules adopted pursuant to section 14 of the Securities Exchange Act for associations subject to such rules.

(c) *Denial of right to examine.* The right to examination authorized by paragraph (b) of this section may be denied to any stockholder or group of stockholders upon the refusal of any stockholder or group of stockholders to furnish the association, its transfer agent or registrar an affidavit that such stockholder has not within the five years preceding the date of the affidavit sold or offered for sale, and does not now intend to sell or offer for sale, any list of stockholders of the association, and that such stockholder has not within said five-year period assisted any person in procuring any list of stockholders for purposes of selling or offering for sale such list. A Federal stock association may deny a demand under paragraph (b) if the requesting stockholder has improperly used any information secured through prior examination of the books and records of accounts, or minutes, or record of stockholders or of holders of voting-trust certificates for stock of the association.

(d) *Confidentiality of records.* Notwithstanding any provision of this section or common law, no stockholder, group of stockholders, or any other person shall have the right to obtain, inspect or copy any portion of any books or records of a Federal stock association containing: (1) A list of depositors in or borrowers from such association; (2) their addresses; (3) individual deposit or loan balances or records; or (4) any data from which such information could be reasonably constructed.

(e) *Compelling inspection.* If a Federal association or an agent or officer thereof refuses to permit an inspection sought by a stockholder or his agent or does not reply to the demand within 30 calendar days after the demand has been made, the stockholder may apply to a court having jurisdiction for an order to compel inspection.

**§ 543.9–4 Annual reports to stockholders.**

A Federal stock association shall, within 120 days after the end of its fiscal year, mail to each of its stockholders entitled to vote at its annual meeting an annual report containing financial statements the content of which satisfies the requirements of Rule 14a–3(b) under the Securities Exchange Act of 1934, as supplemented by Part 563c of this Chapter. Concurrently with such mailing, a certification of the mailing signed by the chairman of the board, the president or a vice president of the association, together with three copies of the report, shall be sent by the association to the Federal Home Loan Bank of which the association is a member. Notwithstanding anything in this section, however, a Federal stock association wholly owned by a holding company (disregarding any required qualifying stock of directors), shall not be subject to the requirement to provide an annual report to stockholders.

**§ 543.9–5 Stockholder derivative actions.**

(a) *Right to bring an action.* A stockholder of a Federal stock association may bring an action to enforce a right of the association, *provided that,* no action shall be brought by a stockholder to enforce a right of a Federal stock association unless (1) the plaintiff was a holder of record of stock or of voting-trust certificates therefor at the time of the transaction of which he complains, or his stock or voting-trust certificates thereafter developed upon him by operation of law from a person who was a holder of record at such time and (2) the Principal Supervisory Agent has appoved bringing the action. Any action shall include information as to the efforts, if any, made to obtain the action the stockholder desires from the board of directors and, if necessary, from the stockholders, and the reason for the failure to obtain such action or for not making the effort.

(b) *Payment of expenses.* In any action hereafter instituted to enforce a right of any Federal stock association by the holder or holders of record of stock of such association or of voting-trust certificates therefor, the court having jurisdiction, upon final judgment and a finding that the action was brought without reasonable cause, may require the plaintiff or plaintiffs to pay to the parties named as defendant or the association if it has indemnified those parties, the reasonable expenses, including attorneys fees, incurred by them in the defense of such action.

(c) *Security for expenses.* In any action instituted or maintained to enforce a right of any Federal stock association the association on whose behalf such action is brought shall be entitled at any time before final judgment to require the plaintiff or plaintiffs to give security for the reasonable expenses, including attorneys fees, that may be incurred by the association in connection with such action or may be incurred by other parties named as defendant for which the association may become legally liable. The amount of such security may from time to time be increased or decreased, in the discretion of the court, upon showing that the security provided has or may become inadequate or is excessive. The association shall have recourse to such security in such amount as the court having jurisdiction shall determine upon the termination of such action, whether or not the court finds the action was brought without reasonable cause.

**§ 543.10 Board of directors.**

(a) *General.* All corporate powers shall be exercised by or under authority of, and the business and affairs of a Federal stock association shall be managed under the director of, a board of directors. Directors need not be stockholders of the association unless the bylaws so require. A majority of the directors shall be "independent" as that term is defined in § 543.10–1(c)(2), except when a majority of the voting stock of the association is owned by a holding company. The board of directors shall have authority to fix reasonable compensation of directors and authorize the reimbursement of expenses for actual attendance at any meeting of the Board or its committees. The board of directors shall annually elect a chairman of the board from among its members and shall designate the chairman of the board, when present, to preside at its meetings.

(b) *Performance of duties.* (1) A director shall perform his duties as a director, including his duties as a member of any committee of the board upon which he may serve, in good faith, in a manner he reasonably believes to be in the best interest of the association, and with such care as a prudent person in a like position would use under similar circumstances. In performing his duties, a director shall be entitled to rely on information, opinion, reports or statements, including financial statements and other financial data, in each case prepared or presented by:

(i) One or more officers or employees of the association whom the director reasonably believes to be reliable and competent in the matters presented,

(ii) Counsel, public accountants or other persons as to matters which the director reasonably believes to be within such person's professional or expert competence, or

(iii) A committee of the board upon which he does not serve, duly designated in accordance with a provision of the bylaws, as to matters within its designated authority, which committee the director reasonably believes to merit confidence.

(2) However, a director shall not be considered to be acting in good faith if he has knowledge concerning the matter in question, or would have obtained such knowledge through the exercise of appropriate prudence and diligence, that would cause such reliance to be unwarranted. Reports should be reviewed by each director and verified, and if they appear questionable should not simply be accepted at face value.

(c) *Number and term.* The board of directors shall consist of not fewer than five nor more than fifteen members except where authorized by the Board, which number shall be specified in the bylaws. The directors shall be divided into three classes as nearly equal in number as possible. The members of each class shall be elected for a term of three years and until their successors are elected and qualified. One class shall be elected by ballot annually except in the case of converting or *de novo* associations where all directors shall be elected at the first election of directors for first terms which shall be staggered in length from one to three years.

(d) *Vacancies.* Any vacancy occurring in the board of directors may be filled by the affirmative vote of a majority of the remaining directors even if less than a quorum of the board of directors. A director elected to fill a vacancy shall be elected to serve only until the next election of directors by the stockholders. Any directorship to be filled by reason of an increase in the number of directors may be filled by election by the board of directors for a term of office continuing only until the next election of directors by the stockholders.

(e) *Resignation or removal of directors.* (1) Any director may resign at any time by sending a written notice of such resignation to the home office of the association addressed to the chairman of the board or the president. Unless otherwise specified, such resignation shall take effect upon receipt by the chairman of the board or the president. More than three consecutive absences from regular meetings of the board of directors shall automatically constitute a resignation, effective when such resignation is accepted by the board of directors.

(2) At a meeting of stockholders called expressly for that purpose, any director may be removed only for cause by a vote of the holders of a majority of the stock then entitled to vote at an election of directors.

(3) In associations that allow cumulation of votes, if less than the entire board is to be removed, no one of the directors may be removed if the votes cast against the removal would be sufficient to elect the director if then cumulatively voted at an election of the class of directors of which such director is a part.

(4) Whenever the holders of the shares of stock of any class are entitled to elect one or more directors by the provisions of the charter or supplemental sections thereto, the provisions of this section shall apply, in respect to the removal of a director or directors so elected, to the vote of the holders of the outstanding shares of stock of that class and not to the vote of the outstanding shares of stock as a whole.

(5) In any solicitation of proxies for removal of a director by stockholder vote, opportunity must be provided to the director whose removal is sought to present a defense to stockholders by means of a written statement not to exceed 500 words which must accompany or precede the initial solicitation for removal of such director. Such statement shall be mailed at the expense of the party seeking removal.

(6) For the purposes of this section, the term "clause" shall mean willful failure, neglect or refusal in any material respect to perform duties as a director or commission of any act of willful misconduct, self-dealing, malfeasance or gross negligence. The foregoing description of cause shall in no way limit the power of the Board or the Corporation to bring an action for removal under the National Housing Act of Home Owners' Loan Act.

(f) *Age limitation on directors.* A Federal stock association may provide in its bylaws that no person aged 70 years or older will be eligible for election, reelection, appointment, or reappointment to the board of directors of the association. The bylaws may also provide that no director shall serve as such beyond the annual meeting of the association immediately following the attainment of the specified age.

**§ 543.10-1 Directors' meetings.**

(a) *Meetings.* A regular meeting of the board of directors shall be held immediately after, and at the same place as, the annual meeting of the stockholders. The board of directors shall determine the place, frequency, time and procedure for notice of such meeting shall be at least 24 hours unless waived by the directors, for regular meetings of the board of directors or any committee designated thereby. Meetings may be held with or without notice as prescribed in the bylaws. Members may participate in a meeting of such board or committee by means of a conference telephone or similar communications equipment through which all persons participating in the meeting can hear each other at the same time, and participation by such means shall constitute presence in person at a meeting for all purposes.

(b) *Quorum.* A majority of the authorized number of directors shall constitute a quorum for the transaction of busness at any meeting of the board of directors. The act of the majority of the directors present at a meeting at which a quorum is present shall be the act of the board of directors, unless a greater number is prescribed by regulation of the Board.

(c) *Executive and other committees.* (1) *General.* The board of directors, by resolution adopted by a majority of the authorized number of directors, may designate from among its members an executive committee and one or more other committees each of which, to the extent provided in the resolution or bylaws of the association, shall have and may exercise all of the authority of the board of directors, except that no committee shall have the authority of the board of directors with reference to: (i) The declaration of dividends; (ii) the amendment of the charter or bylaws of the association; (iii) recommending to the stockholders a plan of combination or conversion; (iv) the approval of a plan of combination not requiring stockholder approval; (v) the sale, lease, or other disposition of all, or substantially all of the assets of the association otherwise than in the usual and regular course of its business; (vi) a reduction in the capital of the association; (vii) a voluntary dissolution of the association; (viii) a revocation of any of the foregoing; or (vi) the approval of a transaction in which any member of the executive committee, directly or indirectly, has any material beneficial interest. The designation of any committee and the delegation of authority thereto shall not operate to relieve the board of directors, or any director, of any responsibility or fiduciary duty imposed by law or regulation.

(2) *Audit committee.* Each Federal stock association shall appoint an audit committee of at least three directors the majority of whom shall be independent. A director shall be considered "independent" if he is neither employed by the association, its service corporation, its holding company or its affiliates nor serves as the legal counsel or other professional advisor to the association, its service corporation, its holding company or its affiliates, nor is a member of the immediate family of a person serving in any of the foregoing capacities. The audit committee shall recommend independent auditors, consult with the independent auditors regarding the plan of audit, review that audit report in consulation with the independent auditors, and consult with the independent auditors regrading the adequacy of internal accounting controls.

(3) *Investment committee.* Each Federal stock association shall appoint an investment committee of at least three directors the majority of whom shall be independent as defined in paragraph 2 of this section. The independent directors shall be different persons from those serving on the audit committee. The investment committee will assess the credit and interest rate risk of the association and prepare reports on such risk for the board of directors.

(d) *Notice of special meetings.* Written notice of at least 24 hours regarding any special meeting of the board of directors or of any committee designated thereby shall be given to each director or committee member in accordance with the bylaws, although such notice may be waived by the director. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except where a director attends a meeting for the express purpose of objecting to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, a meeting need be specified in the notice or waiver of notice of such meeting.

(e) *Action without a meeting.* Any action required or permitted to be taken by the board of directors or any committee thereof at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the directors, or committee members.

(f) *Presumption of assent.* A director of the association who is present at a meeting of the board of directors at which action on any matter is taken shall be presumed to have assented to the action taken unless his dissent or abstention shall be entered in the minutes of the meeting or unless a written dissent to such action shall be filed with the person acting as the secretary of the meeting before the adjournment thereof or shall be forwarded by registered mail to the secretary of the association within five days after the date on which a copy of the minutes of the meeting is received. Such right to dissent shall not apply to a director who voted in favor of such action.

**§ 543.10-2 Directors' conflicts of interest.**

(a) *General.* No contract or other transaction between a Federal stock association and one or more of its directors, or between a Federal stock association and any corporation, firm or association in which one or more of the association's directors has a material financial interest, is either void or voidable because such director or directors or such other corporation, firm or association are parties or because such director or directors are present at the meeting of the board or a committee thereof which authorizes, approves or ratifies the contract or transaction: *Provided,* that

(1) The material facts regarding the transaction and the director's interest therein are fully disclosed or known to the stockholders and such contract or transaction is approved by the stockholders, with the stock owned by the interested director or directors not being entitled to vote thereon or be counted as outstanding for purposes of determining a quorum and the contract or transaction is just and reasonable as to the association at the time it is authorized, approved or ratified; or

(2) The material facts regarding the transaction and the director's interest are fully disclosed or known to the board or committee, and the board or committee authorizes, approves or ratifies the contract or transaction in good faith by a vote sufficient without counting the vote of the interested

director or directors, and the contract or transaction is just and reasonable as to the association at the time it is authorized, approved or ratified.

(b) *Interested directors.* A mere common directorship does not constitute a material financial interest within the meaning of this section. Nor is a director "interested" within the meaning of this section in a resolution fixing the compensation of another director as a director, officer or employee of the association, notwithstanding the fact that the first director is also receiving compensation from the association.

(c) *Presence of interested directors at meeting.* Except with regard to contracts or other transactions addressed in paragraph (a) of this section, no contract or other transaction between a Federal stock association and any corporation or association of which one or more of its directors are directors is either void or voidable because such director or directors are present at the meeting of the board or a committee thereof which authorizes, approves or ratifies the contract or transaction: *Provided,* that (1) The material facts regarding the transaction and the director's other directorship are fully disclosed or known to the board or committee, and the board or committee authorizes, approves or ratifies the contract or transaction in good faith by a vote sufficient without counting the vote of the interested director or directors, or the contract or transaction is approved by the stockholders in good faith; or

(2) The contract or transaction is just and reasonable to the association at the time it is authorized, approved or ratified.

(d) *Determining a quorum.* Interested directors may be counted in determining the presence of a quorum at a meeting of the board or a committee thereof which authorizes, approves or ratifies a contract or transaction involving an interested director.

(e) *Transactions with affiliates.* Compliance with this section shall not effect the right of the Board or the Corporation to object to the contract or transaction under §§ 563.40 through 563.44, § 584.3 or any other section of this Chapter or any other law or regulation.

**§ 543.10-3 Liability of directors for improper distributions.**

(a) *Director liability.* In addition to any other liabilities, a director who votes for or assents to any distribution contrary to the provisions of the Home Owners' Loan Act, this Chapter or the charter of the association shall, unless he complies with the standards provided in § 543.10(b) of this Part for the performance of duties of directors, be liable to the association jointly and severally with all other directors so voting or assenting, for the amount of such distribution which is paid or the value of such distribution in excess of the amount of such distribution which could have been made without a violation of the cited provisions.

(b) *Right to contribution from stockholders.* Any director against whom a claim shall be asserted pursuant to this section for the making of a distribution and who shall be held liable thereon, shall be entitled to contribution from any stockholder[s] who accepted or received any such distribution with knowledge that it had been made in violation of this Part, in proportion to the amounts received by such stockholder[s].

(c) *Right to contribution from other directors.* Any director against whom a claim shall be asserted pursuant to this section shall be entitled to contribution from any other director[s] who voted for or assented to the action upon which the claim is asserted and who did not comply with the standard provided in § 543.10(b) regarding the performance of the duties of directors.

(d) *Distribution.* For purposes of this section, the term "distribution" shall have the same meaning as specified in § 543.12-2(a).

**§ 543.10-4 Officers.**

(a) *Positions.* The officers of the association shall be a president, one or more vice presidents, a secretary, and a treasurer or comptroller, each of whom shall be elected by the board of directors. The board of directors may also designate the chairman of the board as an officer. The president shall be the chief executive officer, unless the board of diretors designates the chairman of the board as chief executive officer. The president need not be a director of the association. The offices of the secretary and treasurer may be held by the same person and a vice president may also be either the secretary or the treasurer. The board of directors may designate one or more vice presidents as executive vice president or senior vice president. The board of directors may also elect or authorize the appointment of such other officers as the business of the association may require. The officers shall have such authority and perform such duties as the board of directors may from time to time authorize or determine. In the absence of action by the board of directors, the officers shall have such powers and duties as generally pertain to their respective offices.

(b) *Removal.* Any officer may be removed by the board of directors whenever in its judgment the best interests of the association will be served thereby; but such removal, other than for cause, shall be without prejudice to the contractual rights, if any, of the person so removed. "Cause" with respect to removal of an officer shall mean willful failure, neglect or refusal in any material respect to perform duties as an officer or commission of any act of willful misconduct, self-dealing, malfeasance or gross negligence.

(c) *Employment contracts.* Upon specific approval of the board of directors a Federal stock association may enter into employment contracts with its officers and other employees in accordance with § 563.39 of this Chapter.

(d) *Age limitation on officers.* A Federal stock association may provide in its bylaws that no person aged 70 years or older will be eligible for election, reelection, appointment or reappointment as an officer of the association. The bylaws may also provide that no officer shall serve as such byond the annual meeting of the association immediately following the attainment of the specified age.

**§ 543.10-5 Indemnification of directors, officers and employees.**

A Federal stock association may indemnify its directors, officers and employees and the directors, officers and employees of any wholly-owned subsidiary, provided that indemnification may be made only in accordance with the following requirements:

(a) *General.* Subject to the provisions of this section, a Federal stock association may indemnify any person against whom an action is brought or threatened because that person is or was a director, officer or employee of the association or any wholly-owned subsidiary, for:

(1) Any amount for which that person becomes liable under a judgment or settlement in such action; and

(2) Reasonable costs and expenses, including attorney's fees, actually paid or incurred by that person in defending or settling such action, or in enforcing his rights under this section if he obtains a favorable judgment in such action; *Provided,* that nothing in this section authorizes indemnification by a Federal stock association of directors, officers or employees of affiliates, affiliated persons, or subsidiaries of the association for actions in their capacity

as such except as provided in this section.

(b) *Conditions.* (1) *Favorable judgment.* Indemnification may be made to a person described in paragraph (a) of this section if final judgment on the merits are in his favor.

(2) *No favorable judgment.* Indemnification may be made to a person described in paragraph (a) if final judgment is not in his favor, but only as provided in this paragraph (b).

(i) *General.* In the case of settlement, final judgment against the person, or final judgment in his favor other than on the merits, indemnification may be made if it is determined that the person was acting in good faith within the scope of his employment or authority as he could reasonably have perceived it under the circumstances and for a purpose he could reasonably have believed under the circumstances was in the best interests of the association and in the case of a criminal action, he had no reasonable cause to believe his conduct was unlawful. Such determination shall be made by the board of directors by a majority vote of a quorum consisting of disinterested directors, or if such a quorum is not obtainable or, even if obtainable, if a quorum of disinterested directors so directs, by the stockholders with only the shares of disinterested stockholders allowed to vote or to be counted for purposes of determining a quorum. However, in no case shall any indemnification be made unless the association gives the Board at least 60 days' notice of its intention to make such indemnification. Such notice shall state the facts on which the action arose, the terms of any settlement, and any disposition of the action by a court. A copy of such notice, and a certified copy of the resolution containing the required determination by the board of directors, shall be sent to Office of Examination and Supervision, the Office of General Counsel and the Supervisory Agent. The Supervisory Agent shall promptly acknowledge receipt thereof. The notice period shall run from the date of such receipt. No such indemnification shall be made if the Board or the designee advises the association in writing, within such notice period, of its objection thereto. The Office of Examination and Supervision with the concurrence of the Office of General Counsel has delegated authority to make a determination under this paragraph (b)(2)(i).

(ii) *Action by or on behalf of the association.* In addition to the requirements of paragraph (b)(2)(i), when the action is brought or threatened by the association or on behalf of the association, indemnification shall be limited to resonable costs and expenses as described in paragraph (a)(2) of this section and no indemnification shall be made in connection with any claim, issue or matter for which there has been a final judgment that the person was liable for negligence or misconduct in the performance of his duty to the association.

(c) *Insurance.* An association may obtain insurance to protect it and its directors, officers and employees or the directors, officers and employees of its wholly-owned subsidiaries from potential losses arising from claims against any of them for alleged wrongful acts, or wrongful acts committed in their capacity as directors, officers or employees. However, associations may not obtain insurance which provides for payment of losses of any person incurred as a consequence of his willful or criminal misconduct.

(d) *Advance payment of expenses.* If a majority of the disinterested directors or the stockholders of an association concludes that, in connection with an action, any person ultimately may become entitled to indemnification under this section, the directors or stockholders may authorize payment of reasonable costs and expenses, including attorneys' fees, arising from the defense or settlement of such action. In any vote of the stockholders to authorize such advances, only the stocks of disinterested stockholders shall be voted or counted towards a quorum. Nothing in this paragraph (d) shall prevent the directors of an association from imposing such conditions on a payment of expenses as they deem warranted and in the interests of the association. Before making advance payment of expenses under this paragraph, the association shall obtain an agreement in writing that the association will be repaid if the person on whose behalf is made is later determined not be to entitled to such indemnification.

(e) *Prohibited indemnification.* Nothing in this section shall authorize or require the Board to approve indemnification of directors, officers, or employees, of the association when such indemnification would contravene public policy as expressed by Federal statutes or the regulations of the Board.

(f) *Exclusiveness of provisions.* No association shall indemnify any person referred to in paragraph (a) of this section or obtain insurance referred to in paragraph (c) of this section other than in accordance with this section. However, an association which had a bylaw in effect on October 1, 1969, relating to indemnification of its personnel shall be governed solely by that bylaw, if such is still in effect, except that the association's authority to obtain insurance shall be governed by paragraph (c) of this section.

(g) *Definitions and rules of construction.* (1) Definitions for purposes of this section:

(i) *Action.* Any judicial or administrative proceeding, or threatened proceeding, whether civil, criminal, or otherwise, including any appeal or other proceeding for review;

(ii) *Court.* Includes, without limitation, any court to which or in which any appeal or any proceeding for review is brought.

(iii) *Disinterested.* When applied to a stockholder or director, a person not named as party to the action in connection with which indemnification or advancement of expenses is sought;

(iv) *Final judgment.* A judgment, decree, or order which is not appealable or as to which the period for appeal has expired with no appeal taken;

(v) *Settlement.* Includes entry of a judgment or dismissal by consent or confession or a plea of guilty or *nolo contendere*.

(2) References in this section to any individual or other person, including any association, shall include any person acting as administrator, executor, guardian, conservator, trustee, legal representative, successor and assign thereof.

**§ 543.11 Certificates for stock and their transfer.**

(a) *Certificates for stock.* Certificates representing shares of capitol stock of the association shall be in such form as shall be determined by the board of directors and approved by the Board. Certificates shall be signed by the chief executive officer or by any other officer of the association authorized by the board of directors, attested by the secretary or an assistant secretary, and sealed with the corporate seal or a facsimile thereof. The signatures of such officers upon a certificate may be facsimiles if the certificate is manually signed on behalf of a transfer agent or a registrar other than the association itself or one of its employees. Each certificate for shares of capital stock shall be consecutively numbered or otherwise identified. The name and address of the person to whom the shares are issued, with the number of shares and date of issue, shall be entered on the stock transfer books of the association. All certificates surrendered to the association for transfer shall be cancelled and no new certificate shall be issued until the former certificate for

a like number of shares of stock have been surrendered and cancelled, except that in the case of a lost or destroyed certificate a new certificate may be issued upon such terms and indemnity to the association as the board of directors may prescribe.

(b) *Transfer of shares of stock.* Transfer of shares of capital stock of the association shall be made only on its transfer books. Authority for such transfer shall be given only by the holder of record, a legal representative who shall furnish proper evidence of such authority, or by an attorney authorized by a duly executed power of attorney and filed with the association. The transfer shall be made only upon surrender for cancellation of the certificate, a restriction on transfer imposed by the issuer even though otherwise lawful is ineffective except against a person with actual knowledge of it.

**§ 543.11-1 Consideration for stock.**

(a) *General.* Stock may be issued from time to time for such consideration as shall be authorized in accordance with the charter by the board of directors through action which establishes a price in cash or other consideration, or both, or a minimum price or a general formula or method by which price can be determined.

(b) *Treasury stock.* Treasury stock may be disposed of by the association for such consideration expressed in dollars as may be fixed from time to time by the board of directors.

(c) *Stock dividends.* That part of the retained earnings of an association which is transferred to paid-in capital upon the issuance of shares of stock as a stock dividend shall be deemed to be the consideration for the issuance of such shares of stock.

(d) *Stock issued in exchange.* Except as provided in § 543.11-2 of this Part, in the event of the issuance of shares of stock upon the conversion or exchange of indebtedness or stock, the consideration for the stock so issued shall be (1) in the case of indebtedness, the principal sum of, and any accrued and unpaid interest on, the indebtedness so exchanged or converted; (2) in the case of shares of stock, the paid-in capital then represented by the shares of stock so exchanged or converted; (3) that part of retained earnings, if any, transferred to paid-in capital upon the issuance of shares of stock for the shares of stock so exchanged or converted, and (4) any additional consideration paid to the association upon the issuance of shares of stock.

**§ 543.11-2 Stock rights and options.**

(a) *Creation and issuance.* A Federal stock association may create and issue, whether or not in connection with the issuance and sale of any of its shares of stock or other securities, rights or options entitling the holders thereof to purchase from the association shares of stock of any class or classes. Such rights or options shall be evidenced in such manner as the board of directors shall approve and, subject to the provisions of the charter, shall set forth the terms upon which, the time or times within which, and the price or prices at which, such shares of stock may be purchased from the association upon the exercise of any such right or option. If such rights or options are to be issued to directors, officers or employees of the association or of any subsidiary thereof, and not to the stockholders generally, their issuance or the plan under which they would be issued shall be approved by the majority of the votes eligible to be cast at a legal meeting of stockholders. In the absence of fraud, the judgment of the board of directors as to the adequacy of the consideration received for such rights or options shall be conclusive. The price or prices to be received for any shares of stock having a par value, other than treasury shares of stock to be issued upon the exercise of such rights or options, shall not be less than the par value thereof.

(b) *Restriction on grants to non-employee directors.* (1) No Federal stock association shall adopt any stock option plan providing for the grant of stock options or rights to non-employee directors, unless all of the following conditions are met:

(i) The plan is fully and fairly disclosed in a proxy statement meeting the disclosure requirements of Schedule 14A of the Proxy Rules under the Securities Exchange Act of 1934, 17 CFR 240.14a-1 *et seq.*;

(ii) The plan is approved by a majority of the total votes eligible to be cast at a legal meeting of stockholders;

(iii) The duration of any options or rights and the amount of stocks allocable to non-employee directors are limited to reasonable duration and amounts and are not, when aggregated with all other forms of compensation received by such non-employee directors from the association, in excess of that which is reasonable and commensurate with their duties and responsibilities;

(iv) The exercise price of the option or rights is not less than the fair market value of the underlying shares of common stock on the date of grant; and

(v) The terms of the plan do not contravene public policy as expressed by Federal statutes or the regulations of the Board.

(2) For purposes of this paragraph (b), the term "non-employee directors" means any director, trustee, advisory director, honorary director, director emeritus or other similar person not currently employed on a full-time basis by the association, its service corporation, its holding company or its affiliates, and notwithstanding the provisions of § 563.17(b) of this Chapter regarding the compensation of officers, directors and employees of an insured institution, shall also include any director who is a former officer or employee of the association, regardless of whether such director regularly performs service for the association under consulting contracts or similar arrangements.

(c) *Payment of stock rights or options.* (1) Notwithstanding the provisions of § 543.11-1(d) of this Part or § 563b.3(g)(1) of this Chapter, a Federal stock association shall have the authority to adopt a stock rights or option plan which provides for the repurchase or redemption of the shares of any class of the association's outstanding common or preferred stock tendered as payment for the exercise of stock rights or options by plan participants: *Provided*, that such authority shall not extend to any repurchase or redemption which, after giving effect to the repurchase or redemption, would cause the association's net worth to be less than the amount required of the association by § 563.13 of this Chapter.

(2) Nothing in this paragraph (c) shall authorize a Federal stock association to repurchase or redeem its shares of stock from any officer or director of the association in contravention of the provisions of § 563b.3(c)(17) of this Chapter.

**§ 543.11-3 Fractional shares of stock.**

A Federal stock association may: (a) issue fractions of a share of stock; (b) arrange for the disposition of fractional interests by those entitled to them; (c) pay in cash the fair value of fractions of a share of stock as of the time when those entitled to receive such fractions are determined, and (d) issue scrip in registered or bearer form which shall entitle the holder to receive a certificate for a full share of stock upon the surrender of such scrip aggregating a full share of stock. A certificate for a fractional share of stock shall, but scrip shall not unless otherwise provided therein, entitle the holder to exercise

voting rights, to receive dividends thereon, and to participate in a distribution of any of the assets of the association in the event of liquidation. The Board of directors may cause scrip to be issued subject to the condition that it shall become void if not exchanged for certificates representing full shares of stock before a specified date, or subject to the condition that the shares of stock for which scrip is exchangeable may be sold by the association and the proceeds thereof distributed to the holders of scrip, or subject to any other conditions which the board of directors may deem advisable.

**§ 543.11-4 Liability of stockholders.**

A holder of or subscriber to shares of stock of a Federal stock association shall be under no obligation to the association or its creditors with respect to such shares of stock other than the obligation to pay to the association the full consideration for which such shares of stock were issued or to be issued. Any person becoming an assignee or transferee of shares of or of a subscription for shares of stock in good faith and without knowledge or notice that the full consideration therefor has not been paid shall not be personally liable to the association or its creditors for any unpaid portion of such consideration.

**§ 543.12 Authority to acquire own stock.**

Subject to the limitations in § 543.12-2 and other applicable laws or regulations, a Federal stock association shall have the power to acquire its own stock. All such reacquired stock shall, upon acquisition, constitute authorized by uninssued stock or may be deemed treasury stock, provided that in either case, stockholders' equity is reduced by the amount paid to reacquire the stock.

**§ 543.12-1 Authority to pay dividends to stockholders.**

Subject to the limitations of § 543.12-2, a Federal stock association, may,from time to time, by resolution of its board of directors, pay dividends on its shares of stock out of retained earnings in cash, in its own securities or in other property, including the securities of other corporations or entities.

**§ 543.12-2 Limitations on distributions ot stockholders.**

(a) *Distribution.* For purposes of this section, the term "distribution" means a direct or indirect transfer of money or other property (except its own shares of stock) or incurrence of indebtedness, by an association to or for the benefit of any of its stockholders in respect to any of its shares of stock, whether by dividend or by purchase, redemption or other acquisition of its stock, or otherwise.

(b) *Limitation in distributions.* No distribution to stockholders may be made by a Federal stock association if, after giving effect to the distribution, the association's net worth would be less than the amount required of the association by § 563.13 of this Chapter.

(c) *Measurement date.* The effect of a distribution under paragraph (a) of this section is measured as of the earlier of:

(1) The date of its authorization if payment occurs within 120 days after the date of authorization, or the date of payment if payment occurs more than 120 days after the date of authorization; or

(2) In the case of distribution by purchase, redemption, or other acquisition of the association's stock, the earlier of the date money or other property is transferred or debt incurred by the association, or the date stockholders cease to be stockholders of record.

**§ 543.12-3 Reduction of paid-in capital.**

(a) *General.* A Federal stock association may, by resolution of its board of directors, reduce its paid-in capital by charging against it:

(1) All or any part of any deficit arising from operating or other losses or from diminution in the value of its assets in accordance with generally accepted accounting principles;

(2) Distributions as liquidating dividends as permitted by this chapter;

(3) The paid-in capital represented by stock acquired by the association as permitted by law, to the extent such paid-in capital has not previously been reduced on account of such acquisition; and

(4) Expenses, including commissions, paid or incurred by the association in connection with the issuance of stock.

(b) *Exception.* Nothing in this section shall be construed to permit an association to reduce its paid-in capital where such action would be specifically prohibited by other regulations of the Board or conditions imposed by the Board or to prohibit any such reduction in any other manner permitted by this Part or as directed by the Board.

**§ 543.13 Fiscal year; annual audit.**

The bylaws of a Federal stock association shall specify the fiscal year for the association. The association shall be subject to an annual audit as of the end of its fiscal year by independent public accountants appointed by and responsible to the board of directors. The appointment of such accountants shall be subject to annual ratification by the stockholders.

**§ 543.14 Corporate procedures.**

(a) *Execution of instruments generally.* The board of directors shall establish procedures for the execution, verification, acknowledgement, and delivery of instruments or writings of any nature.

(b) *Seal.* The association may have a corporate seal, which may be modified from time to time, and may use the same by causing it, or a facsimile thereof, to be impressed or affixed or in any other manner reproduced.

(c) *Miscellaneous.* The bylaws may also address subjects which comply with applicable Federal law, rules, or regulations such as emergency preparedness or any other subjects necessary or appropriate for effective operation of the association.

**§ 543.15-543.19 [Reserved]**

**§ 543.20 Combinations involving Federal stock associations.**

Federal stock associations may enter into combinations, which for the purposes of this Part include bulk purchases or sales of assets, mergers and consolidations, only in accordance with the provisions of this Part.

**§ 543.21 Merger or consolidation.**

(a) *Permissible mergers or consolidation.* Federal stock associations may merge or consolidate with other associations: *Provided,* that—

(1) All constituent associations have accounts insured by the Federal Savings and Loan Insurance Corporation, except for Federal associations the deposits of which are insured by the Federal Deposit Insurance Corporation, and (2) if any constituent is a mutual association, the resulting association shall be mutually held, except in cases involving supervisory combinations, mergers approved under Part 563b of this Chapter or combinations in which one of the constituents is an interim Federal association or an interim state institution; and (3) as to any constituent association which is not a Federal association, the merger is in accordance with the laws of the jurisdiction in which the association was organized.

(b) *Board approval.* Prior written approval of the Board is required for every combination. In determining whether to confer such approval, the Board shall apply the criteria set out in § 571.5 of this Chapter and shall impose any condition it deems necessary or appropriate to ensure conformity with those criteria and the requirements of this Chapter. Prior written approval of the Federal Deposit Insurance Corporation is required for every combination involving a Federal

association insured by the Federal Deposit Insurance Corporation.

(c) *Approval by the Board's Principal Supervisory Agent.* (1) The specific approval of the Board (including recommending modifications of the combination agreement) required by paragraph (b) of this section may be given by the Board's Principal Supervisory Agent in accordance with the conditions set forth in § 563.22 of this Chapter.

(2) In approving a merger under paragraph (c) of this section, the Principal Supervisory Agent may approve maintenance of an office of the merging association as a facility of the resulting association and may approve a temporary increase in the number of directors of the resulting association, provided that the association submits an acceptable plan for bringing the board of directors into compliance with the requirements of § 543.3 of this Subchapter within a reasonable period of time.

(d) *Approval of board of directors.* Before filing for Board approval, the combination and the combination agreement shall be approved by each constituent association's board of directors: (1) By a two-thirds vote of the entire board of each Federal association, and (2) as required by state law or other applicable law for other constituents.

(e) *Conservator or receiver action.* A conservator or receiver for an association appointed under Part 547 of this Subchapter may merge the association with another under § 543.21 without submitting the combination agreement to the association's board of directors or stockholders for their approval.

(f) *Combination agreement.* (1) All terms, conditions, agreements or understandings, or other provisions with respect to the combination, shall be set forth fully in a written combination agreement.

(2) The combination agreement shall state: (i) That the combination shall not be effective unless and until approved by the Board: (ii) which constituent association is to be the resulting association; (iii) the name of the resulting association; (iv) the location of the home office and any other offices of the resulting association; (v) the terms and conditions of the combination and method of effectuation; (vi) any charter amendments or, if no such amendments are to be made, a statement that the charter of one of the constituent associations, naming it, shall be the charter of the surviving or resulting association, or the new charter in the event of consolidation; (vii) the manner of converting or exchanging the stock of each constituent association into stock, insured accounts, or other securities of the resulting association or cash, property, rights, or securities of any other entity in connection with the combination, including any provision for the payment of cash in lieu of the issuance or recognition of fractional shares, interests or rights, or for any other arrangements with respect thereto consistent with the provisions of § 543.11–3 of this Part; (viii) the basis upon which the insured accounts of the resulting association shall be issued; (ix) the number, names and residence addresses, and terms of directors; (x) the effect upon and assumption of any liquidation account of a disappearing association by the resulting association; and (xi) such other provisions, agreements, or understandings as relate to the combination.

(g) *Corporate title; change of location.* If a combination agreement provides for the resulting association's name or location to be changed, and it is a Federal association, its charter shall be amended accordingly.

(h) *Application for Board approval.* (1) *Contents.* Application shall be in a form prescribed by the Board and shall include appropriate information responsive to the factors enumerated in § 571.5 of this Chapter.

(2) *Filing requirement.* Constituent associations shall file three copies of the application prepared pursuant to this section with the Supervisory Agent. The combination agreement for a bulk purchase of assets shall state the information required by § 543.21(f)(2) of this Subchapter. Applicants shall also comply with section 7A of the Clayton Act (15 U.S.C. 18A) and regulations issued thereunder (16 CFR Parts 801, 802 and 803).

(i) *Notice.* (1) *Public Notice.* Constituent associations shall jointly publish notice pursuant to § 542.4 of this Subchapter, except that the required newspaper publication of notice shall be made in the communities in which the home offices of the constituent associations are located. Promptly after joint publication the constituent associations shall jointly file with the Supervisory Agent a copy of the notice and publisher's affidavit of publication.

(2) *Notice to stockholders.* If the combination agreement is not subject to the approval by stockholders of a Federal stock association pursuant to §§ 543.22 or 543.23, such constituent Federal stock association shall mail notice of the application to its stockholders, within 10 days of being notified by the Supervisory Agent that the application is complete, with a copy of such notice to the Supervisory Agent. The contents of the notice shall include: (i) A statement that an application under this section has been filed with the Board; (ii) the name and address of the home or principal office of each constituent association; (iii) a brief summary of the principal terms of the combination agreement; (iv) the name and address of the home office of the resulting association; (v) a statement as to which offices of constituent associations are to be maintained as home office or branches and which are to be discontinued; (vi) a statement that any person may file written comments concerning the application which will be considered by the Board if filed with the Supervisory Agent within 10 days (or within 17 days if a request is filed within the first 10 days stating that more time is needed to furnish additional information) of publication or such later date as may be permitted by the Supervisory Agent; (vii) a statement notifying each stockholder that pursuant to § 543.27 of this Part, that appraisal rights are not available, and including in such notice a copy of § 543.27; and (viii) a statement that the application and all comments filed pursuant to the notice shall be available for public inspection by any person at the Office of the Supervisory Agent, except for any material exempt from disclosure prsuant to the Freedom of Information Act.

(3) *Procedure.* Processing of an application under this section shall follow the procedures set forth in paragraph (h)(1) and in §§ 542.4(b) and 542.4(c) of this Subchapter: *Provided,* that in the case of mergers involving an acquisition subject to Part 574, instead of the public notice procedures of paragraph (i)(1), the public notice procedures of Part 574 shall be applicable.

(4) *Supervisory exception.* This paragraph (i) does not apply to combinations instituted for supervisory reasons.

**§ 543.22 Short-form merger.**

(a) *General.* In any case in which at least 90 percent of the outstanding shares of each class of the stock of an insured institution or institutions is owned by another insured institution, and one of the insured institutions is a Federal association and the other insured institution or institutions are Federal associations or are insured state-chartered institutions and with respect to the state-chartered institution, state law permits and insured institution of such jurisdiction to merge with another insured institution, the insured institution having such stock ownership may either merge the other insured

institution into itself and assume all of its obligations, or merge itself into one of the other insured institutions. Such merger may be effected by executing and filing with the Supervisory Agent a copy of the resolution of the parent insured institution's board of directors to so merge, a copy of the combination agreement and the date of the adoption: *Provided*, that in the event the parent insured institution shall end up not owning all the oustanding stock (disregarding any required qualifying shares of stock of directors) of the subsidiary insured institution or institutions that are parties to the merger, the resolution of the board of directors of the parent insured institution shall state the terms and conditions of the merger, including the securities, cash, property, or rights to be issued, paid, delivered or granted by the survivor upon surrender of each share of stock of the disappearing entity or entities not owned by the parent insured institution.

(b) *Subsidiary resulting association.* If the parent insured institution is not the resulting association, the resolution shall include provision for *pro rata* issuance of stock of the resulting association to the holders of stock of the parent insured institution shall file evidence with the Supervisory Agent that the proposed merger has been approved by an affirmative vote of the majority of the outstanding stock of the parent insured institution entitled to vote thereon at a meeting duly called.

(c) *Corporate title.* The resulting association may change its corporate name by the inclusion of a provision to that effect in the resolution of merger adopted, and upon the effective date of the merger the name of the insured institution shall be so changed: *Provided*, that any Federal association which is the resulting association pursuant to this section may only change its corporate title in conformance with § 542.2 of this Subchapter.

(d) *Processing; delegation.* Processing of an application under this section shall follow the procedures set forth in § 543.21(h)(3). Approval by the Board shall be governed by § 543.21(c).

(e) *Appraisal rights.* Whenever any constituent Federal association party to a merger affected by this section is the disappearing association, any notice or proxy materials furnished to stockholders must contain information that the stockholders of the constituent Federal association or associations shall have appraisal rights as set forth in § 543.27 except when the Federal association is wholly owned (disgregarding any required qualifying shares of stock of directors).

**§ 543.23 Approval by stockholders for merger or consolidation.**

(a) *General rule.* Unless a greater percentage is specified in the association's charter, an affirmative vote of two-thirds of the outstanding voting stock shall be required for approval of any combination agreement. If any class of shares of stock is entitled to vote as a class pursuant to § 543.4 of this Part, an affirmative vote of a majority of shares of stock of each voting class and two-thirds of the total voting shares of stock shall be required unless a greater percentage is specified in the charter.

(b) *General exception.* Stockholders of the resulting association need not authorize a combination agreement if: (1) It does not involve an interim Federal association or an interim state institution; (2) the association's charter is not amended; (3) each share of stock outstanding immediately prior to the effective date of the combination is to be an identical outstanding share of a stock or a treasury share of stock of the resulting association after such effective date; and (4) either (i) no shares of voting stock of the resulting association and no securities convertible into such stock are to be issued or delivered under the plan of combination, or (ii) the authorized unissued shares or the treasury shares of voting stock of the resulting association to be issued or delivered under the plan of combination, plus those shares of stock initially issuable upon conversion of any securities to be issued or delivered under such plan, do not exceed 15 percent of the total shares of voting stock of such association outstanding immediately prior to the effective date of the combination.

(c) *Exceptions for certain combinations involving an interim institution.* Stockholders of a Federal stock association need not authorize by a two-thirds affirmative vote combinations involving an interim Federal association or an interim state institution where a company acquires the resulting Federal stock association pursuant to § 574.4 of this Chapter. In those cases, the required approval voting stock of the Federal association. If any class of stock is entitled to vote as a class pursuant to §543.4 of this Part, an affirmative vote of a majority of the stock of each voting class shall be required.

(d) *Disclosure.* The Board may require, in connection with a combination under this section, such disclosure of information as it deems necessary or desirable for the protection of investors in any of the constituent associations.

**§ 543.24 Articles of combination for merger or consolidation.**

(a) *Contents.* Following stockholder approval, articles of combination shall be executed in duplicate by each association, by its chief executive officer or executive vice president and by its secretary or an assistant secretary, and verified by one of the officers of each association signing such articles, and shall contain: (1) The terms of the combination agreement (either set forth or attached as an exhibit); (2) the number of shares of stock in each association; and (3) the number of shares of stock in each association voted for and against such combination agreement.

(b) *Filing.* Both sets of articles of combination shall be filed with the Supervisory Agent who shall, if he finds that such articles conform to the requirements of this regulation, endorse the articles and return one set to the resulting association.

**§ 543.25 Effective date; date of consummation for merger or consolidation.**

(a) *Effective date.* No combination under this agreement shall be effective until approved by the Board or its delegate. The effective date of a combination in which the resulting association is a Federal stock association shall be the date of endorsement of the articles of combination by the Supervisory Agent. A later effective date, up to 90 days after the date of approval of the combination, may be requested by the applicant as part of the application subject to approval by the Board or its delegate. The effective date of a combination in which the resulting association is not a Federal association shall be a date subsequent to Board approval prescribed by the law of the state under which the resulting association is chartered, or other applicable law. If a disappearing association combining under this section is a Federal association, its charter shall be deemed to be cancelled as of the effective date of the combination; such charter shall be surrendered to the Supervisory Agent at the time of filing of the articles of combination.

(b) *Date of consummation.* No combination under this section may be concluded until all necessary compliance materials, as required by any conditions to the resolution approving such combination by the Board or its delegate, have been

submitted to the satisfaction of the Supervisory Agent. The effective date and the date of consummation may be simultaneous only if the above noted materials have been submitted to and approved by the Supervisory Agent. Until the compliance materials have been submitted to and approved by the Supervisory Agent, the Board or its delegate shall have the right to alter, suspend or withdraw its approval should any interim development be deemed by the Board or its delegate to be a material change in circumstances warranting such action.

**§ 543.26 Continuity of corporate existence after merger or consolidation.**

On the effective date of a combination in which the resulting association is a Federal association, all assets and property (real, personal, and mixed, tangible, and intangible, choses in action, rights and credits) of the association shall immediately, without any further act, become the property of the resulting association to the same extent as they were the property of the disappearing association, and the resulting association shall be a continuation of the entity which absorbed the association. All rights, obligations, duties and liabilities of the association shall remain unimpaired, and the resulting association shall, on the effective date of the combination, succeed to all those rights and obligations.

**§ 543.27 Dissenters' appraisal rights in merger or consolidation.**

(a) *Right to demand payment of fair value.* Except as provided in paragraph (b) of this section, any stockholder of record of a Federal stock association combining in accordance with § 543.21, 543.22 or 543.30 of this Part shall have the right to demand payment of the fair value of his stock: *Provided,* that such stockholder complies with the provisions of paragraph (c) of this section and, where a stockholder vote to approve a combination involving a Federal association is required, such stockholder has not voted in favor of the combination.

(b) *Exceptions.* No stockholder required to accept only qualified consideration for his stock shall have the right under this section to demand payment of the stock's fair value, if (1) such stock was listed on a national securities exchange or quoted on the NASDAQ on the date of the meeting of stockholders at which the combination was acted upon, where a stockholder vote is required; or (2) stockholder action is not required for a combination made pursuant to § 543.21 or 543.22(b).

(c) *Procedure.* (1) *Notice.* If the combination agreement is not subject to the approval by the stockholders of a Federal stock association, such constituent Federal stock association shall notify all stockholders in accordance with the applicable notification provisions set forth in § 543.21(i)(2) of this Part. If the combination agreement is subject to the approval by the stockholders of a Federal stock association, such Federal stock association shall include a statement notifying each stockholder entitled to appraisal rights pursuant to this section of the effective date of the combination, and of the fact that appraisal rights are available for any or all shares of stock pursuant to this section, in the proxy materials furnished to the stockholders, and the association shall also include in such proxy materials a copy of this § 543.27.

(2) *Demand for appraisal and payment.* Each stockholder electing to make a demand under this section shall deliver to the Federal stock association, prior to the later of the effective date of the combination or twenty days after receipt of the notice required in paragraph (c)(1) of this section, a writing identifying himself and stating his intention to demand appraisal of and payment for his stock. Where a stockholder vote is required, such demand must be in addition to and separate from any proxy or vote against the combination by the stockholder.

(3) *Written offer.* Within ten days after the effective date of the combination, the resulting association shall (i) give written notice by mail to stockholders of constituent Federal stock associations who have complied with the provisions of paragraph (c)(2) of this section and have not voted in favor of the combination, of the effective date of the combination; (ii) make a written offer to each stockholder to pay for dissenting shares of stock at a specified price deemed by the resulting association to be the fair value thereof; and (iii) inform those stockholders that, within sixty days of such date, the respective requirements of paragraphs (c) (5) and (6) of this section must be satisfied. The notice and offer shall be accompanied by a balance sheet and statement of income of the association, for a fiscal year ending not more than sixteen months before the date of notice and offer, together with the latest available interim financial statements.

(4) *Acceptance of offer.* If, within sixty days of the effective date of the combination, the fair value is agreed upon between the resulting association and any stockholder who has complied with the provisions of paragraph (c)(2), payment therefor shall be made withn ninety days of the effective date of the combination.

(5) *Petition to be filed if offer not accepted.* If, within sixty days of the effective date of the combination, the resulting association and any stockholder who has complied with the provisions of paragraph (c)(2) do not agree as to the fair value, then any such stockholder may file a petition with the Office of General Counsel of the Board, with a copy by registered or certified mail to the resulting association, demanding a determination of fair value of the stock of all such stockholders. A stockholder entitled to file a petition under this section who fails to file such petition within sixty days of the effective date of the combination shall be deemed to have accepted the terms offered under the combination.

(6) *Stock certificates to be noted.* Within sixty days of the effective date of the combination, each stockholder demanding appraisal and payment under this section shall submit to the transfer agent his certificates of stock for notation thereon that an appraisal and payment have been demanded with respect to such stock and that appraisal proceedings are pending. Any stockholder who fails to submit his stock certificates for such notation shall no longer be entitled to appraisal rights under this section and shall be deemed to have accepted the terms offered under the combination.

(7) *Withdrawal of demand.* At any time within sixty days after the effective date of the combination, any stockholder shall have the right to withdraw his demand for appraisal and to accept the terms offered upon the combination.

(8) *Voting and distribution.* Any stockholder who has demanded appraisal rights as provided in paragraph (c)(2) shall thereafter neither be entitled to vote such stock for any purpose nor be entitled to the payment of dividends or other distributions on the stock (except dividends or other distribution payable to, or a vote to be taken by, stockholders of record at a date which is on or prior to, the effective date of the combination): *Provided:* that if any stockholder becomes unentitled to appraisal and payment of appraised value with respect to such stock and accepts or is deemed to have accepted

the terms offered upon the combination, such stockholder shall thereupon be entitled to vote and receive the distribution described above.

(9) *Status.* Shares of stock of the resulting association into which stock of the stockholders demanding appraisal rights would have been converted or exchanged, had they assented to the combination, shall have the status of authorized and unissued stock of the resulting association.

(d) *Valuation by the Board or its delegate.* (1) *Procedures.* The Board or its delegate shall, as it may elect, either appoint one or more independent persons or direct an appropriate Office of the Board to appraise the shares to determine their fair value, as of the effective date of the combination, exclusive of any element of value arising from the accomplishment or expectation of the combination. The Board, after consideration of the appraisal report or the advice of the appropriate Office, shall, if it concurs in the valuation of the shares, direct payment by the resulting association of the appraised fair value of the shares of stock, upon surrender of the certificates representing such stock. Payment by the resulting association shall be made, together with interest from the effective date of the combination, at a rate deemed equitable by the Board within 30 days after the Board's determination of fair value.

(2) *Cost and expenses.* The cost and expenses of any proceeding under this section may be apportioned and assessed by the Board as it may deem equitable against all or some of the parties. In making this determination the Board shall consider whether any party had acted arbitrarily, vexatiously, or not in good faith in respect to the rights provided by this section.

(e) *Reorganizations using interims.* For reorganizations involving the use of an interim Federal association pursuant to Part 574 herein, the holding company shall constitute the resulting association for purposes of satisfying dissenters' appraisal rights.

(f) *Definitions.* The following definitions shall apply for purposes of this section:

(1) *Fair value.* The term "fair value" shall mean the appraisal of, and valuation assigned by the Board or its delegate to, the stock of a Federal stock association combining in accordance with §§ 543.21, 543.22 or 543.30 of this Part, pursuant to a duly perfected stockholder demand for appraisal, and payment for such stock pursuant to the § 543.27 of this Part. In determining the fair value of the stock of a Federal stock association, the Board or its delegate shall in its discretion take into consideration any factors it deems relevant in appraising the value of shares of stock of an insured institution on a "going concern" basis, including, but not limited to, an evaluation of any arms' length trades in the stock, the association's net asset value, historical earnings, future prospects for earnings, financial condition, dividends record, investment value, and book value.

(2) *NASDAQ.* The term "NASDAQ" shall mean the National Association of Securities Dealers' Automated Quotation system.

(3) *National securities exchange.* The term "national securities exchange" shall mean the New York Stock Exchange or American Stock Exchange.

(4) *Qualified consideration.* The term "qualified consideration" shall mean cash, shares of stock of any association or corporation which at the effective date of the combination are listed on a national securities exchange or quoted on the NASDAQ, or any combination or shares of such stock and cash.

**§ 543.28 Supervisory combinations.**

Notwithstanding anything in this Part, the Board may determine to waive or deem inapplicable any provision of §§ 543.21–543.27 if the Board determines that severe financial conditions exit that threaten the stability of such an association and that such action is likely to improve the financial condition of the association, or to avert insolvency or imminent failure of an association as defined in § 541.3 of this Subchapter. For purposes of such action under section 5(d) of the Home Owners' Loan Act, the term "member" shall include stockholders of a Federal stock association. The term "insolvency" shall mean that the assets of the association are less than its obligation to its creditors and others, including its depositors.

**§ 543.29 [Reserved]**

**§ 543.30 Bulk purchase or sale of assets.**

(a) *Permissible bulk purchase of assets.* Federal stock associations may enter into bulk-purchase-of-asset transactions as transferee with other entities: *Provided:* That (1) all transferor entities are depository institutions, and (2) the transferee Federal stock association (i) will meet the requirements of Federal Home Loan Bank membership and insurance of accounts after the transaction; and (ii) conforms, within the time prescribed by the Board, to the requirements of section 5(c) of the Home Owners' Loan Act; and (3) the transferor is not a mutual association chartered by the Board or insured by the FSLIC, except in cases involving combinations approved under Part 563b of Subchapter D.

(b) *Permissible bulk sale of assets.* Federal stock associations may enter into bulk sales of assets transactions as transferor only in connection with combinations instituted for supervisory reasons.

(c) *Bulk purchase or sale of assets defined.* A purchase or sale of assets by a Federal stock association shall be deemed a bulk purchase or sale if it involves the acquisition or disposition by the Federal stock association of all or substantially all of the association's assets other than in the ordinary course of business. An acquisition or disposition shall be deemed to involve substantially all of an association's assets if the association's and its subsidiaries' net book value of the assets to be acquired or disposed or the amount paid or to be received by the association for such acquisition exceeds fifty percent of the total assets of the association and its subsidiaries prior to the acquisition or disposition.

(d) *Board approval.* Prior written approval of the Board is required for every bulk purchase or sale of assets. In determining whether to confer such approval, the Board shall apply the criteria set out in § 571.5 of this Chapter and shall impose any condition it deems necessary or appropriate to ensure conformity with those criteria and the requirements of this Chapter. Prior written approval of the Federal Deposit Insurance Corporation is required for every combination involving both a Federal association insured by the Federal Deposit Insurance Corporation and an association not insured by such Corporation.

(e) *Approval by the Board's Principa Supervisory Agent.* The specific approval of the Board (including recommending modifications of the combination agreement) required by paragraph (b) of this section may be given by the Board's Principal Supervisory Agent in accordance with the conditions set forth in § 563.22 of this Chapter.

(f) *Approval of board of directors.* Before filing for Board approval of a bulk purchase or sale of assets, the combination shall be approved by each constituent association's board of directors: (1) By a two-thirds vote of the entire board of each Federal association, and (2) as required by state law or other applicable law for other constituents.

(g) *Combination agreement.* (1) All terms, conditions, agreements, understandings, or other provisions with respect to a combination involving a

bulk purchase of assets shall be set forth fully in a written combination agreement.

(2) The combination agreement for a bulk purchase of assets shall state the information required by § 543.21(f)(2).

(h) *Application for Board approval.* Application for Board approval of a bulk purchase of assets shall follow the procedures of § 543.21(h).

(i) *Notice.* Notice requirements for a bulk purchase of assets shall follow the procedures of § 543.21(i).

**§ 543.31 Approval by stockholders.**

Approval by stockholders of a federal stock association for a bulk purchase of assets shall be required under the circumstances specified in § 543.23 of this Part.

**§ 543.32 Articles of combination.**

Articles of combination for a bulk purchase of assets shall be executed pursuant to the requirements of § 543.24 of this Part.

**§ 543.33 Effective date; date of consummation.**

The effective date and the date of consummation for a bulk purchase or sale of assets shall be determined pursuant to § 543.25 of this Part.

**§ 543.34 Continuity of corporate existence after bulk purchase or sale of assets.**

The continuity of corporate existence of a Federal stock association shall not be affected by a bulk purchase or sale of assets.

**§ 543.35 Dissenters' appraisal rights in bulk purchase or sale of assets.**

Dissenters' appraisal rights in connection with a bulk purchase or sale of assets shall exist under the circumstances set forth in § 543.27 of this Part.

**§ 543.36 Partial purchase or sale of assets.**

(a) *General.* A purchase or sale of assets by a Federal stock association shall be considered a partial purchase or sale of assets if the transaction involves the acquisition or disposition by the Federal stock association of assets, other than in the ordinary course of business, in any amount which is less than "all or substantially all of the association's assets," as defined in § 543.30(c) of this Part.

(b) *Percentage of assets test.* A partical purchase or sale of assets by a Federal stock association shall not be deemed to involve all or substantially all of the association's assets if the association's and its subsidiaries' equity in the net book value of such assets to be acquired or disposed or the total amount paid or received for such acquisition or disposition does not exceed fifty percent of the total assets of the association and its subsidiaries prior to the purchase or sale, except where the purchase or sale is part of an overall plan contemplating the sale or purchse of greater than fifty percent of the total assets of the association and its subsidiaries. Partial purchases or sales of assets shall be governed by § 563.22 of this Chapter.

**§ 543.37–543.39 [Reserved]**

**§ 543.40 Reorganization [Reserved]**

**§ 543.41–543.49 [Reserved]**

**§ 543.50 Dissolution.**

Federal stock associations may voluntarily dissolve themselves only in accordance with the provisions of this Part.

**§ 543.51 Voluntary dissolution.**

(a) *Plan for dissolution.* A Federal stock association's board of directors may propose a plan for dissolution of the association. The plan shall be approved by a two-thirds vote of the authorized number of directors. The plan may provide for: (1) Appointment of the Federal Savings and Loan Insurance Corporation (under section 5 of the Home Owners' Loan Act or section 406 of the National Housing Act) as receiver for the purpose of liquidation; (2) transfer of all the association's assets to a depository institution under Federal or State charter either for cash sufficient to pay all obligations of the association and retire all outstanding accounts or in exchange for that institution's payment of all the association's outstanding obligations or other evidence of interest to the association's accountholders on a *pro rata* basis; or (3) dissolution in a manner proposed by the directors which they consider best for all concerned. The plan, and a statement of reasons for proposing dissolution and for proposing the plan, shall be submitted to the Board for approval.

(b) *Board approval.* The Board may approve the plan if the Board believes dissolution is advisable and the plan best for all concerned, but if the Board considers the plan inadvisable, the Board may either make recommendations to the association concerning the plan or disapprove the plan.

**§ 543.52 Approval by stockholders for dissolution.**

(a) *Stockholder vote.* When a plan of dissolution is approved by the association's board of directors and by the Board, the plan shall be submitted to the association's stockholders at a legal meeting, and shall become effective when approved by the affirmative vote of two-thirds of the outstanding voting stock. If any class of stock is entitled to vote as a class pursuant to § 543.4 of this Part, an affirmative vote of a majority of the stock of each voting class and two-thirds of the total voting stock shall be required.

(b) *Dissenters' appraisal rights.* Nothing in this Part shall be interpreted as providing dissenters' appraisal rights to any stockholder of an association dissolving in accordance with this Part.

**§ 543.53 Notice of dissolution.**

(a) *Notice to creditors.* Upon filing of a plan of dissolution with the Board, the dissolving association shall immediately cause notice thereof to be mailed to each known creditor of the association.

(b) *Notice to accountholders.* Notice of the stockholders' affirmative vote to approve the plan of dissolution shall be furnished to any affected accountholder pursuant to § 565.5 of this Subchapter.

**§ 543.54 Procedure for dissolution after Board and stockholder approval.**

Upon approval of the plan of dissolution by the Board and a vote of stockholders, the dissolving association shall immediately proceed to collect its assets, convey and dispose of its properties that are not to be distributed in kind to its stockholders, pay, satisfy and discharge its liabilities and obligations, and do all other acts required to liquidate its business and affairs, and after paying or adequately providing for the payment of all its obligations an liabilities, distribute the remainder of its assets, either in cash or in kind, among its class or classes of stockholders according to their respective rights and preferences.

**§ 543.55 Termination of corporate existence.**

(a) *Completion of dissolution.* After dissolution in accordance with the plan, a certificate evidencing dissolution, supported by such evidence as the Board may require, shall immediately be filed with the Board. When the Board receives such evidence satisfactory to it, it will terminate the corporate existence of the dissolved association and the association's charter shall thereby be cancelled.

(b) *Continuation of corporate existence after dissolution.* Any association dissolving in accordance with this Part shall nevertheless continue its corporate existence for a period of three years from such dissolution, or for such longer period as the Board in its discretion may direct,

solely for the purposes of prosecuting and defending legal actions, suits, or proceedings, whether civil, criminal or administrative, brought by or against such association, settling and closing business, disposing of or otherwise conveying property and discharging liabilities, and for the distribution to stockholders of any remaining assets, but not for the purpose of continuing the business for which the association was organized. Any association dissolved pursuant to this Part shall, with respect to any action, suit or proceeding, whether civil, criminal or administrative, brought by or against such association, either prior to or within three years of the date of its dissolution, be deemed to continue its corporate existence beyond the three-year period until any and all final judgments, orders or decrees in connection with such action, suit or proceeding have been fully executed.

**§ 543.56 Involuntary dissolution.**

Notwithstanding the foregoing provisions of this Part, the Board may determine to waive or deem inapplicable any provision of §§ 543.51–543.55 of this Part for dissolutions instituted for supervisory reasons or pursuant to Part 574 of this Subchapter.

**§543.57–543.59 [Reserved]**

**§ 543.60 Supervisory waiver.**

Notwithstanding the foregoing provisions of Part 543, the Board may determine to waive or deem inapplicable any provision of §§ 543.1–543.59 of this Part to facilitate: (a) an acquisition to prevent the failure of an institution chartered by the Board or insured by the Corporation; or (b) a transfer of accounts in payment of insurance; or, for (c) supervisory reasons or pursuant to Part 574 of this Subchapter.

**Appendix A to Part 543—Model Bylaws for Stock Associations**

*Article I—Home Office*

The home office of the association shall be at ——— in the County of ———, in the State of ———.

*Article II—Stockholders*

Section 1. *Place of Meetings.* All annual and special meetings of stockholders shall be held at the home office of the association or at such other place in the state in which the principal place of business of the association is located or in which the association maintains branches, as the board of directors may determine.

Section 2. *Annual Meeting.* A meeting of the stockholders of the association for the election of directors and for the transaction of any other business of the association shall be held annually within 150 days after the end of the association's fiscal year on the ——— of ——— if not a legal holiday, and if a legal holiday, then on the next day following which is not a legal holiday, at ———, or at such other date and time within such 150-day period as the board of directors may determine.

Section 3. *Special Meeting.* Special meetings of the stockholders for any purpose or purposes, unless otherwise prescribed by the regulations of the Federal Home Loan Bank Board ("Board") (which as hereinafter used includes the Federal Savings and Loan Insurance Corporation), may be called at any time by the chairman of the board, the president, or a majority of the board of directors, and shall be called by the chairman of the board, the president, or the secretary upon the written request of the holders of not less than one-tenth of all of the oustanding capital stock of the association entitled to vote at a legal meeting. Such written request shall state the purpose or purposes of the meeting and shall be delivered to the home office of the association addressed to the chairman of the board, the president, or the secretary.

Section 4. *Conduct of Meetings.* Annual and special meetings shall be conducted in accordance with the most current edition of Robert's Rules of Order unless otherwise prescribed by regulations of the Board or these bylaws. The board of directors shall designate, when present, either the chairman of the board or the president, if the president is a director, to preside at such meetings.

Section 5. *Notice of Meetings* Written notice stating the place, day, and hour of the meeting and the purpose(s) for which the meeting is called shall be delivered not fewer than 20 nor more than 50 days before the date of the meeting, either personally or by mail, by or at the direction of the chairman of the board, the president, or the secretary, or the directors calling the meeting, to each stockholder of record entitled to vote at such meeting. If mailed, such notice shall be deemed to be delivered when deposited in the United States mail, addressed to the stockholder at the address as it appears on the stock transfer books or records of the association as of the record date prescribed in section 6 of this Article II, with postage prepaid. When any stockholders' meeting, either annual or special, is adjourned for 30 days or more, notice of the adjourned meeting shall be given as in the case of an original meeting. It shall not be necessary to give any notice of the time and place of any meeting adjourned for fewer than 30 days or of the business to be transacted at the meeting, other than an announcement at the meeting at which such adjournment is taken.

Section 6. *Fixing of Record Date.* For the purpose of determining stockholders entitled to notice or to vote at any meeting of stockholders or any adjournment, or stockholders entitled to receive payment of any dividend, or in order to make a determination of stockholders for any other proper purpose, the board of directors shall fix in advance a date as the record date for any such determination of stockholders. Such date in any case shall be not more than 50 days and, in the case of a meeting of stockholders, not fewer than 20 days prior to the date on which the particular action requiring such determination of stockholders is to be taken. When a determination of stockholders entitled to vote at any meeting of stockholders has been made as provided in this section, such determination shall apply to any adjournment.

Section 7. *Voting Lists.* At least 20 days before each meeting of the stockholders, the officer or agent having charge of the stock transfer books for shares of stock of the association shall make a complete list of the stockholders entitled to vote at such meeting, or any adjournment, arranged in alphabetical order, with the address and the number of shares of stock held by each. This list of stockholders shall be kept on file at the home office of the association and shall be subject to inspection for any purpose germane to the meeting, by any stockholder of record or his agent at any time during usual business hours for a period of 20 days prior to such meeting. Such list shall also be produced and kept open at the time and place of the meeting and shall be subject to inspection by any stockholder of record during the entire time of the meeting. The original stock transfer book shall constitute *prima facie* evidence of the stockholders entitled to examine such list or transfer books or to vote at any meeting of stockholders.

Section 8. *Books and Records; Stockholder Access.* Stockholder access to books and records shall be governed by § 543.9–3 of the Board's Federal Regulations (12 CFR 543.9–3) as now in effect or any successor provision thereto.

Section 9. *Quorum.* A majority of the outstanding shares of stock of the association entitled to vote, represented in person or by proxy, shall constitute a quorum at a meeting of stockholders. If less than a majority of the outstanding shares of stock is represented at a meeting, a majority of the shares of stock so represented may adjourn the meeting from time to time without further notice. At such adjourned meeting at which a quorum shall be present or represented, any business may be transacted which might have transacted at the meeting as originally notified. The stockholders present at a legal meeting may continue to transact business until adjournment, notwithstanding that the remaining stockholders constitute less than a quorum.

If a quorum is present, the affirmative vote of the majority of the shares of stock represented at the meeting and entitled to vote on the subject matter shall be the act of the stockholders unless the vote of a greater number of stockholders or voting by classes is required by law or the charter.

Section 10. *Proxies.* At all meetings of stockholders a stockholder may vote in person or by a duly authorized attorney in fact. Proxies may be given telephonically or electronically as long as the holder uses a reasonable procedure for identifying the stockholder. Proxies shall have been placed on file with the secretary of the association for verification, prior to the meeting. Notwithstanding § 569.3 of the Board's Insurance Regulations, 12 CFR 569.3, a proxy may designate as holder a corporation, partnership or company as defined in Part

574 of the Board's Insurance Regulations, 12 CFR Part 574. Proxies solicited on behalf of the managment shall be voted as directed by the stockholer or in the absence of such direction, as determined by a majority of the proxy committee, or in its absence, by the board of directors. No proxy shall be valid more than eleven months from the date of its execution except for a proxy coupled with an interest.

Section 11. *Voting stock in the Name of Two or More Persons.* When ownership stands in the name of two or more persons, in the absence of written directions to the association to the contrary, at any meeting of the stockholders of the association any one or more of such stockholders may cast, in person or by proxy, all votes to which such ownership is entitled. In the event an attempt is made to cast conflicting votes, in person or by proxy, by the several persons in whose names shares of stock stand, the vote or votes to which those persons are entitled shall be cast as directed by a majority of those holding such and present in person or by proxy at such meeting, but no votes shall be cast for such stock if a majority cannot agree.

Section 12. *Voting Stock by Certain Holders.* Stock standing in the name of another company may be voted by any officer, agent, or proxy as the bylaws of such company may prescribe, or in the absence of such provision, as the board of directors of such company may determine. Stock held by an administrator, executor, guardian, or conservator may be voted by that person, either in person or by proxy, without a transfer of such stock into his name. Stock held in the name of a trustee may be voted by him, either in person or by proxy, but no trustee shall be entitled to vote stock held by him without a transfer of such stock into his name. Stock held in the name of a receiver may be voted by such receiver, and stock held by or under the control of a receiver may be voted by such receiver without the transfer into his name if authority to do so is contained in an appropriate order of the court or other public authority by which such receiver was appointed.

A stockholder whose stock is pledged shall be entitled to vote such stock until the stock has been transferred into the name of the pledgee, and thereafter the pledgee shall be entitled to vote the stock so transferred.

Neither treasury shares of its own stock held by the association nor stock held by another company, if such other company is controlled by the association as defined in section 574 of the Board's Insurance Regulations, 12 CFR 574, shall be voted at any meeting or counted in determining the total number of outstanding shares of stock at any given time for purposes of any meeting.

Section 13. *Cumulative Voting.* Every stockholder entitled to vote at an election for directors shall have the right to vote, in person or by proxy, the number of shares of stock owned by the stockholder for as many persons as there are directors to be elected and for whose election the stockholder has a right to vote, or to cumulate the votes by giving one candidate as many votes as the number of such directors to be elected multiplied by the number of shares of stock shall equal or by distributing such votes on the same principle among any number of candidates.

Section 14. *Inspectors of Election.* In advance of any meeting of stockholers, the board of directors may appoint any persons other than nominees for office as inspectors of election to act at such meeting or any adjournment. The number of inspectors shall be either one or three. Any such appointment shall not be altered at the meeting. If inspectors of election are not so appointed, the chairman of the board or the president may, or on the request of not fewer than 10 percent of the votes represented at the meeting shall, make such appointment at the meeting. If approinted at the meeting, the majority of the votes present shall determine whether one or three inspectors are to be appointed. In case any person appointed as inspector fails to appear or fails or refuses to act, the vacancy may be filled by appointment by the board of directors in advance of the meeting or at the meeting by the chairman of the board or the president.

Unless otherwise prescribed by regulations of the Board, the duties of such inspectors shall include: Determining the number of shares of stock and the voting power of stock, the stock represented at the meeting, the existence of a quorum, and the authenticity, validity and effect of proxies; receiving votes, ballots, or consents; hearing and determining all challenges and questions in any way arising in connection with the right to vote; counting and tabulating all votes or consents; determining the result; and such acts as may be proper to conduct the election or vote with fairness to all stockholders.

Section 15. *Nominating Committee.* The board of directors or a committee of directors appointed by a majority of directors shall act as a nominating committee for selecting the management nominees for election as directors. Except in the case of a nominee substituted as a result of the death or incapacity of a management nominee, the nominating committee shall deliver written nominations to the secretary at least 20 days prior to the date of the annual meeting. Upon delivery, such nominations shall be posted in a conspicuous place in each office of the association. No nominating committee shall be voted upon at the annual meeting unless other nominations by stockholders of record are made in writing and delivered 10 days prior to the date of the annual meeting. Upon delievery, such nominations shall be posted in a conspicuous place in each office of the association. Ballots bearing the names of all persons nominated by the nominating committee and by stockholders shall be provided for use at the annual meeting. However, if the nominating committee shall fail or refuse to act at least 20 days prior to the annual meeting, nominations for directors may be made at the annual meeting by any stockholder entitled to vote and shall be voted upon.

Section 16. *New Business.* Any new business to be taken up at the annual meeting, including any proposal to increase or decrease the number of directors, shall be stated in writing and filed with the secretary of the association at least 10 days before the date of the annual meeting, and all business so stated, proposed, and filed shall be considered at the annual meeting. Any stockholder may make any other proposal at the annual meeting and the same may be discussed and considered, but unless stated in writing and filed with the secretary at least 10 days before the meeting, such proposal shall be laid over for action at an adjourned, special, or annual meeting of the stockholders taking place 30 days or more thereafter. This provision shall not prevent the consideration and approval or disapproval at the annual meeting of reports of officers, directors, and committees; but in connection with such reports, no new business shall be acted upon at such annual meeting unless stated and filed as provided in this section.

Section 17. *Informal action by stockholders.* Any action required to be taken at a meeting of the stockholders, or any other action which may be taken at a meeting of stockholders, may be taken without a meeting if consent in writing, setting forth the action so taken, has been given by all of the stockholders entitled to vote with respect to the subject matter.

*Article III—Board of Directors*

Section 1. *General Powers.* The business and affairs of the association shall under the direction of its board of directors. The board of directors shall annually elect a chairman of the board and a president from among its members and shall designate, when present, either the chairman of the board or the president to preside at its meetings.

Section 2. *Number and term.* The board of directors shall consist of —— members and shall be divided into three classes as nearly equal in number as possible. The members of each class shall be elected for a term of three years and until their successors are elected and qualified. One class shall be elected by ballot annually.

Section 3. *Regular Meetings.* A regular meeting of the board of directors shall be held without other notice than this bylaw immediately after, and at the same place as, the annual meeting of stockholders. The board of directors may provide, by resolution, the time and place for the holding of additional regular meetings without other notice than such resolution.

Section 4. *Qualification.* Each director shall at all times be the beneficial owner of not less than 100 shares of capital stock of the association unless the association is a wholly owned subsidiary of a holding company.

Section 5. *Special Meetings.* Special meetings of the board of directors may be called by or at the request of the chairman of the board, the president, or one-third of the directors. The persons authorized to call special meetings of the board of directors may fix any place for holding any special meeting of the board of directors called by such persons.

Members of the board of directors may participate in special meetings by means of conference telephone or similar communications equipment by which all persons participating in the meeting can hear each other. Such participation shall constitute presence in person for all purposes.

Section 6. *Notice.* Written notice of any special meeting shall be given to each director at least 24 hours prior thereto when delivered personally or by telegram or at least five days prior thereto when delivered by mail at the address at which the director is most likely to be reached. Such notice shall be deemed to be delivered when deposited in the mail so addressed, with postage prepaid if mailed, and when delivered to the telegraph company if sent by telegram. Any director may waive notice of any meeting by a writing filed with the secretary. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting unless the director is attending the meeting for the express purpose of objecting to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any meeting of the board of directors need be specified in the notice of or waiver of notice of such meeting.

Section 7. *Quorum.* A majority of the number of directors fixed by section 2 of this Article II shall constitute a quorum for the transaction of business at any meeting of the board of directors; but if less than such majority is present at a meeting, a majority of the directors present may adjourn the meeting from time to time. Notice of any adjourned meeting shall be given in the same manner as prescribed by section 6 of this Article III.

Section 8. *Manner of Acting.* The act of the majority of the directors present at a meeting at which a quorum is present shall be the act of the board of directors, unless a greater number is prescribed by regulation of the Board or by these bylaws.

Section 9. *Action Without a Meeting.* Any action required or permitted to be taken by the board of directors at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the directors eligible to vote thereon.

Section 10. *Resignation.* Any director may resign at any time by sending a written notice of such resignation to the home office of the association addressed to the chairman of the board or the president. Unless otherwise specified, such resignation shall take effect upon receipt by the chairman of the board or the president. More than three consecutive absences from regular meetings of the board of directors, unless excused by resolution of the board of directors, shall automatically constitute a resignation, effective when such resignation is accepted by the board of directors.

Section 11. *Vacancies.* Any vacancy occurring on the board of directors may be filled by the affirmative vote of a majority of the remaining directors, although less than a quorum of the board of directors. A director elected to fill a vacancy shall be elected to serve until the next election of directors by the stockholders. Any directorship to be filled by reason of an increase in the number of directors may be filled by election by the board of directors for a term of office continuing only until the next election of directors by the stockholders.

Section 12. *Compensation.* Directors, as such, may receive a stated salary for their services. By resolution of the board of directors, a reasonable fixed sum and reasonable expenses of attendance, if any, may be allowed for attendance at each regular or special meeting of the board of diectors. Members of either standing or special committees may be allowed such compensation for attendance at committee meetings as the board of directors may determine.

Section 13. *Presumption of Absent.* A director of the association who is present at a meeting of the board of directors at which action on any association matter is taken shall be presumed to have assented to the action taken unless his dissent or abstention shall be entered in the minutes of the meeting or unless he shall file a written dissent to such action with the person acting as the secretary of the meeting before the adjournment thereof or shall forward such dissent by registered mail to the secretary of the association within five days after the date a copy of the minutes of the meeting is received. Such right to dissent shall not apply to a director who voted in favor of such action.

Section 14. *Removal of Directors.* At a meeting of stockholders called expressly for that purpose, any director may be removed only for cause by a vote of the holders of a majority of stock then entitled to vote at an election of directors. If less than the entire board is to be removed, no one of the directors may be removed if the votes cast against the removal would be sufficient to elect a director if cumulatively voted at an election of the class of directors of which such director is a part, where the association's stockholders are permitted to vote cumulatively. Whenever the holders of the shares of stock of any class are entitled to elect one or more directors by the provisions of the association's charter or supplemental sections thereto, the provisions of this section shall apply, in respect to the removal of a director or directors so elected, to the vote of the holders of the outstanding shares of stock of that class and not to the vote of the outstanding shares of stock as a whole.

In any solicitation of proxies for removal of a director by stockholder vote, opportunity must be provided to the director whose removal is sought to present a defense to stockholders by means of a written statement not to exceed 500 words which must accompany or pecede the initial solicitation for removal of such director. Such statement shall be made at the expense of the party seeking removal. For the purpose of this section, the term "cause" shall mean willful failure, neglect or refusal in any material respect to perform duties as a director or commission of any act of willful misconduct, self-dealing, malfeasance or gross negligence.

Section 15. *Age Limitation on Directors.* No person [fill in any age, 70 or above] years of age shall be eligible for election, reelection, appointment, or reappointment to the board of directors of the association. No director shall serve as such beyond the annual meeting of the association immediately following the directors becoming [fill in any age, 70 or above] except that a director serving on [fill in bylaw adoption date] may complete the term as director. This age limitation does not apply to an advisory director.

*Article IV—Executive and Other Committees*

Section 1. *Appointment.* The board of directors, by resolution adopted by a majority of the full board, may designate the chief executive officer and two or more of the other directors to constitute an executive committee. The designation of any committee pursuant to this Article IV and the delegation of authority shall not operate to relieve the board of directors, or any director, of any responsibility imposed by law or regulation.

Section 2. *Authority.* The executive committee, when the board of directors is not in session, shall have and may exercise all of the authority of the board directors except to the extent, if any, that such authority shall be limited by the resolution appointing the executive committee; and except also that the executive committee shall not have the authority of the board of directors with reference to: The declaration of dividends; the amendment of the charter or bylaws of the association, or recommending to the stockholders a plan of merger, consolidation, or conversion; the sale, lease, or other disposition of all or substantially all of the property and assets of the association otherwise than in the usual and regular course of its business; a voluntary dissolution of the association; a revocation of any of the foregoing; or the approval of a transaction in which any member of the executive committee, directly or indirectly, has any material beneficial interest.

Section 3. *Tenure.* Subject to the provisions of section 8 of this Article IV, each member of the executive committee shall hold office until the next regular meeting of the board of directors following his designation and until a successor is designated as a member of the executive committee.

Section 4. *Meetings.* Regular meetings of the executive committee may be held without notice at such times and places as the executive committee may fix from time to time by resolution. Special meetings of the executive committee may be called by any member thereof upon not less than one day's notice stating the place, date, and hour of the meeting, which notice may be written or oral. Any member of the executive committee may waive notice of any meeting and no notice of any meeting need be given to any member thereof who attends in person. The notice of a meeting of the executive committee need not state the business proposed to be transacted at the meeting.

Section 5. *Quorum.* A majority of the members of the executive committee shall constitute a quorum for the transaction of business at any meeting thereof, and action of the executive committee must be authorized by the affirmative vote of a majority of the members present at a meeting at which a quorum is present.

Section 6. *Action without a meeting.* Any action required or permitted to be taken by the executive committee at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the members of the executive committee eligible to vote thereon.

Section 7. *Vacancies.* Any vacancy in the executive committee may be filled by a resolution adopted by a majority of the authorized board of directors.

Section 8. *Resignations and removal.* Any member of the executive committee may be removed at any time with or without cause by resolution adopted by a majority of the authorized board of directors. Any member of the executive committee may resign at any time by giving written notice to the president or secretary of the association. Unless otherwise specified, such resignation shall take effect upon its receipt; the acceptance of such resignation shall not be necessary to make it effective.

Section 9. *Procedure.* The executive committee shall elect a presiding officer from its members and may fix its own rules of procedure which shall not be inconsistent with these bylaws. It shall keep regular minutes of its proceedings and report the same to the board of directors for its information at the meeting held next after the proceedings shall have occurred.

Section 10. *Audit Committee.* The board of directors, by resolution adopted by a majority of the authorized board, shall appoint an audit committee of at least three directors the majority of whom shall be independent. A director shall be considered independent if he or she is neither employed by the association, its service corporation, its holding company or its affiliates nor serving as legal counsel or other professional advisor to the association, its service corporation, its holding company or its affiliates, nor is a member of the immediate family or a person serving in any of the foregoing capacities. The audit committee shall recommend independent auditors, consult with the independent auditors regarding the plan of audit, review the audit report in consultation with the independent auditors, and consult with the independent auditors regarding the adequacy of internal accounting controls.

Section 11. *Other committees.* The board of directors may by resolution establish a loan committee or other committee composed of directors as it may determine to be necessary or appropriate for the conduct of the business of the association, and may prescribe the duties, membership, and procedures thereof.

*Article V—Officers*

Section 1. *Positions.* The officers of the association shall be president, one or more vice presidents, a secretary, and a treasurer, each of whom shall be elected by the board of directors. The board of directors may also designate the chairman of the board as an officer. The president shall be the chief executive officer, unless the board of directors designates the chairman of the board as chief executive officer. The president need not be a director of the association. The offices of the secretary and treasurer may be held by the same person and a vice president may also be either the secretary or the treasurer. The board of directors may designate one or more vice presidents as executive vice president or senior vice president. The board of directors may also elect or authorize the appointment of such other officers as the business of the association may require. The officers shall have such authority and perform such duties as the board of directors may from time to time authorize or determine. In the absence of action by the board of directors, the officers shall have such powers and duties as generally pertain to their respective offices.

Section 2. *Election and Term of Office.* The officers of the association shall be elected annually at the first meeting of the board of directors held after each annual meeting of the stockholders. If the election is not held at such meeting, such election shall be held as soon thereafter as possible. Each officer shall hold office until a successor has been duly elected and qualified or until the officer's death, resignation, or removal in the manner provided in this Article V. Election or appointment of an officer, employee, or agent shall not of itself create contractual rights. The board of directors may authorize the association to enter into an employment contract with any officer in accordance with regulations of the Board; but not such contract shall impair the right of the board of directors to remove any officer at any time in accordance with section 3 of this Article V.

Section 3. *Removal.* Any officer may be removed by the board of directors whenever in its judgment the best interests of the association will be served thereby, but such removal, other than for cause, shall be without prejudice to the contractual rights, if any, of the person so removed. "Cause" with respect to removal of an officer shall have the same meaning as set forth in section 14 of Article III as applied to directors.

Section 4. *Vacancies.* A vacancy in any office because of death, resignation, removal, disqualification, or otherwise may be filled by the board of directors for the unexpired portion of the term.

Section 5. *Renumeration.* The renumeration of the officers shall be fixed from time to time by the board of directors.

Section 6. *Age Limitation for Officers.* No person [fill in any age, 70 or above] years of age shall be eligible for election, reelection, appointment, or reappointment as an officer of the association. No officer shall serve beyond the annual meeting of the association immediately following the officer becoming [fill in any age used above] except that an officer serving on [fill in bylaw adoption date] may complete the term. However, an officer shall, at the option of the Board, retire at age 65 if the officer has served in an executive or high policymaking post for at least two years immediately prior to retirement and is immediately entitled to nonforfeitable annual retirement benefits of at least ——— [44,000 (1985) must be in accordance with the Age Discrimination in Employment Act].

*Article VI—Indemnification of Directors, Officers, and Employees*

Section 1. *General.* The association may indemnify any person against whom an action is brought or threatened because that person is or was a director, officer or employee of the association or a director, officer or employee of any wholly-owned subsidiary, only as provided in this Article VI, for any amount for which that person becomes liable under a judgment or settlement in such action; and reasonable costs and expenses, including attorney's fees, actually paid or incurred by that person in defending or settling such action, or in enforcing his rights under this section if he obtains a favorable judgment in such action: *Provided,* that nothing herein shall authorize indemnification by the association of directors, officers or employees of affiliates, affiliated persons, or subsidiaries of the association for actions in their capacity as such unless such person was a director, officer or employee of a wholly-owned subsidiary.

Section 2. *Conditions.* Indemnification may be made to a person described in Section 1 if final judgment on the merits is in his favor. In addition, in the case of settlement, final judgment against him or final judgment in his favor other than on the merits, indemnification may be made to a person described in Section 1 if it is determined that he was acting in good faith within the scope of his employment or authority as he could reasonably have perceived it under the circumstances and for a purpose he could reasonably have believed under the circumstances was in the best interests of the association, and, in the case of a criminal action, he had no reasonable cause to believe his conduct was unlawful. Such determination shall be made by the board of directors by a majority vote of a quorum consisting of disinterested directors, or if such a quorum is not obtainable, or, even if obtainable, a quorum of disinterested directors so directs, by the stockholders with only the shares of stock of disinterested stockholders allowed to vote or to be counted for purposes of determinating a quorum. However, no indemnification shall be made unless the association gives the Board at least 60 days' notice of its intention to make such indemnification. Such notice shall state the facts on which action arose, the terms of any settlement, and any disposition of the action by a court. A copy of such notice, and a certified copy of the resolution containing the required determination by the board of directors, shall be sent to the Board in accordance with its regulations. No such indemnification shall be made if the Board or its designee advises the association in writing, within such notice period, of its objection thereto. In addition, when the action is brought or threatened by the association or on behalf of the association, indemnification shall be limited to reasonable costs and expenses as described in section 1. Under no circumstances may indemnification be made in connection with any claim, issue or matter with regard to which there has been a final judgment that the person was liable for negligence or misconduct in the performance of his duty to the association.

Section 3. *Insurance.* An association may obtain insurance to protect it and its directors, officers and employees or the directors, officers and employees of a wholly-owned subsidiary from potential losses arising from claims against any of them for alleged wrongful acts, or wrongful acts committed in their capacity as directors, officers or employees: *Provided,* that the association may not obtain insurance which

provides for payment of losses of any person incurred as a consequence of his willful or criminal misconduct.

Section 4. *Advance Payment of Expenses.* If a majority of the disinterested directors of a majority of the disinterested stockholders of the association concludes that, in connection with an action, any person ultimately may become entitled to indemnification under this section, such directors or stockholders may authorize payment of reasonable costs and expenses, including attorneys' fees, arising from the defense or settlement of such action. In any vote of the stockholders to authorize such advances, only the shares of disinterested stockholders shall be voted or counted towards a quorum. Nothing in this section shall prevent the directors of an association from imposing such conditions on a payment of expenses as they deem warranted and in the interests of the association. Before making advance payment of expenses under this section, the association shall obtain an agreement in writing that the association will be repaid if the person on whose behalf payment is made is later determined not to be entitled to such indemnification.

Section 5. *Indemnification.* Nothing in this section shall authorize indemnification of directors, officers or employees, of the association when such indemnification would contravene public policy as expressed by federal statutes or the regulations of the Board.

Section 6. *Exclusive of Provisions.* No association shall indemnify any person referred to in section 1 of this Article or obtain insurance referred to in section 3 of this Article other than in accordance with this Article.

Section 7. *Definitions and Rules of Construction.* Definitions and rules of construction for purposes of this Article shall be in accordance with Board regulations on indemnification of directors, officers or employees.

*Article VII—Contractors, Loans, Checks and Deposits*

Section 1. *Contracts.* To the extent permitted by regulations of the Board, and except as otherwise prescribed by these bylaws with respect to certificates for shares of stock, the board of directors may authorize any officer, employee, or agent of the association to enter into any contract or execute and deliver any instrument in the name of and on behalf of the association. Such authority may be general or confined to specific instances.

Section 2. *Loans.* No loans shall be contracted for on behalf of the association and no evidence of indebtedness shall be issued in its name unless authorized by the board of directors. Such authority may be general or confined to specific instances.

Section 3. *Checks, Drafts, etc.* All checks, drafts, or other orders for the payment of money, notes, or other evidences of indebtedness issued in the name of the association shall be signed by one or more officers, employees or agents of the association in such manner as shall from time to time be determined by the board of directors.

Section 4. *Deposits.* All funds of the association not otherwise employed shall be deposited from time to time to the credit of the association in such duly authorized federally insured depositories as the board of directors may select.

*Article VIII—Certificates for Shares and Their Transfer*

Section 1. *Certificate for Capital Stock.* Certificates representing capital stock of the association shall be in a form or forms determined by the board of directors and approved by the Board. Such certificates shall be signed by the chief executive officer or by any other officer of the association authorized by the board of directors, attested by the secretary or an assistant secretary, and sealed with the corporate seal or a facsimile thereof. The signatures of such officers upon a certificate may be facsimiles if the certificate is manually signed on behalf of a transfer agent or a registrar other than the association itself or one of its employees. Each certificate for capital stock shall be consecutively numbered or otherwise identified. The name and address of the person to whom the stock is issued, with the number of shares of stock and date of issue, shall be entered on the stock transfer books of the association. All certificates surrendered to the association for transfer shall be cancelled and no new certificate shall be issued until the former certificate for a like number of shares of stock has been surrendered and cancelled, except that in case of a lost or destroyed certificate, a new certificate may be issued upon such terms and indemnity to the association as the board of directors may prescribe.

Section 2. *Transfer of Capital Stock.* Transfer of shares of capital stock of the association shall be made only on its stock transfer books. Authority for such transfer shall be given only by the holder of record or his legal representative who shall furnish proper evidence of such authority, or by his attorney authorized by a duly executed power of attorney and filed with the association. Such transfer shall be made only on surrender for cancellation of the certificate for such shares of stock. The person in whose name shares of capital stock are held on the books of the association shall be deemed by the association to be the owner for all purposes.

*Article IX—Fiscal Year; Annual Audit*

The fiscal year of the association shall end on the —— of —— of each year. The association shall be subject to an annual audit as of the end of its fiscal year by independent public accountants appointed by and responsible to the board of directors. The appointment of such accountants shall be subject to annual ratification by the stockholders.

*Article X—Dividends*

Subject to the terms of the association's charter and the regulations and orders of the Board, the board of directors may, from time to time, declare, and the association may pay, dividends on its outstanding shares of capital stock.

*Article XI—Corporate Seal*

The board of directors shall provide an association seal which shall be two concentric circles between which shall be the name of the association. The year of incorporation or an emblem may appear in the center.

*Article XII—Amendments*

These bylaws may be amended in a manner consistent with regulations of the Board at any time by a majority vote of the full board of directors or by a majority vote of the votes cast by the stockholders of the association at any legal meeting.

2. Revise Part 544 as follows:

## PART 544—FEDERAL MUTUAL ASSOCIATIONS

Sec.


544.1 Procedures for organization of Federal mutual association; initial collection of pledged capital; organizational meeting.
544.2 Powers of Federal mutual associations.
544.3 Charters for Federal mutual association.
544.4 Preapproved charter amendments.
544.4–1 Additional charter provisions [Reserved]
544.5 Procedures for obtaining Board approval of charter amendments.
544.6 Reissuance of charter.
544.7 Bylaws.
544.8 Effect of subsequent charter or bylaw amendment.
544.9 Members' meetings.
544.9–1 Voting by proxy.
544.9–2 Communication between members.
544.9–3 Annual reports to members.
544.10 Board of directors.
544.10–1 Directors' meetings.
544.10–2 Directors' conflict of interest.
544.10–3 [Reserved]
544.10–4 Officers.
544.10–5 Indemnification of directors, officers and employees.
544.11–544.12 [Reserved]
544.13 Fiscal year; annual audit.
544.14 Corporate procedures.
544.15–544.19 [Reserved]
544.20 Combinations involving Federal mutual associations.
544.21 Merger or consolidation.
544.22–544.23 [Reserved]
544.24 Articles of combination for merger or consolidation.
544.25 Effective date; date of consummation for merger or consolidation.
544.26 Continuity of corporate existence after merger or consolidation.
544.27 [Reserved]
544.28 Supervisory combinations.
544.29 [Reserved]
544.30 Bulk purchase or sale of assets.
544.31 [Reserved]
544.32 Articles of combination for bulk purchase or sale of assets.
544.33 Effective date; date of consummation for bulk purchase or sale of assets.
544.34 Continuity of corporate existence after bulk purchase or sale of assets.
544.35 [Reserved]
544.36 Partial purchase or sale of assets

Sec.

544.37–544.39 [Reserved]
544.40 Reorganization [Reserved]
544.41–544.49 [Reserved]
544.50 Dissolution.
544.51 Voluntary dissolution.
544.52 Approval by membrs of dissolution.
544.53 Notice of dissolution.
544.54 Procedure for dissolution after Board and member approval.
544.55 Termination of corporate existence.
544.56 Involuntary dissolution.
544.57–544.59 [Reserved]
544.60 Supervisory Waiver.
Appendix A to Part 554—Model Bylaws for Mutual Associations.

Authority: 12 U.S.C. 1464; Reorg. Plan No. 3 of 1947, 3 CFR, 1943–1948 Comp., P. 1071.

**§ 544.1 Procedures for organization of Federal mutual association; initial collection of pledged capital; organizational meeting.**

(a) *General.* Applications for permission to organize a Federal mutual association shall be subject to the provisions of §§ 542.1 through 542.12 of this Subchapter.

(b) *Initial collection of pledged capital.* No pledges may be collected until the organizers have received conditional approval of the application for permission to organize. Upon the conditional approval of an application for permission to organize a Federal mutual association and after the interim officers, directors, employees and agents have been bonded to the extent required by § 563.19 of this Chapter, such association shall proceed to collect its pledged capital. All money collected as pledges shall be placed in escrow with an independent financial institution insured by the Federal Savings and Loan Insurance Corporation or Federal Deposit Insurance Corporation until the association has received the certificate of authority specified in § 542.7 and, unless specifically approved by the Board consideration for the initial minimum capitalization shall consist of cash or tangible property to the extent investment in such property would be permitted to the association.

(c) *Organizational meeting.* Within six months of receiving a certificate of authority to commence business the association shall provide notice, pursuant to § 544.9(a) of this Part, of a meeting of its members to elect a board of directors. Until such time, the interim board of directors shall be governed by the Model Bylaws. Immediately following such election, the directors shall meet to adopt permanent bylaws and to elect the officers of the association and to undertake any other action necessary to complete corporate organization.

**§ 544.2 Powers of Federal mutual associations.**

In addition to the authority contained in this Part and in its charter, a Federal mutual association may make any loan or investment or engage in any activity authorized for a Federal association in Parts 545, 550, 555, or 556 of this Subchapter or pursuant to the Home Owners' Loan Act of 1933, as amended, or the successor provisions of any of the foregoing.

**§ 544.3 Charters for Federal mutual association.**

(a) *Initial Charter.* The charter of a Federal mutual association shall be in the form specified in paragraph (c) of this section and may also include any preapproved optional provision contained in § 544.4 of this Part.

(b) *Federal savings bank charter.* A charter for a Federal mutual savings bank shall substitute the term "savings bank" for "association" and, for savings banks converting pursuant to §546.10 of this Subchapter shall include the following sentence at the end of Section 4 of the charter set forth at paragraph (c) of this section: "In addition, the savings bank may make any investment and engage in any activity as may be specifically authorized by action of the Board, including authorization by delegated authority, in connection with action approving the issuance of the chapter."

(c) *Federal mutual charter.* The following is the standard form of Federal mutual charter. Associations may vary the wording of charters only in accordance with bracketed instructions.

**Federal Mutual Charter**

Section 1. *Corporate title.* The full corporate title of the association is ————.

Section 2. *Office.* The home office shall be located at————.

Section 3. *Duration.* The duration of the association is perpetual.

Section 4. *Purpose and powers.* The purpose of the association is to pursue any or all of the lawful objectives of a Federal mutual association chartered under section 5 of the Home Owners' Loan Act and to exercise all the express, implied, and incidental powers conferred thereby and by all acts amendatory thereof and supplemental thererto, subject to the Constitution and laws of the United States as they are now in effect, or as they may hereafter be amended, and subject to all lawful and applicable rules, regulations, and orders of the Federal Home Loan Bank Board ("Board").

Section 5. *Capital.* The association may raise capital by accepting payments on savings and demand accounts and by any other means authorized by the Board.

Section 6. *Members.* All holders of the association's savings, demand, or other authorized accounts are members of the association. In the consideration of all questions requiring action by the members of the association, each holder of an account shall be permitted to cast one vote for each $100, or fraction thereof, of the withdrawal value of the member's account. All accounts shall be nonassessable. Borrowers as of the date of this charter shall continue to have one vote for the period of time such borrowings are in existence. No member, however, shall cast more than 1000 votes. Voting may be by proxy, which is subject to the rules and regulations of the Board.

[Associations adopting this charter with existing borrower members must "grandfather" those borrower members i.e. grant them voting rights, if they were members on the date of issuance of the new charter by the Board.]

Section 7. *Directors.* The association shall be under the direction of a board of directors. The authorized number of directors shall not be fewer than five nor more than fifteen persons, as fixed in the association's bylaws, except that the number of directors may be increased to a number greater than fifteen with the prior approval of the Board or its delegate.

[State-chartered savings banks converting to Federal savings banks may retain the term "trustees" and substitute such term throughout the charter and bylaws for the term "director," and may include alternative provisions for the election and term of office of trustees so long as such provisions (1) are authorized by the Board, including authorization pursuant to delegated authority, and (2) provide for compliance with the standard provisions of this section no later than six years after conversion to a Federal association.]

Section 8. *Reserves, surplus, and distribution of earnings.* The association shall maintain for the purpose of meeting losses the amount of general reserves that the Board requires for insurance of accounts referred to in the Board's regulations as "regulatory net worth" or any successor term. Any losses may be charged against general reserves. The association shall distribute net earnings on its accounts on such basis and in accordance with such terms and conditions as may from time to time be authorized by the Board: *Provided*, that the association may establish minimum-balance requirements for accounts to be eligible for distribution of earnings.

All holders of accounts of the association shall be entitled to equal distribution of assets, *pro rata* to the value of their accounts, in the event of voluntary or involuntary liquidation, dissolution, or winding up of the association. Moreover, in any such event, or in any other situation in which the priority of such accounts is in controversy, all such accounts shall, to the extent of their withdrawal value, be debts of the association having the same priority as the claims of general creditors of the association not having priority (other than any priority arising or resulting from consensual subordination) over other general creditors of the association.

Section 9. *Amendment of charter.* Adoption of any preapproved charter amendment pursuant to § 544.4 or 546.10 of the Board's

regulations (12 CFR 544.4, 546.10) or any successor provision shall be effective upon filing the amendment with the Board in accordance with regulatory procedures, after such preapproved amendment has been submitted to and approved by the members at a legal meeting. Any other amendment, addition, alteration, change, deletion to or repeal of this charter must be submitted to and preliminarily approved by the Board prior to submission to and approval by the members at a legal meeting. Any amendment, addition, alteration, change, deletion to or repeal so acted upon and approved shall be effective upon filing it with the Board in accordance with regulatory procedures.

Attest: _____

Secretary of the Association.

By: _____

President or Chief Executive Officer of the Association.

Federal Home Loan Bank Board.

Attest: _____

Secretary of the Board.

By: _____

Effective Date.

**§ 544.4 Preapproved charter amendments.**

This section constitutes preliminary approval by the Board of proposals to members by the board of directors of any Federal mutual association for the adoption or deletion of any of the following amendments to the charter of a Federal mutual association, including the adoption of the Federal mutual charter as set forth in § 544.3(c) of this Part: *Provided*, that the association follows the requirements of its charter in adopting the amendments; and *Provided further*, that where a paragraph specifies wording for an amendment, such amendment uses the exact wording as specified in that paragraph.

(a) *Purposes and powers.* Add a second paragraph to Section 4, as follows:

Section 4. Purpose and Powers. * * *

The association shall have the express power: (i) To act as fiscal agent of the United States when designated for that purpose by the Secretary of the Treasury, under such regulations as the Secretary may prescribe, to perform all such reasonable duties as fiscal agent of the United States as may be required, and to act as agent for any other instrumentality of the United States when designated for that purpose by any such instrumentality; (ii) To sue and be sued, complain and defend in any court of law or equity; (iii) To have a corporate seal, affixed by imprint, facsimile or otherwise; (iv) To appoint officers and agents as its business shall require and allow them suitable compensation; (v) To adopt bylaws not inconsistent with the Constitution or laws of the United States and rules and regulations adopted thereunder and under this Charter; (vi) To raise capital, which shall be unlimited, by accepting payments on savings, demand, or other accounts, as are authorized by regulations made by the Board, and the holders of all such accounts or other accounts as shall, to such extent as may be provided by such regulations, be members of the association and shall have such voting rights and such other rights as are thereby provided; (vii) To issue notes, bonds, debentures, or other obligations, or securities, provided by or under any provision of Federal statute as from time to time is in effect; (viii) To provide for redemption of insured accounts; (ix) To borrow money without limitation and pledge and otherwise encumber any of its assets to secure its debts; (x) To lend and otherwise invest its funds as authorized by statute and the rules and regulations of the Board; (xi) To wind up and dissolve, merge, consolidate, convert, or reorganize; (xii) To purchase, hold and convey real estate and personalty consistent with its objects, purposes, and powers; (xiii) to mortgage or lease any real estate and personalty and take such property by gift, devise, or bequest; and (xiv) To exercise all powers conferred by law. In addition to the foregoing powers expressly enumerated, this association shall have power to do all things reasonably incident to the accomplishment of its express objects and the performance of its express powers.

(b) *Title change.* A Federal mutual association may amend its charter by substituting a new corporate title upon satisfaction of the requirements of this paragraph. Prior to submitting the proposed amendment to its members, the association shall file with the Supervisory Agent a written notice setting forth the proposed title. The Supervisory Agent shall provide to the association a timely written acknowledgment of receipt. If, within 30 days of receipt of notice, the Supervisory Agent does not notify the association of his objection on the grounds set forth in § 542.2 of this Subchapter, the association may change its title by amending its charter in accordance with § 544.5(b) of this Part and the amendment provisions of its charter, except that an association chartered as a Federal savings and loan association may change its title to indicate that it is a Federal savings bank, and an association chartered as a Federal savings bank may change its title to indicate that it is a Federal savings and loan association, only pursuant to paragraph (d) of this section.

(c) *Change of location.* A Federal mutual association that has complied with § 545.95 of this Subchapter may amend its charter by substituting a new home office in section 2.

(d) *Savings bank charter.* A Federal mutual savings and loan association may amend its charter to read in the form of a Federal mutual savings bank charter as specified in § 544.3(b) of this Part and a Federal mutual savings bank may amend its charter to read in the form of a Federal mutual savings and loan association charter: *Provided*, that such association complies with the requirements of § 546.10 of this Subchapter.

(e) *Mutual capital certificates.* Renumber existing section 9 as section 10, add new section 9 to read as set forth below, and add an additional provision to renumbered section 10 as provided below:

Section 9. *Mutual capital certificates.* The association may issue mutual capital certificates pursuant to the rules and regulations of the Board. Subject to such rules and regulations and without the prior approval of the members, the board of directors of the association is authorized, by resolutions from time to time adopted by it, to provide in supplementary sections hereto for the issuance of mutual capital certificates and to fix and state the voting powers, designations, preferences, and the relative participating, optional, or other special rights of the certificates, and the qualifications, limitations, and restrictions thereon.

Members of the association shall not be entitled to preemptive rights with respect to the issuance of mutual capital certificates, nor shall holders of such certificates be entitled to preemptive rights with respect to any additional issues of mutual capital certificates.

Section 10. Amendment of charter. * * *

[Additional provisions may be added to the section to grant holders of mutual capital certificates the right to vote on amendments, additions, alterations, changes, or repeal of the charter in any of the instances set forth in § 563.7–4 of the Board's regulations.]

(f) *Maximum number of votes for members.* A Federal mutual association may amend its charter by substituting 1,000 votes per member in section 6.

**§ 544.4–1 Additional charter provisions. [Reserved]**

**§ 544.5 Procedures for obtaining Board approval of charter amendments.**

(a) *Procedure for obtaining preliminary approval of amendments.* Preliminary approval is the approval required before submitting charter amendments to a vote of the members. Amendments listed in § 544.4 are granted preliminary approval of the Board. The board of directors of a Federal mutual association may request preliminary approval of amendments to the association's Federal mutual charter by filing with the Office of General Counsel, with a copy to the Supervisory Agent, a certified resolution of the board of directors proposing the amendment and setting forth the text of the amendment. Any such provision must be consistent with applicable statutes, regulations and Board policies. If the effect of the proposed amendment would be to render more difficult a change in control of the institution, the

filing shall include an opinion, acceptable to the Board, or counsel independent from the association, demonstrating that the proposed charter provision is consistent with applicable statutes, regulations and Board policies and indicating whether such a provision would be permissible for a corporation incorporated under the laws of Delaware. Any amendment not consistent with regulations or policy of the Board need not be approved by the Board or its delegate, regardless of their purported permissibility under state law. The General Counsel or his designee has delegated authority to make determinations under this section and to grant or deny the preliminary approval of the Board for amendments to all Federal mutual charters. Upon making such a determination, the General Counsel shall notify the Supervisory Agent who shall forward a copy of that determination to the Association.

(b) *Procedures for obtaining final approval of amendments.* Whenever a Federal mutual association whose charter specifies that amendments shall be effective upon filing completes the procedures necessary to amend its charter, or adds supplementary sections thereto, the association shall submit three signed copies of such amendment, along with a certification by the secretary of the association that the amendment is validly authorized and approved, to the Supervisory Agent, who shall return to the association a signed copy of the charter amendment stamped to demonstrate its filing and forward one copy to the Office of District Banks. Such filing shall constitute filing with the Board for purposes of determining the effectiveness of the amendment. A Federal mutual association whose charter provides that any amendment shall be effective on the date it receives final approval of the Board shall be deemed to have obtained such final approval on the date it files a copy of the properly adopted amendment what the Supervisory Agent in the manner specified in the first sentence of this paragraph (b).

**§ 544.6 Reissuance of charter.**

A Federal mutual association that has amended its charter may apply to have its charter, including the amendments, reissued by the Board by filing three executed copies, with the signatures required under § 544.3 of this Part, with the Board's Office of District Banks, with such supporting documents as may be needed to demonstrate that the amendments were properly adopted. Supporting documents shall include copies of the letters granting preliminary approval of the amendments and certifications regarding the vote of the members. The General Counsel or his designee has delegated authority to sign on the Board's behalf charters submitted for reissuance pursuant to this paragraph. Following attestation by the Secretary to the Board or his designee, a copy shall be returned to the association with copies forwarded to the Supervisory Agent and the Office of District Banks.

**§ 544.7 Bylaws.**

(a) *General.* At its first meeting following election by the members, the board of directors of a Federal mutual association shall adopt a set of bylaws for the administration and regulation of its affairs. Except as otherwise provided herein or in the charter, bylaws may be adopted, amended, or repealed by either a majority of the votes cast by the members at a legal meeting or a majority of the board of directors. The bylaws shall contain sufficient provisions to govern the association in accordance with the requirements of §§ 544.8 through 544.14 of this Part.

(b) *Permissible bylaws.* The bylaws and all amendments thereto shall not contain any provision that is inconsistent with §§ 544.8 through 544.14 or with other applicable laws, rules, regulations, the policies underlying such rules or the charter of the institution. Bylaw provisions that adopt the language of the Model Bylaws set out in the Appendix to this Part shall be deemed to comply with the requirements of this section.

(c) *Effectiveness.* Bylaws and amendments thereto that adopt the wording of the Model Bylaws in the Appendix shall be effective upon filing with the Supervisory Agent along with a statement that such provisions conform to the Model Bylaws. Bylaws and amendments that do not adopt the wording of the Model Bylaws shall not be effective unless approved by the Supervisory Agent. Approval by the Supervisory Agent shall constitute the approval of the Board for associations whose bylaws require such approval for amendment. The Supervisory Agent shall not accept any bylaw for amendments thereto for filing that do not conform to the Model Bylaws unless accompanied by an opinion of counsel independent from the association that states with specificity the reasons that such bylaws or amendments conform to the requirements of paragraph (b) of this section. Any bylaw or amendment whose effect would be to render more difficult a change in control of the institution or which adversely affects the ability of members to participate in the governance of the institution shall not be effective and shall be void unless such bylaw or amendment has been approved by the General Counsel or his designee. Any such provision must be filed with the Office of General Counsel, together with an opinion, acceptable to be Board, of counsel independent from the association, demonstrating that the proposed provision is consistent with applicable statutes, regulations and Board policies and indicating whether such provision would be permissible for a corporation incorporated under the laws of Delaware. The General Counsel may condition approval on the favorable vote of the members or such other conditions as he may deem appropriate.

(d) *Procedure.* Three copies of all bylaws and amendments thereto shall be filed with the Supervisory Agent with a copy of any required legal opinion and a certification from the secretary of the association stating such bylaws or amendments thereto were adopted by resolution of the board of directors or members by the requisite vote, who upon approval shall return one copy to the association, and forward one copy to the Office of District Banks, except that with respect to bylaws requiring the approval of the General Counsel, the association shall file two copies with the General Counsel and one copy with the Supervisory Agent and upon approval the General Counsel shall return one copy to the Supervisory Agent who shall notify the association.

**§ 544.8 Effect of subsequent charter or bylaw amendment.**

Notwithstanding any subsequent change to its charter or bylaws, the authority of a Federal mutual association to engage in any transaction shall be determined only the association's charter or bylaws then in effect, unless otherwise provided by Federal law or regulation.

**§ 544.9 Members' meetings.**

(a) *Annual meetings of members.* An association shall provide for and conduct an annual meeting of its members for the election of directors and at which any other business of the association may be conducted. Such meeting shall be held at such place as the board of directors may determine in the state in which the association has its principal place of business or in which the association maintains branches. Such annual meetings shall be held at a date and time within 150 days after the end of the association's fiscal year. At each annaul meeting, the officers shall make a full report of the financial condition of the association and of its

progress for the preceding year and shall outline a program for the succeeding year.

(b) *Special meetings of members.* Procedures for calling any special meeting of the members and for conducting such a meeting shall be set forth in the bylaws. The subject matter of such special meeting must be established in the notice for such meeting. The board of directors of the association or the holders of 10 percent or more of the votes eligible to be cast at a legal meeting shall be entitled to call a special meeting.

(c) *Notice of meeting of members.* Notice specifying the date, time, and place of the annual or any special meeting and adequately describing any business to be conducted shall be published in the business section of a newspaper printed in the English language in the community in which the home office of the association is located for one day for each of two successive weeks immediately prior to the week in which such meeting shall convene. If it is determined that the primary language of a significant number of adult residents of the community is a language other than English, notice may be required to be published simultaneously in the appropriate language(s). Notice shall be published in manner that is conspicuous to the average reader. A similar notice shall be posted in a conspicuous place in each of the offices of the association during the 20 days immediately preceding the date on which such meeting shall convene. Notice may also be mailed, postage prepaid and delivered not fewer than 20 or more than 50 days before the date of the meeting to each member of record at the last address appearing on the books of the association. When any annual meeting is adjourned for 30 days or more, notice of the adjournment shall be given as in the case of an original meeting.

(d) *Fixing of record date.* For purpose of determining members entitled to notice of or to vote at any meeting of members or any adjournment thereof, or in order to make a determination of members for any other proper purpose, the bylaws shall provide for the fixing of a record date and a method for determining from the books of the association the members entitled to vote. Such date shall be not more then 50 days nor fewer than 20 days prior to the date on which the action, requiring such determination of members, is to be taken. When a determination of members entitled to vote at any meeting of members has been made as provided in this section, such determination shall apply to any adjournment thereof.

(e) *Member quorum.* Any number of members present and voting, represented in person or by proxy, at a properly called annual or special meeting of the members shall constitute a quorum. A majority of all votes cast at any meeting of the members shall determine any question. At any adjourned meeting any business may be transacted which might have been transacted at the meeting as originally ratified. The members present at a duly organized meeting may continue to transact business until adjournment.

(f) *Nomination for directors.* The board of directors or a committee of directors appointed by a majority of the directors shall act as a nominating committee for selecting the management nominees for election as directors. Except in the case of a nominee substituted as a result of death or other incapacity, such nominations shall be prominently posted in each office of the association at least 20 days prior to the date of the meeting. The bylaws shall provide that nominations for directors may be made at the annual meeting by any member of record and shall be voted upon, except that the bylaws may require that nominations by a member be submitted to the secretary and then prominently posted in each office of the association at least 10 days prior to the date of the annual meeting.

(g) *New business.* Any new business to be taken up at the annual meeting shall be stated in writing and filed with the secretary of the association at least 10 days before the date of the annual meeting, and all business so stated, proposed, and filed shall be considered at the annual meeting. No other proposal shall be acted upon at the annual meeting although it may, but need not, be discussed and considered; unless stated in writing and filed with the secretary at least 10 days before the meeting, such proposal shall be laid over for action at an adjourned, special, or next annual meeting of the members taking place 30 days or more thereafter. Nothing in this paragraph (g) shall prevent the consideration and approval or disapproval at the annual meeting of reports of officers, directors, and committees, but in connection with such reports, no new business shall be acted upon at such annual meeting unless stated and filed as provided in this paragraph.

**§ 544.9-1 Voting by proxy.**

(a) *General.* At all meetings of members a member may vote in person or by a duly authorized attorney in fact. Proxies may be given telephonically or electronically as long as the holder uses a procedure for identifying the member which is determined to be acceptable by the General Counsel or his designee. Proxies shall have been placed on file with the secretary of the association for verification prior to the meeting. Notwithstanding §569.3(b) of this Chapter, a proxy may designate as holder a corporation, partnership or company as defined in Part 574 of this Chapter. Proxies solicited on behalf of the management shall be voted as directed by the member or, in the absence of such direction, as determined by a majority of the proxy committee, or in its absence, by the board of directors. All proxies with a term greater than eleven months or solicited at the expense of the association must run to the board of directors as a whole, or to a committee of directors appointed by a majority of such board.

(b) *Other voting arrangements.* (1) Accounts held by an administrator, executor, guardian or conservator may be voted by him, either in person or by proxy, without a transfer of such shares into his name. Accounts shown on the books of the association in the name of a trustee may be voted by such trustee, either in person or by proxy in accordance with the terms of the trust agreement, but no trustee shall be entitled to vote shares held by him without a transfer of such shares into his name.

(2) Accounts held in the name of a receiver may be voted by such receiver, and accounts held by or under the control of a receiver may be voted by such receiver without the transfer thereof into his name if authority to do so is contained in an appropriate order by which such receiver was appointed.

(3) A member whose shares are pledged shall be entitled to vote such shares until the shares have been transferred into the name of the pledgee, and thereafter the pledgee shall be entitled to vote the shares so transferred.

(c) *Joint accounts.* (1) For voting purposes, funds in any type of joint account with identical joint or co-tenants shall be entitled to not more than 1000 votes. If the joint or co-tenants are not indentical, each such joint account shall be entitled to not more than 1000 votes.

(2) For voting purposes, a joint account shall be considered as being held by a single entity in undivided possession. Thus, only the entity rather than its joint owners may cast the votes to which the account is entitled. Nothing in this section, however, shall prevent the joint account from splitting the votes

to which it is entitled as the joint owners may in writing agree.

(3) If joint owners cannot agree on how to cast the votes of the joint account, neither the joint account or its joint owners shall be entitled to vote.

**§ 544.9-2 Communication between members.**

Provisions relating to communications between members shall be consistent with § 545.131 of this Subchapter. Notwithstanding any provision of this section or common law, no members or any other person shall have the right to obtain, inspect or copy any portion of any books or records of a Federal mutual association containing: (1) A list of depositors in or borrowers from such association; (2) their addresses; (3) individual deposit or loan balances or records; or (4) any data from which such information could be reasonably constructed.

**§ 544.9-3 Annual reports to members.**

Provisions relating to annual reports to members shall be consistent with § 545.115 of this Subchapter.

**§ 544.10 Board of directors.**

(a) *General.* All corporate powers shall be exercised by or under authority of, and the business and affairs of a Federal mutual association shall be managed under the direction of, a board of directors. Each director of the association shall be a member of the association. A majority of the Directors shall be independent as that term is defined in § 544.10-1(c)(2). The board of directors shall have authority to fix reasonable compensation of directors and authorize the reimbursement of expenses for actual attendance at any meeting of the board or its committee. The board of directors shall annually elect a chairman of the board from among its members and shall designate the chairman of the board, when present, to preside at its meetings.

(b) *Performance of duties.* A director shall perform his duties as a director, including his duties as a member of any committee of the board upon which he may serve, in good faith, in a manner he reasonably believes to be in the best interests of the association, and with such care as a prudent person in a like position would use under similar circumstances. In performing his duties, a director shall be entitled to rely on information, opinions, reports or statements, including financial statements and other financial data, prepared or presented by:

(1) One or more officers or employees of the association whom the director reasonably believes to be reliable and competent in the matters presented,

(2) Counsel, public accountants or other persons as to matters which the director reasonably believes to be within such person's professional or expert competence, or

(3) A committee of the board upon which he does not serve, duly designated in accordance with a provision of the bylaws, as to matters within its designated authority, which committee the director reasonably believes to merit confidence.

(2) However, a director shall not be considered to be acting in good faith if he has knowledge concerning the matter in question, or would have obtained such knowledge through the exercise of appropriate prudence and diligence, that could cause such reliance to be unwarranted. Reports should be reviewed by each director and verified, and if they appear questionable should not simply be accepted at face value.

(c) *Number and term.* The board of directors shall consist of not fewer than five nor more than fifteen members, except where authorized by the Board, which number shall be specified in the bylaws. The directors shall be divided into three classes as nearly equal in number as possible. The members of each class shall be elected for a term of three years and until their successors are elected and qualified. One class shall be elected by ballot annually except in the case of converting or *de novo* associations where all directors shall be elected at the first election of directors for first terms which shall be staggered in length from one to three years.

(d) *Vacancies.* Any vacancy occuring in the board of directors may be filled by the affifmative vote of a majority of the remaining directors even if they constitute less than a quorum of the board of directors. A director elected to fill a vacancy shall be elected to serve only until the next election of directors by the members. Any directorship to be filled by reason of an increase in the number of directors may be filled by election by the board of directors for a term of office continuing only until the next election of directors by the members.

(e) *Resignation or removal of directors.* (1) Any director may resign at any time by sending a written notice of such resignation to the home office of the association addressed to the chairman of the board or the president. Unless otherwise specified, such resignation shall take effect upon receipt by the chairman of the board or the president. More than three consecutive absences from regular meetings of the board of directors, unless excused by resolution of the board of directors, shall automatically constitute a resignation, effective when such resignation is accepted by the borad of directors.

(2) At a meeting of members called expressly for that purpose, any director may be removed only for cause by a vote of the majority of the shares then entitled to vote at an election of directors.

(3) In any solicitation of proxies for removal of a director by member vote, opportunity must be provided to the director whose removal is sought to present a defense to members by means of a written statement not to exceed 500 words which must accompany or precede the initial solicitation for removal of such director. Such statement shall be mailed at the expense of the party seeking removal.

(4) For the purposes of this section, the term "cause" shall mean willful failure, neglect or refusal in any material respect to perform duties as a director or commission of any act of willful misconduct, self-dealing, malfeasance or gross negligence. The foregoing description of cause shall in no way limit the power of the Board of the Corporation to bring an action for removal under the National Housing Act, Home Owners' Loan Act or other authority.

(f) *Age limitation on directors.* A Federal mutual association may provide in its bylaws that no person of an age 70 years or older will be eligible for election, reelection, appointment, or reappointment to the board of directors of the association. The bylaws may also provide that no director shall serve as such beyond the annual meeting of the association immediately following the attainment of the specified age.

**§ 544.10-1 Director's meetings.**

(a) *Meetings.* A regular meeting of the board of directors shall be held immediately after, and at the same plae as, the annual meeting of the members. The board of directors shall determine the place, frequency, time, and procedure for notice of such meeting and other meetings of the board of directors. Notice of meetings shall be at least 24 hours unless waived by the directors for regular meeting of the board of directors or any committee designated thereby. Members of the board of directors or any committee designated thereby may participate in a meeting of such board or committee by means of a conference telephone or similar communications equipment through which all persons participating in the meeting can hear each other at the same time, and

participation by such means shall constitute presence in person at a meeting for all purposes.

(b) *Quorum.* A majority of the authorized number of directors shall constitute a quorum for the transaction of business at any meeting of the board of directors. The act of the majority of the directors present at a meeting at which a quorum is present shall be the act of the board of directors, unless a greater number is prescribed by regulation of the Board.

(c) *Executive and other committees.* (1) *General.* The board of directors, by resolution adopted by a majority of the authorized number of directors, may designate from among its members an executive committee and one or more other committees each of which, to the extent provided in the resolution or bylaws of the association, shall have and may exercise all of the authority of the board of directors, except that no committee shall have the authority of the board of directors with reference to: (i) The amendment of he charter of bylaws of the association; (ii) recommending to the members a plan of combination or conversion; (iii) the approval of a plan of merger not requiring member approval; (iv) the sale, lease, or other disposition of all or substantially all of the assets of the association otherwise than in the usual and regular course of its business; (v) a reduction in the capital of the association; (vi) a voluntary dissolution of the association; (vii) a revocation of any of the foregoing; or (viii) the approval of a transaction in which any member of the executive committee, directly or indirectly, has any material beneficial interest. The designation of any committee and the delegation of authority thereto shall not operate to relieve the board of directors, or any director, of any responsibility or fiduciary duty imposed by law or regulation.

(2) *Audit committee.* Each Federal mutual association shall appoint an audit committee of at least three directors the majority of whom shall be independent. A director shall be considered independent if he is neither employed by the association, its service corporation, or any person or persons deemed to control the association under § 563.18–1 of this Chapter, or its affiliates or serving as legal counsel or other professional advisor to the association, its service corporation, or any person or persons deemed to control the association under Part 563, or its affiliates. The audit committee shall recommend independent auditors, consult with the independent auditors regarding the plan of audit, review the audit report in consultation with the independent auditors, and consult with the independent auditors regarding the adequacy of internal accounting controls.

(3) *Investment Committee.* Each Federal mutual association shall appoint an investment committee of at least three directors the majority of whom shall be independent, as defined in paragraph 2 of this section. The independent directors shall be different persons from those serving on the audit committee.The investment committee will assess the credit and interest rate risk of the association and prepare reports on such risk for the board of directors.

(d) *Notice of special meetings.* Written notice of at least 24 hours regarding any special meeting of the board of directors or of any committee designated thereby shall be given to each director or committee member in accordance with the bylaws, although such notice may be waived by the director. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except where a director attends a meeting for the express purpose of objecting to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any meeting need be specified in the notice or waiver of notice of such meeting.

(e) *Action without a meeting.* Any action required or permitted to be taken by the board of directors at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the directors.

(f) *Presumption of assent.* A director of the association who is present at a meeting of the board directors at which action on any matter is taken shall be presumed to have assented to the action taken unless his dissent or abstention shall be entered in the minutes of the meeting or unless a written dissent to such action shall be filed with the person acting as the secretary of the meeting before the adjournment thereof or shall be forwarded by registered mail to the secretary of the association within five days after the date on which a copy of the minutes of the meeting is received. Such right to dissent shall not apply to a director who voted in favor of such action.

**§ 544.10–2 Directors' conflicts of interest.**

(a) *General.* No contract or other transaction between a Federal mutual association and one or more of its directors, or between a Federal mutual association and any corporation, firm or association in which one or more of the association's directors has a material financial interest, is either void or voidable because such director or directors or such other corporation, firm or association are parties or because such director or directors are present at the meeting of the board or a committee thereof which authorizes, approves or ratifies the contract or transaction; *Provided,* that

(1) The material facts regarding the transaction and the director's interest therein are fully disclosed or known to the members and such contract or transaction is approved by the members with the eligible votes of the interested director or directors not entitled to vote on or be counted for purposes of determining a quorum, and the contract or transaction is just and reasonable as to the association at the time it is authorized, approved or ratified; or

(2) The material facts regarding the transaction and the director's interest herein are fully disclosed or known to the board or committee, and the board or committee authorizes, approves or ratiifies the contract or transaction in good faith by a vote sufficient without counting the vote of the interested director or directors, and the contract or transaction is just and reasonable as to the association at the time it is authorized, approved or ratified.

(b) *Interested directors.* A mere common directorship does not constitute a material financial interest within the meaning of this section. Nor is a director "interested" within the meaning of this section in voting upon a resolution fixing the compensation of another director as a director, officer or employee of the association, notwithstanding the fact that the first director is also receiving compensation from the association.

(c) *Presence of interested directors at meeting.* Except with regard to other transactions addresed in paragraph (a) of this section, no contract or other transaction between a Federal mutual association and any corporation or association of which one or more of its directors are directors is either void or voidable because such director or directors are present at the meeting of the board or a committee thereof which authorizes, approves or ratifies the contract or transaction: *Provided,* that

(1) The material facts regarding the transaction and such director's other directorship are fully disclosed or known to the board or committee, and the board or committee authorizes, approves or ratifies the contract or transaction in good faith by a vote sufficient without counting the vote of

the interested director or directors, or the contract or transaction is approved by the members; or

(2) The contract or transaction is just and reasonable to the association at the time it is authorized, approved or ratified.

(d) *Determining a quorum.* Interested directors may be counted in determining the presence of a quorum at a meeting of the board or a committee thereof which authorizes, approves or ratifies a contract or transaction.

(e) *Transactions with affiliates.* Compliance with this section shall not affect the right of the Board or the Corportion to object to the contract or transaction under §§ 563.40 through 563.44, § 584.3, or any other section of this Chapter or any other law or regulation.

**§ 544.10-3 [Reserved]**

**§ 544.10-4 Officers.**

(a) *Positions.* The officers of the association shall be a president, one or more vice presidents, a secretary, and a treasurer or comptroller, each of whom shall be elected by the board of directors. The board of directors may also designate the chairman of the board as an officer. The president shall be the chief executive officer, unless the board of directors designates the chairman of the board as chief executive officer. The president need not be a director of the association. The offices of the secretary and treasurer may be held by the same person and a vice president may also be either the secretary or the treasurer. The board of directors may designate one or more vice presidents as executive vice president or senior vice president. The board of directors may also elect or authorize the appointment of such other officers as the business of the association may require. The officers shall have such authority and perform such duties as the board of directors may from time to time authorize or determine. In the absense of action by the board of directors, the officers shall have such powers and duties as generally pertain to their respective offices.

(b) *Removal.* Any officer may be removed by the board of directors whenever in its judgment the best interests of the association will be served thereby; but such removal, other than for cause, shall be without prejudice to the contractual rights, if any, of the person so removed. "Cause" shall mean willful failure, neglect, or refusal in any material respect to perform duties as an officer or commission of any act of willful misconduct, self-dealing, malfeasance or gross negligence.

(c) *Employment contracts.* Upon specific approval of the board of directors, a Federal mutual association may enter into employment contracts with its officers and other employees in accordance with § 563.39 of this Chapter.

(d) *Age limitation on officers.* A Federal mutual association may provide in its bylaws that no person of an age 70 years or older will be eligible for election, reelection, appointment or reappointment as an officer of the association. The bylaws may also provide that no officer shall serve as such beyond the annual meeting of the association immediately following the attainment of the specified age.

**§ 544.10-5 Indemnification of directors, officers and employees.**

A Federal mutual association may indemnify its directors, officers and employees and directors, officers and employees of any wholly-owned subsidiary, provided that indemnification may be made only in accordance with the following requirements:

(a) *General.* Subject to the provisions of this section, a Federal mutual association may indemnify any person against whom an action is brought or threatened because that person is or was a director, officer or employee of the association or any wholly-owned subsidiary for:

(1) Any amount for which that person become liable under a judgment or settlement in such action; and

(2) Reasonable costs and expenses, including attorney's fees, actually paid or incurred by that person in defending or settling such action or in enforcing his rights under this section if he obtains a favorable judgment in such action; *Provided,* that nothing in this section authorizes indemnification by a Federal mutual association of directors, officers or employees of affiliates, affiliated persons, or subsidiaries of the association for actions in their capacity as such except as provided in this section.

(b) *Conditions.* (1) *Favorable judgment.* Indemnification may be made to a person described in paragraph (a) of this section if final judgment on the merits is in his favor.

(2) *No favorable judgment.* Indemnification may be made to a person described in paragraph (a) if final judgment is not in his favor, but only as provided in this paragraph (b).

(i) *General.* In the case of settlement, final judgment against the person, or final judgment in his favor other than on the merits, indemnification may be made if it is determined that the person was acting in good faith within the scope of his employment or authority as he could reasonably have perceived it under the circumstances and for a purpose he could reasonably have believed under the circumstances was in the best interests of the association or its members and, in the case of a criminal action, he had no reasonable cause to believe his conduct was unlawful. Such determination shall be made by the board of directors by a majority vote of a quorum consisting of disinterested directors. However, in no case shall any indemnification be made unless the association gives the Board at least 60 days' notice of its intentions to make such indemnification. Such notice shall state the facts on which the action arose, the terms of any settlement, and any disposition of the action by a court. A copy of such notice, and a certified copy of the resolution containing the required determination by the board of directors, shall be sent to the Office of Examination and Supervision, the Office of General Counsel and the Supervisory Agent. The Supervisory Agent shall promptly acknowledge receipt thereof. The notice period shall run from the date of such receipt. No such indemnification shall be made if the Board or its designee advises the association in writing, within such notice period, of its objection thereto. The Office of Examination and Supervision with the concurrence of the Office of General Counsel has delegated authority to make a determination under this paragraph (b)(2)(i).

(ii) *Action by or on behalf of the association.* In addition to the requirements of paragraph (b)(2)(i), when the action is brought or threatened by the association or on behalf of the association indemnification shall be limited to reasonable costs and expenses as described in paragraph (a)(2) of this section, and no indemnification shall be made in connection with any claim, issue or matter for which there has been a final judgment that the person was liable for negligence or misconduct in the performance of his duty to the association.

(c) *Insurance.* An association may obtain insurance to protect it and its directors, officers and employees or the directors, officers and employees of its wholly-owned subsidiaries from potential losses arising from claims against any of them for alleged wrongful acts, or wrongful acts committed in their capacity as directors, officers or employees. However, associations may

not obtain insurance which provides for payment of losses of any person incurred as a consequence of his willful or criminal misconduct.

(d) *Advanced payment of expenses.* If a majority of the disinterested directors of an association concludes that, in connection with an action, any person ultimately may become entitled to indemnification under this section, the directors may authorize payment of reasonable costs and expenses, including attorneys' fees, arising from the defense or settlement of such action. Nothing in this paragraph (d) shall prevent the directors of an association from imposing such conditions on a payment of expenses as they deem warranted and in the interests of the association. Before making advance payment of expenses under this paragraph, the association shall obtain an agreement in writing that the association will be repaid if the person on whose behalf payment is made is later determined not to be entitled to such indemnification.

(e) *Prohibited indemnification.* Nothing in this section shall authorize or require the Board to approve indemnification of directors, officers or employees of the association when such indemnification would contravene public policy as expressed by Federal statutes or the regulations of the Board.

(f) *Exclusiveness of provisions.* No association shall indemnify any person referred to in paragraph (a) of this section or obtain insurance referred to in paragraph (c) of this section other than in accordance with this section. However, an association which had a bylaw in effect on October 1, 1969, relating to indemnification of its personnel shall be governed solely by that bylaw, is such is still in effect, except that the association's authority to obtain insurance shall be governed by paragraph (c) of this section.

(g) *Definitions and rules of construction.* (1) Definitions for purposes of this section:

(i) *Action.* Any judicial or administrative proceeding or threatened proceeding, whether civil, criminal, or otherwise, incuding any appeal or other proceeding for review;

(ii) *Court.* Includes, without limitation, any court to which or in which any appeal or any proceeding for review is brought;

(iii) *Disinterested.* When applied to members or a director, a person not named as party to the action in connection with which indemnification or advancement of expenses is sought;

(iv) *Final judgment.* A judgment, decree, or order which is not appealable or as to which the period for appeal has expired with no appeal taken;

(v) *Settlement.* Includes entry of a judgment or dismissal by consent or confession or a plea of guilty or *nolo contendere.*

(2) References in this section to any individual or other person, including any association, shall include any person acting as administrator, executor, guardian, conservator, trustee, legal representative, successor and assign thereof.

**§ 544.11-544.12 [Reserved]**

**§ 544.13 Fiscal year; annual audit.**

The bylaws of a Federal mutual association shall specify the fiscal year for the association. The association shall be subject to an annual audit as of the end of its fiscal year by independent public accountants appointed by and responsible to the board of directors. The appointment of such accountants shall be subject to annual ratification by the members.

**§ 544.14 Corporate procedures.**

(a) *Execution of instruments, generally.* The board of directors shall establish procedures for the execution, verification, acknowledgment, and delivery of instruments or writings of any nature.

(b) *Seal.* The association may have a corporate seal, which may be modified from time to time, and may use the same by causing it, or a facsimile thereof, to be impressed or affixed or in any other manner reproduced.

(c) *Miscellaneous.* The bylaws may also address subjects which comply with applicable Federal law, rules, or regulations such as emergency preparedness or any other subjects necessary or appropriate for effective operation of the association.

**§ 544.15-544.19 [Reserved]**

**§ 544.20 Combinations involving Federal mutual associations.**

Federal mutual associations may enter into combinations, which for the purposes of this Part include bulk purchase or sale of assets, mergers and consolidations, only in accordance with the provisions of this Part.

**§ 544.21 Merger or consolidation.**

(a) *Permissible mergers or consolidation.* Federal mutual associations may merge or consolidate with other associations: *Provided,* that—

(1) All constituent associations have accounts insured by the Federal Savings and Loan Insurance Corporation, except for Federal associations the deposits of which are insured by the Federal Deposit Insurance Corporation, (2) if any constituent is a mutual association, the resulting association shall be mutually held, except in cases involving supervisory combinations, mergers approved under Part 563b of this Chapter or combinations in which one of the constituents, is an interim Federal association or an interim state institution, and (3) as to any constituent association which is not a Federal association, the merger is in accordance with the laws of the jurisdiction in which the association was organized.

(b) *Board approval.* Prior written approval of the Board is required for every combination. In determining whether to confer such approval, the Board shall apply the criteria set out in § 571.5 of this Chapter and shall impose any condition it deems necessary or appropriate to ensure conformity with those criteria and the requirements of this Chapter. Prior written approval of the Federal Deposit Insurance Corporation is required for every combination involving a Federal association insured by the Federal Deposit Insurance Corporation.

(c) *Approval by the Board's Principal Supervisory Agent.* (1) The specific approval of the Board (including recommending modifications of the combination agreement) required by paragraph (b) of this section may be given by the Board's Principal Supervisory Agent in accordance with the conditions set forth in § 563.22 of this Chapter.

(2) In approving a merger under paragraph (c) of this section, the Principal Supervisory Agent may approve maintenance of an office of the merging association as a facility of the resulting association and may approve a temproary increase in the number of directors of the resulting association, provided that the association submits an acceptable plan for bringing the board of directors into compliance with the requirements of § 544.3 of this Subchapter within a reasonable period of time.

(d) *Approval of board of directors.* Before filing for Board approval, the combination and the combination agreement shall be approved by each constituent association's board of directors: (1) By a two-thirds vote of the entire board of each Federal association, and (2) as required by state law or other applicable law for other constituents.

(e) *Approval by members.* Notwithstanding any other provision of this part, the Board may require that a plan or merger be submitted to the voting members of any of the associations at a duly called meeting(s)

and that the plan to be effective, be approved by them.

(f) *Conservator or receiver action.* A conservator or receiver for an association appointed under Part 547 of this Subchapter may merge the association with another under § 544.21 without submitting the combination agreement to the association's board of directors or members for their approval.

(g) *Combination agreement.* (1) All terms, conditions, agreements, understandings, or other provisions with respect to the combination, shall be set forth fully in a written combination agreement.

(2) The combination agreement shall specify: (i) Which association will be the resulting association; (ii) the name it will use; (iii) the location of its home office and branch offices; (iv) the bases on which its savings accounts will be issued; and (v) the number of its directors and their names, addresses, and length of their terms.

(h) *Corporate title; change of location.* If a combination agreement provides for the resulting association's name or location to be changed, and it is a Federal association, its charter shall be amended accordingly.

(i) *Application for Board approval.* (1) *Contents.* Applications shall be in a form prescribed by the Board and shall include appropriate information responsive to the factors enumerated in § 571.5.

(2) *Filing requirement.* Constituent associations shall file three copies of the application prepared pursuant to this section with the Supervisory Agent. The combination agreement for a bulk purchase of assets shall state the information required by § 544.21(g)(2) of this subchapter. Applicants shall also comply with section 7A of the Clayton Act (15 U.S.C. § 18A) and regulations issued thereunder (16 CFR Parts 801, 802, and 803).

(j) *Notice.*—(1) *Public Notice.* Constituent associations shall jointly publish notice pursuant to § 542.4 of this Subchapter, except that the required newspaper publication of notice shall be made in the communities in which the home offices of the constiuent associations are located. Promptly after joint publication the constituent associations shall jointly file with the Supervisory Agent a copy of the notice and publisher's affidavit of publication.

(2) *Procedure.* Processing of an application under this section shall follow the procedures set forth in paragraph (i)(1) and in §§ 542.4(b) and 542.4(c) of this Subchapter: *Provided,* that in the case of mergers involving an interim Federal association or an interim state institution where the disappearing institution is immediately acquired under Part 574.4, instead of the public notice procedures of paragraph (j)(1), the public notice procedures of Part 574 shall be applicable.

(3) *Supervisory exception.* This paragraph (j) does not apply to combination instituted for supervisory reasons.

**§ 544.22–544.23 [Reserved]**

**§ 544.24 Articles of combination for merger or consolidation.**

(a) *Contents.* Articles of combination shall be executed in duplicate by each association, by its chief executive officer or executive vice president and by its secretary or an assistant secretary, and verified by one of the officers of each association signing such articles, and shall contain the terms of the combination agreement (either set forth or attached as an exhibit).

(b) *Filing.* Both sets of articles of combination shall be filed with the Supervisory Agent who shall, if he finds that such articles conform to the requirements of this regulation, endorse the articles and return one set to the resulting association.

**§ 544.25 Effective date; date of consummation for merger or consolidation.**

(c) *Effective date.* No combination under this section shall be effective until approved by the Board or its delegate. The effective date of a combination in which the resulting association is a Federal mutual association shall be the date of endorsement of the articles of combination by the Supervisory Agent. A later effective date, up to 90 days after the date of approval of the combination, may be requested by the applicant as part of the application subject to approval by the Board or its delegate. The effective date of a combination in which the resulting association is not a Federal association shall be a date subsequent to Board approval prescribed by the law of the state under which the resulting associated is chartered, or other applicable law. If a disappearing association combining under this section is a Federal association, its charter shall be deemed to be cancelled as of the effective date of the combination; such charter shall be surrendered to the Supervisory Agent at the time of filing of the articles of combination.

(b) *Date of consummation.* No combination under this section may be concluded until all necessary compliance materials, as required by any conditions to the resolution approving such consummation by the Board or its delegate, have been submitted to the satisfaction of the Supervisory Agent. The effective date and the date of consummation may be simultaneous only if the above noted materials have been submitted to and approved by the Supervisory Agent. Until the compliance materials have been submitted to and approved by the Supervisory Agent, the Board or its delegate shall have the right to alter, suspend or withdraw its approval should any interim development be deemed by the board or its delegate to be a material change in circumstances warranting such action.

**§ 544.26 Continuity of corporate existence after merger or consolidation.**

On the effective date of a combination in which the resulting association is a Federal association, all assets and property (real, personal, and mixed, tangible, and intangible, choses in action, rights and credits) of the association shall immediately, without any further act, become the property of the resulting association to the same extent as they were the property of the disappearing association, and the resulting association shall be a continuation of the entity which absorbed the association. All rights, obligations, duties and liabilities of the association shall remain unimpaired, and the resulting association shall, on the effective date of the combination, succeed to all those rights and obligations.

**§ 544.27 [Reserved]**

**§ 544.28 Supervisory Combinations.**

Notwithstanding anything in this Part, the Board may determine to waive or deem inapplicable any provision of §§ 544.21–544.27 if the Board determines that severe financial conditions exist that threaten the stability of such an association and that such action is likely to improve the financial condition of the association, or to avert insolvency or imminent failure of an association as defined in § 541.3 of this Subchapter. For purposes of such action under § 5(d) of the Home Owners' Loan Act, the term "member" shall include the members as defined in the charter of a Federal mutual association. The term "insolvency" shall mean that the assets of the association are less than its obligation to it creditors and others, including its depositors.

**§ 544.29 [Reserved]**

**§ 544.30 Bulk purchase or sale of assets.**

(a) *Permissible bulk purchase of assets.* Federal mutual associations may enter into bulk purchase-of-asset transactions as transferee with other

entities: *Provided*, that (1) all transferor entities are depository institutions, and (2) the transferee Federal mutual association (i) will meet the requirements of Federal Home Loan Bank membership and insurance of accounts after the transaction; and (ii) conforms, within the time prescribed by the Board, to the requirements of section 5(c) of the Home Owners' Loan Act.

(b) *Permissible bulk sale of assets.* Federal mutual associations may enter into bulk sales of assets transactions as transferor only in connection with combinations instituted for supervisory reasons.

(c) *Bulk purchase or sale of assets defined.* A purchase or sale of assets by a Federal mutual association shall be deemed a bulk purchase or sale if it involves the acquisition or disposition by a Federal mutual institution of all or substantially all of the association's assets other than in the ordinary course of business. An acquisition or disposition shall be deemed to involve substantially all of an association's assets if the association's and its subsidiaries' net book value of the assets to be acquired or disposed or the amount paid or to be received by the association exceeds fifty percent of the total assets of the association and its subsidiaries prior to the acquisition or disposition.

(d) *Board approval.* Prior written approval of the Board is required for every bulk purchase of assets. In determining whether to confer such approval, the Board shall apply the criteria set out in § 571.5 of this Chapter and shall impose any condition it deems necessary or appropriate to ensure conformity with those criteria and the requirements of this Chapter. Prior written approval of the Federal Deposit Insurance Corporation is required for every combination involving both a Federal association insured by the Federal Deposit Insurance Corporation and an association not insured by such Corporation.

(e) *Approval by the Board's Principal Supervisory Agent*—The specific approval of the Board (including recommending modifications of the combination agreement) required by paragraph (b) of this section may be given by the board's Principal Supervisory Agent in accordance with the conditions set forth in § 563.22 of this Chapter.

(f) *Approval of board of directors.* Before filing for Board approval of a bulk purchase of assets, the combination shall be approved by each constituent association's board of directors: (1) By a two-thirds vote of the entire board of each Federal association, and (2) as required by state law or other applicable law for other constituents.

(g) *Combination agreement.* (1) All terms, conditions, agreements, understandings, or other provisions with respect to a combination involving a bulk purchase of assets shall be set forth fully in a written combination agreement.

(2) The combination agreement for a bulk purchase of assets shall state the information required by § 544.21(g)(2).

(h) *Application for Board approval.* Application for Board approval of a bulk purchase of assets shall follow the procedures of § 544.21(i).

(i) *Notice.* Notice requirements for a bulk purchase of assets shall follow the procedures of § 544.21(j).

**§ 544.31 [Reserved]**

**§ 544.32 Articles of combination for bulk purchase or sale of assets.**

Articles of combination for a bulk purchase of assets shall be executed pursuant to § 544.24 of this Part.

**§ 544.33 Effective date; date of consummation for bulk purchase or sale of assets.**

The effective date and the date of consummation for a bulk purchase or sale of assets shall be determined pursuant to § 544.25 of this Part.

**§ 544.34 Continuity of corporate existence after bulk purchase or sale of assets.**

The continuity of corporate existence of a Federal mutual association shall not be affected by a bulk purchase or sale of assets.

**§ 544.35 [Reserved]**

**§ 544.36 Partial purchase or sale of assets.**

(a) *General.* A purchase or sale of assets by a Federal mutual association shall be considered a partial purchase or sale of assets if the transaction involves the acquisition or disposition by the Federal mutual association of assets, other than in the ordinary course of business, in any amount which is less than "all or substantially all of the associations assets" as defined in § 544.30(c).

(b) *Percentage of assets test.* A partial purchase or sale by a Federal mutual association shall not be deemed to involve all or substantially all of the association's assets if the association's and its subsidiaries' equity in the net book value of such assets to be acquired or disposed or the total amount paid or received for such acquisition or disposition does not exceed fifty percent of the total assets of the association and its subsidiaries prior to the purchase or sale, except where the purchase or sale is part of an overall plan contemplating the sale or purchase of greater than fifty percent of the total assets of the association and its subsidiaries. Partial purchases or sales of assets shall be governed by § 563.22 of this Chapter.

**§ 544.37–544.39 [Reserved]**

**§ 544.40 Reorganization [Reserved]**

**§ 544.41–544.49 [Reserved]**

**§ 544.50 Dissolution.**

Federal mutual associations may voluntarily dissolve themselves only in accordance with the provisions of this Part.

**§ 544.51 Voluntary dissolution.**

(a) *Plan for dissolution.* A Federal mutual association's board of directors may propose a plan for dissolution of the association. The plan shall be approved by a two-thirds vote of the authorized number of directors. The plan may provide for (1) appointment of the Federal Savings and Loan Insurance Corporation (under section 5 of the Home Owners' Loan Act or section 406 of the National Housing Act as receiver for the purpose of liquidation; (2) transfer of all the association's assets to a depository institution under Federal or State charter either for cash sufficient to pay all obligations of the association and retire all outstanding accounts or in exchange for that institution's payment of all the association's outstanding obligations or other evidence of interest to the association's accountholders on a *pro rata* basis; or (3) dissolution in a manner proposed by the directors which they consider best for all concerned. The plan, and a statement of reasons for proposing dissolution and for proposing the plan, shall be submitted to the Board for approval.

(b) *Board approval.* The Board may approve the plan if the Board believes dissolution is advisable and the plan best for all concerned, but if the Board considers the plan inadvisable, the Board may either make recommendations to the association concerning the plan or disapprove the plan.

**§ 544.52 Approval by members for dissolution.**

When a plan of dissolution is approved by the association's board of directors and by the Board, the plan shall be submitted to the association's members at a legal meeting, and shall become effective when approved by the affirmative vote of two-thirds of the votes present at a legal meeting.

**§ 544.53 Notice of dissolution.**

(a) *Notice to creditors.* Upon filing of a plan of dissolution with the Board, the dissolving association shall immediately cause notice thereof to be mailed to each known creditor of the association.

(b) *Notice to accountholders.* Notice of the members' affirmative vote to approve the plan of dissolution shall be furnished to any affected accountholder pursuant to § 565.5 of this Subchapter.

**§ 544.54 Procedure for dissolution after Board and member approval.**

Upon approval of the plan of dissolution by the Board and a vote of members, the dissolving association shall immediately proceed to collect its assets, convey and dispose of its properties pay, satisfy and discharge its liabilities and obligations, and do all other acts required to liquidate its business and affairs, and after paying or adequately providing for the payment of all its obligations and liabilities, distribute the remainder of its assets, either in cash or in kind, among its members according to their respective rights and preferences.

**§ 544.55 Termination of corporate existence.**

(a) *Completion of dissolution.* After dissolution in accordance with the plan, a certificate evidencing dissolution, supported by such evidence as the Board may require, shall immediately be filed with the Board. When the Board receives such evidence satisfactory to it will terminate the corporate existence of the dissolved association and the association's charter shall thereby be cancelled.

(b) *Continuation of corporate existence after dissolution.* Any association dissolving in accordance with this Part shall nevertheless continue its corporate existence for a period of three years from such dissolution, or for such longer period as the Board in its discretion may direct, solely for the purposes of prosecuting and defending legal actions, suits, or proceedings, whether civil, criminal or administrative, brought by or against such association, settling and closing business, disposing of or otherwise conveying property and discharging liabilities, but not for the purpose of continuing the business for which the association was organized. Any association dissolved pursuant to this Part shall, with respect to any action, suit or proceeding, whether civil, criminal or administrative, brought by or against such association, either prior to or within three years of the date of its dissolution, be deemed to continue its corporate existence beyond the three-year period until any and all final judgments, orders or decrees in connection with such action, suit or proceeding have been fully executed.

**§ 544.56 Involuntary dissolution.**

Notwithstanding the foregoing provisions of this Part, the Board may determine to waive or deem inapplicable any provision of §§ 544.51–544.55 of this Part for dissolutions instituted for supervisory reasons or pursuant to Part 547 of this Subchapter.

**§ 544.57–544.59 [Reserved]**

**§ 544.60 Supervisory waiver.**

Notwithstanding the foregoing provisions of Part 544, the Board may determine to waive or deem inapplicable any provision of §§ 544.1–544.59 of this Part to facilitate: (1) An acquisition to prevent the failure of an institution chartered by the Board or insured by the Corporation; or (2) a transfer of accounts in payment of insurance; or, (3) for supervisory reasons or pursuant to Part 574 of this Subchapter.

**Appendix A to Part 544 Model Bylaws for Mutual Associations**

*Article I—Home Office*

The home office of the association shall be at———in the County of———, in the State of———.

*Article II—Members*

Section 1. *Place of Meetings.* All annual and special meetings of members shall be held at the home office of the association or at such other place in the state in which the principal place of business of the association is located or in which the association maintains branches, as the board of directors may determine.

Section 2. *Annual Meeting.* A meeting of the members of the association for the election of directors and for the transaction of any other business of the association shall be held annually within 150 days after the end of the association's fiscal year on the———of———is not a legal holiday, and if a legal holiday, then on the next day following which is not a legal holiday, at———, or at such other date and time within such 150-day period as the board of directors may determine.

Section 3. *Special Meetings.* Special meetings of the members for any purpose or purposes, unless otherwise prescribed by the regulations of the Federal Home Loan Bank Board ("Board") (which as hereinafter used includes the Federal Savings and Loan Insurance Corporation), may be called at any time by the chairman of the board, the president, or a majority of the board of directors, and shall be called by the chairman of the board, the president, or the secretary upon the written request of the holders of not less than one-tenth of all of the votes eligible to be cast at a legal meeting. Such written request shall state the purpose or purposes of the meeting and shall be delivered to the home office of the association addressed to the chairman of the board, the president, or the secretary.

Section 4. *Conduct of Meetings.* Annual and special meetings shall be conducted in accordance with the most current edition of Robert's Rules of Order unless otherwise prescribed by regulations of the Board or these bylaws. The board of directors shall designate, when present, either the chairman of the board or president, if the president is a director, to preside at such meetings.

Section 5. *Notice of Meeting.* Written notice stating the place, day, and hour of the meeting and the purpose(s) for which the meeting is called shall be published in the business section of a newspaper printed in the English language in the community in which the home office of the association is located for one day for each of two successive weeks immediately prior to the week in which the meeting shall convene. If it is determined that the primary language of a significant number of adult residents of the community is a language other than English, notice may be required to be published simultaneously in the appropriate language. Notice shall be published in a manner that is conspicuous to the average reader. A similar notice shall be posted in a conspicuous place in each office of the association during the 20 days immediately preceding the date on which the meeting shall convene. Notice may also be mailed, postage prepaid and delivered not fewer than 20 or more than 50 days prior to the date of the meeting, to each member of record at the last address appearing on the books of the association. When any members' meeting, either annual or special, is adjourned for 30 days or more, notice of the adjourned meeting shall be given as in the case of an original meeting. It shall not be necessary to give any notice of the time and place of any meeting adjourned for fewer than 30 days or of the business to be transacted at the meeting, other than an announcement at the meeting at which such adjournment is taken.

Section 6. *Fixing of Record Date.* For the purpose of determining members entitled to notice of or to vote at any meeting of members or any adjournment, or in order to make a determination of members for any other proper purpose, the board of directors shall fix in advance a date as the record date for any such determination of members. Such date in any case shall be not more than 50 days nor fewer than 20 days prior to the date on which the particular action requiring such determination of members is to be taken. When a determination of members entitled to vote at any meeting of members has been made as provided in this section, such determination shall apply to any adjournment.

Section 7. *Quorum.* Any number of members present and voting, represented in person or by proxy, shall constitute a quorum at a properly called meeting of members. A majority of all votes cast at any meeting shall determine any question. At any adjourned meeting any business may be transacted which might have been transacted at the meeting as originally notified. The members present at a duly organized meeting may

continue to transact business until adjournment.

Section 8. *Proxies.* At all meetings of members a member may vote in person or by a duly authorized attorney in fact. Proxies may be given telephonically or electronically as long as the holder uses a reasonable procedure for identifying the member. Proxies shall have been placed on file with the secretary of the association for verification, prior to the meeting. Nothwithstanding § 569.3(b) of the Board's Insurance Regulations, 12 CFR 569.3, a proxy may designate as holder a corporation, partnership or company as defined in Part 574 of the Insurance Regulations, 12 CFR Part 574. Proxies solicited on behalf of the management shall be voted as directed by the member or, in the absence of such direction, as determined by a majority of the proxy committee or, in its absence, by the board of directors. All proxies with a term greater than eleven months or solicited at the expense of the association must run to the board of directors as a whole, or to a committee of directors appointed by a majority of the authorized board of directors.

Section 9. *Joint accounts.* When ownership stands in the name of two or more persons, in the absence of written directions to the association to the contrary, at any meeting of the members of the association, any one or more of such members may cast, in person or by proxy, all votes to which such ownership is entitled. Nothing in this section shall prevent the joint owners from splitting their votes if written direction has been provided to the association prior to the meeting. In the event an attempt is made to cast conflicting votes, in person or by proxy, by the several persons in whose names the account(s) are held, the vote or votes to which those persons are entitled shall not be cast.

Section 10. *Voting by Certain Holders.* Accounts will in the name of another company may be voted by any officer, agent, or proxy as the bylaws of such company may prescribe, or, in the absence of such provisions, as the board of directors of such company may determine. Accounts held by an administrator, executor, guardian, or conservator may be voted by that person, either in person or by proxy, without a transfer of such shares into his name. Accounts held in the name of a trustee may be voted by him, either in person or by proxy, but no trustee shall be entitled to vote accounts held by him without a transfer or such shares into his name. Accounts held in the name of a receiver may be voted by such receiver, and accounts held by or under the control of a receiver may be voted by such receiver without the transfer into his name if authority to do so is contained in an appropriate order of the court or other public authority by which such receiver was appointed.

A member whose accounts are pledged shall be entitled to vote such accounts until the accounts have been transferred into the name of the pledgee, and thereafter the pledgee shall be entitled to vote the accounts so transferred.

Section 11. *Communication Between Members.* Communications between members shall be subject to § 545.131 of the Board's regulations (12 CFR 545.131) as now in effect or any successor provision. Notwithstanding any provision of this section or common law, no member or any other person shall have the right to obtain, inspect or copy a portion of any books or records of a Federal mutual association containing: (1) A list of depositors in or borrowers from such association; (2) their addresses; (3) individual deposit or loan balances or records; or (4) any data from which such information could be reasonably constructed.

Section 12. *Inspectors of Election.* In advance of any meeting of members, the board of directors may appoint any persons other than nominees for office as inspectors of election to act at such meeting or any adjournment. The number of inspectors shall be either one or three. Any such appointment shall not be altered at the meeting. If inspectors of election are not so appointed, the chairman of the board or the president may, or on the request of not fewer than 10 percent of the votes eligible to be cast at the meeting shall, make such appointment at the meeting. If appointed at the meeting, the majority of the votes present shall determine whether one or three inspectors are to be appointed. In case any person appointed as inspector fails to appear or fails or refuses to act, the vacancy may be filled by appointment by the board of directors in advance of the meeting or at the meeting by the chairman of the board or the president.

Unless otherwise prescribed by regulations of the Board, the duties of such inspectors shall include: Determining the number of members and the voting power of each member, the members represented at the meeting, the existence of a quorum, and the authenticity, validity and effect of proxies; receiving votes, ballots, or consents; hearing and determining all challenges and questions in any way arising in connection with the right to vote; counting and tabulating all votes or consents; determining the result; and such acts as may be proper to conduct the election or vote with fairness to all members.

Section 13. *Nominating Committee.* The board of directors or a committee of directors appointed by a majority of the authorized board of directors shall act as a nominating committee for selecting the management nominees for election as directors. Except in the case of a nominee substituted as a result of death or the incapacity of a management nominee, the nominating committee shall deliver written nominations to the secretary at least 20 days prior to the date of the annual meeting. Upon delivery, such nominations shall be posted in a conspicuous place in each office of the association. No nominations for directors except those made by the nominating committee shall be voted upon at the annual meeting unless other nominations by members are made in writing and delivered to the secretary 10 days prior to the date of the annual meeting. Upon delivery, such nominations shall be posted in a conspicuous place in each office of the association. Ballots bearing the names of all persons nominated by the nominating committee and by members shall be provided for use at the annual meeting. However, if the nominating committee shall fail or refuse to act at least 20 days prior to the annual meeting, nominations for directors may be made at the annual meeting by any member entitled to vote and shall be voted upon.

Section 14. *New Business.* Any new business to be taken up at the annual meeting, including any proposal to increase or decrease the number of directors, shall be stated in writing and filed with the secretary of the association at least 10 days before the date of the annual meeting, and all business so stated, proposed, and filed shall be considered at the annual meeting. Any member may make any other proposal at the annual meeting and the same may be discussed and considered, but unless stated in writing and filed with the secretary at least 10 days before the meeting, such proposal shall be laid over for action at an adjourned, special, or annual meeting of the members taking place 30 days or more thereafter. This provision shall not prevent the consideration and approval or disapproval at the annual meeting of reports of officers, directors, and committees; but in connection with such reports, no new business shall be acted upon at such annual meeting unless stated and filed as provided in this section.

*Article III—Board of Directors*

Section 1. *General Powers.* The business and affairs of the association shall be under the direction of its board of directors. The board of directors shall annually elect a chairman of the board and a president from among its members and shall designate, when present, either the chairman of the board or the president to preside at its meetings.

Section 2. *Number and Term.* The board of directors shall consist of ——— members and shall be divided into three classes as nearly equal in number as possible. The members of each class shall be elected for a term of three years and until their successors are elected and qualified. One class shall be elected by ballot annually.

Section 3. *Regular Meetings.* A regular meeting of the board of directors shall be held without other notice than this bylaw immediately after, and at the same place as, the annual meeting of members. The board of directors may provide, by resolution, the time and place for the holding of additional regular meetings without other notice than such resolution.

Section 4. *Qualification.* Each director shall at all times be a member of the association.

Section 5. *Special Meetings.* Special meetings of the board of directors may be called by or at the request of the chairman of the board, the president, or one-third of the directors. The persons authorized to call special meetings of the board of directors may fix any place for holding any special meeting of the board of directors called by such persons.

Members of the board of directors may participate in special meetings by means of conference telephone or similar communications equipment by which all persons participating in the meeting can hear each other. Such participation shall constitute presence in person for all purposes.

Section 6. *Notice.* Written notice of any special meeting shall be given to each

director at least 24 hours prior thereto when delivered personally or by telegram or at least five days prior thereto when delivered by mail at the address at which the director is most likely to be reached. Such notice shall be deemed to be delivered when deposited in the mail so addressed, with postage prepaid if mailed, and when delivered to the telegraph company if sent by telegram. Any director may waive notice of any meeting by a writing filed with the secretary. The attendance of a director at a meeting shall constitute a waiver of notice of such meeting unless the director is attending the meeting for the express purpose of objecting to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any meeting of the board of directors need be specified in the notice of or waiver of notice of such meeting.

Section 7. *Quorum.* A majority of the number of directors fixed by section 2 of this Article II shall constitute a quorum for the transaction of business at any meeting of the board of directors; but if less than such majority is present at a meeting, a majority of the directors present may adjourn the meeting from time to time. Notice of any adjourned meeting shall be given in the same manner as prescribed by section 6 of this Article III.

Section 8. *Manner of Acting.* The act of the majority of the directors present at a meeting at which a quorum is present shall be the act of the board of directors, unless a greater number is prescribed by regulation of the Board or by these bylaws.

Section 9. *Action Without a Meeting.* Any action required or permitted to be taken by the board of directors at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the directors, eligible to vote thereon.

Section 10. *Resignation.* Any director may resign at any time by sending a written notice of such resignation to the home office of the association addressed to the chairman of the board or the president. Unless otherwise specified, such resignation shall take effect upon receipt by the chairman of the board or the president. More than three consecutive absences from regular meetings of the board of directors, unless excused by resolution of the board of directors, shall automatically constitute a resignation, effective when such resignation is accepted by the board of directors.

Section 11. *Vacancies.* Any vacancy occurring on the board of directors may be filled by the affirmative vote of a majority of the remaining directors, although less than a quorum of the board of directors. A director elected to fill a vancancy shall be elected to serve until the next election of directors by the members. Any directorship to be filled by reason of an increase in the number of directors may be filled by election by the board of directors for a term of office continuing only until the next election of directors by the members.

Section 12. *Compensation.* Directors, as such, may receive a stated salary for their services. By resolution of the board of directors, a reasonable fixed sum, and reasonable expenses of attendance, if any, may be allowed for attendance at each regular or special meeting of the board of directors. Members of either standing or special committees may be allowed compensation and reasonable expenses of attendance for attendance at committee meetings as the board of directors may determine.

Section 13. *Presumption of Assent.* A director of the association who is present at a meeting of the board of directors at which action on any association matter is taken shall be presumed to have assented to the action taken unless his dissent or abstention shall be entered in the minutes of the meeting or unless he shall file a written dissent to such action with the person acting as the secretary of the meeting before the adjournment thereof or shall forward such dissent by registered mail to the secretary of the association within five days after the date a copy of the minutes of the meeting is received. Such right to dissent shall not apply to a director who voted in favor of such action.

Section 14. *Removal of Directors.* At a meeting of members called expressly for that purpose, any director may be removed for cause by a vote of a majority of the votes then entitled to vote at an election of directors. In any solicitation of proxies for removal of a director by member vote, opportunity must be provided to the director whose removal is sought to present a defense to members by means of a written statement not to exceed 500 words which must accompany or precede the initial solicitation for removal of such director. Such statement shall be mailed at the expense of the party seeking removal. For purposes of this section, the term "cause" shall mean willful failure, neglect or refusal in any material respect to perform duties as a director or commission of any act of willful misconduct, self-dealing, malfeasance, or gross negligence.

Section 15. *Age Limitations on Directors.* No person [fill in any age, 70 or above] years of age shall be eligible for election, reelection, appointment, or reappointment to the board of the association. No director shall serve as such beyond the annual meeting of the association immediately following the director's becoming [fill in age used above], except that a director serving on [fill in bylaw adoption date] may complete the term as director. This age limitation does not apply to an advisory director.

*Article IV—Executive and Other Committees*

Section 1. *Appointment.* The board of directors, by resolution adopted by a majority of the authorized board, may designate the chief executive officer and two or more of the other directors to constitute an executive committee. The designation of any committee pursuant to this Article IV and the delegation of authority shall not operate to relieve the board of directors, or any director, of any responsibility imposed by law or regulation.

Section 2. *Authority.* The executive committee, when the board of directors is not in session, shall have and may exercise all of the authority of the board of directors except to the extent, if any, that such authority shall be limited by the resolution appointing the executive committee; and except also that the executive committee shall not have the authority of the board of directors with reference to: the amendment of the charter or bylaws of the association, or recommending to the members a plan of merger, consolidation, or conversion; the sale, lease, or other disposition of all or substantially all of the property and assets of the association otherwise than in the usual and regular course of its business; a voluntary dissolution of the association; a revocation of any of the foregoing; or the approval of a transaction in which any member of the executive committee, directly or indirectly, has any material beneficial interest.

Section 3. *Tenure.* Subject to the provisions of section 8 of this Article IV, each member of the executive committee shall hold office until the next regular annual meeting of the board of directors following his designation and until a successor is designated as a member of the executive committee.

Section 4. *Meetings.* Regular meetings of the executive committee may be held without notice at such times and places as the executive committee may fix from time to time by resolution. Special meetings of the executive committee may be called by any member thereof upon not less than one day's notice stating the place, date, and hour of the meeting, which notice may be written or oral. Any member of the executive committee may waive notice of any meeting and no notice of any meeting need be given to any member thereof who attends in person. The notice of a meeting of the executive committee need not state the business proposed to be transacted at the meeting.

Section 5. *Quorum.* A majority of the members of the executive committee shall constitute a quorum for the transaction of business at any meeting thereof, and action of the executive committee must be authorized by the affirmative vote of a majority of the members present at a meeting at which a quorum is present.

Section 6. *Action without a meeting.* Any action required or permitted to be taken by the executive committee at a meeting may be taken without a meeting if a consent in writing, setting forth the action so taken, shall be signed by all of the members of the executive committee eligible to vote thereon.

Section 7. *Vacancies.* Any vacancy in the executive committee may be filled by a resolution adopted by a majority of the authorized board of directors.

Section 8. *Resignations and removal.* Any member of the executive committee may be removed at any time with or without cause by resolution adopted by a majority of the authorized board of directors. Any member of the executive committee may resign at any time by giving written notice to the president or secretary of the association. Unless otherwise specified, such resignation shall take effect upon its receipt; the acceptance of such resignation shall not be necessary to make it effective.

Section 9. *Procedure.* The executive committee shall elect a presiding officer from its members and may fix its own rules of procedure which shall not be inconsistent with these bylaws. It shall keep regular

minutes of its proceedings and report the same to the board of directors for its information at the meeting held next after the proceedings shall have occurred.

Section 10. *Audit committee.* The board of directors, by resolution adopted by a majority of the authorized board, shall appoint an audit committee of at least three directors the majority of whom shall be independent. A director shall be considered independent if he or she is neither employed by the association, its service corporation, or any person or persons deemed to control the association under § 563.18–1 of the Insurance Regulations, 12 CFR 563.18–1, or its affiliates, or serving as legal counsel or other professional advisor to the association. The audit committee shall recommend independent auditors, consult with the independent auditors regarding the plan of audit, review the audit report in consultation with the independent auditors, and consult with the independent auditors regarding the adequacy of internal accounting controls.

Section 11. *Other committees.* The board of directors may by resolution establish a loan, or other committees composed of directors as it may determine to be necessary or appropriate for the conduct of the business of the association, and may prescribe the duties, membership, and procedures thereof.

*Article V—Officers*

Section 1. *Positions.* The officers of the association shall be a president, one or more vice presidents, a secretary, and a treasurer, each of whom shall be elected by the board of directors. The board of directors may also designate the chairman of the board as an officer. The president shall be the chief executive officer, unless the board of directors designates the chairman of the board as chief executive officer. The president need not be a director of the association. The offices of the secretary and treasurer may be held by the same person and a vice president may also be either the secretary or the treasurer. The board of directors may designate one or more vice presidents as executive vice president or senior vice president. The board of directors may also elect or authorize the appointment of such other officers as the business of the association may require. The officers shall have such authority and perform such duties as the board of directors may from time to time authorize or determine. In the absence of action by the board of directors, the officers shall have such powers and duties as generally pertain to their respective offices.

Section 2. *Election and Term of Office.* The officers of the association shall be elected annually at the first meeting of the board of directors held after each annual meeting of the members. If the election of officers is not held at such meeting, such election shall be held as soon thereafter as possible. Each officer shall hold office until a successor has been duly elected and qualified or until the officer's death, resignation, or removal in the manner provided in this Article V. Election or appointment of an officer, employee, or agent shall not of itself create contractual rights. The board of directors may authorize the association to enter into an employment contract with any officer in accordance with regulations of the Board; but no such contract shall impair the right of the board of directors to remove any officer at any time in accordance with section 3 of this Article V.

Section 3. *Removal.* Any officer may be removed by the board of directors whenever in its judgment the best interests of the association will be served thereby, but such removal, other than for cause, shall be without prejudice to the contrattual rights, if any, of the person so removed. "Cause" with respect to removal of an officer shall have the same meaning as set forth in Section 14 of Article III as applied to directors.

Section 4. *Vacancies.* A vacancy in any office because of death, resignation, removal, disqualification, or otherwise may be filled by the board of directors for the unexpired portion of the term.

Section 5. *Remuneration.* The remuneration of the officers shall be fixed from time to time by the board of directors.

Section 6. *Age Limitation for Officers.* No person [fill in any age, 70 or above] years of age shall be eligible for election, reelection, appointment, or reappointment as an officer of the association. No officer shall serve beyond the annual meeting of the assocaition immediately following the officer becoming [fill in age used above] except that an officer serving on [fill in bylaw adoption date] may complete the term. However, an official shall, at the option of the board, retire at age 65 if the officer has served in the executive or high policymaking post for at least two years immediately prior to retirement and is immediately entitled to nonforfeitable annual retirement benefits of at least ——— [$44,000 (1985) must be in accordance with the Age Discrimination in Employment Act.]

*Article VI—Indemnification of Directors, Officers and Employees*

Section 1. *General.* The association may indemnify any person against whom an action is brought or threatened because that person is or was a director, officer or employee of the association or a director,officer, or employer of any wholly-owned subsidiary, only as provided in this Article VI, for any amount for which that person becomes liable under a judgment or settlement in such action; and reasonable costs and expenses, including attorney's fees, actually paid or incurred by that person in defending or settling such action, or in enforcing his rights under this section if he obtains a favorable judgment in such action: *Provided,* that nothing herein shall authorize indemnification by the association of directors, officers or employees of affiliates, affilated persons, or subsidiaries of the association for actions in their capacity as such unless such person was a director, officer or employee of a wholly-owned subsidiary.

Section 2. *Conditions.* Indemnification may be made to a person described in sectiion 1 if final judgment on the merits is in his favor. In addition, in the case of settlement, final judgment against him, or final judgment in his favor other than on the merits, indemnification may be made to a person described in Section 1 if it is determined that he was acting in good faith within the scope of his employment or authority as he could reasonably have perceived it under the circumstances and for a purpose he could reasonably have believed under the circumstances was in the best interests of the association or its members, and, in the cae of a criminal action, he had no reasonable cause to believe his conduct was unlawful. Such determination shall be made by the board of directors by a majority vote of a quorum consisting of disinterested directors. However, no indemnification shall be made unless the association gives the Board at least 60 days' notice of its intention to make such indemnification. Such notice shall state the facts on which the action arose, the terms of any settlement, and any disposition of the action by a court. A copy of such notice, and a certified copy of the resolution containing the required determination by the board of directors, shall be sent to the Board in accordance with its regulatiosn. No such indemnification shall be made if the Board or its designee advises the association in writing, within such notice period, of its objection thereto. In addition, when the action is brought or threatened by the association or on behalf the associatioin, indemnification shall be limited to reasonable costs and expenses as described in section 1. Under no circumstances may indemnification be made in connection with any claim, issue or matter with regard to which there has been a final judgment that the person was liable for negligence or misconduct in the performance of his duty to the association.

Section 3. *Insurance.* An association may obtain insurance to protect it and its directors, officers and employees or the directors, officers and employees of a wholly-owned subsidiary from potential losses arising from claims against any of them for alleged wrongful acts, or wrongful acts committed in their capacity as directors, officers or employees: *Provided,* that the association may not obtain insurance which provides for payment of losses of any person incurred as a consequence of his willful or criminal misconduct.

Section 4. *Advance Payment of Expenses.* If a majority of the disinterested directors of the association concludes that, in connection with an action, any person ultimately may become entitled to indemnification under this section, such directors may authorize payment of reasonable costs and expenses, including attorney's fees, arising from the defense or settlement of such action. Nothing in this section shall prevent the directors of an association from imposing such conditions on a payment of expenses as they deem warranted in the interests of the association. Before making advance payment of expenses under this section, the association shall obtain an agreement in writing that the association will be repaid if the person on whose behalf payment is made is later determined not to be entitled to such indemnification.

Section 5. *Indemnification.* Nothing in this section shall authorize indemnification of directors, officers or employees of the association when such indemnification would contravene public policy as expressed by

Federal statutes or the regulations of the Board.

Section 6. *Exclusiveness of Provisions.* No association shall indemnify any person referred to in section 1 of this Article or obtain insurance referred to in section 3 of this Article other than in accordance with this Article.

Section 7. *Definitions and rules of construction.* Definitions and rules of construction for purposes of this Article shall be in accordance with Board regulations on indemnification of directors, officers or employees.

*Article VII—Fiscal Year; Annual Audit*

The fiscal year of the association shall end on the ——— of ——— of each year. The association shall be subject to an annual audit as of the end of its fiscal year by independent public accountants appointed by and responsible to the board of directors. The appointment of such accountants shall be subject to annual ratification by the members.

*Article VIII—Contracts, Loans, Checks and Deposits*

Section 1. *Contracts.* To the extent permitted by regulations of the Board, and except as otherwise prescribed by these bylaws with respect to certificates for shares, the board of directors may authorize any officer, employee, or agent of the association to enter into any contract or execute and deliver any instrument in the name of and on behalf of the association. Such authority may be general or confined to specific instances.

Section 2. *Loans.* No loans shall be contracted for on behalf of the association and no evidence of indebtedness shall be issued in its name unless authorized by the board of directors. Such authority may be general or confined to specific instances.

Section 3. *Checks, Drafts, etc.* All checks, drafts, or other orders for the payment of money, notes, or other evidences of indebtedness issued in the name of the association shall be signed by one or more officers, employees or agents of the association in such manner as shall from time to time be determined by the board of directors.

Section 4. *Deposits.* All funds of the association not otherwise employed shall be deposited from time to time to the credit of the association in such duly authorized federally insured depositories as the board of directors may select.

*Article IX—Corporate Seal*

The board of directors shall provide an association seal which shall be two concentric circles between which shall be the name of the association. The year of incorporation or an emblem may appear in the center.

*Article X—Amendments*

These bylaws may be amended in a manner consistent with regulations of the Board at any time by a majority vote of the full board of directors or by a majority vote of the votes cast by the members of the association at any legal meeting.

By the Federal Home Loan Bank Board.

**Nadine Y. Penn,**

*Acting Secretary.*

[FR Doc. 85-30059 Filed 12-23-85; 8:45 am]

BILLING CODE 6720-01-M

## DEPARTMENT OF TRANSPORTATION

### Federal Aviation Administration

### 14 CFR Part 71

**[Airspace Docket No. 85-AWP-9]**

*Correction*

In FR Doc. 85-29038, beginning on page 50174 in the issue of Monday, December 9, 1985, make the following corrections:

1. On page 50176, third column, in the fifth line of the paragraph beginning "Area A", "21°8'41" N." should read "21°18'41" N.";

2. On page 50177, first column, in the eighth line of the paragraph beginning "Area G", "239°T(239°M)" should read "239°T(228°M)"; and

3. On page 50177, first column, same paragraph, in the eleventh line, "286°T(095°M)" should read "286°T(275°M)".

BILLING CODE 1505-01-M

## DEPARTMENT OF THE TREASURY

### Customs Service

### 19 CFR Part 141

### Proposed Customs Regulations Amendments Relating to Entry of Merchandise

**AGENCY:** U.S. Customs Service, Treasury.

**ACTION:** Proposed rule.

**SUMMARY:** The Tariff Act of 1930 allows the consignee of imported merchandise to designate a customs broker to make entry. Small shipments of merchandise having various consignees are more efficiently and effectively handled if consolidated into large shipments under a master bill of lading or master air waybill prepared by a foreign freight consolidator which covers the numerous individual packages in the shipment. The foreign freight consolidator normally consigns the consolidated shipment to a freight forwarder, courier service or other person in the U.S. This consignee is normally not the same consignee identifed on the individual bills of lading or individual air waybills which make up the master bill of lading or master air waybill. When the consignee named in the master bill of lading or master air waybill appoints a broker of its own choosing to make entry, the actual consignees of the merchandise named in the individual bills are often frustrated in two respects. First, entry is made by a broker not of their choosing and, second, entry is often made at a port not of their choosing. Further, additional expenses may be incurred. This document proposes to amend the entry procedures to prevent frustration of the wishes of the actual consignees identified on the individual bills.

**DATE:** Comments must be received on or before February 24, 1986.

**ADDRESS:** Comments (preferably in triplicate) may be submitted to and inspected at the Regulations Control Branch, Room 2426, U.S. Customs Service, 1301 Constitution Avenue, NW., Washington, DC 20229. Comments relating to the information collection aspects of the proposal should be addressed to Customs, as noted above, and also the Office of Information and Regulatory Affairs, Attention: Desk Officer for U.S. Customs Service, Office of Management and Budget, Washington, DC 20503.

**FOR FURTHER INFORMATION CONTACT:** Jerry Laderberg, Entry, Licensing, and Restricted Merchandise Branch, Office of Regulations and Rulings, U.S. Customs Service, 1301 Constitution Avenue, NW., Washington, DC 20229; 202-566-5765.

**SUPPLEMENTARY INFORMATION**

Background

A customs broker is a person who is licensed by the Customs Service to transact Customs business on behalf of importers and other persons. Section 484, Tariff Act of 1930, as amended (19 U.S.C. 1484), provides for the entry of merchandise. Section 484(a)(1)(C) provides that when an entry of merchandise is made, the required documentation shall be filed either by the owner or purchaser of the merchandise or, when appropriately designated by the owner, purchaser, or consignee of the merchandise, a broker. A problem has arisen with respect to the appointment of a broker by the consignee of consoldiated shipments.

Small shipments of merchandise having various consignees are more efficiently and effectively handled if consolidated into a large shipment. Consolidated shipments to the U.S., usually by containers, have two sets of documents. One set of documents consists of a master bill of lading or master air waybill covering the container and its contents. Individual

bills of lading or individual air waybills, also known as "house" bills of lading or "house" air waybills comprise the second set of documents. The master bill of lading or master air waybill is prepared by a foreign freight consolidator who ordinarily consigns the ontainer to a freight forwarder, courier service or similar party in the U.S. The consignee designated by the foreign freight consolidator is normally not the same consignee identified on the individual bills of lading or individual air waybills which make up the master bill of lading or master air waybill. When the consignee named in the master bill of lading or master air waybill appoints a broker of its own choosing to make entry, the actual consignees of the merchandise named in the individual bills are often frustrated in two respects. First, entry is made by a broker not of their choosing and second, entry is often made at a port of entry not of their choosing. Further, additional expenses may be incurred.

To prevent the foregoing situation from happening, Customs proposes to amend § 141.11, Customs Regulations (19 CFR 141.11), relating to evidence of the right to make entry for importations by common carrier by adding a new paragraph (c) covering consolidated shipments. The proposal would provide that in the case of consolidated shipments by common carrier, entry will not be made by a broker appointed by the consignee named in the master bill of lading or master air waybill, if (1) a consignee on any one of the individual bills of lading or individual air waybills which make up the master bill of lading or master air waybill, has designated another broker to make entry, or (2) any one of the individual bills of lading or individual air waybills indicates that entry will be made by the actual owner or purchaser. However, if the broker designated on an individual bill of lading or individual air waybill is contacted and fails to timely respond to make entry, the consignee named in the master bill of lading or master air waybill may disregard the designation and appoint a broker of its choosing to make entry. Under the proposal, the consignee named in the master bill of lading or master air waybill will submit with the entry filed with Customs a signed statement to the effect that none of the individual bills of lading or individaul air waybill which make up the master bill of lading or master air waybills have designated a broker, or a different broker from the one identified in the master bill of lading or master air waybill, or have indicated that entry will be made by the actual owner or purchaser, or in the case of an actual designation, the designated broker was contacted and failed to timely respond to make entry. The statement may be stamped, typed or printed on the entry documentation provided to Customs. It will not be treated as a missing document for which a bond may be provided. If the signed statement is not submitted, entry will be made by the broker designated by the consignee of each individual bill of lading or individual air waybill which makes up the master bill of lading or master air waybill or by the actual owner or purchaser.

Because the proposed amendment applies only to consolidated shipments, it will not apply to those aspects of express delivery operations, courier service operations or similar delivery operations that do not involve consolidated shipments, or delivery operations that do not use individual house bills of lading or air waybills. Nor will it apply to any carrier where the shipper contractually agrees that the carrier is the consignee and may appoint a broker of its own choosing to make entry.

### Comments

Before adopting this proposal, consideration will be given to any written comments (preferably in triplicate) that are submitted timely to Customs. Comments submitted will be available for public inspection in accordance with the Freedom of Information Act (5 U.S.C. 552), § 1.4, Treasury Department Regulations (31 CFR 1.4) and § 103.11(b), Customs Regulations (19 CFR 103.11(b)), on regular business days between the hours of 9:00 a.m. and 4:30 p.m. at the Regulations Control Branch, Room 2426, Customs Headquarters, 1301 Constitution Avenue, NW., Washington, DC 20229.

### Executive Order 12291

This document does not meet the criteria for a "major rule" as specified in section 1(b) of E.O. 12291. Accordingly, no regulatory impact analysis has been prepared.

### Regulatory Flexibility Act

Pursuant to the provisions of the Regulatory Flexibility Act (5 U.S.C. 605(b)), it is certified that, if adopted, the proposed regulation will not have a significant economic impact on a substantial number of small entities. Accordingly, it is not subject to the regulatory analysis requirement of 5 U.S.C. 603 and 604.

### Paperwork Reduction Act

This document is subject to the Paperwork Reduction Act. Accordingly, a copy has been submitted to the Office of Management and Budget for review and comment pursuant to 44 U.S.C. 3504(h). Public comments relating to the information collection aspects of the proposal should be addressed to Customs and to the Office of Management and Budget at the addresses set forth in the **ADDRESS** portion of this document.

### Drafting Information

The principal author of this document was John E. Elkins, Regulations Control Branch, U.S. Customs Service. However, personnel from other Customs offices participated in its development.

### List of Subjects in 19 CFR Part 141

Customs duties and inspection, Imports, Brokers.

### Amendments to the Regulations

It is proposed to amend Part 141, Customs Regulations (19 CFR Part 141), as set forth below.

### Proposed Amendments

## PART 141—ENTRY OF MERCHANDISE

1. It is proposed that the general authority citation for Part 141, Customs Regulations (19 CFR Part 141), continues to read as set forth below:

**Authority:** 19 U.S.C. 66, 1448, 1484, 1624.

2. It is proposed to amend § 141.11 by adding a new paragraph (c) to read as follows:

**§ 141.11 Evidence of right to make entry for importations by common carrier.**

* * * * *

(c) *Consolidated shipments by common carrier.* In the case of consolidated shipments by common carrier, entry shall not be made by a broker appointed by the consignee named in the master bill of lading or master air waybill, if (1) a consignee on any one of the individual bills of lading or individual air waybills, which makes up the master bill of lading or master air waybill, has designated on the individual bills of lading or individual air waybills another broker to make entry, or (2) any one of the individual bills of lading or individual air waybills indicates that entry will be made by the actual owner or purchaser. Except that, if the broker designated on the individual bill of lading or individual air waybill is contracted and fails to timely respond to make entry, the consignee named in the master bill of lading or

master air waybill may disregard the designation and appoint a broker of its choosing to make entry. The consignee named in the master bill of lading or master air waybill shall submit with the entry a signed statement to the effect that none of the individual bills of lading or individual air waybills which makes up the master bill of lading or master air waybill have designated a broker, or a different broker from the one identified in the master bill of lading or master air waybill, or have indicated that entry will be made by the actual owner or purchaser, or in the case of an actual designation, the designated broker was contacted and failed to timely respond to make entry. The required statement may be stamped, typed or printed on the entry documentation provided to Customs. The signed statement shall not be treated as a missing document for which a bond may be provided. If the signed statement is not submitted, entry shall be made by the broker designated by the consignee of each individual bill of lading or individual air waybill which makes up the master bill of lading or master air waybill or by the actual owner or purchaser.

**William von Raab,**

*Commissioner of Customs.*

Approved December 9, 1985.

**David D. Queen,**

*Assistant Secretary of the Treasury.*

[FR Doc. 85-29999 Filed 12-23-85; 8:45 am]

BILLING CODE 4820-02-M

## DEPARTMENT OF TRANSPORTATION

### Federal Highway Administration

### 23 CFR 625 and 655

**[FHWA Docket No. 85-18, Notice 2]**

### National Standards for Traffic Control Devices; Manual on Uniform Traffic Control Devices; Standards For Performance of Retroreflective Traffic Control Devices

**AGENCY:** Federal Highway Administration (FHWA), DOT.

**ACTION:** Extension of comment period.

**SUMMARY:** This document extends the period of comments on the notice of proposed rulemaking published on April 26, 1985 (50 FR 16515), which requested comments by February 15, 1986, on proposed standards for retroreflective illumination of traffic control devices. If adopted, these standards could be incorporated into the Manual on Uniform Traffic Control Devices (MUTCD). The comment period is being extended upon request until June 15, 1986, in order to provide interested parties additional time to respond to the notice.

**DATE:** Written comments must be received on or before June 15, 1986.

**ADDRESS:** Submit comments, preferably in triplicate, to FHWA Docket No. 85-18, Federal Highway Administration, Room 4205, HCC-10, 400 Seventh Street SW., Washington, DC 20590. All comments received will be available for examination at the above address between 8:30 a.m. and 3:30 p.m., ET, Monday through Friday. Those desiring notification of receipt of comments must include a self-addressed, stamped postcard.

**FOR FURTHER INFORMATION CONTACT:** Mr. Philip O. Russell, Office of Traffic Operations, (202) 426-0411, or Mr. Michael J. Laska, Office of the Chief Counsel, (202) 426-0762, 400 Seventh Street SW., Washington, DC 20590. Office hours are from 7:45 a.m. to 4:15 p.m., e.t., Monday through Friday, except legal holidays.

(23 U.S.C. 315; 49 CFR 1.48)

Issued on: December 17, 1985.

**Anthony J. McMahon,**

*Chief Counsel, Federal Highway Administration.*

[FR Doc. 85-30344 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-02-M

## Coast Guard

### 33 CFR Parts 166 and 167

**[CGD 84-021]**

### Port Access Route Study Results

*Correction*

In FR Doc. 85-28910 beginning on page 49861 in the issue of Thursday, December 5, 1985, make the following corrections:

1. On page 49861, third column, **SUMMARY,** sixth line, "f" should read "of".

2. On page 49863, first column, in the seventh line of the paragraph of block numbers, "5485" should read "5385".

BILLING CODE 1505-01-M

## POSTAL SERVICE

### 39 CFR Part 111

### Plant-Load Operations

**AGENCY:** Postal Service.

**ACTION:** Proposed rule.

**SUMMARY:** The Postal Service proposes to amend the Domestic Mail Manual (DMM) to provide uniform and comprehensive regulations governing plant-load operations, which involves the Postal Service receiving mail at a mailer's plant and transporting it to bypass handling that otherwise would be required at one or more postal facilities. The proposed regulations provide procedures for the review of applications for authorizing plant load operations. The regulations would make it clear that plant-load applications would only be authorized when the plant-load would result in a benefit to the Postal Service. To ensure more consistent service, and to more efficiently process plant-loaded mail, the regulations would require that plant-loaded vehicles be prepared according to the destination of the mail and the class or type of mail plant-loaded. The regulations would also require that the Postal Service be reimbursed for charges it incurs in providing nonpostal services to the mailer.

**DATE:** Comments must be received on or before February 7, 1986.

**ADDRESS:** Written comments should be directed to the Director, Office of Transportation & International Services, Mail Processing Department, 475 L'Enfant Plaza, W. SW., Washington, DC 20260-7130. Copies of all written comments will be available for public inspection and photocopying between 9 a.m. and 4 p.m., Monday through Friday, in Room 7914, U.S. Postal Service Headquarters, 475 L'Enfant Plaza W. SW., Washington, DC 20260-7130.

**FOR FURTHER INFORMATION CONTACT:** James E. Orlando, Director, Office of Transportation & International Services, Mail Processing Department, 475 L'Enfant Plaza W. SW., Washington, DC 20260-7130, 202-268-4360.

**SUPPLEMENTARY INFORMATION:** The Postal Service has for more than 20 years allowed mailers to have their mail accepted and verified at their plants and to then load their mail into Postal Service vehicles. Plant loaded mail is transported so that one or more handlings at postal facilities are bypassed. The Postal Service benefits from plant loading because it results in cost savings and eases mail processing capacity problems at some postal facilities, since one or more postal facilities are bypassed. Mailers benefit because their mail is verified, accepted and transported at their plant.

In administering plant load operations, each region and many management sectional centers (MSCs) have developed their own procedures for authorizing plant-load operations, for verifying and collecting postage for

plant-loaded mail, and for having the mailer reimburse the Postal Service for charges incurred as a result of providing certain nonpostal services, such as detaining trailers. These different procedures have resulted in a lack of uniformity in adminsitering plant-load operations. In addition, each region and many MSCs have developed different definitions of plant-load operations. Furthermore, there have been no comprehensive regulations governing plant-load operations for either the Postal Service or mailers to follow.

The Postal Service seeks to make plant-load operations available throughout the United States on a uniform basis. The Postal Service believes that adoption of these propsoed DMM regulations would benefit both the Postal Service and mailers by implementing uniform and comprehensive procedures governing every aspect of plant-load operations, by considering the current and future volume of plant-load mailers in deciding whether to authroizing plant-load operations, and by allowing the Postal Service to provide plant-loading wherever equipment is available and the operations will result in cost savings to the Postal Service. It is the Postal Service's belief that adoption of these proposed DMM regulations would result in plant-load operations being provided throughout the United States to all qualified mailers on a uniform basis.

The proposed amendment to the DMM would delete Chapter 154, General Delivery, which contains only a single sentence that refers the reader to Chapter 953 for the regulations concerning general delivery, and substitute Chapter 154, Plant-Load Operations, in its place. Existing Chapter 154 would be deleted because it is unnecessary and redundant.

The following is a detailed discussion of the proposed regulations.

**1. Definitions**

Section 154.1 would provide uniform and comprehensive definitions for all aspects of plant-load operations. Plant-load operations would be distinguished from the collection of mail so that mailers and the Postal Service would know when each operation should be provided. Section 154.11 would define a plant-load operation as an operation in which the Postal Service receives mail at a mailer's plant and transports it in order to bypass handling that otherwise would be required at one or more postal facilities. Section 154.19 would define collection of mail as an operation where the mail is verified and accepted at the mailer's plant and is transported by the Postal Service to the local post office or other designated postal facility without bypassing any handlings. The proposed regulations do not apply to the collection of mail.

**2. Review of Applications for Plant Loading**

Current procedures for reviewing an application for plant loading differ virtually from postal facility to postal facility; there is no appeal process if the application is denied; and there is no procedure for the Postal Service to reevaluate plant-load authorizations after they have been granted. Section 154.2 would provide uniform and comprehensive procedures for approving a plant-load application. An application would be reviewed by the MSC manager and the transportation management office (TMO) manager to determine whether the conditions for approving an application set forth in section154.3 have been met. The mailer could appeal a denial of an application by either of those officials to the Regional Plant-Load Committee. If the application is denied by the Regional Plant-Load Committee, the mailer could appeal to the National Plant-Load Policy Committee. The reasons for the denial of an application would have to be set forth in writing by the postal official denying an application. If, at any time, the mailer failed to meet the requirement for plant-load operations or any other provision of these regulations for two consecutive postal accounting periods or some other period agreed to by the Postal Service and the mailer, the plant-load authorization would have to be reevaluated by the Regional Plant-Load Committee.

**3. Requirements for Authorizing Plant-Load Operations**

There are no current uniform and comprehensive requirements for authorizing plant-load operations. Virtually each postal facility has a different interpretation of existing procedures. Section 154.3 would set forth uniform and comprehensive requirements for approval of an application for authoriztion of plant loads. If the postal facility to which the mail is destined is within the service area of the origin postal facility, the plant load would be an intra-service-area move. An intra-service-area application would be approved if there were equipment available to transport the mail and the plant load would result in cost savings to the Postal Service. Cost savings are demonstrated under either Alternative 1 *or* 2. Under Alternative 1, the current and future volume of mail would have to fill at least 50 percent of a vehicle by weight or cube *and* the mileage from the mailer's plant to the destination postal facility could not exceed 150 miles. Under Alternative 2, if the requirements of Alternative 1 were not met, a detailed cost analysis would have to demonstrate cost savings to the Postal Service.

If the postal facility to which the mail is destined is outside of the service area of the origin postal facility, the plant load would be an inter-service-area move. An application for an inter-service-area plant-load would be granted if equipment is available to transport plant-loaded mail and the plant load would result in cost savings to the Postal Service. Cost savings are demonstrated under either Alternative 1 *or* 2 *or* 3. Under Alternative 1, cost savings would be demonstrated if the current and future volume of mail to be plant loaded filled at least 60 percent of a vehicle by weight or cube *and* the mileage from the mailer's plant to the destination postal facility did not exceed 275 miles, if the origin sectional center facility (SCF) and at least one bulk mail center (BMC), auxiliary service facility (ASF), or area distribution center (ADC) is bypassed, *or* the mileage did not exceed 150 miles, if only the origin SCF is bypassed. Under Alternative 2, if the requirements of Alternative 1 were not met, a detailed cost analysis would have to demonstrate cost savings. Under Alternative 3, if the requirements of Alternatives 1 and 2 were not met, cost savings would be demonstrated if the local origin postal facility was operating at or near its mail processing capacity for the class or type of mail to be plant-loaded.

The cost savings to the Postal Service of providing plant loads are determined by balancing the costs avoided and the costs incurred in providing such operations. Plant loads reduce costs because mail handlings at one or more facilities that are bypassed are avoided. The greater the number of facilities bypassed, the greater the cost savings. At the same time, plant loads result in the incurrence of additional plant load highway transportation costs to the extent that conventional two-way highway transportation movements are supplanted by more expensive one-way transportation movements. Cost savings are determined by adding the costs of the handlings bypassed, and then subtracting the additional transportation costs incurred in providing the plant load. If the result is positive, the plant load will result in cost savings and, hence, be a benefit to the Postal Service.

Using this methodology, the Postal Service has determined that a plant load meeting the minimum volume and maximum mileage requirements under Alternative 1 for either intra- or inter-service-area moves would always result in cost savings to the Postal Service and, hence, a detailed cost analysis would not be necessary. Not meeting the minimum volume and maximum mileage criteria does not necessarily mean there is no cost savings. If these criteria are not met, then a detailed cost savings analysis must be performed to determine if a particular plant load will result in cost savings to the Postal Service.

**4. Verification of Plant-Loaded Mail**

Plant-loaded mail can now be verified only at a mailer's plant. This has resulted in the denial of some plant-load applications where postal personnel were not available at the mailer's plant to verify and accept the mail. Under section 154.4, intra-service-area plant-loaded mail could be verified and accepted at a mailer's plant *or* at the bulk mail acceptance unit of the origin BMC, ASF, MSC or SCF, if authorized. Due to the difficulty of verifying zone-rated inter-service-area plant-load mail at the destination postal facility, inter-service-area plant-loaded mail would be verified and accepted only at the mailer's plant. In order to avoid any revenue protection problems, payment of postage and fees for plant-loaded mail would have to be made to the origin post office prior to the plant-loaded vehicle's being transported from the mailer's facility.

**5. Preparation Requirements for Plant-Loaded Vehicles**

Plant-loaded mail now receives inconsistent service in major part because there are no requirements that each vehicle be prepared to the destination ZIP Code or postal facility. Under section 154.5, by definition, intra-service-area plant-loaded vehicles could be filled only with mail addressed to the service area of the origin facility. Inter-service-area plant-loaded vehicles would have to be prepared with mail addressed to the destination ZIP Code or postal facility, depending on the volume of mail plant-loaded, the appropriate class or type of mail, and the number of mailings plant-loaded. These preparation requirements would enable the Postal Service to provide more consistent service.

**6. Reimbursement to the Postal Service for Furnishing Nonpostal Services**

Under § 154.6, the Postal Service would obtain reimbursement from mailers for nonpostal services furnished by the Postal Service in providing plant-load service where the Postal Service incurs a charge due to some action or inaction of the mailer. These nonpostal services include the detention or demurrage of trailers, and bobtailing, deadheading and waiting/holding charges for trailers before plant-loaded mail is loaded into a trailer, verified, and accepted by the Postal Service. (See § 154.18 for definitions of above terms.) The Postal Service proposes to continue obtaining reimbursement for trailers detained by a mailer. The proposed revisions would make such reimbursement uniform regardless of the mode of transportation utilized. Reimbursement would be obtained where the mailer makes a request in advance to detain trailers and holds them for more than 24 hours, excluding Saturdays, Sundays, and holidays, or if the mailer does not submit a request to detain trailers in advance, but nevertheless detains trailers longer than necessary to load them. The proposed revisions would also make reimbursement for bobtailing, deadheading or waiting/holding uniform. The proposed regulations would enable the Postal Service and mailers to determine the amount of and conditions under which the Postal Service will obtain reimbursement. The Postal Service would not obtain reimbursement from plant-load mailers where trailers are detained, or bobtailing, deadheading or waiting/holding charges are incurred as a result of some action or inaction of the Postal Service.

**7. Transportation of Plant-Loaded Mail**

Some mailers have on occasion made arrangements with the TMO serving their plant to utilize highway transportation in lieu of railroad transportation. This practice has not been uniform. Under § 154.7, the TMO would select the least costly mode of transportation that will meet the service objectives of the class or type of mail plant-loaded. As a result, the mode of transportation will not be changed at the request of the mailer.

The current requirement that mailers may transport their own plant-loaded mail only if there is a highway contract between the Postal Service and the mailer has not been uniformly followed. Under § 154.7, this requirement would be made uniform. In addition, under § 154.7, the Postal Service would no longer relocate trailers at a mailer's plant.

If these proposed regulations governing plant loading are adopted, existing plant-load operations will continue without the mailer having to file a plant-load application. The Regional Plant-Load Committee will reevaluate existing plant-load authorizations within one year of the adoption of these regulations to determine if the plant load meets these requirements and conditions for plant loading. An application for plant loading filed after the adoption of these regulations will be reviewed pursuant to these regulations.

Although exempt from the notice and comment requirements of the Administrative Procedure Act (5 U.S.C. of 553 (b), (c)) regarding proposed rulemaking by 39 U.S.C. 410(a), the Postal Service invites comments on the following proposed revision of the Domestic Mail Manual, incorporated by reference in the Code of Federal Regulations. *See* 39 CFR 111.1.

**List of subjects in 39 CFR Part 111**

Postal Service.

**Part 111—(AMENDED)**

**CHAPTER 1, DOMESTIC MAIL SERVICES**

1. The authority citation for 39 CFR Part 111 is revised to read as follows:

**Authority:** 5 U.S.C. 552(a); 39 U.S.C. 101(e), 101(f), 401, 404, 407, 408, 3001–3011, 3201–3219, 3403–3405, 3621, 5001; 42 U.S.C. 1973cc–13, 1973cc–14.

2. Revise Part 154 to read as follows:

154 PLANT-LOAD OPERATIONS

*154.1 Definitions.*

.11 Plant Loading. Plant loading is an operation in which the Postal Service receives mail at a mailer's plant and transports it in order to bypass handling that otherwise would be required at one or more postal facilities. Plant loads are authorized when they result in a benefit to the Postal Service.

.12 Mailer's Plant. The mailer's plant is the non-Postal Service location where the mail is plant loaded.

.13 Service Area.

.131 First- and Second-Class Mail. The service area for plant-loaded First-class and second-class mail is the service area of the sectional center facility (SCF) in which the mailer's plant is located.

.132 Third- and Fourth-Class Mail. The service area for plant-loaded third- and fourth-class mail is the service area of the bulk mail center (BMC) or auxiliary service facility (ASF) in which the mailer's plant is located.

.14 Intra-Service-Area Plant Loads. Intra-service-area plant loads are movements of mail from the mailer's plant to a mail processing facility located within the service area of the

appropriate mail processing facility in which the plant is located. Handling at the local origin post office or other local acceptance facility is bypassed.

.15 Inter-Service-Area Plant Loads. Inter-Service-area plant loads are movements of mail from the mailer's plant to a mail processing facility located outside the service area of the appropriate mail processing facility in which the plant is located. Handling at the local origin post office or other local acceptance facility and one or more intermediate processing facilities is bypassed.

.16 Vehicle. A vehicle is a trailer, straight truck, or other container used to transport mail by highway, railroad, or water.

.17 Trailers.

.171 Highway Transportation Trailer. A highway transportation trailer is a trailer owned or leased for any term by the Postal Service or provided by a Postal Service highway transportation contractor for the transportation of mail exclusively over highways.

.172 Rail Tranportation Trailer. A rail transportation trailer is a trailer provided by a Postal Service rail transportation contractor for the transportation of mail in whole or in part by rail.

.18 Other Operations.

.181 Bobtailing. Bobtailing is the movement of a tractor without a trailer to or from a mailer's plant.

.182 Deadheading. Deadheading is the movement of a tractor and trailer or other container or straight truck to or from a mailer's plant without transporting any mail.

.183 Waiting/Holding. Waiting/holding occurs when a vehicle waits or is held at a mailer's plant for mail to be loaded into the vehicle.

.19 Collection. Collection of mail is different from plant loading. Collection is an operation in which the Postal Service verifies and accepts mail at the mailer's plant or at an authorized location other than a postal facility and transports it to the local post office or other designated local acceptance point. No handlings are bypassed in collection.

Note.—These regulations do not apply to the collection of mail.

*154.2 Procedures for Authorization of Plant Loads.*

.21 Application. A mailer desiring to have mail plant loaded must complete Form 3815, *Application for Plant-Load Authorization,* and submit it to the postmaster of the post office serving the mailer's plant.

.22 Review. The local postmaster must review the application for completeness and forward it to his management sectional center (MSC) manager. The MSC manager must review the application and approve or deny it in accordance with 154.23 or 154.24. If approved, he will forward the application to the transportation management office (TMO) manager. The TMO manager will review the application and approve or deny it in accordance with 154.23 or 154.24. If approved, he will forward the application to the Regional Plant Load Committee. This committee consists of the following officials or their designees: the Regional General Manager, Logistics Division, (chairman), and the Regional General Managers of the Budget and Cost, Accounting and Revenue Protection, Customer Programs, and Delivery Divisions. The Regional Plant Load Committee must review the application and approve or deny it in accordance with 154.23 or 154.24. Each official or group of officials reviewing the application must act upon it within two business day of receipt.

.23 Approval.

.231 Conditions. The application will be approved if it meets all of the requirements set forth in 154.3 for either intra- or inter-service-area plant loads, as appropriate. If the application is approved, the mailer must enter into the standard Plant Load Agreement with the Postal Service.

.232 Failure to Meet Requirements. The local postmaster of the post office which serves the mailer's plant is responsible for monitoring plant-load operations and must notify the Regional Plant Load Committee if, at any time, a mailer fails to meet the requirements set forth in these regulations for two consecutive postal accounting periods, or a period set forth in the mailer's plant-load agreement. The plant-load authorization must then be reevaluated by the Regional Committee.

.24 Denial. The application will be denied if it does not meet all of the requirements set forth in 154.3 for either intra- or inter-service-area plant loads. Any official or group of officials denying an application must notify the mailer in writing of the denial and the reasons therefor within three business days of the receipt of the application.

.25 Appeal.

.251 Appeal to Regional Plant Load Committee. If the application is denied by the MSC manager or TMO manager, the mailer may appeal in writing to the Regional Plant Load Committee. Such an appeal must be filed with the Chairman of the Regional Plant Load Committee, Regional General Manager Logistics Division, within 10 calendar days of the date of the mailer's receipt of the notice of denial. The Regional Committee must notify the mailer in writing of the action taken on appeal within three business days of receipt of the appeal. If the application is denied, the Regional Committee must also inform the mailer of the reasons for the denial.

.252 Appeal to National Plant Load Policy Committee. If an application is denied by the Regional Plant Load Committee, the mailer may appeal to the National Plant Load Policy Committee at Postal Service Headquarters, which will issue a final ruling on the application. Such an appeal must be filed with the Chairman of the National Committee, the Director, Office of Transportation and International Services, Mail Processing Department, Washington, D.C. 20260–7130, within 10 calendar days of the date of the mailer's receipt of the Regional Plant Load Committee's notice of denial. The National Committee consists of the following officials or their designees: Director, Office of Transportation and International Services, Mail Processing Department, (chairman); Director, Office of In-Plant Processing, Mail Processing Department; Director, Office of Mail Classification, Rates and Classification Department; Director, Office of Fleet Management, Delivery Services Department; Director, Office of Commercial Marketing, Customer Services Department; and Associate General Counsel, Office of Rate and Classification Law, Law Department.

*154.3 Requirements for Approval of Plant Load Applications.*

.31 Intra-Service Area.

.311 General. An application for an intra-service-area plant load will be approved if there is equipment available (154.312) and cost savings to the Postal Service are demonstrated under *either* Alternative 1 (154.313a) *or* Alternative 2 (154.313b).

.312 Equipment Availability. There must be equipment available to transport the vehicle to the BMC, ASF, MSC, or SCF, in the service area of the mailer's plant. If equipment is not available, sufficient additional transportation equipment must be obtained, if possible. The application will not be granted until additional transportation equipment is obtained.

.313 Cost Savings. The plant load must result in cost savings to the Postal Service. A cost savings can be demonstrated *either* under Alternative 1 (154.313a) *or* Alternative 2 (154.313b) below.

a. Alternative 1: Minimum Volume and Maximum Mileage. The current and future volume of mail to be plant loaded must be at least 50 percent of a vehicle

by weight or cube, and the mileage from the mailer's plant to the destination postal facility must be 150 miles or less. For mail verified and accepted at a mailer's plant, the Postal Service may allow mailings verified at the plants of two or more mailers located in the same service area to be combined to meet the minimum volume requirement. For mail verified and accepted at the bulk mail acceptance unit of the origin BMC, ASF, MSC, or SCF, the minimum volume requirement must be met by the mailings of only one mailer. (See 154.423 for requirements for verification at postal facility.)

b. Alternative 2: Detailed Cost Saving Analysis. If the mailer does not meet the criteria in Alternative 1 (154.313a), cost savings to the Postal Service must be demonstrated using the detailed analysis on Form 3815.

.32 Inter-Service-Area.

.321 General. An application for an inter-service-area plant load will be approved if there is equipment available (154.322) and cost savings to the Postal Service are demonstrated under *either* Alternative 1 (154.323a) *or* Alternative 2 (154.323b) *or* Alternative 3 (154.323c).

.322 Equipment Availability. There must be equipment available to transport the vehicle to the BMC, ASF, MSC, or SCF outside the postal facility's service area in which the mailer's plant is located. If equipment is not available, sufficient additional transportation equipment must be obtained, if possible. The application will not be granted until additional transportation equipment is obtained.

.323 Cost Savings. The plant load must result in cost savings to the Postal Service. A cost savings can be demonstrated under *either* Alternative 1 (154.323a) *or* Alternative 2 (154.323b) *or* Alternative 3 (154.323c) below.

a. Alternative 1: Minimum Volume and Maximum Mileage.

(1) Minimum Volume. The current and future volume of mail to be plant loaded must be at least 60 percent of a vehicle by weight or cube. Mailings of two or more mailers located in the same service area may be combined to make up the minimum volume.

(2) Maximum Mileage for Highway.

(a) If the plant-load transportation is via highway and bypasses the origin SCF and at least one BMC, ASF, or ADC, the mileage from the mailer's plant to the destination postal facility must be 275 miles or less.

(b) If the plant-load transportation is by highway and bypasses only the origin SCF, the mileage from the mailer's plant to the destination postal facility must be 150 miles or less.

(c) There is no mileage criterion for plant-load transportation by railroad or water.

b. Alternative 2: Detailed Cost Savings Analysis. If the mailer does not meet the applicable criteria in Alternative 1 (154.323a), cost savings to the Postal Service must be demonstrated by using the detailed analysis on Form 3815.

c. Alternative 3: Mail Processing Capacity. Even if the mailer does not satisfy either Alternative 1 (154.232a) or Alternative 2 (154.323b), the cost savings criteria may de deemed to be satisfied if the local origin postal facility is operating at or near its mail processing capacity for the type of mail plant-loaded. The Regional Plant Load Committee shall determine whether a facility is at or near its mail processing capacity and whether to authorize plant load in such cases. If the Regional Plant Load Committee subsequently determines that the local origin postal facility is operating below its mail processing capacity for the class or type of mail plant-loaded, the Regional Committee must reevaluate the plant-load authorization.

*154.4 Verification and Collection of Postage.*

.41 General. All plant-loaded mail must be verified and postage and fees collected in accordance with the Domestic Mail Manual (DMM) and Management Instruction, DM–120–84–1, *National Bulk Mail Verification Program*, or subsequent reissues thereof, except as provided below.

.42 Verification of Intra-Service-Area Plant Loads.

.421 General. Intra-service-area plant-loaded mail must be verified at the mailer's plant, at the origin MSC or SCF if authorized by the MSC manager, or at the origin BMC or ASF, if authorized by the ASF or BMC manager.

.422 Verification at the Mailer's Plant. Intra-service-area plant-loaded mail must be verified at the plant by a clerk qualified to perform verification procedures unless authorization to verify mail at the origin BMC, ASF, MSC or SFC has been granted under 154.423 and .424.

.423 Verification at Postal Facility. Authorization to verify mail at the origin BMC, ASF, MSC, or SCF may be granted only if all of the following conditions are met:

a. There is no Detached Mail Unit (DMU) at the mailer's plant.

b. The mailer is located within the service area of the BMC, ASF, MSC or SCF where verification will take place.

c. Each vehicle contains the mail of only one mailer.

d. Each vehicle contains no more than five mailings and each mailing is physically separated.

e. If a Form 3541, 3541A, 3602, 3602, 3602PC, or 3605, *Mailing Statement*, is required to be completed, the original mailing statement must accompany each vehicle if there is only one mailing on the vehicle, or mailing in the vehicle. Where a single mailing is contained in more than one vehicle, a separate mailing statement must accompany each vehicle for each mailing segment.

f. The mailer must maintain a plant load control log containing a copy of each mailing statement, numbered sequentially, the number of each vehicle used to transport the plant-loaded mail, and the name of the BMC, ASF, MSC, or SCF where verification will take place.

g. The mail can be physically verified at the BMC, ASF, MSC, or SCF, *i.e.*, the mailing is not shrink-wrapped or otherwise prepared so that an in-depth verification could not be performed.

.424 Conditions for Verification at Postal Facility. If mail is to be verified at the origin BMC, ASF, MSC, or SCF:

a. Before the vehicle leaves the mailer's plant, the mailer must place on the vehicle a distinctive placard provided by the Postal Service which indicates that verification is required. The driver will not pick up the vehicle unless this placard is on the vehicle.

b. The TMO must report the empty weight of the vehicle to the BMC, ASF, MSC, or SCF verification unit prior to the vehicle's arrival at the verification unit.

.425 Corrective Action. If intra-service-area plant-loaded mail is verified at the BMC, ASF, MSC, or SCF verification unit and the verification shows an error rate of 10 percent or more, the mailer has the following two options:

a. The mailer pays the single-piece rate on that portion of the mailing estimated to be improperly prepared.

b. Within 24 hours, the mailer either transports the mailing or arranges for Postal Service to transport the mailing to the mailer's plant, at the mailer's expense, for reworking the mailing to comply with the applicable make-up requirements for its class. If the mailer does not transport the mail or request transportation for it within 24 hours, the mailer will reimburse the Postal Service for detention in accordance with 154.6.

.43 Verification of Inter-Servie-Area Plant Loads. Inter-service-area plant-loaded mail must be verified at the plant by a clerk qualified to perform verification procedures.

.44 Payment of Postage and Fees. Payment of postage and fees for plant-

loaded mail must be made to the origin post office prior to the vehicle being transported from the mailer's plant.

*154.5 Preparation Requirements for Plant-Loaded Vehicles.*

.51 Intra-Service-Area Plant Loads. Intra-service-area plant-loaded vehicles must fill 50 percent or more of a vehicle by weight or cube addressed to that service area.

.52 Inter-Service-Area Plant Loads.

.521 Vehicles Containing Five or Fewer Mailings. Inter-service-area plant-loaded vehicles containing five or fewer mailings must be prepared in accordance with the following preparation requirements for the appropriate class or type of mail.

a. First-Class Mail.

(1) 3-Digit ZIP Code Destination. When mail filling 60 percent or more of a vehicle by weight or by cube is addressed to the same 3-digit ZIP Code, the mailer must prepare a direct vehicle for that 3-digit ZIP Code.

(2) SCF Destination. When, after making up all possible 3-digit vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same SCF service area, the mailer must prepare a direct vehicle for that SCF.

(3) ADC Destination. When, after making up all possible 3-digit and SCF vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same area distribution center (ADC) service area, the mailer must prepare a direct vehicle for that ADC.

b. Second-Class Mail.

(1) 3-Digit ZIP Code Destination. When mail filling 60 percent or more of a vehicle by weight or by cube is addressed to the same 3-digit ZIP Code, the mailer must prepare a direct vehicle for that 3-digit ZIP Code.

(2) SCF Destination. When, after making up all possible 3-digit vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same SCF service area, the mailer must prepare a direct vehicle for that SCF.

(3) SDC Destination. When, after making up all possible 3-digit and SCF vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same state distribution center (SDC) service area, the mailer must prepare a direct vehicle for that SDC.

(4) Transfer Hubs. When, after making up all possible 3-digit, SCF, and SDC vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the service area of the same transfer hub the mailer must prepare a direct vehicle for that transfer hub.

c. Third-Class and Non-Machinable Fourth-Class Mail.

(1) 3-Digit ZIP Code Destination. When mail filling 60 percent or more of a vehicle by weight or by cube is addressed to the same 3-digit ZIP Code, the mailer must prepare a direct vehicle for that 3-digit ZIP Code.

(2) SCF Destination. When, after making up all possible 3-digit vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same SCF service area, the mailer must prepare a direct vehicle for that SCF.

(3) BMC or ASF Destination. When, after making up all possible 3-digit and SCF vehicles, there is mail filling 60 percent or more or a vehicle by weight or by cube addressed to the same BMC or ASF service area, the mailer must prepare a direct vehicle for that BMC or ASF.

d. Machinable Fourth-Class Mail (Except Bound Printed Matter).

(1) 5-Digit ZIP Code Destination. When mail filling 60 percent or more of a vehicle by weight or by cube is addressed to the same 5-digit ZIP Code, the mailer must prepare a direct vehicle for that 5-digit ZIP Code.

(2) BMC or ASF Destination. When, after making up all possible 5-digit vehicles, there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same BMC or ASF service area, the mailer must prepare a direct vehicle for that BMC or ASF.

e. Machinable Bound Printed Matter.

(1) SCF Destination. When mail filling 60 percent or more of a vehicle by weight or cube is addressed to the same SCF service area, the mailer must prepare a direct vehicle for that SCF service area.

(2) BMC or ASF Destination. When, after making up all possible SCF vehicles there is mail filling 60 percent or more of a vehicles by weight or by cube addressed to the same BMC or ASF service area, the mailer must prepare a direct vehicle for that BMC or ASF.

f. Residue. Residue is the part of a mailing which remains after all of the above preparation requirements for the appropriate class of mail have been met. The Postal Service, using appropriate transportation, will transport such residue to the postal facility selected by the TMO.

.522 Vehicles Containing Six or More Mailings. Inter-service-area plant-loaded vehicles containing six or more mailings must be prepared in accordance with the following preparation requirements for the appropriate class or type of mail.

a. First-Class Mail. When there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same ADC service area, the mailer must prepare a direct vehicle for that ADC.

b. Second-Class Mail. When there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the service area of the same transfer hub, the mailer must prepare a direct vehicle for that transfer hub.

c. Third- and Fourth-Class Mail. When there is mail filling 60 percent or more of a vehicle by weight or by cube addressed to the same BMC or ASF service area, the mailer must prepare a direct vehicle for that BMC or ASF.

d. Residue. Residue is the part of a mailing which remains after all of the above preparation requirements for the appropriate class or type of mail have been met. The Postal Service, using appropriate transportation, will transport such residue to the postal facility selected by the TMO.

154.6 Reimbursement for Nonpostal Services.

.61 General. The Postal Service will obtain reimbursement from mailers for nonpostal services furnished by the Postal Service in providing plant-load service only as authorized below.

.62 Detention of Trailers.

.621 General. The Postal Service will obtain reimbursement in accordance with 154.622–.625 from plant-load mailers for detention of trailers where trailers furnished by the Postal Service to provide plant-load service are detained as a result of some action or inaction of the mailer.

.622 Request to Detain Trailers.

a. Plant-load mailers desiring to detain trailers longer than the time necessary to load them must make such a request to the Postal Service at least 24 hours in advance of the requested date and time of the trailer's arrival. The mailer must agree to reimburse the Postal Service for the cost of detaining the trailers. The Postal Service must approve the request to detain trailers before the trailers will be sent to the mailer's plant.

b. If the mailer did not submit a timely request to detain trailers, but nevertheless detains trailers longer than the time necessary to load them, the mailer must reimburse the Postal

Service for the cost of detaining the trailers.

.623 Non-reimbursable Detention Period. Plant-load mailers who submit timely requests to detain trailers may do so for 24 hours without reimbursing the Postal Service for detention. The non-reimbursable period begins at the date and time the trailer arrives at the mailer's plant or, at the date and time at which the mailer requested the trailer to arrive, whichever is later, and ends 24 hours later, excluding Saturdays, Sundays, and holidays. For example, if a trailer arrives at 5:00 p.m. Friday, the non-reimbursable period ends 5:00 p.m. Monday, or 5:00 p.m. Tuesday if Monday is a holiday.

.624 Determination of Reimbursable Detention Period.

a. If the plant-load mailer has submitted timely requests to detain trailers, the reimbursable detention period begins at the expiration of the non-reimbursable detention period.

B. If the mailer did not submit timely requests to detain trailers, the reimbursable detention period begins at the date and time the trailer arrives at the plant, or at the date and time at which the mailer requested the trailer to arrive, whichever is later.

c. The reimbursable period ends when the trailer is ready for dispatch and the mailer so notifies the Postal Service.

.625 Calculation of Reimbursement. Reimbursement will be made for each 24 hours, or fraction thereof, of the reimbursable detention period that a vehicle is detained. After the non-reimbursable detention period ends, Saturdays, Sundays, and holidays will be included in the calculation of detention reimbursement.

a. Highway Transportation Trailers. Reimbursement for each highway transportation trailer will be equal to the average daily cost to the Postal Service of leasing a trailer in the origin TMO service area during the preceding postal quarter.

b. Rail Transportation Trailers. Reimbursement for each rail transportation trailer will be equal to the demurrage or detention charge payable by the Postal Service under the rail transportation contract under which the trailer is furnished to the Postal Service by the railroad.

.63 Bobtailing, Deadheading, Waiting/Holding Charges. The Postal Service will obtain reimbursement from plant-load mailers for bobtailing, deadheading, or waiting/holding, where such charges are incurred in order to provide plant-load service as a result of some action or inaction by the mailer. Reimbursement will equal to the charge for such service payable by the Postal Service under the transportation contract.

.64 Non-Reimbursable Charges.

.641 The Postal Service will not obtain reimbursement from plant-load mailers for detention of trailers which results from some action or inaction of the Postal Service.

.642 The Postal Service will not obtain reimbursement from plant-load mailers where bobtailing, deadheading or waiting/holding charges are incurred as a result of some action or inaction of the Postal Service.

.643 The Postal Service will not obtain reimbursement from plant-load mailers for user's charges paid by the Postal Service to a railroad contractor for the movement of railroad trailers beyond the commercial zone of the railroad terminus.

*154.7 Transportation.*

.71 Selection of Mode of Transportation. The TMO will select the least costly mode of transportation that will meet the service objectives for the class of mail plant-loaded. The mode of transportation will *not* be changed at the request of the mailer.

.72 Mailer Transportation. Mailers may not transport their own plant-loaded mail unless there is a highway contract between the Postal Service and the mailer. The awarding of a highway contract to the mailer will not be considered in deciding whether to authorize the plant load.

.73 Holding, Storing, or Delaying Dispatch. The Postal Service will not hold, store, or otherwise delay the dispatch of plant-loaded mail released to the Postal Service, except as provided in the plant-load agreement with the mailer.

.74 Relocation of Trailers. The Postal Service will not relocate trailers at a mailer's plant.

154.8 Service Objectives. The service objectives that apply to the class of mail being transported will apply to the plant-loaded mail. Plant-loaded mail may have deferred service objectives, if provided for in the plant-load agreement.

An appropriate amendment to 39 CFR 111.3 to reflect these changes will be published if the proposal is adopted.

**W. Allen Sanders,**

*Association General Counsel, Office of General Law and Administration.*

[FR Doc. 85-30389 Filed 12-23-85; 8:45 am]

BILLING CODE 7710-12-M

## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 131

**[OW-FRL-2920-2]**

### Water Quality Standards for Surface Waters of the Commonwealth of Kentucky

**AGENCY:** Environmental Protection Agency.

**ACTION:** Proposed rule.

**SUMMARY:** On April 8, 1985, the Kentucky Natural Resources & Environmental Protection Cabinet adopted revisions to the Commonwealth's Water Quality Standards in accordance with section 303(c) of the Clean Water Act. Subsequent to adoption by the Commonwealth, a Johnson County Circuit Court judge issued an injunction blocking the Commonwealth's enforcement of portions of the revised state standards. The most significant enjoined revision is the new chloride criterion for warmwater aquatic life. This notice proposes a rule establishing a chloride criterion to protect warmwater aquatic life in Kentucky to replace the enjoined State criterion. A proposed rule addressing the remaining enjoined provisions of Kentucky's water quality standards will be handled in a separate action.

**DATES:** All written comments received on or before March 1, 1986, will be considered in the preparation of the final rule. Public Hearings will be held on February 19, 1986 and February 20, 1986 in Slade, Kentucky and Owensboro, Kentucky See Addresses below.

**ADDRESSES:** Written comments should be addressed to Rosemary M. Patton, Water Quality Section, Water Management Division, Environmental Protection Agency, 345 Courtland Street NE., Atlanta, Georgia 30365. Hearing addresses: Activity Center, Natural Bridge State Park, Slade, Kentucky, February 19, 1986, 7:00 p.m.; Ohio Room, Executive Inn Rivermont, 1 Executive Boulevard, Owensboro, Kentucky, February 20, 1986, 7:00 p.m.

Both oral and written comments will be accepted at the hearings. The Hearing Officer reserves the right to fix reasonable limits on the time allowed for oral presentations. Written comments are encouraged.

**FOR FURTHER INFORMATION CONTACT:** Rosemary M. Patton, Water Management Division, Environmental Protection Agency, 345 Courtland Street

NE., Atlanta, Georgia 30365, 404/881-3116.

**SUPPLEMENTARY INFORMATION:** Section 303 of the Clean Water Act, amended, (hereinafter the Act) requires the adoption of water quality standards, consisting of designated uses and in-stream water criteria to protect such uses, for all waters of the United States. Section 303(c)(4) provides that in any case where it is determined that a revised or new water quality standard is necessary to meet the requirements of the Act, the Administrator shall publish proposed regulations setting forth a revised or new water quality standard for the navigable waters involved. The Administrator shall promulgate any new or revised standard not later than ninety (90) days after publication of the proposed standard. The Agency's regulations for implementing section 303(c) of the Act are codified at 40 CFR Part 131. Guidance for these regulations is contained in the Water Quality Standards Handbook (December 1983) and Technical Support Manual: Waterbody Surveys and Assessments for Conducting Use Attainability Analyses (Volumes I, II and III).

### A. Background

Kentucky's water quality standards are found at Chapter 401 of the Kentucky Administrations Regulations (KAR), Sections 5:026, 5:029, and 5:031. On April 8, 1985, the Kentucky Natural Resources and Environmental Protection Cabinet (hereinafter the Cabinet) adopted revisions to its water quality standards pursuant to the requirements of section 303(c) of the Act. The revisions were submitted to EPA on May 24, 1985 and approved on July 10, 1985.

Subsequent to adoption of the revised standards by the Cabinet, a Johnson County Circuit Court Judge issued a temporary injunction prohibiting enforcement of the revisions to 401 KAR 5:031. The injunction was the result of a complaint filed by several individuals claiming that portions of 401 KAR 5:031 were not properly promulgated and are contrary to law. The most significant, and perhaps controversial, change to 401 KAR 5:031 was the addition of a chloride criterion for warmwater aquatic life. Heretofore, the standards included a chloride criterion only for domestic water supply.

Chloride represents a significant problem in many of Kentucky's waters and has been shown to be directly related to discharges of brine from oil "stripper" wells. (A stripper well is defined as one that produces less than ten barrels per day.) In an effort to address this significant problem, the Commonwealth has taken several actions in the last few years. One such action was approval of a regulation which mandates underground injection or the transport and disposal off-site of produced water (brine) wherever economically feasible.

Another action by the Commonwealth was the commission of a study to develop numerical criteria for chloride that would assure protection of warmwater aquatic species in the Commonwealth of Kentucky. These criteria would be used to establish water quality based effluent limitations for dischargers who are unable to utilize underground injection techniques or off-site disposal and must continue to discharge to surface waters of the Commonwealth.

The study was conducted by the University of Kentucky in accordance with a Memorandum of Agreement between the Cabinet and the University. The objective of the study was to perform both toxicity tests and monitoring studies to determine the effects of chloride on warmwater species of aquatic life and to recommend numerical criteria appropriate for protecting warmwater species in Kentucky. Direct toxicological monitoring was conducted in the field on both impacted and unimpacted waters and comparative acute toxicity tests were performed in the laboratory. In conducting side-by-side acute toxicity tests on an aquatic invertebrate using the same concentration of chloride in both reconstituted laboratory water and in natural stream water, chloride was found to be approximately twice as toxic in the laboratory water as in the natural water. An extensive field study, involving biotic surveys of a second order stream receiving a chloride effluent, also revealed that standard laboratory tests apparently overestimated the impact of chloride on the natural biotic communities.

Considering the field data and best overall interpretation of laboratory toxicity data, the Commonwealth determined that the average concentration of chloride should not exceed 600 mg/1 and the maximum concentration should not exceed 1,200 mg/1 to protect freshwater aquatic life. Therefore, Kentucky adopted a 600 mg/1 criterion for waters with a freshwater aquatic life designated use.

Numerical criteria represent the most practical and direct mechanism for establishing water quality based treatment controls to protect the designated or existing uses of a waterbody. As a result of the court injunction, Kentucky is unable to implement the numerical criterion for chloride it adopted and is thus hindered in its ability to readily control this significant pollutant.

### B. Statutory Basis and Purpose

Under section 303(c) of the Act, a water quality standard for a specific waterbody basically consists of two components: a designated use for which a waterbody is to be protected (such as recreation, fish and wildlife, or agriculture) and numercial or qualitative pollutant criteria which will support the designated use.

Section 303(c) of the Act requires that State water quality standards ". . . be such as to protect the public health or welfare, enhance the quality of water and serve the purposes of this Act. Such standards shall be established taking into consideration their use and value for propagation of fish and wildlife, . . ." Key concerns of this statutory section are the enhancement of water quality and the protection of the propagation of fish. The ultimate purpose of water quality of water quality standards, as with the other sections of the Act, is to achieve the national goal, wherever attainable, of water quality which provides for the protection and propagation of fish, shellfish, and wildlife and provides for recreation in and on the water [section 101(a)(2)]

EPA's Water Quality Standards regulations at 40 CFR Part 131 provide that States must review water quality data and information on discharges to identify specific water bodies where toxic pollutants may be adversely affecting water quality or the attainment of the designated use or where the levels of toxic pollutants are at a level to warrant concern and must adopt criteria for such pollutants to protect the designated uses.

The adoption of a chloride criterion by Kentucky represents an effort by the Commonwealth to satisfy this requirement [48 FR 51400, 131.11(a)(2)]. The Court's injunction prohibiting enforcement of the standard results in a situation which is inconsistent with EPA's regulation in that a specific pollutant adversely affecting the attachment of a use was identified by the State, but the State is now constrained from putting into place environmental controls to resolve a known problem. Accordingly, under the provisions of section 303(c)[4][B], of the CWA, the Administrator has determined that a new or revised standard is necessary to meet the requirements of the Act and is proposing to promulgate a Federal chloride criterion for Kentucky.

### C. The Proposed Criteria

The Agency's proposed rule would establish a chloride criterion to protect warmwater aquatic life in Kentucky. In the absence of published national criteria for chloride under section 304(a) of the Act, EPA is proposing to promulgate the chloride criterion developed by the Commonwealth of Kentucky. In the study conducted by the University of Kentucky, this criterion was found to be protective of warmwater aquatic life in significant stream systems in the State. For warmwater aquatic life, the allowable instream concentration for chloride shall be 600 mg/1 as a 30-day average with a maximum concentration of 1,200 mg/1 not be exceeded at any time. These criteria protect aquatic life from both acute and chronic toxicity.

The Agency's proposed rule does not endorse establishment of this criterion on a national basis nor does it preclude EPA, at some later date, from reconsidering and revising through rulemaking the chloride criterion proposed herein for Kentucky. Development and publication of water quality criteria is an ongoing process and as new scientific information becomes available, criteria are reevaluated and revised as appropriate.

### D. Initial Regulatory Flexibility Analysis

Section 303(c) specifies that water quality standards be established for all water which consist of designated use for the segment and criteria to protect the uses. EPA's regulations implementing § 303 provide that criteria must contain sufficient parameters or constituents to protect the designated use.

Because there is a documented chloride problem in Kentucky which can interfere with the uses designated by the Commonwealth the standards for Kentucky waters must include a criterion at a level which protects such uses from chloride. Since the court action has effectively repealed the chloride criterion adopted by Kentucky, its standards no longer meet the requirements of the Act. In such circumstances, section 303(c)(4) directs EPA to promulgate standards which do meet the requirements of the Act.

Accordingly, under the scheme contemplated by Congress and these facts, EPA has no alternative but to promulgate a water quality standard, and in promulgating such a standard, to develop one which contains a criterion which protects the use(s) designated by Kentucky. (Under section 510 of the Act, EPA does not have the option of downgrading a State-designated use.)

The proposed WQS will potentially affect anyone who discharges chloride into navigable waters of the Commonwealth of Kentucky, since anyone discharging into such waters must comply with a NPDES permit whose terms assure compliance with water quality standards. The primary group that potentially will be affected are producers of oil and gas. Produced water which is generally high in chlorides accompanies all production of oil and gas. However, currently all gas producers and oil producers with the exception of those producing from stripper wells are subject to a technology-based no-discharge regulation, 40 CFR 435.32. Therefore, the only producers potentially affected by these proposed water quality standards are those producing oil from stripper wells.

There are approximately 15,500 producing oil wells in the State and 77 percent of these wells are stripper wells, i.e., wells that produce less than 10 barrels of oil per day. Of the wells which produce less than 10 barrels of oil per day, the amount of produced water varies generally from 1 to 10 barrels of produced water for every barrel of oil. The Commonwealth data also indicates that the oil-producing wells are owned by 1,920 producers. Of these, 1,684 are considered as small operators, i.e., owning less than 10 wells each. Approximately 900 own only one well each. The total number of wells owned by small operators (1,684) is approximately 4,000 of the 15,500 total. The fact that a producer may own one well or less than 10 wells, even assuming they are all stripper wells, does not necessarily mean it is a small entity. Many of these wells would not be expected to provide the sole or primary source of income for the producers. For example, the average production of oil from a stripper well, based on Commonwealth research, is approximately 1 barrel of oil a day. This would generate approximately $40 in gross revenue, with a profit range of $5–$10 a barrel. The Agency does not have sufficient data to document the impact on earnings of meeting the standard and requests specific comment on this question during the comment period.

Surface water discharges will be subject to water quality based effluent limitations compatible with the Federal water quality criterion for chloride. Producers on large streams with sufficient assimilative capacity could perhaps meet the instream criteria for chloride with a modest investment whereas dischargers to small, low-flow streams probably would require disposal by reinjection methods. Transportation to a centralized reinjection facility would be the most cost-effective means of disposal for operators on small, low-flow streams. Small operators will probably bear the greatest burden because some large operators are currently achieving zero-discharge through reinjection. Well closures could possibly result in some cases where the cost of compliance prohibits viable production. It is estimated by the Commonwealth that there would be a 5-percent reduction in oil production as a result of this criterion. The Agency invites comment on the economic impact of the proposed rule.

As part of its regulatory flexibility analyses, the Agency also considered possible recordkeeping or reporting impact on small entities. Such recordkeeping and reporting impacts which might occur are minimal and result from the need for a discharger discharging brine directly to surface waters to obtain a national pollutant discharge elimination system permit and then to follow the discharge conditions set forth in that permit. If underground injection or transport and disposal of brine off-site are the methods used, no NPDES permit is required.

Current Commonwealth regulation requires underground injection of transport and disposal of brine off-site wherever economically feasible. The criteria proposed in this rule, if finally promulgated, would be used by the State to establish water quality based effluent limitations for dischargers who are unable to use these techniques and must continue to discharge to surface waters of the Commonwealth.

It is these currently unregulated dischargers who have no current treatment controls in place that the Commonwealth was attempting to control through its adoption of a criterion for chlorides and who would be most directly affected by the Federal proposal. Since this proposed rule is aimed at eventually establishing treatment controls for the discharge of brine from small entities, it is clear that this rule cannot provide exemptions for such small entities.

Under the current EPA water quality standards regulation, short-term variances to water quality standards may be granted to individual dischargers based on any one of several factors including "substantial and widespread economic and social impact" (40 CFR 131.10(g)(6)). It is doubtful, however, that an operator of only one or a few wells could meet the economic test for a variance.

### E. Executive Order 12291

Executive Order 12291 requires EPA and other agencies to perform regulatory and impact analyses of major regulatons. Major rules are those which impose a cost on the economy of $100 million a year or more or have certain other economic impacts. This regulation is not a major rule because its annualized cost, as discussed above, is significantly less that $100 million and it meets none of the other criteria specified in section 1(b) of the Executive Order. Also, as required by Executive Order 12291, this proposed rule has been reviewed by the Office of Management and Budget.

### F. Regulatory Flexibility Act Requirements

Under the Regulatory Flexibility Act, 5 U.S.C. 601 et seq., the Administrator is required to conduct an initial regulatory flexibility analysis describing the impact of the proposed rule. A summary of the analysis is included as Part D of this proposal. Copies of the complete analysis are available from the person listed under the section "For Further Information Contact".

### G. Availability of the Record

The entire administrative record concerning the Kentucky Water Quality Standards discussed in this preamble, including the University of Kentucky study on chloride toxicity, is available for public inspection and copying at the Environmental Protection Agency, Region IV Office, Water Quality Section, 345 Courtland Street, NE., Atlanta, Georgia 30365, and the U.S. Environmental Protection Agency Library, 401 M Street SW., Washington, DC 20460.

### H. List of Subjects in 40 CFR Part 131

Water pollution control, Intergovernmental relations, Administrative practices and procedures, Reporting and recordkeeping.

Dated: December 12, 1985.

**Lee M. Thomas,**

*Administrator.*

## PART 131—[AMENDED]

1. The authority citation for Part 131 continues to read as follows:

**Authority:** 33 U.S.C. 1313(c).

2. Part 131 of Chapter 1, Title 40 of the Code of Federal Regulations is proposed bo be amended by adding § 131.35 as follows:

### § 131.35 Kentucky.

The water quality standards applicable to the waters of Kentucky adopted by the Kentucky Natural Resources and Environmental Protection Cabinet on April 8, 1985, are amended as follows:

Section 4. Aquatic Life. (1) Warmwater aquatic habitat. The following parameters and associated criteria are for the protection of productive warmwater aquatic communities, fowl, animal wildlife, arborous growth, agricultural and industrial uses:

(i) Toxics:

4. Allowable instream concentrations of specific parameters are outlined in Table I. These values are based on protecting aquatic life from both acute and chronic toxicity.

TABLE I.—WARMWATER AQUATIC HABITAT CRITERIA

| Parameter | Concentration |
|---|---|
| Chloride | 600 mg/l as a 30-day average, not to exceed a maximum of 1,200 mg/l at any time. |

[FR Doc. 85-30249 Filed 12-23-85; 8:45 am]

BILLING CODE 6560-50-M

## FEDERAL COMMUNICATIONS COMMISSION

### 47 CFR Part 100

**[MM Docket No. 85-32]**

### In Matter of the Rules Concerning Technical Standards for Direct Broadcast Satellite Service

**AGENCY:** Federal Communications Commission.

**ACTION:** Proposed rule; Order extending time for filing comments.

**SUMMARY:** This Order extends the time for filing comments in MM Docket No. 85-32 regarding technical standards for direct broadcast satellite service (50 FR 6971; February 19, 1985). This extension is in response to a Motion for Extension of Time filed by the Direct Broadcast Satellite Association (DBSA).

**DATES:** Comments must be filed on or before February 14, 1986, and reply comments on or before March 15, 1986.

**ADDRESS:** Federal Communications Commission, Washington, DC 20554.

**FOR FURTHER INFORMATION CONTACT:** Bernard Gorden, Policy and Rules Division, Mass Media Bureau, (202) 632-9660.

### Order Extending Time for Filing Comments to Notice of Proposed Rule Making

In the matter of amendment of Subpart C of Part 100 of the Commission's Rules and Regulations with Respect to Technical Standards for Direct Broadcast Satellite Service, MM Docket No. 84-32.

Adopted: December 13, 1985.

Released: December 17, 1985.

By the Chief, Mass Media Bureau.

1. The deadlines for filing comments and reply comments in this proceeding, as extended twice by earlier *Orders*, are now December 6, 1985, and January 10, 1986, respectively. On November 27, 1985, the Direct Broadcast Satellite Association (DBSA), the principal industry coordinating respondent in this proceeding, filed its third request for additional time for submission of comments.

2. In support of its request, DBSA stated that its plans for comprehensive tests of alternative proposed Direct Broadcast Satellite (DBS) systems (including alternative signal formats) have been completed. It also reported that the tests included comparative testing of the NTSC system used for planning at RARC-83, a B-NTSC system, and a B-MAC system. DBSA claimed that the test results should show whether the B-NTSC and B-MAC systems cause more or less interference to other systems than the RARC-83 (NTSC-M) signal format. The DBSA standards committee believes that the results of the tests will be a major contribution to the formulation of voluntary industry standards. However, DBSA stated that the tests produced a voluminous amount of data which its standards committee must fully analyze in order to make a recommendation. Consequently, DBSA claimed that because of the amount of time consumed in making the tests and the time necessary for analysis, it cannot meet the December 6, 1985, comment date. Therefore, DBSA requested an extention of time to March 1, 1986, to file initial comments on the voluntary standards and standards of good industry practice proposed in the *Notice* (adopted February 6, 1985), and until April 4, 1986, to file reply comments.

3. We note that this is the third request for extention of the comment period, resulting in a total delay of a year. We reiterate that our goal in this proceeding is to adopt only those standards which are required to limit interference and to assure a reasonable degree of interoperability among DBS systems and receivers in the hands of the public. While the results of DBSA's

system testing may be pivotal in the selection of a standard signal format, we emphasize that this will be an industry "voluntary" standard as identified in the initiating *Notice*. Thus, any final signal format selection may not necessarily be of benefit to rule amendments, if any are adopted by the Commission in this proceeding. As also stated in the previous *Order* and initiating *Notice*, we do have some reservations as to whether it is necessary to adopt any standards, either mandatory or voluntary.

4. In as much that this proceeding may have only marginal impact on the industry's consensus on voluntary standards, we are reluctant to unduly prolong this proceeding. However, since it does not appear that a further delay will cause undue harm to any party in this proceeding, we are granting a final and limited extention of the comment and reply comment periods.

5. Accordingly, it is ordered that the time for filing comments and replies to comments to the above referenced *Notice* is extended to and including February 14, 1986, for comments and March 15, 1986, for reply comments.

6. This action is taken pursuant to authority found in sections 4(i), 5(c)(i), and 303(r) of the Communications Act of 1934, as amended, and section 01281 of the Commission's Rules.

Federal Communications Commission.

**James C. McKinney,**

*Chief, Mass Media Bureau.*

[FR Doc. 85-30197 Filed 12-23-85; 8:45 am]

BILLING CODE 6712-01-M

## DEPARTMENT OF TRANSPORTATION

### National Highway Traffic Safety Administration

### 49 CFR Part 571

### Federal Motor Vehicle Safety Standards; Denial of Petition for Rulemaking

**AGENCY:** National Highway Traffic Safety Administration (NHTSA), DOT.

**ACTION:** Denial of petition for rulemaking.

**SUMMARY:** This notice denies the petition of Chrysler Corporation for an amendment to Motor Vehicle Safety Standard No. 108 *Lamps, Reflective Devices, and Associated Equipment* to allow the use of removable transparent headlamp covers on motor vehicles. Currently, the standard prohibits such covers. The petition argued that such an amendment would contribute to an improvement in the aerodynamics of a vehicle and therefore enhance fuel economy. Chrysler averred that it would provide headlamps whose photometrics exceeded the minimum required by Standard No. 108 to compensate for the reduction in light ouput created by the covers. The petition is being denied primarily because of the difficulty of insuring that replacement headlamps used with headlamp covers will provide photometrics exceeding the mimimum sufficiently to compensate for the reduction in light caused by the covers.

**FOR FURTHER INFORMATION CONTACT:** Richard Van Iderstine, Office of Vehicle Safety Standard, National Highway Traffic Safety Administration, 400 Seventh Street, SW., Washington, DC 20590, (202-426-2720).

**SUPPLEMENTARY INFORMATION:**

Paragraph S4.1.3 of Standard No. 108 prohibits the installation of motor vehicle equipment that impairs the effectiveness of lighting equipment that the standard requires. Furthermore SAE J580 *Sealed Beam Headlamp Assembly*, incorporated by reference and made applicable to replaceable bulb headlamp assemblies by paragraph S4.1.1.36, prohibits styling features in front of headlamps when they are activated. These provisions have been interpreted as forbidding the use of transparent headlamp covers as original equipment on motor vehicles.

On July 24, 1984, Chrysler Corporation petitioned the agency for rulemaking to allow the use of such covers provided that they met performance specifications which the company had developed. These included the assurance that beam pattern and photometrics would continue to be met with the covers in place, durability tests to insure that plastic covers retain their transparency over a period of time, moisture and dust tests, vibration integrity requirements, and requirements relating to corrosion, abrasion and chemical resistance performance. In addition, to facilitate mechanical aiming and cleaning, covers would be capable of being removed and reinstalled without tools.

Chrysler stated that it intended to provide the covers in conjunction with original equipment "halogen" headlamps (this is not a term used in Standard No. 108, but Chrysler has petitioned that the headlamps and covers in combination should be required to meet the Photometrics of SAF J579c). Chrysler indicates that its tests has shown that "non-halogen incandescent headlamps" (meeting SAE J579c) would nevertheless also meet Standard No. 108 with covers in place. According to Chrysler, a change of the nature requested would "allow greater freedom in designing lower drag coefficient front ends for improved fuel economy" with no diminution in motor vehicle safety.

The agency has carefully evaluated Chrysler's petition. NHTSA's primary concern in this review has been the performace of headlamp-covered vehicles with replacement headlamps. Approximately two of every three headlamps manufactured are sold in the aftermarket for replacement purposes. According to Chrysler, use of headlamp covers will cause a reduction in light output between 7.2% and 15.5%, although care will be taken by Chrysler to insure that new vehicles comply with the standard. However, Chrysler cannot assure equivalent performance when original equipment headlamps are replaced by those available in the aftermarket. Although replacement headlamps are certified as complying with Standard No. 108, their actual performance appears to vary widely. Recent experience indicates that a significant portion of replacement headlamps may not meet photometrics at all specified test points, and that some of those that do, will fail to continue to comply when a reduction factor, such as would be the case with lens covers, is applied to test measurements. In 1984, under a contract with NHTSA is connection with an unrelated project, the University of Michigan Transportation Research Institute (UMTRI) measured photometric performance on 20 sealed beam headlamps purchased at random in the aftermarket. Only 15 met the minimum photometric requirements at all test points. When NHTSA applies a reduction factor of 11.35% to these test results (the average of the 7.2% to 15.5% submitted by Chrysler), only 8 of the 15 headlamps would continue to meet or exceed the minimum required for all test points. Given these two factors, NHTSA has concluded that it is impossible to insure that headlamps of equivalent or better performance than originally supplied by Chrysler will be used as replacements.

Chrysler sought to alleviate agency concern on this issue by theorizing that owners bought lamps by part numbers, and that it would provide an advisory statement on headlamp replacement in the operator's manual. The agency is not persuaded. However, NHTSA is concerned that a significant number of owners might ignore a safety warning in the operator's manual, advising of proper headlamp replacement, since consumers normally do not have to refer to an owner's manual to replace sealed

beam headlamps and used car owners are unlikely to have an owner' manual. Further, with a commonly-used commonly-available part such as the standardized sealed beam headlamp, the agency believes that owners tend to comparison shop for the best bargains at self-service stores, as they do for air filters or other commonly replaced parts, rather than to obtain an identical item from their vehicle dealer.

The predicate of NHTSA's actions in permitting additional headlighting systems adopted in the past few years has been that their performance would be at least equivalent to those already in use. However, with the proposed Chrysler system, performance would be degraded *ab initio* and extra care would be required for the life of the vehicles through the use of headlamps with performance higher than that required by the standard, to insure that lighting performance remains above the minimum specified by the standard. Although the agency has other concerns as to the efficacy of the tests proposed by Chrysler for the covers, its primary concern is the potential for noncompliance that exists when the covers are used, and it has concluded that the existing level of motor vehicle safety might be compromised by the allowance of headlamp covers. NHTSA appreciates Chrylser's interest in exploring new technologies which might enhance fuel economy, but notes that safety considerations must prevail in any proposal to amend the Federal motor vehicle safety standards.

At the conclusion of the technical review, the agency has determined that there is not a reasonable possibility that, at the end of the rulemaking proceeding, Standard No. 108 would be amended to allow headlamp covers on motor vehicles. The petition is hereby denied.

The program official and attorney principally responsible for the development of this agency position are Richard Van Iderstine and Taylor Vinson, respectively.

(Secs. 103, 119, and 124, Pub. L. 89-563, 80 Stat. 718 (15 U.S.C. 1392, 1407, and 1410a); delegations of authority at 49 CFR 1.50 and 49 CFR 501.8)

Issued on December 19, 1985.

Barry Felrice,

*Associate Administrator for Rulemaking.*

[FR Doc. 85-30385 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-59-M

# Notices

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

This section of the FEDERAL REGISTER contains documents other than rules or proposed rules that are applicable to the public. Notices of hearings and investigations, committee meetings, agency decisions and rulings, delegations of authority, filing of petitions and applications and agency statements of organization and functions are examples of documents appearing in this section.

## DEPARTMENT OF COMMERCE

### National Bureau of Standards

[Docket No. 41027-5163]

### Approval of Federal Information Processing Standards Publication 68-1, Minimal BASIC and Federal Information Processing Standards Publication 69-1, FORTRAN

**AGENCY:** National Bureau of Standards, Commerce.

**ACTION:** The purpose of this notice is to announce that the Secretary of Commerce (Secretary) has approved two revised standards, which will be published as FIPS Publications 68-1, Minimal BASIC, and 69-1 FORTRAN.

**SUMMARY:** On November 20, 1984, notice was published in the **Federal Register** (49 FR 45774) and a correction notice published December 6, 1984 (49 FR 47647) that two Federal Information Processing Standards for Minimal BASIC and FORTRAN were being proposed for Federal use.

The written comments submitted by interested parties and other material available to the Department relevant to these standards were reviewed by NBS. On the basis of this review, NBS recommended that the Secretary approve the revised standards and prepared a detailed justification document for the Secretary's review in support of that recommendation.

The detailed justification document which was presented to the Secretary, and which includes an analysis of the written comments recieved, is part of the public record and is available for inspection and copying in the Department's Central Reference and Records Inspection Facility, Room 6628, Herbert C. Hoover Building, 14th Street between Pennsylvania and Constitution Avenues NW., Washington, DC 20230.

Each approved standard contains two portions: (1) An announcement portion which provides information concerning the applicability, implementation, and maintenance of the standard, and (2) a specifications portion which deals with the technical requirements of the standard. The technical specifications, which are voluntary industry standards, have not been changed. Only the announcement portions of the standards are revised and are provided in this notice.

**ADDRESS:** Interested parties may purchase copies of these revised standards, including the technical specifications portions, from the National Technical Information Service (NTIS). Specific ordering information from NTIS for these standards is set out in the Where to Obtain Copies Section of the announcement portion of each standard.

**FOR FURTHER INFORMATION CONTACT:** Ms. Mabel Vickers, Center for Programming Science and Techology, Institute for Computer Sciences and Technology, National Bureau of Standards, Gaithersburg, MD 20899, (301) 921-2431.

Dated: December 18, 1985.

**Ernest Ambler,**
*Director.*

### Federal Information Processing Standards Publication 68-1

(date)

*Announcing the Standard for Minimal BASIC*

Federal Information Processing Standards Publications (FIPS PUBS) are issued by the National Bureau of Standards pursuant to section 111(f)(2) of the Federal Property and Administrative Services Act of 1949, as amended, Public Law 89-306 (79 Stat. 1127), Executive Order 11717 (38 FR 12315, dated May 11, 1973), and Part 6 of Title 15 Code of Federal Regulations (CFR).

1. *Name of Standard.* Minimal BASIC (FIPS PUB 68-1)

2. *Category of Standard.* Software Standard, Programming Language.

3. *Explanation.* This publication announces the revision of Federal Information Processing Standard (FIPS) Minimal BASIC. This revision supersedes FIPS PUB 68 and reflects changes to the Objectives, Applicability, and Implementation portions of FIPS Minimal BASIC. FIPS Minimal BASIC is the adoption of American National Standard Programming Language Minimal BASIC, X3.68-1978. The American National Standard defines the syntax of the Minimal BASIC programming language and the semantics for its interpretation. The standard is used by implementors as the reference authority in developing compilers, interpreters, or other forms of high level language processors and by other computer professionals who need to know the precise syntactic and semantic rules of the standard language.

4. *Approving Authority.* Secretary of Commerce.

5. *Maintenance Agency.* Department of Commerce, National Bureau of Standards (Institutes for Computer Sciences and Technology).

6. *Cross Index.* American National Standard Programming Language Minimal BASIC, X3.68-1978.

7. *Related Documents.*

a. Federal Information Resources Management Regulation 201-8.1, Federal ADP and Telecommunications Standards.

b. Federal Information Processing Standards Publication 29-1, Interpretation Procedures for Federal Information Processing Standard Programming Languages.

c. NBS Special Publication 500-117, Selection and Use of General-Purpose Programming Languages.

8. *Objectives.* Federal standards for high level programming languages permit Federal departments and agencies to exercise more effective control over the production, management, and use of the Government's information resources. The primary objectives of Federal programming langauge standards are:

—to encourage more effective utilization and management of programmers by insuring that programming skills acquired on one job are transportable to other jobs, thereby reducing the cost of programming re-training;

—to reduce the cost of program development by achieving the increased programmer productivity that is inherent in the use of high level programming languages;

—to reduce the overall software costs by making it easier and less expensive to maintain programs and to transfer programs among different computer systems, including replacement systems;

—to protect this existing software assets of the Federal Government by insuring to the maximal feasible extent that Federal programming language standards are technically sound and that subsequent revisions are compatible with the installed base.

Government-wide attainment of the above objectives depends upon the widespread availability and use of comprehensive and precise standard language specifications.

9. *Applicability.*

a. Federal standards for high level programming languages should be used for computer applications and programs that are either developed or acquired for Government use. FIPS Minimal BASIC is one of the high level programming language standards provided for use by all Federal departments and agencies. FIPS Minimal BASIC is especially suited for: (1) the rapid development of computer programs to solve small nonrecurrent problems, particularly on computers providing time-shared or interactive service; and (2) for use in computing environments in which ease of learning and casual use are dominant factors.

b. The use of FIPS high level programming languages is strongly recommended when one or more of the following situations exist:

—It is anticipated that the life of the program will be longer than the life of the presently utilized equipment.
—The application or program is under constant review for updating of the specifications, and changes may result frequently.
—The application is being designed and programmed centrally for a decentralized system that employs computers of different makes, models and configurations.
—The program will or might be run on equipment other than that for which the program is initially written.
—The program is to be understood and maintained by programmers other than the original ones.
—The advantages of improved program design, debugging, documentation and intelligibility can be obtained through the use of this high level language regardless of interchange potential.
—The program is or is likely to be used by organizations outside the Federal Government (i.e., State and local governments, and others).

c. Non-standard language features should be used only when the needed operation or function cannot reasonably be implemented with the standard features alone. Although non-standard language features can be very useful, it should be recognized that their use may make the interchange of programs and future conversion to a revised standard or replacement processor more difficult and costly.

d. It is recognized that programmatic requirements may be more economically and efficiently satisfied through the use of report application-oriented software packages. The use of any facility should be considered in the context of system life, system cost, data integrity, and the potential for data sharing.

e. Programmatic requirements may be also more economically and efficiently satisfied by the use of automatic program generators. However, if the final output of a program generator is a BASIC source program, then the resulting program should conform to the conditions and specifications of FIPS Minimal BASIC.

10. *Specifications.* FIPS Minimal BASIC specifications are the language specifications contained in American National Standard Programming Language Minimal BASIC, X3.68–1978.

The X3.68–1978 document specifies the form of a program written in Minimal BASIC, formats of data for input and output, minimal precision and range of numeric representations for input and output, semantic rules for program and data interpretation, and errors and exceptional circumstances that must be detected by a standard-conforming BASIC processor.

The standard does not specify limits on the size of programs, minimum system requirements, the means of supervisory control of programs, or the means of transforming programs internally for processing. Although Minimal BASIC is primarily an interactive language, the standard does not restrict implementations to the interactive mode.

11. *Implementation.* The implementation of FIPS Minimal BASIC involves three areas of consideration: acquisition of Minimal BASIC processors, interpretation of FIPS Minimal BASIC, and validation of Minimal BASIC processors.

11.1 *Acquisition of Minimal BASIC Processors.* This publication is effective December 24, 1985. Minimal BASIC processors acquired for Federal use after this date should implement FIPS Minimal BASIC. Conformance to FIPS Minimal BASIC should be considered whether Minimal BASIC processors are developed internally, acquired as part of an ADP system procurement, acquired by separate procurement, used under an ADP leasing management, or specified for use in contracts for programming services.

11.2 *Interpretation of FIPS Minimal BASIC.* NBS provides for the resolution of questions regarding FIPS Minimal BASIC specifications and requirements, and issues official interpretations as needed. All questions about the interpretation of FIPS Minimal BASIC should be addressed to: Director, Institute for Computer Sciences and Technology, Attn: BASIC Interpretation, National Bureau of Standards, Gaithersburg, MD 20899.

11.3 *Validation of Minimal BASIC Processors.* The General Services Administration (GSA), through its Federal Software Management Support Center (FSMSC), provides a service for the purpose of validating the conformance to this standard of language processors offered for Federal procurement. The validation system reports the nature of any deviations that are detected. This service is offered on a reimbursable basis. Further information about the validation service can be obtained from the FSMSC which is located at 5203 Leesburg Pike, Suite 1100, Falls Church, Virginia 22041–3467 (703–756–6153).

12. *Where to Obtain Copies.* Copies of this publication are for sale by the National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161. (Sale of the included specifications document is by arrangement with the American National Standards Institute.) When ordering, refer to Federal Information Processing Standards Publication 68–1 (FIPS PUB 68–1), and title. Payment may be made by check, money order, or deposit account.

**Federal Information Processing Standards Publication 69–1**

(date)

*Announcing the Standard for FORTRAN*

Federal Information Processing Standards Publications (FIPS PUBS) are issued by the National Bureau of Standards pursuant to Section 111(f)(2) of the Federal Property and Administrative Services Act of 1949, as amended, Pub. L. 89–306 (79 Stat. 1127), Executive Order 11717 (38 FR 12315, dated May 11, 1973), and Part 6 of Title 15 Code of Federal Regulations (CFR).

1. *Name of Standard.* FORTRAN (FIPS PUB 69).

2. *Category of Standard.* Software Standard, Programming Language.

3. *Explanation.* This publication announces the revision of Federal Information Processing Standard FORTRAN. This revision supersedes FIPS PUB 69 and reflects changes to the Objectives, Applicability, and Implementation portions of FIPS FORTRAN. FIPS FORTRAN is the

adoption of American National Standard Programming Language FORTRAN, X3.9–1978. The American National Standard specifies the form and establishes the interpretation of programs expressed in the FORTRAN programming language. The Standard consists of a full language and a subset language. The purpose of the standard is to promote portability of FORTRAN programs for use on a variety of data processing systems. The standard is used by implementors as the reference authority in developing compilers, interpreters, or other forms of high level language processors, and by other computer professionals who need to know the precise syntactic and semantic rules of the standard.

4. *Approving Authority.* Secretary of Commerce.

5. *Maintenance Agency.* Department of Commerce, National Bureau of Standards (Institute for Computer Sciences and Technology).

6. *Cross Index.* American National Standard Programming Language FORTRAN, X3.9–1978.

7. *Related Documents.*

a. Federal Information Resources Management Regulation 201–8.1, Federal ADP and Telecommunications Standards.

b. Federal Information Processing Standards Publication 29–1, Interpretation Procedures for Federal Information Processing Standard Programming Languages.

c. NBS Special Publication 500–117, Selection and Use of General-Purpose Programming Languages.

8. *Objectives.* Federal standards for high level programming languages permit Federal departments and agencies to exercise more effective control over the production, management, and use of the Government's information resources. The primary objectives of Federal programming language standards are:

—to encourage more effective utilization and management of programmers by insuring that programming skills acquired on one job are transportable to other jobs, thereby reducing the cost of programmer re-training;

—to reduce the cost of program development by achieving the increased programmer productivity that is inherent in the use of high level programming languages;

—to reduce the overall software costs by making it easier and less expensive to maintain programs and to transfer programs among different computer systems, including replacement systems;

—to protect the existing software assets of the Federal Government by insuring to the maximal feasible extent that Federal programming language standards are technically sound and that subsequent revisions are compatible with the installed base.

Government-wide attainment of the above objectives depends upon the widespread availability and use of comprehensive and precise standard language specifications.

9. *Applicability.*

a. Federal standards for high level programming languages should be used for computer applications and programs that are either developed or acquired for government use. FIPS FORTRAN is one of the high level programming language standards provided for use by all Federal departments and agencies. FIPS FORTRAN is especially suited for: (1) the generation of programs to solve recurrent numerical, scientific and engineering problems, particularly those which depend upon efficient computation or access to mathematical or statistical libraries of subprograms; (2) the efficient implementation of algorithms on a wide range of computing equipment of varying power and structure.

b. The use of FIPS high level programming languages is strongly recommended when one or more of the following situations exist:

—It is anticipated that the life of the program will be longer than the life of the presently utilized equipment.

—The application or program is under constant review for updating of the specifications, and changes may result frequently.

—The application is being designed and programmed centrally for a decentralized system that employs computers of different makes, models and configurations.

—The program will or might be run on equipment other than that for which the program is initially written.

—The program is to be understood and maintained by programmers other than the original ones.

—The advantages of improved program design, debugging, documentation and intelligibility can be obtained through the use of the high level language regardless of interchange potential.

—The program is or is likely to be used by organizations ouside the Federal Government (i.e., State and local governments, and others).

c. Non-standard language features should be used only when the needed operation or function cannot reasonably be implemented with the standard features alone. Although non-standard language features can be very useful, it should be recognized that their use may make the interchange of programs and future conversion to a revised standared or replacement processor more difficult and costly.

d. It is recognized that programmatic requirements may be more economically and efficiently satisfied through the use of statistical or numerical software packages. The use of any facility should be considered in the context of system life, system cost, data integrity, and the potential for data sharing.

e. Programmatic reqirements may be also more economically and efficiently satisfied by the use of automatic program generators. However, if the final output of a program generator is a FORTRAN source program, then the resulting program should conform to the conditions and specifications of FIPS FORTRAN.

10. *Secifications.* FIPS FORTRAN specifications are the language specifications contained in American National Standard Programming Language FORTRAN, X3.9–1978. The FORTRAN standard describes two levels of the FORTRAN language. FORTRAN referes to the full language and Subset FORTRAN refers to the subset of the full language.

The X3.9–1978 document specifies the form of a program written in FORTRAN, formats of data for input and output, and semantic rules for program and data interpretation.

The standard does not specify limits on the size or complexity of programs, the range or precision of numeric quantities or the method of rounding of numeric results, the results when the rules of the standard fail to establish an interpretation, minimum system requirements, the means of supervisory control of programs, or the means of transforming programs internally for processing.

A facility should be available in the processor that allows a FORTRAN source program to be analyzed with respect to FIPS FORTRAN. Any statement appearing in the source program that does not conform syntactically to the specifications of FIPS FORTRAN should be explicitly identified.

11. *Implementation.* The implementation of FIPS FORTRAN Involves three areas of consideration: acquisition of FORTRAN processors, interpretation of FIPS FORTRAN, and validation of FORTRAN processors.

11.1 Acquisition of FORTRAN Processors. This publication is effective December 24, 1985. FORTRAN processors acquired for Federal use after this date should implement FIPS FORTRAN. Conformance to FIPS

FORTRAN should be considered whether FORTRAN processors are developed internally, acquired as part of an ADP system procurement, acquired by separate procurement, used under an ADP leasing management, or specified for use in contracts for programming services.

11.2 *Interpretation of FIPS FORTRAN.* NBS provides for the resolution of questions regarding FIPS FORTRAN specifications and requirements, and issues official interpretations as needed. All questions about the interpretation of FIPS FORTRAN should be addressed to: Director, Institute for Computer Sciences and Technology, Attn: FORTRAN Interpretation, National Bureau of Standards, Gaithersburg, MD 20899.

11.3 *Validation of FORTRAN Processors.* The General Services Administration (GSA), through its Federal Software Management Support Center (FSMSC), provides a service for the purpose of validating the conformance to this standard of language processors offered for Federal procurement. The validation system reports the nature of any deviations that are detected. This service is offered on a reimbursable basis. Further information about the validation service can be obtained from the FSMSC which is located at 5203 Leesburg Pike, Suite 1100, Falls Church, Virginia 22041-3467-6153).

12. *Where to Obtain Copies.* Copies of this publication are for sale by the National Technical Information Service, U.S. Department of Commerce, Springfield, VA 22161. (Sale of the included specifications document is by arrangement with the American National Standards Institute.) When ordering, refer to Federal Information Processing Standards Publication 69-1 (FIPS PUB 69-1), and title. Payment may be made by check, money order, or deposit account.

[FR Doc. 85-30335 12-23-85; 8:45 am]
BILLING CODE 3510-CN-M

## National Oceanic and Atmospheric Administration

### Marine Mammals; Proposed Permit Modification; Dr. Robert C. Schneider

Notice is hereby given that Dr. Robert C. Schneider, Department of Anesthesia, Massachusetts General Hospital, Boston, MA 02114 has requested a modification to Permit No. 526 issued on October 11, 1985 (50 FR 42747), under the authority of the Marine Mammal Protection Act of 1972 (16 U.S.C. 1361-1407), and the Regulations Governing the Taking and Importing of Marine Mammals (50 CFR Part 216).

The Permit Holder is requesting to use an electrical method of immobilizing the seals for tagging purposes using high frequency, low amperage current.

Concurrent with the publication of this notice in the **Federal Register**, the Secretary of Commerce is forwarding copies of the modification request to the Marine Mammal Commission and the Committee of Scientific Advisors.

Written data views, or requests for a public hearing on this modification request should be submitted to the Assistant Administrator for Fisheries, National Marine Fisheries Service, U.S. Department of Commerce, Washington, DC 20235, within 30 days of the publication of this notice. Those individuals requesting a hearing should set forth the specific reasons why a hearing on this particular request would be appropriate. The holding of such hearing is at the discretion of the Assistant Administrator for Fisheries.

All statements and opinions contained in this application are summaries of those of the Applicant and do not necessarily reflect the views of the National Marine Fisheries Service.

The permit and modification are available for review by interested persons in the following offices:

Assistant Administrator for Fisheries, National Marine Fisheries Service, 3300 Whitehaven Street, NW, Washington, DC; and

Director, Northeast Region, National Marine Fisheries Service, 14 Elm Street, Federal Building, Gloucester, MA 01930-3799.

**Richard B. Roe,**

*Director, Office of Fisheries Management, National Marine Fisheries Service.*

December 16, 1985.

[FR Doc. 85-30314 Filed 12-23-85; 8:45 am]
BILLING CODE 3510-22-M

## COMMITTEE FOR THE IMPLEMENTATION OF TEXTILE AGREEMENTS

### Announcing an Import Restraint Level for Certain Cotton Textile Products, Produced or Manufactured in Turkey

December 18, 1985.

On October 24, 1985, a notice was published in the **Federal Register** ( 50 F.R. 43267) announcing that, on September 30, 1985 the United States Government, under Article 3 of the Arrangement Regarding International Trade in Textiles, had requested the Government of Turkey to enter into consultations concerning exports to the United States of cotton sheets in Category 361, produced or manufactured in Turkey.

The purpose of this notice is to advise the public that, inasmuch as no agreement has been reached on a mutually satisfactory solution concerning this category, the United States Government has decided to control imports of cotton sheets in Category 361, produced or manufactured in Turkey and exported during the twelve-month period which began on September 30, 1985 and extends through September 29, 1986 at a level of 189,073 numbers. Should further consultations result in agreement, further notice will be published in the **Federal Register**.

Accordingly, in the letter published below, the Chairman of the Committee for the Implementation of Textile Agreements directs the Commissioner of Customs to prohibit entry into the United States for consumption, or withdrawal from warehouse for consumption, of cotton textile products in Category 361, exported during the period which began on September 30, 1985 and extends through September 29, 1986 in excess of the designated restraint limit.

**FOR FURTHER INFORMATION CONTACT:** Ann Fields, International Trade Specialist, Office of Textiles and Apparel, U.S. Department of Commerce, Washington, D.C. (202/377-4212).

A description of the textile categories in terms of T.S.U.S.A. numbers was published in the **Federal Register** on December 13, 1982 (47 FR 55709), as amended on April 7, 1983 (48 FR 15175), May 3, 1983 (48 FR 19924), December 14, 1983 (48 FR 55607), December 30, 1983 (48 FR 57584), April 4, 1984 (49 FR 13397), June 28, 1984 (49 FR 28622), July 16, 1984 (49 FR 28754), November 9, 1984 (49 FR 44782), and in Statistical Headnote 5, Schedule 3 of the Tariff Schedules of the United States Annotated (1985).

**Walter C. Lenahan,**

*Chairman, Committee for the Implementation of Textile Agreements.*

December 18, 1985.

**Committee for the Implementation of Textile Agreements**

Commissioner of Customs,
*Department of the Treasury, Washington, D.C.*

Dear Mr. Commissioner: Under the terms of section 204 of the Agriculture Act of 1956, as amended (7 U.S.C. 1854), and the Arrangement Regarding International Trade in Textiles done at Geneva on December 20, 1973, as extended on December 15, 1977 and December 22, 1981; and in accordance with the provisions of Executive Order 11651 of March 3, 1972, as amended, you are directed to prohibit, effective on December 24, 1985,

entry into the United States for consumption and withdrawal from warehouse for consumption of cotton textile products in Category 361 produced or manufactured in Turkey and exported during the twelve-month period beginning on September 30, 1985 and extending through September 29, 1986, in excess of 189,073 numbers.[1]

Textile products in Category 361 which have been exported to the United States prior to September 30, 1985 shall not be subject to this directive.

Textile products in Category 361 which have been released from the custody of the U.S. Customs Service under the provisions of 19 U.S.C. 1448(6) or 1484(a)(1)(A) prior to the effective date of this directive shall not be denied entry under this directive.

A description of the textile categories in terms of T.S.U.S.A. numbers was published in the **Federal Register** on December 13, 1982 (47 FR 55709), as amended on April 7, 1983 (48 FR 15175), May 3, 1983 (48 FR 19924), December 14, 1983 (48 FR 55607), December 30, 1983 (48 FR 57584), April 4, 1984 (49 FR 13397), June 28, 1984 (49 FR 26822), July 16, 1984 (49 FR 28754), November 9, 1984 (49 FR 44782), and in Statistical Headnote 5, Schedule 3 of the Tariff Schedules of the United States Annotated (1985).

In carrying out the above directions, the Commissioner of Customs should construe entry into the United States for consumption to include entry for consumption into the Commonwealth of Puerto Rico.

The Committee for the Implementation of Textile Agreements has determined that this action falls within the foreign affairs exception to the rulemaking provisions of 5 U.S.C. 553.

Sincerely,

**Walter C. Lenahan,**

*Chairman, Committee for the Implementation of Textile Agreements.*

[Fr Doc. 85-30322, Filed 12-23-85; 8:45 am]

BILLING CODE 3510-DR-M

## DEPARTMENT OF DEFENSE

### Office of the Secretary of Defense

### DOD Advisory Group on Electron Devices; Advisory Committee Meeting

**SUMMARY:** Working Group B (Microelectronics) of the DoD Advisory Group on Electron Devices (AGED) announces a closed session meeting.

**DATE:** The meeting will be held at 0900, Tuesday, 14 January 1986.

**ADDRESS:** The meeting will be held at Palisades Institute for Research Services, Inc., 2011 Crystal Drive, Suite 307, Arlington, VA 22202.

**FOR FURTHER INFORMATION CONTACT:** Becky Terry, AGED Secretariat, 2011 Crystal Drive, Arlington, Virginia 22202.

**SUPPLEMENTARY INFORMATION:** The mission of the Advisory Group is to provide the Under Secretary of Defense for Research and Engineering, the Director, Defense Advanced Research Projects Agency and the Military Departments with technical advice on the conduct of economical and effective research and development programs in the area of electron devices .

The Working Group B meeting will be limited to review of research and development programs which the military propose to initiate with industry, universities or in their laboratories. The Microelectronics area includes such programs as integrated circuits, charge coupled devices and memories. The review will include classified program details throughout.

In accordance with section 10(d) of Pub. L. No. 92-463, as amended, (5 U.S.C App. II, section 10(d) (1982)), it has been determined that this Advisory Group meeting concerns matters listed in 5 U.S.C. 552b(c)(1) (1982), and that accordingly, this meeting will be close to the public.

**Patricia H. Means,**

*OSD Federal Register Liaison Officer, Department of Defense.*

December 18, 1985.

[FR Doc. 85-30339 Filed 12-23-85; 8:45 am]

BILLING CODE 3810-01-M

### Defense Advisory Committee; on Military Personnel Testing; Meeting

Pursuant to Pub. L. 92-463, notice is hereby given that a meeting of the Defense Advisory Committee on Military Personnel Testing is scheduled to be held from 2:00 pm-5:00 pm on January 9, 1986; 8:00 am-5:00 pm on January 10, 1986; and 8:00 am-11:30 am on January 11, 1986, at the Embassy Suite Hotel, 7750 Briar Ridge Drive, San Antonio, Texas. Meeting sessions will be open to the public.

The purpose of the meeting is to (1) review the development of DoD's computerized adaptive testing (CAT) system scheduled for nationwide implementation as the operational military selection and classification test (2) review the validation of the Armed Services Vocational Aptitude Battery (ASVAB); and (3) review the DoD Student Testing Program. The next Committee meeting will also be discovered.

Persons desiring to make oral presentations or submit written statements for consideration at the Committee meeting must contact Dr. A. R. Lancaster, Executive Secretary, Defense Advisory Committee on Military Personnel Testing, Office of the Assistant Secretary of Defense (Force Management and Personnel), Room 2B271, The Pentagon, Washington, DC 20301-4000, telephone (202) 697-9271 no later than January 3, 1986.

**Patricia H. Means,**

*OSD Federal Register Liaison Officer, Department of Defense.*

December 19, 1985.

[FR Doc. 85-30372 Filed 12-23-85; 8:45 am]

BILLING CODE 3810-01-M

## DEPARTMENT OF EDUCATION

### Fund for the Improvement of Postsecondary Education; Application Notice for Comprehensive Program for FY 1986

**AGENCY:** Department of Education.

**ACTION:** Application Notice for Comprehensive Program for Fiscal Year 1986.

Preapplications and applications are invited for new awards under the Comprehensive Program of the Fund for the Improvement of Postsecondary Education.

Under this competition the Secretary of Education makes grants to and enters into cooperative agreements with institutions of postsecondary education and other public and private educational institutions and agencies for the purpose of improving postsecondary educational opportunities.

Authority for this program is contained in Title X of the Higher Education Act, as amended. (20 U.S.C. 1135)

*Closing Date for Transmittal of Preapplications and Applications:* Preapplications for awards must be mailed or hand-delivered by February 18, 1986. Applications must be mailed or hand-delivered by May 20, 1986.

*Preapplications and Applications Delivered by Mail:* A preapplication or application sent by mail must be addressed to the Department of Education, Application Control Center, Attention: 84.116A, Washington, D.C. 20202.

To establish proof of mailing, an applicant must show one of the following:

(1) A legibly dated U.S. Postal Service postmark.

(2) A legible mail receipt with the date of mailing stamped by the U.S. Postal Service.

(3) A dated shipping label, invoice, or receipt from a commercial carrier.

(4) Any other proof of mailing acceptable to the Secretary.

If an application is sent through the U.S. Postal Service, the Secretary does not accept a private metered postmark

[1] The level has not been adjusted to reflect any imports exported after September 29, 1985.

or a receipt that is not dated by the U.S. Postal Service as proof of mailing. An applicant should note that the U.S. Postal Service does not uniformly provide a dated postmark. Before relying on this method, an applicant should check with its local post office.

An applicant is encouraged to use registered or at least first class mail. Each late applicant will be notified that its application will not be considered.

*Preapplications and Applications Delivered by Hand:* A preapplication or application that is hand delivered must be taken to the Department of Education, Application Control Center, Attention: 84.116A, 7th and D Streets, S.W., Room 3633, Regional Office Building 3, Washington, D.C. 20202.

The Secretary will accept hand delivered preapplications and applications between 8:00 a.m. and 4:30 p.m. (Washington, D.C. time) daily, except Saturdays, Sundays, and Federal holidays. Preapplications that are hand-delivered will not be accepted after 4:30 p.m. on February 18, 1986. Applications that are hand-delivered will not be accepted after 4:30 p.m. on May 20, 1986.

**Program Information**

*Type of Competition and Guidelines:* The Secretary supports a broad range of projects that seek to improve postsecondary education. In accordance with 34 CFR 75.105(c)(1) the following guidelines suggest areas in which proposals would be especially welcome. However, the list is not meant to be exhaustive. Projects that do not fit any of these guideline areas are also eligible for support if they address other significant problems in postsecondary education. Proposals are solicited which seek to—

(1) Ensure that undergraduate curricula provide the knowledge and skills which an educated citizen needs—including knowledge of our intellectual and cultural heritage;

(2) Ensure that recent increases in access to postsecondary education are made meaningful by improving retention and completion rates without compromising program standards;

(3) Improve the quality of undergraduate education by—

(i) Raising academic standards for the bachelor's degree;

(ii) Strengthening the liberal arts component of undergraduate professional programs;

(iii) Developing means of assessing and comparing programs and institutions; and

(iv) Recognizing and rewarding outstanding undergraduate teaching through hiring, tenure, and promotion policies;

(4) Reform the education of school teachers by—

(i) Making it easier for able people to qualify as teachers who have earned degrees in fields other than education and who currently lack pedagogical training;

(ii) Increasing current and prospective teachers' mastery of the subjects they teach;

(iii) Ensuring that prospective teachers have a solid grounding in the liberal arts; and

(iv) Attracting more people of commitment and intellectual ability to the teaching profession;

(5) Reform graduate education by—

(i) Fostering the teaching skills of Ph.D. candidates bound for careers in teaching; and

(ii) Broadening the social ethical perspectives of students in professional graduate programs generally;

(6) Strengthen postsecondary educational instutitions and organizations by providing incentives to develop the abilities of their leaders, administrators, faculty, and staff;

(7) Provide education for a changing economy by offering educational programs and services for workers, unemployed individuals, businesses, and communities; and

(8) Develop educational uses of technology, including computers, television, and other electronic media.

In the coming year the Secretary will solicit suggestions from the field to assist in the development of future priorities.

*Preapplications:* Preapplications are required for this competition. They are reviewed in the same manner as applications, including review by independent field readers, and are evaluated on the basis of the selection criteria announced below.

*Selection Criteria:* The Secretary evaluates preapplications and applications on the basis of the following selection criteria:

(a) *Significance for Postsecondary Education.* The Secretary reviews each proposed project for its significance in improving postsecondary education by determining the extent to which it would—

(1) Address an important problem or need;

(2) Represent an improvement upon, or important department from, existing practice;

(3) Involve learner-centered improvements;

(4) Achieve far-reaching impact through improvements that will be useful in a variety of ways and in a variety of settings; and

(5) Increase the cost-effectiveness of services.

(b) *Feasibility.* The Secretary reviews each proposed project for its feasibility by determining the extent to which—

(1) The proposed project represents an appropriate response to the problem or need addressed;

(2) The applicant is capable of carrying out the proposed project, as evidenced by—

(i) The applicant's understanding of the problem or need;

(ii) The quality of the project design, including objectives, approaches and evaluation plan;

(iii) The adequacy of resources, including money, personnel, facilities, equipment, and supplies;

(iv) The qualifications of key personnel who would conduct the project; and

(v) The applicant's relevant prior experience; and

(3) The applicant and any other participating organizations are committed to the success of the proposed project, as evidenced by—

(i) Contribution of resources by the applicant and by participating organizations;

(ii) Their prior work in the area; and

(iii) Potential for continuation of the proposed project beyond the period of the Fund's support (unless the project would be self-terminating).

(c) *Appropriateness of funding projects.* The Secretary reviews each application to determine whether support of the proposed project by the Fund in appropriate in terms of the availability of other funding sources for the proposed activities.

For purposes of reviewing *preapplications*, the selection criteria grouped under "significance" ((a) above) are more important than those grouped under "feasibility" ((b) above) and "appropriateness" ((c) above). The group of criteria under "feasibility" ((b) above) is equal in importance to the "appropriateness" criteria ((c) above).

In reviewing *applications*, the selection criteria (a)(1), (a)(2), (a)(3), (a)(4), (a)(5), (b)(1), (b)(2), (b)(3), and (c) are of equal importance.

In applying the criteria, the Secretary first analyzes preapplications and applications in terms of individual criteria. The Secretary then bases the final judgment of a preapplication or application on an overall assessment of the extent to which the application satisfactorily addresses the selection criteria.

*Other Information To Be Requested From Applicants:* In the final stage of the selection process, applicants whose

applications are being considered for funding will be contacted by telephone to verify or clarify information relevant to the their applications.

*Available Funds:* The Department of Education Appropriation Act, 1986, appropriated $12,710,000 for the Fund for the Improvement of Postsecondary Education. Of the amount, approximately $5,260,000 will be available for new award under the Comprehensive Program. It is estimated that 75 grants ranging from $5,000 to $200,000 per year will be funded. These estimates do not bind the Department of Education to a specific number of grants or the amount of any grant unless that amount is otherwise specified by statute or regulations.

Applications may be submitted for project periods of up to 36 months. In the case of projects approved for multi-year funding, grants awarded in Fiscal Year 1986 will be for the first year of operation only.

*Preapplication and Application Forms:* Preapplication and application forms are included in the program information package. These materials have been sent directly to everyone on the mailing list for the Fund for the Improvement of Postsecondary Education. Institutions and persons not on this list can obtain these materials from the Comprehensive Program, Attention: 84.116A, Department of Education, Fund for the Improvement of Postsecondary Education, 400 Maryland Avenue, S.W. (Room 3100, Regional Office Building 3), Washington, D.C. 20202.

The program information is intended to aid applicants in applying for assistance under this competition. Nothing in the program information package is intended to impose any paperwork, application content, reporting, or grantee performance requirement beyond those specifically imposed under the statute and regulation governing the competition. (Approved by the Office of Management Budget under Control Number 1840-0514)

*Applicable Regulations:* The regulations governing award made by the Fund for the Improvement of Postsecondary Education are contained in:

(1) The Education Department General Administrative Regulations (EDGAR) in 34 CFR Parts 74, 75, 77, and 78, with the exception noted in 34 CFR Part 630.4(b).

(2) The regulations in 34 CFR Part 630.

*Further Information:* For further information contact the Fund for the Improvement of Postsecondary Education regarding the Comprehensive Program (84.116A). Telephone (202) 245-8091/8100.

(20 U.S.C. 1135)

(Catalog of Federal Domestic Assistance No. 84.116A, Fund for the Improvement of Postsecondary Education)

Dated: December 17, 1985.

**William J. Bennett,**

*Secretary of Education.*

[FR Doc. 85-30340 Filed 12-23-85; 8:45 am]

BILLING CODE 4000-01-M

## National Advisory Council on Women's Educational Programs; Meeting

**AGENCY:** National Advisory Council on Women's Educational Programs.

**ACTION:** Notice of meeting.

**SUMMARY:** This sets forth the schedule and proposed agenda of the National Advisory Council on Women's Educational Programs and its Executive; Federal Policies, Practices and Programs; WEEA Program; and Civil Rights Committees. The agenda will include discussion of Council goals and objectives, evaluation of Forum proposals, budget review, revisions of draft of annual report, up-date on Civil Rights legislation, Committee reports and general discussion. This notice also describes the function of the Council. Notice of this meeting is required under section 10(a)(2) of the Federal Advisory Committee Act. This document is intended to notify the general public of their opportunity to attend.

**DATES:**

January 20, 1986, 7:30 p.m. to 9:00 p.m. Executive Committee.

January 21, 1986, 2:30 p.m. to 3:30 p.m. Meetings of Federal Policies, Practices and Programs Committee; Civil Rights Committee and WEEA Program Committee.

January 22, 1986, 8:00 a.m. to 3:00 p.m. Full Council Meeting.

**ADDRESS:** All meetings will be held at the Mayflower Hotel, 1127 Connecticut Avenue, NW., Washington, DC 20036

For further information contact: Patricia A. Weber, Deputy Director, National Advisory Council on Women's Educational Programs, 2000 "L" Street, NW., Suite 568, Washington, DC 20036, (202) 634-6105.

**SUPPLEMENTARY INFORMATION:** The National Advisory Council on Women's Educational Programs is established pursuant to Pub. L. 95-561. The Council is mandated to (a) advise the Secretary on matters relating to equal education opportunities for women and policy matters relating to the administration of the Women's Educational Equity Act of 1978; (b) make recommendations to the Secretary with respect to the allocation of any funds pursuant to the Act, including criteria developed to insure an appropriate geographical distribution of approved programs and projects throughout the Nation; (c) recommend criteria for the establishment of program priorities; (d) make such reports as the Council determines appropriate to the President and Congress on the activities of the Council; and (e) disseminate information concerning the activities of the Council.

The meeting of the Executive Committee will take place on Monday, January 20, 1986 from 7:30 p.m. to 9:00 p.m. The agenda will include Forum review, the Council's 1986 budget, unfinished business and new business.

The meetings of the Federal Policies, Practices, and Programs; Civil Rights; and WEEA Program Committees, will take place on Tuesday, January 21, 1986, from 2:30 to 3:30 p.m.

The agenda for the Federal Policies, Practices and Programs Committee will include the election of officers, unfinished business and new business.

The agenda for the Civil Rights Committee will include new legislation, unfinished business and new business.

The agenda for the WEEA Program Committee will include discussion of site visits, unfinished business and new business.

The meeting of the Council is open to the public. Records will be kept of the proceedings and will be available for public inspection at the office of the National Advisory Council on Women's Educational Programs, 2000 L Street NW., Suite 568, Washington, DC 20036.

Signed at Washington, DC, on December 19, 1985.

**Sally A. Todd,**

*Executive Director.*

[FR Doc. 85-30343 Filed 12-23-85; 8:45 am]

BILLING CODE 4000-01-M

## DEPARTMENT OF ENERGY

### Office of Assistant Secretary for International Affairs and Energy Emergencies

### Proposed Subsequent Arrangement

Pursuant to section 131 of the Atomic Energy Act of 1954, as amended (42 U.S.C. 2160) notice is hereby given of a proposed "subsequent arrangement".

The subsequent arrangement involves the shipment to U.S. Department of Energy facilities of fuel rods from a research reactor containing approximately 25,500 kilograms of

natural uranium for reprocessing and storage of recovered nuclear materials.

In accordance with section 131 of the Atomic Energy Act of 1954, as amended, it has been determined that this subsequent arrangement will not be inimical to the common defense and security.

This subsequent arrangement will take effect no sooner than fifteen days after the date of publication of this notice.

Dated: December 18, 1985.

For the Department of Energy.

George J. Bradley, Jr.,

*Acting Assistant Secretary for International Affairs and Energy Emergencies.*

[FR Doc. 85-30329 Filed 12-23-85; 8:45 am]

BILLING CODE 6450-01-M

## Finding of No Significant Impact, Remedial Action at the Lakeview Uranium Mill Tailings Site, Lakeview, OR

**AGENCY:** Department of Energy.

**ACTION:** Finding of No Significant Impact.

**SUMMARY:** The Department of Energy (DOE) has prepared an environmental assessment (DOE/AE-0271) on the proposed remedial action at the inactive uranium milling site located on private property owned by Precision Pine Company in Lakeview, Oregon. Based on the analyses in the EA, DOE has determined that the proposed action does not constitute a major Federal action significantly affecting the quality of the human environment within the meaning of the National Environmental Policy Act (NEPA) of 1969 (42. U.S.C. 4321 *et seq.*).

### Background.

On November 8, 1978, the Uranium Mill Tailings Radiation Control Act (UMTRCA), Pub. L. 95-604, was enacted in order to address a Congressional finding that uranium mill tailings located at inactive processing sites may pose a potential health hazard to the public. On November 8, 1979, DOE designated 24 inactive processing sites for remedial action under Title I of UMTRCA including the inactive uranium mill tailings site at Lakeview, Oregon (44 FR 74892).

UMTRCA charges the Environmental Protection Agency (EPA) with the responsibility for promulgating remedial action standards for inactive mill sites. The purpose of these standards is to protect the public health and safety and the environment from radiological and non-radiological hazards associated with residual radioactive materials at the sites. The final standards (40 CFR Part 192) were published on January 5, 1983, and became effective on March 7, 1983. The DOE has proposed a plan of remedial action that will satisfy the EPA standards. Under UMTRCA, the DOE and the State of Oregon entered into a cooperative agreement, effective June 29, 1984, for remedial action at the Lakeview designated site. Under the agreement, the State of Oregon must concur with the remedial action plan to be developed for the site, comment on the EA, assist in site characterization and disposal site selection, participate in and comment upon the final design, and provide 10 percent of site acquisition, engineering, and construction costs. The DOE will provide the remaining 90 percent of these costs.

All remedial actions must be selected and performed with the concurrence of the Nuclear Regulatory Commission (NRC).

### Project Description

The Lakeview mill site and tailings are located in south-central Oreon, in Lake County. The closest town is Lakeview, one mile to the southeast. Klamath Falls is about 96 miles west of the site. The site is about 16 miles north of the California-Oregon border.

The 258-acre Lakeview site, as designated by the DOE, is located in portions of Sections 3, 4, 9, and 10, Township 39 South, Range 20 East, Washington Meridian, at 42 deg 12 min 43 sec north latitude and 120 deg 22 min 09 sec west longitude.

The mill was built in 1958 and operated by the Lakeview Mining Company. The owners of this firm were also the owners of the Gunnison Mining Company, which operated the mill at Gunnison, Colorado. Both companies were acquired in 1961 by Kerr-McGee Oil Industries through its subsidiary, Kermac Nuclear Fuels Corporation.

During the 1958 to 1961 period of operation, 130,000 tons of ore averaging 0.15 percent $U_3O_8$ were processed; 171 tons of uranium oxide were sold to the Atomic Energy Commission (AEC). The mill processed ores from the White King and Lucky Lass mines located in southern Lake County, Oregon.

Between 1960 and 1968 the property had five owners. In 1968, the Lakeview site was obtained by Atlantic Richfield Company, which, in 1974, initiated and performed a cleanup operation on the site under a plan approved by the Oregon State Health Division. By 1977 the mill buildings and their immediate surroundings had been decontaminated to meet the then existing requirements of the Oregon Regulations for the Control of Radiation. The property was sold on March 8, 1978, to Precision Pine Company, the current owner, which uses the site and remaining structures as a lumber mill and stockpile for sawdust and scrap waste.

The total designated site covers 258 acres. This includes the active sawmill area, the tailings (30 acres), and the evaporation ponds (approximately 69 acres). The tailings have been stabilized with an earthen cover 18 to 24 inches thick. The pile is almost square with a very flat surface, although the stabilization cover has depressions that trap moisture. This cover supports a vigorous growth of vegetation. The average depth of the tailings, including cover, is estimated to be seven feet. An earthen dike was formed around the tailings area before the tailings were originally deposited. The tailings have been fenced with a hogwire type of fence and radiation signs are posted. There is also a barbed-wire fence around the entire site.

The mill building and other structures reportedly were decontaminated, along with the machinery and other salvageable items that have been removed. Materials that were not salvageable or were not able to be decontaminated have been placed on the southeastern portion of the tailings pile and stabilized in the same manner as the remainder of the tailings.

Prior to initiation of the EA, the DOE conducted a preliminary assessment of the tailings pile at Lakeview and a review of possible remedial actions. The geotechnical evaluation of the nearby area identified seven active faults or fault zones with potential for disruption of the site. The are also was identified as having high subsurface heat flows with three hot springs and more than 40 geothermal wells nearby. These factors together indicated the existence of a potential hazard which could jeopardize the integrity of on-site stabilization during the project's design life (up to 1000 but in any case not less than 200 years). Because of this potential hazard, the DOE, in concert with the State of Oregon, embarked on a process for the selection of alternate disposal sites. This process investigated several areas for safe disposal of the tailings in compliance with the EPA standards. During the process the public had extensive opportunity to provide input through a local task force. On the basis of this cooperative public process, two sites were selected for detailed analysis in the EA. The DOE initiated, and is continuing, an extensive date gathering program at the tailings site and both alternate disposal sites.

### Proposed Action

The proposed action (Alternative 1) is decontamination of the existing Lakeview mill site with relocation to, and stabilization at, the Collins Ranch site. Located approximately six miles north-northwest of the existing tailing pile on lands adjacent to the Fremont National Forest, the Collins Ranch site (approximately 20 acres) ranges in elevation from 4,886 to 5,000 feet and is characterized by gently sloping terrain without perennial streamflow. Contaminated materials from around the mill site, evaporation ponds, and vicinity properties would be added to the pile and surface runoff diversion ditches would be constructed. The tailings pile would be constructed partially below grade, contoured to be nearly level on top (2 percent slope), and would have 5:1 sideslopes (20 percent). Lesser contaminated materials would be placed on top of the mill tailings thereby reducing the compacted earthen cover to one foot thick. This cover would be capped with a two-foot-thick layer of rock to protect the site from wind and water erosion, limit penetration by plants and animals, and prevent inadvertent human intrusion. A rock-soil matrix would be placed on the erosion protection cover to promote revegetation of the site.

Several alternatives to the proposed action were analyzed in the EA. These include no action (Alternative 2) and decontamination of the Lakeview site and relocation of the wastes to the Flynn Ranch site 26 miles east of the Lakeview site (alternative 3).

### Comments Received

The DOE announced the availability of the EA in the **Federal Register** on May 20, 1985 (50 FR 20826). A 39-day period was provided for public review and comment. Comments were received from the State of Oregon Department of Energy, Environmental Evaluation Branch of the U.S. Environmental Protection Agency, U.S. Nuclear Regulatory Commission, U.S. Department of the Interior, U.S. Department of Agriculture, Lake County Chamber of Commerce, Lake County Task Force on Uranium Mill Tailings Disposal, Forelaws on Board, Fort Bidwell Indian Community Council, and from 27 concerned citizens in the area.

The major concerns expressed relate to the impacts based on specific design details of the stabilized pile, impacts from radiation released during remedial action, health effects from no-action, transportation impacts during remedial action, seismic affects on the stabilized pile, air quality impacts, awarding contracts to local companies, and the potential impacts to historical and cultural significance of the Flynn Ranch area to the Fort Bidwell Indians. All comments received have been reviewed and specific responses are being provided to the commentors.

### Finding

The EA focused on the environmental and economic impacts resulting from the proposed remedial action and identified mitigation measures that will be implemented to reduce these effects to an insignificant level. The Finding of No Significant Impact of stabilization at the Collins Ranch site is based on the following findings which are supported by the information and analyses in the EA:

- Radiation release—the increased radiation exposure above background levels to the general population during the remedial action will be extremely low. The estimated excess health effects were projected to be 0.00019 additional cancer death in 10 years (0.019 additional cancer death in 1000 years). (With no action, these projections were increased to 0.0081 and 0.81, respectively). The projected excess health effects for remedial action workers was 0.0027.

The DOE will closely monitor the release of radon and particulates during the remedial action. The release of radon and contaminated particulates will be reduced by dampening contaminated materials with water, by limiting contaminated material-handling operations during adverse weather conditions, and by using trucks with tight-fitting tailgates and covers when the material is to be moved. All wastewater streams will be isolated from surface-water systems by drainage-control methods.

Human exposure to residual radioactive material will be reduced further by restricting access, by providing worker training program, and by the use of appropriate monitoring and protective equipment by the remedial action workers.

Radiation impacts from the proposed remedial action activities are insignificant.

- Air quality—The site and surrounding area are in attainment of the National Ambient Air Quality Standards for hydrocarbons (HC), nitrogen dioxide ($NO_2$), sulfur dioxide ($SO_2$), carbon monoxide (CO), and total suspended particulates (TSP). Dispersion modeling indicated that combustion emissions from construction equipment will not exceed Federal primary or secondary standards.

However, TSP (24-hour) could exceed the Federal secondary standards (150 microg/$m^3$) and the 24-hour primary standard (260 microg/$m^3$) for a short period of time. The modeling used was conservative in that mitigation measures were credited with only a 50-percent reduction in particulate emissions from the site and the modeling assumed extremely stable wind conditions (i.e., very limited pollutant dispersion). On this basis it was determined that the air-quality impacts of the proposed action will be temporary and will not be significant.

- Surface-water quality—During remedial action, a low possibility exists that surface waters (i.e., Hammersley Creek) would experience an increase in contaminants due to the relocation of tailings and contaminated materials. These impacts would be minimal because of water retention facilities and erosion control measures.

Surface waters would not be impacted after remedial action because the tailings will be isolated from surface-water contact by a one-foot-thick compacted radon cover, a two-foot-thick rock layer for erosion control purposes, and a rock-soil matrix to promote revegetation of the site. A system of drainage diversion ditches will also be installed to control surface runoff. In addition, the nearest perennial stream to the Collins Ranch site is 3000 feet distant.

- Ground-water quality—The proposed remedial action would eliminate further ground-water contamination at the former mill site by removing the principal source of contamination. The design features of the relocated stabilized pile at the Collins Ranch site would essentially prevent further contamination of the shallow aquifers in the area resulting from uranium mill tailings. A two-foot-thick recompacted layer of silty/clayey material will provide the foundation layer beneath the tailings pile. The tailings material will be covered with a 20-foot-thick layer of lesser contaminated materials, averaging 14 pCi/$m^2$ sec. A one-foot-thick compacted soil radon cover, a two-foot-thick rock cover, and a rock-soil matrix over the cover would further inhibit infiltration of precipitation and thereby inhibit potential contamination of the ground water. The shallow ground water in the area is not presently used for domestic consumption. The deeper aquifers would not be effected by the proposal remedial action.

- Threatened and endangered species—No threatened or endangered species, as identified by the U.S. Fish

and Wildlife (FWS), have been identified at or near the Collins Ranch site or the former mill site. The DOE has consulted with state and Federal agencies concerned with the protection of threatened or endangered species and conducted field surveys of the proposed disposal site. No impacts to threatened or endangered species would occur.

• Cultural resources—A class III archeological field reconnaissance survey was conducted at the Collins Ranch site and proposed borrow area. No archaeological sites were identified at the Collins Ranch site, however two historical sites have been identified alongside of the roadway to the borrow site. One of the sites, a hstoric can and bottle dump, does not have sufficient integrity of material remains to warrant further study. The second historic site, a dugout with associated corral, fence, road, and dump, dates back to approximately the turn of the century. This a site appears to meet the criteria for the National Register (36 CFR 800) and will be avoided. The Oregon State Historical Preservation Office (SHPO) has been notified of these findings. Mitigative measures have been implemented to avoid this historic site, and thus, this site would not be impacted during or after remedial action.

• Transportation—Utilization of the Collins Ranch disposal site would require use of a private lumber haul road, currently owned by Fremont Sawmill, which runs in a northwesterly direction from behind the current tailings site, to within one mile of the proposed site. The remainder of the haul distance will be on a U.S. Forest Service road. The haul road will be upgraded and maintained to meet DOE and Forest Service standards. Traffic on these roads is minimal and accident rates are low. No significant impacts resulting from project activities would occur.

• Seismicity—The Collins Ranch disposal site is in a moderate seismic risk zone. The nearest active fault is the Goose Lake graben fault zone, approximately four miles east of the disposal site. Based on the Maximum Credible Earthquake (MCE) calculated for the site and the potential ground accelerations, the Collins ranch disposal site has been designed to withstand these events in compliance with the standard. Thus, potential impacts from seismic events are insignificant.

• Floodplains and wetlands—The Collins Ranch site is not within a floodplain or wetlands area. However, removal of contaminated materials from within the 100-year floodplain during the rerouting of Hammersley Creek will require the elimination of a limited lacustrine, unconsolidated bottom wetlands maintained by seasonal flooding within the creek channel. This activity will be accomplished in such a manner as to minimize environmental harm through consultation with the U.S. Army Corps of Engineers, Oregon Division of State Lands, and the Lake County Planning Department.

Single copies of the EA are available from: John Themelis, UMTRA Project Manager, U.S. Department of Energy, UMTRA Project Office, 5301 Central Avenue NE., Suite 1700, Albuquerque, New Mexico 87108, (505) 844–3941.

**FOR FURTHER INFORMATION CONTACT:** Robert J. Stern, Director, Office of Environmental Guidance EH–23, Office of the Assistant Secretary for Environment, Safety, and Health, Room 3G–092, Forrestal Building, U.S., DOE, Washington, D.C. 20585, (202) 252–4600.

Issued at Washington, D.C. December 16, 1985.

**William A. Vaughan,**

*Assistant Secretary Environment, Safety, and Health.*

[FR Doc. 85–30327 Filed 12–23–85; 8:45 am]

BILLING CODE 6450–01–M

## Floodplain and Wetlands Statement of Findings; Remedial Action at the Lakeview Uranium Mill Tailings Site, Lakeview, OR

**AGENCY:** Department of Energy.

**ACTION:** Floodplain and Wetlands Statement of Findings.

This is a Statement of Findings, prepared pursuant to Executive Orders 11988 and 11990, and 10 CFR Part 1022, Compliance with Floodplain/Wetlands Environmental Review Requirements.

Under authority granted by the Uranium Mill Tailings Radiation Control Act of 1978 (Pub. L. 95–604, dated November 8, 1978), the U.S. Department of Energy (DOE) proposes to clean up the residual radioactive wastes and other contaminated materials at the inactive uranium mill tailings site located just north of Lakeview, Oregon, and relocate these materials to a new disposal site (Collins Ranch site) six miles northwest.

The proposed remedial action will move and stabilize the radioactive wastes according to a plan to be concurred in by the U.S. Nuclear Regulatory Commission and the State of Oregon. The proposed remedial action is in conformance with the Environmental Protection Agency (EPA) Standards for Cleanup of Inactive Uranium Processing Sites (40 CFR 192).

Most of the radioactively contaminated materials (628,000 cubic yards) are located on the edge of the 100-year floodplain of Hammersley Creek. Hammersely Creek traverses the former mill site. As reported in the Environmental Assessment (EA) (UMTRA–DOE/AL–0271), Appendix I, Floodplains and Wetlands Assessment, the U.S. Army Corps of Engineers indicated that wetlands were not present within the area of construction activities. However, since publication of the EA, the U.S. Fish and Wildlife Service indicated that wetlands exist to a limited extent within the confines of Hammerseley Creek. These wetlands are predominately lacustrine, unconsolidated wetlands maintained by seasonal flood events. Therefore, the remedial action involves action in a floodplain/wetlands.

The principal feature of the proposed action is the transportation of tailings and other contaminated soils (from the floodplain, adjacent windblown areas, and the evaporation ponds area) to the Collins Ranch site approximately six miles northwest of the former mill site. The Collins Ranch site is well out of the reach of the nearest perennial stream and is not subject to flood events. At the Collins Ranch site, the materials will be placed on a prepared surface partially below grade, and contoured into an embankment. Below grade excavation would extend to an average depth of five feet. The upper 15 feet of the stabilized embankment would consist of lesser contaminated soils from the mill site. The tailings and contaminated material would be covered with a one-foot-thick earthen cover to control radon exhalation and water infiltration. This cover would be topped with a two-foot-thick layer of graded rock for erosion protection, and a rock-soil matrix cover to promote revegetation of the site.

The former mill site would be restored with uncontaminated fill to conform with the surrounding terrain, recontoured as necessary for service drainage and revegetated.

Specific construction activities related to the floodplain and wetlands area include: (1) Removal of about 628,000 cubic yards of contaminated soils; (2) rerouting of approximately 2,600 feet of Hammersley Creek and fill of the abandoned channel; (3) filling in, grading, and revegetating the floodplain and wetlands area where contaminated soils were excavated.

The DOE examined three alternatives for the remedial actions in the EA. The DOE's proposed action (Alternative 1 in the EA) is decontamination of the Lakeview mill site and relocation of the wastes to the Collins Ranch site. The two other alternatives analyzed in the

EA include: (2) no action; and (3) relocation of the wastes to the Flynn Ranch site.

Pursuant to 10 CFR Part 1022, the DOE prepared a floodplain and wetlands assessment. This assessment was published as Appendix I, Floodplains and Wetlands Assessment, in the EA.

The remedial action has been designed to conform to applicable Federal and state regulations. Before construction begins, all applicable permits and approvals, such as those required under section 404 of the Clean Water Act, will be obtained from the U.S. Army Corps of Engineers, Oregon Division of State Lands, and other agencies having jurisdiction.

Initial consultation with the agencies has taken place, and as a result, the design has been modified to minimize environmental impacts. Principally, rerouting requires the establishment of a seed base for a grass lining to accommodate the flow velocities during the 500-year flood event.

The no action alternative would leave contaminated material in the floodplain. Cleanup of this material (alternatives 1 and 3) inherently involves action within the floodplain and wetlands areas. On the basis of the flood plain and wetlands assessment, the DOE has determined that there is no practicable alternative to the proposed activities in the floodplain and wetlands, and that the proposed action has been designed to minimize potential harm to or within the floodplain and wetlands.

Issued at Washington D.C., December 16, 1985.

**William A.Vaughan,**

*Assistant Secretary, Environment, Safety, and Health.*

[FR Doc. 85-30328 Filed 12-23-85; 8:45 am]

BILLING CODE 6450-01-M

## ENVIRONMENTAL PROTECTION AGENCY

[A-9-FRL-2943-8]

### Approval of Prevention of Significant Air Quality Deterioration (PSD) Permit to Pacific Thermonetics, Inc. (EPA Project Number SFB 85-02)

**AGENCY:** Environmental Protection Agency (EPA), Region 9.

**ACTION:** Notice.

**SUMMARY:** Notice is hereby given that on December 6, 1985 the Environmental Protection Agency issued a PSD permit under EPA's federal regulations 40 CFR 52.21 to the applicant named above. The PSD permit grants approval to construct a combined-cycle cogeneration plant consisting of two General Electric Frame 7 gas turbines, each followed by a heat recovery steam generator (HRSG) and an extraction-type steam turbine. The facility will be located at the existing C&H Sugar Refinery Plant in Crockett, Contra Costa County, California. The permit is subject to certain conditions, including an allowable emission rate as follows: $NO_x$ (gas turbines)—25 ppmv at 15% when firing natural gas and 42 ppmv at 15% when firing fuel oil (fuel oil firing is limited to 330 hrs/yr), $NO_x$ (duct burners—0.1 lb/MMBtu, and particulate matter—0.04 gr/DSCF.

**FOR FURTHER INFORMATION CONTACT:** Copies of the permit are available for public inspection upon request; address request to: Anita Tenley (A-3-1), U.S. Environmental Protection Agency, Region 9, 215 Fremont Street, San Francisco, CA 94105, (415) 974-8240, FTS 454-8240.

**SUPPLEMENTARY INFORMATION:** Best Available Control Technology (BACT) requirements include the use of multiple combustion nozzles, low sulfur fuel oil, limited hours of fuel oil firing, Lo-$NO_x$ burners, and the use of natural gas in the HRSG burners.

**DATE:** The PSD permit is reviewable under section 307(b)(1) of the Clean Air Act only in the Ninth Circuit Court of Appeals. A petition for review must be filed by February 24, 1986.

**Carl C. Kohnert,**

*Acting Director, Air Management Division, Region 9.*

[FR Doc. 85-30347 Filed 12-23-85; 8:45 am]

BILLING CODE 6560-50-M

[Docket No. ECAO-CD-81-1; A-4-FRL 2935-2]

### Draft Air Quality Criteria for Ozone and Other Photochemical Oxidants

**AGENCY:** Environmental Protection Agency.

**ACTION:** Notice of Availability of Second External Review Drafts of Volumes I and V of the Air Quality Criteria for Ozone and Other Photochemical Oxidants.

**SUMMARY:** The second external review draft of Volumes I and V of the revised criteria document for ozone and other photochemical oxidants are being made available for public review and comment.

**DATES:** The Agency will make these volumes available on or about December 16, 1985. Comments must be postmarked by February 17, 1986.

**ADDRESSES:** To obtain a copy of these draft volumes, interested parties should contact the ORD Publications Center, CERI-FRN, U.S. Environmental Protection Agency, 26 W. St. Clair St., Cincinnati, OH 45268, 513/569-7562, (FTS: 684-7562), and request the second external review drafts of Volumes I and V of the revised Air Quality Criteria for Ozone and Other Photochemical Oxidants. Please provide your name, mailing address, and the EPA document number, EPA-600/8-84-020B. The draft volumes will also be available for public inspection and copying at the EPA library, EPA headquarters, Waterside Mall, 401 M Street, SW, Washington, DC 20460.

Comments on these draft volumes should be sent in writing to the: Project Manager, Air Quality Criteria for Ozone/Oxidants, Environmental Criteria and Assessment Office (MD-52), U.S. Environmental Protection Agency, Research Triangle Park, NC 27711.

**FOR FURTHER INFORMATION CONTACT:** Ms. Diane Ray, U.S. Environmental Protection Agency, Environmental Criteria and Assessment Office (MD-52), Research Triangle Park, NC 27711, (919) 541-3637.

**SUPPLEMENTARY INFORMATION:** After close of the public comment period for these volumes, the Clean Air Scientific Advisory Committee (CASAC) of the Agency's Science Advisory Board (SAB) will hold a public meeting to review the volumes. Advance notice of the time and place of the meeting will be provided in a subsequent **Federal Register** notice.

A copy of the volumes, all public comments received, and the Agency's response to these comments will be included in the docket established for the revision of the ozone/oxidants document (Docket No. ECAOCD-81-1). The docket is available for inspection and copying between the hours of 8:00 a.m. and 4:00 p.m. at EPA headquarters in the Central Docket Section (A-130), Gallery 1, West Tower, Waterside Mall, 401 M Street, SW, Washington, DC 20460.

Dated: November 25, 1985.

**Thomas R. Hauser,**

*Acting Assistant Administrator for Research and Development.*

[FR Doc. 85-30464 Filed 12-23-85; 8:45 am]

BILLING CODE 6560-50-M

## FEDERAL DEPOSIT INSURANCE CORPORATION

### Statement of Policy Regarding Disclosure by the FDIC of Statutory Enforcement Actions

**AGENCY:** Federal Deposit Insurance Corporation.

**ACTION:** Change in effective date.

**SUMMARY:** The Federal Deposit Insurance Corporation ("FDIC") is postponing implementation of its May 6, 1985 statement of policy, scheduled to become effective on January 1, 1986, which provides for the FDIC to publicly disclose the final orders it issues in conjunction with formal enforcement actions. In light of the decision by the Office of the Comptroller of the Currency ("OCC") to propose comprehensive disclosure rules, the FDIC's Board of Directors feels that it would be beneficial to review its disclosure policy and to work with the OCC on a uniform disclosure approach. Therefore, the FDIC is delaying the effective date of its statement of policy from January 1 to July 1, 1986.

**EFFECTIVE DATE:** The effective date of the statement of policy published May 17, 1985, is changed from January 1, 1986, to July 1, 1986.

**FOR FURTHER INFORMATION CONTACT:** Robert F. Storch, Planning and Program Development Specialist, Division of Bank Supervision, Federal Deposit Insurance Corporation, Washington, DC 20429, telephone (202) 389-4761.

**SUPPLEMENTARY INFORMATION:** On May 6, 1985, the Board of Directors of the FDIC adopted a statement of policy, scheduled to become effective on January 1, 1986, which provides for the FDIC to publish and make available to the public in agency press releases the names of all banks and persons to whom the FDIC has issued final orders in conjunction with formal enforcement actions. In addition, brief descriptions of the nature of the enforcement actions taken and summaries of the orders are to be incorporated into the press releases for each action disclosed. This policy applies to insurance termination orders, cease-and-desist orders, removal orders, suspension orders, civil money penalty orders, and capital directives.

On October 30, 1985, the OCC published for a 90-day comment period a comprehensive disclosure regulation that would be applicable to all national banks. 50 *FR* 45372 (1985). In light of this action by the OCC, the FDIC's Board of Directors feels that it would be beneficial to review its disclosure policy and to work with the OCC on a uniform disclosure approach. Therefore, the FDIC is delaying the effective date of its policy on disclosure of enforcement actions for six months.

Accordingly, the Statement of Policy Regarding Disclosure by the FDIC of Statutory Enforcement Actions that was adopted by the FDIC's Board of Directors on May 6, 1985 (50 *FR* 20609 (May 17, 1985)) is amended by removing the date "January 1, 1986" from the "**EFFECTIVE DATE**" paragraph on page 20609 and from seventh paragraph of page 20619 and inserting in its place the date "July 1, 1986."

By order of the Board of Directors this 16th day of December 1985.

Federal Deposit Insurance Corporation.

**Hoyle L. Robinson,**

*Executive Secretary.*

[FR Doc. 85-30240 Filed 12-23-85; 8:45 am]

BILLING CODE 6714-01-M

## FEDERAL MARITIME COMMISSION

### Agreement(s) Filed

The Federal Maritime Commission hereby gives notice of the filing of the following agreement(s) pursuant to section 5 of the Shipping Act of 1984.

Interested parties may inspect and obtain a copy of each agreement at the Washington, DC Office of the Federal Maritime Commission, 1100 L Street, NW., Room 10325. Interested parties may submit comments on each agreement to the Secretary, Federal Maritime Commission, Washington, DC 20573, within 10 days after the date of the **Federal Register** in which this notice appears. The requirements for comments are found in § 572.603 of Title 46 of the Code of Federal Regulations. Interested persons should consult this section before communicating with the Commission regarding a pending agreement.

Agreement No.: 224-003945-005.

Title: Oakland Terminal Agreement.

Parties: Port of Oakland (Port), Maersk Line Pacific, Ltd. (Maersk).

Synopsis: This agreement amends the basic agreement between the parties whereby the Port assigned certain marine terminal facilities in the Port's Outer Harbor Terminal Area to Maersk. The amendment extends the time to March 31, 1986 in which Maersk may exercise its right to extend the term of the basic agreement for an additional five years.

Agreement No.: 202-010390-010.

Title: United States Atlantic & Gulf/Ecuador Freight Association.

Parties: Ecuadorian Line, Inc., Lykes Bros. Steamship, Inc., Transportes Navieros Equatorianos.

Synopsis: The proposed amendment would reduce the notice period for a member's independent action from seven calendar days to three business days. It would also provide for amendment of any conference tariff to include the new rate or service item to also be effective not earlier than three business days after receipt of notice and would alter the time for a member to withdraw, review or extend its independent action to reflect a period beyond three business days rather than seven calendar days.

Agreement No.: 202-010689-013.

Title: Transpacific Westbound Rate Agreement.

Parties: American President Lines, Ltd., Evergreen Marine Corp., Hanjin Container Lines, Ltd., Japan Line, Ltd., Kawasaki Kisen Kaisha, Ltd., Korean Marine Transport Co., Ltd., Lykes Bros. Steamship Co., Inc., A.P. Moller-Maersk Line, Mitsui O.S.K. Lines, Ltd., Neptune Orient Lines, Ltd., Nippon Yusen Kaisha, Ltd., Orient Overseas Container Line, Inc., Sea-Land Service, Inc., Showa Line, Ltd., United States Lines, Inc., Yamashita-Shinnihon Steamship Co. Ltd.

Synopsis: The proposed amendment would make clear that an increase in agreement rates would operate to increase an independent action rate to the agreed level (in the absence of notification to the manager to the contrary) only as to independent action rates which have become effective.

Agreement No.: 206-010715-001.

Title: Eurospan.

Parties: North Europe-U.S. Gulf Freight Association, Gulf-European Freight Association.

Synopsis: The proposed amendment would add authority for the parties to establish practices in connection with the self-policing and enforcement of their obligations under their respective conference agreements. The parties have requested a shortened review period.

Agreement No.: 224-010863.

Title: Tampa Terminal Agreement.

Parties: Tampa Port Authority (Authority), St. Philip Towing & Transportation Co. (St. Philip).

Synopsis: This agreement provides for the lease by the Authority to St. Philip of 30,000 sq. ft. of uplands and 10,340 sq. ft. of submerged land including a timber dock and a 3,775 sq. ft. building. St. Philip will use the facility to dock tugs and/or barges in performance of tug and/or barge-tug operations which includes the holding out to perform common carrier services in both interstate offshore and foreign

commerce. The term of the agreement is for 15 years.

Dated: December 19, 1985.

By Order of the Federal Maritime Commission.

**Mary F. Whitmore,**

*Assistant to the Secretary.*

[FR Doc. 85-30380 Filed 12-23-85; 8:45 am]

BILLING CODE 6730-01-M

## FEDERAL MEDIATION AND CONCILIATION SERVICE

### Labor-Management Cooperation Program; Application Solicitation

**AGENCY:** Federal Mediation and Conciliation Service.

**ACTION:** Final FY 1986 Program Announcement/Application Solicitation.

**SUMMARY:** The Federal Mediation and Conciliation Service (FMCS) published the draft Fiscal Year 1986 Program Announcement for the Labor-Management Cooperation Program in the November 14, 1985, issue (50 FR 220) of the **Federal Register.** No written public comments were received, and no changes have been made.

**FOR FURTHER INFORMATION CONTACT:** Peter L. Regner, Director, Labor-Management Grant Programs, Federal Mediation and Conciliation Service, 2100 K Street, NW., Washington, DC 20427.

### Labor-Management Cooperation Program Application Solicitation—FY 1986

*A. Introduction*

The following is the final solicitation for the Fiscal Year 1986 cycle of the Labor-Management Cooperation Program. These guidelines represent the continuing efforts of the Federal Mediation and Conciliation Service to implement the provisions of the Labor-Management Cooperation Act of 1978 which was initially implemented in Fiscal Year 1981. The Act generally authorizes FMCS to provide assistance in the establishment and operation of plant, area, public sector, and industry-wide labor and management committees which:

(A) Have been organized jointly by employers and labor organizations representing employees in that plant, area, government agency, or industry; and

(B) Are established for the purpose of improving labor management relationships, job security, organizational effectiveness, enhancing economic development or involving workers in decisions affecting their jobs including improving communication with respect to subjects of mutual interest and concern.

The Program Description and other sections that follow as well as a separately published FMCS Financial and Administrative Grants Manual make up the basic guidelines, criteria, and program elements a potential applicant for assistance under this program must know in order to develop an application for funding consideration for either a plant, area-wide, industry, or public sector labor-management committee. Directions for obtaining an application kit may be found in Section H. A copy of the Labor-Management Cooperation Act of 1978 follows this solicitation. The Act should be reviewed in conjunction with this solicitation.

*B. Program Description*

Objectives

The Labor-Management Cooperation Act of 1978 identifies the following seven general areas for which financial assistance would be appropriate:

(1) To improve communications between representatives of labor and management;

(2) To provide workers and employers with opportunities to study and explore new and innovative joint approaches to achieving organizational effectiveness;

(3) To assist workers and employees in solving problems of mutual concern not susceptible to resolution within the collective bargaining process;

(4) To study and explore ways of eliminating potential problems which reduce the competitiveness and inhibit the economic development of the plan, area, or industry;

(5) To enhance the involvement of workers in making decisions that affect their working lives;

(6) To expand and improve working relationships between workers and managers; and

(7) To encourage free collective bargaining by establishing continuing mechanisms for communication between employers and their employees through Federal assistance to the formation of labor-management committees.

The primary objective of this program is to encourage and support the establishment and operation of joint labor-management committees to carry out specific objectives that meet the aforementioned general criteria. The term "labor" refers to employees represented by a labor organization and covered by a formal collective bargaining agreement. These committees may be found at either plant (worksite), area, industry, or public sector levels. A plant or worksite committee is generally characterized as restricted to one or more organizational or productive units operated by a single employer. An area committee is generally composed of multiple employers of diverse industries as well as multiple labor unions operating within and focusing upon city, county, contiguous multicounty, or statewide jurisdictions. An industry committee generally consists of a collection of agencies or enterprises and related unions producing a common product or service in the private sector on a local, state, regional, or nationwide level. A public sector committee consists of government employees and managers in one or more units of a local or state government. Those employees must be covered by a formal collective bargaining agreement. Employees covered by so-called "meet and confer" agreements are not eligible under this program. In deciding whether an application is for an area or industry committee, consideration should be given to the above definitions as well as to the focus of the committee.

IN FY86, competition will be open to plant, area, private industry, and public sector committees. In-plant committee applications should offer an innovative or unique effort. All application budget requests should focus directly on supporting the committee. Applicants should avoid seeking funds for activities that are clearly available under other Federal grant programs (e.g., job training).

Required Program Elements

1. *Problem Statement.* The application, which should have numbered pages, must discuss in detail what specific problem(s) face the plant, area, government, or industry and its workforce that will be addressed by the committee. Applicants must document the problems using as much relevant data as possible and discuss the full range of impacts these problems could have or are having on the plant, government, area, or industry. An industrial or economic profile of the area and workforce might prove useful in explaining the problems. This section basically discusses WHY the effort is needed.

2. *Results or Benefits Expected.* By using specific goals and objectives, the application must discuss in detail WHAT the labor-management committee as a demonstration effort will accomplish during the life of the grant. While a goal of "improving communication between employers and employees" may suffice as one overall

goal of a project, the objectives must, whenever possible, be expressed in measurable terms. Applicants should focus on the impacts or changes that the committee's efforts will have. Existing committees should focus on *expansion* efforts/results expected from FMCS funding. The goals, objectives, and projected impacts will become the foundation for future monitoring and evaluation efforts.

3. *Approach.* This section of the application specifies HOW the goals and objective will be accomplished. At a minimum, the following elements must be included in all grant applications:

(a) A discussion of the strategy the committee will employ to accomplish its goals and objectives;

(b) A listing, by name and title, of all existing or proposed members of the labor-management committee. The application should also offer a rationale for the selection of the committee members (e.g. members represent 70% of the area or plant workforce).

(c) A discussion of the number, type, and role of all committee staff persons. Include proposed position descriptions for all staff that will have to be hired as well as résumés for staff already on board;

(d) In addressing the proposed approach, applicants must also present their justification as to why Federal funds are needed to implement the proposed approach;

(e) A statement of how often the committee will meet as well as any plans to form subordinate committees for particular purposes; and

(f) For applications from existing committees (i.e., in existence at least 12 months prior to the submission deadline), a discussion of the past efforts and accomplishments and how they would integrate with the proposed future expanded effort.

4. *Major Milestone.* This section must include an implementation plan that indicates what major steps, operating activities, and objectives will be accomplished as well as a timetable for WHEN they will be finished. A milestone chart must be included that indicates what specified accomplishments (process and impact) will be completed by month over the life of the grant. The chart should identify months as "month 1, 2" etc., rather than by name of month as the grant start date will not be determined until all applications are reviewed. The accomplishment of these tasks and objectives, as well as problems and delays therein, will serve as the basis for quarterly progress reports to FMCS.

5. *Evaluation.* Applicants must provide for an external evaluation or internal assessment of the project's success in meeting its goals and objectives.

An evaluation plan must be developed which will briefly discuss what basic questions or issues the assessment would examine and what baseline data the committee staff would already have/or will gather for the assessment. This section should be written with the application's own goals and objectives clearly in mind and the impacts or changes that the effort is expected to cause.

6. *Letters of Commitment.* Applications must include current letters of commitment from *all* proposed or existing committee participants and chairpersons. These letters should indicate that the participants support the application and are willing to personally attend scheduled committee meetings. A blanket letter signed by a committee chairperson on behalf of all members is not acceptable.

7. *Other Requirements.* Applicants are also responsible for the following:

(a) The submission of data indicating approximately how many employees will be covered or represented through the labor-management committee;

(b) From existing committees, a copy of the existing staffing levels, a copy of the by-laws, a breakout of annual operating costs and identification of all sources and levels of current financial support;

(c) A detailed budget narrative based on plicies and procedures contained in the FMCS Financial and Administrative Grants Manual;

(d) An assurance that the labor-management committee will not interfere with any collective bargaining agreements; and

(e) An assurance that written minutes of all committee meetings will be prepared and made available to FMCS.

Selection Criteria

The following criteria will be used in the scoring and selection of applications for award:

(1) The extent to which the application has clearly identified the problems and jutified the needs that the proposed project will address.

(2) The degree to which appropriate and measurable goals and objectives have been developed to address the problems/needs of the area. For existing committees, the extent to which the committee will focus on expanded efforts.

(3) The feasibility of the approach proposed to attain the goals and objectives of the project and the perceived likelihood of accomplishing the intended project results. For in-plant applicants, this section will address the degree of innovation or uniqueness of the proposed effort.

(4) The appropriateness of committee membership and the degree of commitment of these individuals to the goals of the application.

(5) The feasibility and thoroughness of the implementation plan in specifying major milestones and target dates.

(6) The cost effectiveness and fiscal soundness of the application's budget request, as well as the application's fiscal feasibility vs. its goals and approach.

(7) The overall feasibility of the proposed project in light of all of the information presented for consideration and quality of the application; and,

(8) The cost value to the government of the application in light of the overall objectives of the Labor-Management Cooperation Act of 1978. This includes such factors as innovations, site location, and other qualities that enhance an applicant's value in encouraging the labor-management committee concept.

*C. Eligibility*

Eligible grantees include State and local units of government, private non-profit labor-management committees (or a labor or management entity on behalf of a committee that will be created through the grant), and certain third party private non-profit entities on behalf of one or more committees to be created through the grant. Federal government agencies are not eligible.

Third party non-profit entities which can document that a major purpose or function of their organization has been the improvement of labor relations are eligible to apply. However, all funding must be directed to the functioning of the labor-management committee, and all requirements under Part B must be followed. Applications from third-party entities must document particularly strong support and participation from all labor and management parties with whom the applicant will be working. Applicants from third-parties which do not directly support the operation of a new or expanded committee will not be deemed eligible.

Applicants who received funding under this program in the past for committee funding are not eligible to apply for funding to continue or expand their prior efforts.

*D. Allocations*

FMCS has received an FY86 appropriation of $1 million for this program. However, as a result of the Balanced Budget and Emergency Deficit

Control Act of 1985 (Gramm-Rudman-Hollings Act), this amount may be produced. Specific funding levels will not be established for each type of committee. Instead, the review process will be conducted in such a manner that at least two awards will be made in each category (inplant, industry, public sector, and area), providing that FMCS determines that at least two outstanding applications exist in each cetegory. After these applications are selected for award, the remaining applications will be awarded according to merit without regard to category.

FMCS reserves the right to retain up to 5 percent of the FY86 appropriation to contract for program support purposes (other than administrative).

*E. Dollar Range and Length of Grants and Continuation Policy*

Awards to continue and expand existing labor-management committees (i.e., in existence at least 12 months prior to the submission deadline) will be for a period of 12 months. If successful progress is made during this initial budget period and if sufficient appropriations for expansion and continuation projects are available, these grants may be continued up to an additional 12 months at double the initial cash match ratio.

The total project period will thus normally be no more than 24 months.

Initial awards to establish new labor-management committees (i.e., not yet established or in existence less than 12 months prior to the submission deadline), will be for a period of 18 months. If successful progress is made during this initial budget period and if sufficient appropriations for expansion and continuation projects are available, these grants may be continued up to an additional 18 months at double the initial cash match ratio. The total project period will thus normally be no more than 36 months.

The dollar range of awards is as follows:

—Up to $35,000 in FMCS funds per annum for existing inplant applicants; up to $50,000 over 18 months for new in-plant committee applicants;
—Up to $75,000 in FMCS funds per annum for existing area, industry and public sector committee applicants;
—Up to $100,000 per 18-month period for new area, industry, and public sector committee applicants.

Applicants are reminded that these figures represent maximum Federal funds only. If total costs to accomplish the objectives of the application exceed the maximum allowable Federal funding level and grantee match, applicants may supplement these funds through voluntary contributions from other sources.

*F. Match Requirements and Cost Allowability*

In FY86, applicants for new labor-management committees must provide at least 10 percent of the total allowable project costs. Applicants of existing committees must provide at least 25 percent of the total allowable project costs. All matching funds must be in cash rather than in-kind goods or services. Matching funds may come from state or local government sources or private sector contributions, but may generally not include other Federal funds. Funds generated by grant-supported efforts are considered "project income," and may not be used for matching purposes.

It will be the policy of this program to reject all requests for indirect or overhead costs. In addition, grant funds must not be used to supplant private or local/state government funds currently employed for these purposes. Funding requests from existing committees should focus entirely on the costs associated with the expansion efforts only. Also, under no circumstances will business or labor officials participating on a labor-management committee be compensated out of grant funds for time spent at committee meetings or *time* spent in training sessions. Applicants generally will not be allowed to claim all or a portion of *existing* staff time as an expense or match contribution.

For a more complete discussion of cost allowability, applicants are encouraged to consult the FY86 FMCS Financial and Administrative Grants Manual which will be included in the application kit.

*G. Application Submission and Review Process*

Applications must be signed by *both* a labor and management representative and be postmarked no later than May 17, 1986. No applications or supplementary materials can be accepted after the deadline. It is the responsibility of the applicant to ensure that the application is correctly postmarked by the U.S. Postal Service or other carrier. An orginal application, containing numbered pages, plus three copies should be addressed to the Federal Mediation and Conciliation Service, Labor-Management Grant Programs, 2100 K Street, NW, Washington, DC 20427. Applications submitted without sufficient copies may be returned.

After the deadline has passed, all eligible applications will be reviewed and scored initially by one or more FMCS Grant Review Board(s). The Board(s) will decide which applications will be recommended for funding consideration. The Director, Labor-Management Grant Programs, will finalize the scoring and selection process of those applications recommended by the Board(s).

All FY86 grant applicants will be notified of results, and all grant awards will be made, prior to September 30, 1986. Applications submitted after the deadline dates or that fail to adhere to eligibility or other major requirements will be administratively rejected by the Director, Labor-Management Grant Programs.

*H. Contact*

Individuals wishing to apply for funding under this program should contact the Federal Mediation and Conciliation Service as soon as possible to obtain an application kit. These kits, as well as additional information or clarification, can be obtained by contacting Peter L. Regner, Federal Mediation and Conciliation Service, Labor-Management Grant Programs, 2100 K Street, NW, Washington, DC 20427, or calling 202/653-5320.

**Kay McMurray,**

*Director, Federal Mediation and Conciliation Service.*

[FR Doc. 85-30313 Filed 12-23-85; 8:45 am]
BILLING CODE 6732-01-M

## FEDERAL TRADE COMMISSION

### Granting of Request for Early Termination of the Waiting Period Under the Premerger Notification Rules

Section 7A of the Clayton Act, 15 U.S.C. 18a, as added by Title II of the Hart-Scott-Rodino Antitrust Improvements Act of 1976, requires persons contemplating certain mergers or acquisitions to give the Federal Trade Commission and the Assistant Attorney General advance notice and to wait designated periods before consummation of such plans. Section 7A(b)(2) of the Act permits the agencies, in individual cases, to terminate this waiting period prior to its individual cases, to terminate this waiting period prior to its expiration and requires that notice of this action be published in the Federal Register.

The following transactions were granted early termination of the waiting period provided by law and the premerger notification rules. The grants were made by the Federal Trade Commission and the Assistant Attorney General for the Antitrust Division of the Department of Justice. Neither agency intends to take any action with respect to these proposed acquisitions during the applicable waiting period:

| Transaction | Waiting period terminated effective |
|---|---|
| (1) 86-1024—General Electric Company's proposed acquisition of voting securities of Powerex Inc., a joint venture Corporation to be formed. | Nov. 27, 1985. |
| (2) 86-1025—Westinghouse Electric Corporation's proposed acquisition of voting securities of Powerex Inc., a joint venture Corporation to be formed. | Do. |
| (3) 86-0268—Devon Resource Investor's proposed acquisition assets of Stauffer Oil & Gas, Inc., (Chesebrough Pond's Inc., UPE). | Do. |
| (4) 86-0322—Sudbury Holdings, Inc.'s proposed acquisition of voting securities of Alpha Tube Corporation. | Do. |
| (5) 86-0234—Zayre Corp.'s proposed acquisition of Metro Vermoegensverwaltungs GMBH & Co. KG., (Metro Cash and Cary Wholesale, Inc., UPE). | Dec. 2, 1985. |
| (6) 86-0236—The News Corporation Limited's proposed acquisition of assets of Studio Properties Company. | Do. |
| (7) 86-0239—MKDG II's proposed acquisition of assets of Studio Properties Company. | Do. |
| (8) 86-0310—Laurentian Capital Corp's proposed acquisition of voting securities of Prairie State Life Ins. Co. | Do. |
| (9) 86-0222—Refaat El-Sayed's proposed acquisition of voting securities of Vertac Chemical Corporation. | Dec. 3, 1985. |
| (10) 86-0223—Refaat El-Sayed's proposed acquisition of voting securities of SDS Biotech Corporation, (Diamond Shamrock Corporation, UPE). | Do. |
| (11) 86-0224—Refaat El-Sayed's proposed acquisition of voting securities of SDS Biotech Corporation, (Vanderbilt Development Corporation, UPE). | Do. |
| (12) 86-0233—Claremont Petroleum N.L.'s proposed acquisition of voting securities of Triton Energy Corporation. | Do. |
| (13) 86-0246—The Proctor & Gamble Company's proposed acquisition of assets of G.D. Searle & Co. and voting securities of Searle Consumer Products, Inc., (Monsanto Company, UPE). | Do. |
| (14) 86-0250—United States Steel Corporation's proposed acquisition of voting securities of Texas Oil & Gas Corp. | Do. |
| (15) 86-0251—United States Steel Corporation's proposed acquisition of voting securities of Texas Oil & Gas Corp. | Do. |
| (16) 86-0252—United States Steel Corporation's proposed acquisition of voting securities of Texas Oil & Gas Corp. | Do. |
| (17) 86-0255—Minnesota Mining & Manufacturing Company's proposed acquisition of voting securities of a Newly-Formed Joint Venture. | Do. |
| (18) 86-0261—Harris Corporation's proposed acquisition of voting securities of a Newly-Formed Joint Venture. | Do. |
| (19) 86-0262—Equity Holdings' proposed acquisition of voting securities of Clevepak Corporation. | Do. |
| (20) 86-0271—Pioneer Hi-Bred International, Inc.'s proposed acquisition of voting securities of TLC, Co. | Do. |
| (21) 86-0281—Wolseley—Hughes plc's proposed acquisition of voting securities of Carolina Builders Corporation, (Clifton L. Benson, Jr., UPE). | Do. |
| (22) 86-0291—Primark Corporation's proposed acquisition of voting securities of The Aviation Group, Inc. | Do. |
| (23) 86-0292—Primark Corporation's proposed acquisition of voting securities of The Aviation Group, Inc. | Do. |
| (24) 86-0303—Finevest Partners Limited Partnership's proposed acquisition of assets of Pet Dairy Division and voting securities of Spartanburg Dairies, Inc., (IC Industries, Inc. UPE). | Do. |
| (25) 86-0318—Ernal C. Fraze's proposed acquisition of voting securities of Dayton Reliable Tool & Mfg. Co., (Nestle, S.A., UPE). | Do. |
| (26) 86-0159—National Healthcare, Inc.'s proposed acquisition of voting securities of 5 hospital subsidiaries, (Republic Health Corporation, UPE). | Dec. 4, 1985. |
| (27) 86-0256—Ozark Holdings, Inc.'s proposed acquisition of voting securities of Midcoast Aviation, Inc. | Do. |
| (28) 86-0288—Whirlpool Corporation's proposed acquisition of voting securities of Aspera S.r.L., (Fiat S.p.A., UPE). | Do. |
| (29) 86-0314—Continental Mortgage Investors', (William Davidson, UPE), proposed acquisition of voting securities of G.I.C. Financial Services Corporation, G.I.C. Equipment Leasing Company, (Guardian Industries Corp., William Davidson, UPE). | Do. |
| (30) 86-0316—Exxon Corporation's proposed acquisition of assets of Phillips Petroleum Company. | Do. |
| (31) 86-0294—Masco Corporation's proposed acquisition of voting securities of Flint & Walling Industries, Inc., (Edward L. Benson, UPE). | Dec. 5, 1985. |
| (32) 86-0295—Masco Industries, Inc.'s proposed acquisition of voting securities of Flint & Walling Industries, Inc., (Edward L. Benson, UPE). | Do. |
| (33) 86-0305)—Koninklijke Wessanen N.V.'s proposed acquisition of voting securities of American National Snacks, Inc. and Tree of Life Distribution Company, (Riverside Group, Inc., J. Steven Wilson, UPE). | Do. |
| (34) 86-0336—Bally Manufacturing Corporation's proposed acquisition of voting securities of MGM Grand Hotels, Inc., (Kirk Kerkorian, UPE). | Do. |
| (35) 86-0377—The Goodyear Tire & Rubber Company's proposed acquisition of assets of Chevron Corp. | Do. |
| (36) 86-0337—Alberta Energy Company Ltd.'s proposed acquisition of assets of Royal Dutch Petroleum Company. | Do. |
| (37) 86-0329—Sage Energy Company's (K.K. Amini, UPE) proposed acquisition of assets of Shell Western E & P a subsidiary of Shell Oil Company, (Royal Dutch Petroleum Company, UPE), (Operating in the U.S. as Shell Oil Company). | Dec. 6, 1985. |

**FOR FURTHER INFORMATION CONTACT:** Sandra M. Peay, Legal Technician, Premerger Notification Office, Bureau of Competition, Room 301, Federal Trade Commission, Washington, DC 20580, (202) 523-3894.

By direction of the Commission.

**Emily H. Rock,**

*Secretary.*

[FR Doc. 85-30326 Filed 12-23-85; 8:45 am]

BILLING CODE 6750-01-M

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Alcohol, Drug Abuse, and Mental Health Administration

### Alcohol, Drug Abuse, and Mental Health Aspects of Acquired Immunodeficiency Syndrome (AIDS)

**AGENCY:** Alcohol, Drug Abuse, and Mental Health Administration, HHS.

**ACTION:** Issuance of program announcement for research of alcohol, drug abuse, and mental health aspects of Acquired Immunodeficiency Syndrome (AIDS).

**SUMMARY:** The Alcohol, Drug Abuse, and Mental Health Administration announces the availability of a program announcement for research on the Alcohol, Drug Abuse, and Mental Health Aspects of Acquired Immunodeficiency Syndrome (AIDS). This announcement is to encourage research directed toward the psychological and neuropsychiatric problems, important consequences of AIDS which may also represent risk factors for it. Among the concerns are durg abusers who represent an avenue of AIDS infection to the general public. Concern over AIDS also reemphasizes the importance of research on the effects of alcohol consumption on immunologic functioning. Support may be requested for up to 5 years.

#### Receipt And Review Dates Of Applications

Applications will be accepted and reviewed according to the usual Public Health Service schedule and procedures.

**FOR FURTHER INFORMATION CONTACT:** Ellen Simon Stover, Ph.D., Deputy Director, Division of Basic Sciences, National Institute of Mental Health, Room 10-104, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, Telephone: (301) 443-4337.

**Robert L. Trachtenberg,**

*Acting Administrator Alcohol, Drug Abuse, and Mental Health Administration.*

[FR Doc. 85-30316 Filed 11-23-85; 8:45 am]

BILLING CODE 4160-20-M

### Food and Drug Administration

**[Docket No. 85E-0444]**

### Determination of Regulatory Review Period for purposes of Patent Extension; Fortaz; Correction

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice; correction.

**SUMMARY:** The Food and Drug Administration (FDA) is correcting the notice that announced that it had determined the regulatory review period for Fortaz. This document corrects the title of the person who signed the document.

**FOR FURTHER INFORMATION CONTACT:** Agnes B. Black, Regulations Editorial Staff (HFC–222), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–2994.

**SUPPLEMENTARY INFORMATION:** In FR Doc. 85–28927 appearing on page 50014 in the issue of Friday, December 6, 1985, the following correction is made: In the third column, at the end of the document, "Deputy Associate Commissioner for Regulatory Affairs" should have read "Deputy Associate Commissioner for Health Affairs."

Dated: December 18, 1985.

**Stuart L. Nightingale,**

*Associate Commissioner for Health Affairs.*

[FR Doc. 85–30319 Filed 12–23–85; 8:45 am]

BILLING CODE 4160–01–M

---

[Docket No. 85E–0472]

## Determination of Regulatory Review Period For Purposes of Patent Extension; Hexabrix Injection; Correction

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice; correction.

**SUMMARY:** The Food and Drug Administration (FDA) is correcting the notice that announced that it had determined the regulatory review period for Hexabrix injection. This document corrects the title of the person who signed the document.

**FOR FURTHER INFORMATION CONTACT:** Agnes B. Black, Regulations Editorial Staff (HFC–222), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–2994.

**SUPPLEMENTARY INFORMATION:** In FR Doc. 85–28925 appearing on page 50014 in the issue of Friday, December 6, 1985, the following correction is made on page 50015: In the second column, at the end of the document, "Deputy Associate Commissioner for Regulatory Affairs" should have read "Deputy Associate Commissioner for Health Affairs."

Dated: December 18, 1985.

**Stuart L. Nightingale,**

*Associate Commissioner for Health Affairs.*

[FR Doc. 85–30318 Filed 12–23–85; 8:45 am]

BILLING CODE 4160–01–M

---

[Docket No. 76F–0118]

## Kureha Chemical Industry Co., Ltd.; Withdrawal of Food Additive Petition

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the withdrawal without prejudice of a petition (FAP 3B2835) proposing that the food additive regulations be amended to provide for the safe use of di-$\beta$-butoxyethyl peroxydicarbonate as a polymerization initiator for vinyl chloride.

**FOR FURTHER INFORMATION CONTACT:** Mary W. Lipien, Center for Food Safety and Applied Nutrition (HFF–335), Food and Drug Administration, 200 C Street SW., Washington, DC 20204, 202–472–5690.

**SUPPLEMENTARY INFORMATION:** In the **Federal Register** of May 12, 1976 (41 FR 19363), FDA published a notice that it had filed a petition (FAP 3B2835) from Kureha Chemical Industry Co., Ltd., c/o Kreha Corp. of America, 420 Lexington Ave., New York, NY 10017, that proposed to amend the food additive regulations to provide for the safe use of di-$\beta$-butoxyethyl peroxydicarbonate as a polymerization initiator for vinyl chloride. Kureha Chemical Industry Co., Ltd., has now withdrawn the petition without prejudice to a future filing (21 CFR 171.7).

Dated: December 16, 1985.

**Richard J. Ronk,**

*Acting Director, Center for Food Safety and Applied Nutrition.*

[FR Doc. 85–30321 Filed 12–23–85; 8:45 am]

BILLING CODE 4160–01–M

---

## Advisory Committees; Meetings

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice.

**SUMMARY:** This notice announces forthcoming meetings of public advisory committees of the Food and Drug Administration (FDA). This notice also summarizes the procedures for the meetings and methods by which interested persons may participate in open public hearings before FDA's advisory committees.

**MEETINGS:** The following advisory committee meetings are announced:

### Workshop on Allergenic Extract Standardization and Allergenic Products Advisory Committee

*Date, time, and place.* January 8, 8:30 a.m., Wilson Hall, Bldg. 1, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD; January 9 and 10, Conference Rm. 6, Bldg. 31C, National Institutes of Health, 9000 Rockville Pike, Bethesda, MD.

*Type of meeting and contact person.* Open public workshop, January 8, 8:30 a.m. to 5 p.m.; open public hearing, January 9, 9 a.m. to 10 a.m.; open committee discussion, 10 a.m. to 5 p.m.; closed presentation of data, January 10, 9 a.m. to 12:30 p.m.; Clay Sisk, Center for Drugs and Biologics (HFN–32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–4695.

*General function of the committee.* The committee reviews and evaluates available data on the safety and effectiveness of marketed and investigational allergenic biological products administered to humans for the diagnosis, prevention, or treatment of allergies and allergic disease.

*Agenda—Open public workshop.* The public workshop on January 8 is directed to the manufacturers of allergenic extracts. Topics include (1) the proposed adoption of additional reference preparations for standardized allergenic extracts, (2) an update on analytical methods of standardization, and (3) information on the assignment of "allergy units" to describe the potency of allergenic extracts.

*Agenda—Open public hearing.* Interested persons requesting to present data, information, or views, orally or in writing, on issues pending before the committee should communicate with the committee contact person.

*Open committee discussion.* January 9 will be an orientation of the new members to the their role on the committee, the organization and function of the Food and Drug Administration (FDA), and the advice and involvement expected from the committee at future meetings followed by an introduction to some scientific issues which may be topics for future meetings. These include (1) guidelines for the clinical testing of allergenic extracts for use in immunotherapy and (2) the potential toxicity of the aluminum component of Alum-Precipitated Allergenic Extracts.

*Closed presentation of data.* The committee will receive briefings on trade secret or confidential commercial information relevant to pending biological product license applications for allergenic products such as new allergenic extracts. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

**Ophthalmic Devices Panel**

*Date, time, and place.* January 23 and 24, 9 a.m., Auditorium, HHS Bldg., 330 Independence Ave. SW. (enter at C St. entrance), Washington, DC.

*Type of meeting and contact person.* Open public hearing, January 23, 9 a.m. to 10 a.m.; open committee discussion, 10 a.m. to 1 p.m.; closed committee deliberations, 2 p.m. to 5 p.m.; open public hearing, January 24, 9 a.m. to 10 a.m.; open committee discussion, 10 a.m. to 1 p.m.; closed committee deliberations, 2 p.m. to 3 p.m.; open committee discussion, 3 p.m. to 5 p.m.; Richard E. Lippman, Center for Devices and Radiological Health (HFZ–460), Food and Drug Administration, 8757 Georgia Ave., Silver Spring, MD 20910, 301–427–7940.

*General function of the committee.* The committee reviews and evaluates available data on the safety and effectiveness of devices currently in use and makes recommendations for their regulations. The committee also reviews data on new devices and makes recommendations regarding their safety and effectiveness and their suitability for marketing.

*Agenda—Open public hearing.* Interested persons may present data, information, or views, orally or in writing, on issues pending before the committee. Those desiring to make formal presentations should notify the contact person before December 20, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, and an indication of the approximate time required to make their comments.

*Open committee discussion.* On January 23, the committee will discuss general issues relating to approvals of premarket approval applications (PMA's) for intraocular lenses (IOL's) and neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers, and may discuss specific PMA's for these devices. If discussion of all pertinent IOL or Nd:YAG laser issues is not completed, discussion will be continued the following day. On January 24, the committee will discuss PMA's for contact lenses and other ophthalmic devices and requirements for PMA approval.

*Closed committee deliberations.* On January 23, the committee will conduct reviews of PMA's for IOL's and Nd:YAG lasers. On January 24, the committee may discuss trade secret or confidential commercial information relevant to PMA's for contact lenses or other ophthalmic devices. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

**Vaccines and Related Biological Products Advisory Committee**

*Date, time, and place.* January 23, 8:30 a.m., Bldg. 29, Rm. 115, 8800 Rockville Pike, Bethesda, MD; January 24, 8:30 a.m., Bethesda Marriott Hotel, 5151 Pooks Hill Rd., Bethesda, MD.

*Type of meeting and contact person.* Closed committee deliberations, January 23, 8:30 a.m. to 10:30 a.m.; open public hearing, 10:30 a.m. to 11:30 a.m., unless public participation does not last that long; open committee discussion, 11:30 a.m. to 4 p.m.; closed committee deliberation, 4 p.m. to 6 p.m.; open committee deliberations, January 24, 8:30 a.m. to 3:30 p.m.; closed committee deliberations (if necessary), 3:30 p.m. to 4:30 p.m.; Jack Gertzog, Center for Drugs and Biologics (HFN–31), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–5455.

*General function of the committee.* The committee reviews and evaluates available data on the safety and effectiveness of vaccines and related biological products intended for use in the diagnosis, prevention, or treatment of human diseases. The committee also reviews and evaluates the quality and relevance of FDA's research program which provides scientific support for the regulation of these products.

*Agenda—Open public hearing.* Interested persons requesting to present data, information, or views, orally or in writing, on issues pending before the committee should communicate with the committee contact person.

*Open committee discussion.* On January 23, the committee will discuss the influenza vaccine formulation for the 1986–1987 season. On January 24, the committee will have deliberations to review the safety and effectiveness of live varicella virus vaccine.

*Closed committee deliberations.* On January 23 and 24 (if necessary), the committee will review trade secret or confidential commercial information relevant to pending license applications. This portion of the meeting will be closed to permit discussion of this information (5 U.S.C. 552b(c)(4)).

Each public advisory committee meeting listed above may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. The dates and times reserved for the separate portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairman determines will facilitate the committee's work.

Public hearings are subject to FDA's guideline (Subpart C of 21 CFR Part 10) concerning the policy and procedures to expedite electronic media coverage of FDA's public administrative proceedings, including hearings before public advisory committees under 21 CFR Part 14. Under 21 CFR 10.205, representatives of the electronic media may be permitted, subject to certain limitations, to videotape, film, or otherwise record FDA's public administrative proceedings, including presentations by participants.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this **Federal Register** notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairman's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

A list of committee members and members and summary minutes of meetings may be requested from the Dockets Management Branch (HFA–305), Rm. 4–62, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday.

The Commissioner, with the concurrence of the Chief Counsel, has determined for the reasons stated that those portions of the advisory committee meetings so designated in this notice shall be closed. The Federal Advisory Committee Act (FACA), as amended by the Government in the Sunshine Act (Pub. L. 94–409), permits

such closed advisory committee meetings in certain circumstances. Those portions of a meeting designated as closed, however, shall be closed for the shortest possible time, consistent with the intent of the cited statutes.

The FACA, as amended, provides that a portion of a meeting may be closed where the matter for discussion involves a trade secret; commercial or financial information that is privileged or confidential; information of a personal nature, disclosure of which would be a clearly unwarranted invasion of personal privacy; investigatory files compiled for law enforcement purposes; information the premature disclosure of which would be likely to significantly frustrate implementation of a proposed agency action; and information in certain other instances not generally relevant to FDA matters.

Examples of portions of FDA advisory committee meetings that ordinarily may be closed, where necessary and in accordance with FACA criteria, include the review, discussion, and evaluation of drafts of regulations or guidelines or similar preexisting internal agency documents, but only if their premature disclosure is likely to significantly frustrate implementation of proposed agency action; review of trade secrets and confidential commercial or financial information submitted to the agency; consideration of matters involving investigatory files compiled for law enforcement purposes; and review of matters, such as personnel records or individual patient records, where disclosure would constitute a clearly unwarranted invasion of personal privacy.

Examples of portions of FDA advisory committee meetings that ordinarily shall not be closed include the review, discussion, and evaluation of general preclinical and clinical test protocols and procedures for a class of drugs or devices; consideration of labeling requirements for a class of marketed drugs or devices; review of data and information on specific investigational or marketed drugs and devices that have previously been made public; presentation of any other data or information that is not exempt from public disclosure pursuant to the FACA, as amended; and, notably deliberative sessions to formulate advice and recommendations to the agency or matters that do not independently justify closing.

This notice is issued under section 10(a) (1) and (2) of the Federal Advisory Committee Act (Pub. L. 92-463, 86 Stat. 770-776 (5 U.S.C. App. I)), and FDA's regulations (21 CFR Part 14) on advisory committees.

Dated: December 20, 1985.

**Frank E. Young,**

*Commissioner of Food and Drugs.*

[FR Doc. 85-30480 Filed 12-20-85; 2:24 pm]

BILLING CODE 4160-01-M

---

**[Docket No. 85E-0522]**

## Determination of Regulatory Review Period for Purposes of Patent Extensions; Sulcosyn Solution

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) has determined the regulatory review period for Sulcosyn solution and is publishing this notice of that determination as required by law. FDA has made the determination because of the submission of an application to the Commissioner of Patents and Trademarks, Department of Commerce, for the extension of a patent which claims that human drug product.

**ADDRESS:** Written comments and petitions should be directed to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** Philip L. Chao, Office of Health Affairs (HFY-20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-1382.

**SUPPLEMENTARY INFORMATION:** The Drug Price Competition and Patent Term Restoration Act of 1984 (Pub. L. 98-417) generally provides that a patent may be extended for a period of up to 5 years so long as the patented item (human drug product, medical device, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under that act, a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period consists of two periods of time: a testing phase and an approval phase. For human drug products, the testing phase begins when the exemption to permit the clinical investigations of the drug becomes effective and runs until the approval phase begins. The approval phase starts with the initial submission of an application to market the human drug product and continues until FDA grants permission to market the drug product. Although only a portion of a regulatory review period may count toward the actual amount of extension that the Commissioner of Patents and Trademarks may award (for example, half the testing phase must be subtracted as well as any time that may have occurred before the patent was issued), FDA's determination of the length of a regulatory review period for a human drug product will include all of the testing phase and approval phase as specified in 35 U.S.C. 156(g)(1)(B).

FDA recently approved for marketing the human drug product Sulcosyn, a solution of sulconazole nitrate which is indicated for the treatment of tinea cruris and tinea corporis caused by *Trichophyton mentagrophytes, Epidermophyton floccosum,* and *Microsporum canis,* and for the treatment of tinea versicolor. Based on this approval, Syntex (U.S.A.) Inc. now seeks patent term restoration.

FDA has determined that the applicable regulatory review period for Sulcosyn solution is 1,956 days. Of this time, 1,148 days occurred during the testing phase of the regulatory review period, while 808 days occurred during the following dates:

1. *The date an exemption under section 505(i) of the Federal Food, Drug, and Cosmetic Act became effective:* April 24, 1980. FDA verified that the notice of claimed investigational exemption became effective on April 24, 1980.

2. *The date the application was initially submitted with respect to the human drug product under section 505(b) of the Federal Food, Drug, and Cosmetic Act:* June 15, 1983. The applicant claims that the new drug application for the drug (NDA 18-738) was initially submittd on June 13, 1983. However, FDA did not receive the full application until June 15, 1983.

3. *The date the application was approved:* August 30, 1985. FDA verified that NDA 18-738 was approved on August 30, 1985.

This determination of the regulatory review period establishes the maximum potential length of a patent extension. However, the U.S. Patent and Trademark Office applies several statutory limitations in its calculations of the actual period for patent extension. In its application for patent extension, this applicant seeks 730 days of patent extension.

Anyone with knowledge that any of the dates as published is incorrect may, on or before February 21, 1986, submit to the Dockets Management Branch (address above) written comments and ask for a redetermination. Furthermore, any interested person may petiton FDA, on or before June 23, 1986, for a determination regarding whether the applicant for extension acted with due diligence during the regulatory review

period. To meet its burden, the petition must contain sufficient facts to merit an FDA investigation. (See H. Rept. 857, Part 1, 98th Cong., 2d Sess., pp. 41–42, 1984.) Petitions should be in the format specified in 21 CFR 10.30.

Comments and petitions should be submitted to the Dockets Management Branch (address above) in three copies (except that individuals may submit single copies) and identified with the document number found in brackets in the heading of this document. Comments and petitions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: Decembr 18, 1985.

**Stuart L. Nightingale,**

*Associate Commissioner for Health Affairs.*

[FR Doc. 85-30320 Filed 12-23-85; 8:45 am]

BILLING CODE 4160-01-M

## DEPARTMENT OF THE INTERIOR

### Bureau of Land Management

### Kemmerer Resource Area, Rock Springs District, WY; Availability of Proposed Resource Management Plan and Final Environmental Impact Statement

**AGENCY:** Bureau of Land Management, Interior.

**ACTION:** Public notice that the proposed resource management plan and final environmental impact statement for the Kemmerer Resource Area, Rock Springs District, Wyoming, is available for public review.

**SUMMARY:** The Kemmerer Resource Management Plan (RMP) and Environmental Impact Statement (EIS) presents the proposed plan for managing the Kemmerer Resource Area in southwestern Wyoming. Copies are available from the Rock Springs District Office at the address listed below. The document is also available for review at the Kemmerer Resource Area Office in Kemmerer, Wyoming. Note that this final EIS is an abbreviated document. The draft and final EIS's collectively, provide the complete description and analyses of all alternatives that were considered.

The protest period on the proposed RMP and final EIS will begin on the date the Environmental Protection Agency publishes the notice of filing in the **Federal Register** and will end 30 days later. Any person who participated in the planning process and who has an interest which is or may be adversely affected by adoption of the proposed plan may protest its approval. A protest may raise only those issues the person(s) submitted for the record during the planning process.

Protests must be sent in writing to Director (202), Room 906, Premier Building, Bureau of Land Management, 1800 C Street, NW., Washington, DC 20240, before the end of the 30-day protest period. A protest must contain:

1. The name, mailing address, telephone number, and interest of the person filing the protest.

2. A statement of the issue or issues being protested.

3. A statement of the part or parts of the plan being protested.

4. A copy of all documents addresing the issue or issues that were submitted during the planning process by the protesting party, or an indication of the date the issue or issues were discussed for the record.

5. A concise explaining why the proposed management plan is believed to be wrong.

Following the 30-day protest period, the proposed plan, excluding any portion under protest, will be approved and a record of decision will be prepared. Approval will be withheld on any portion of the plan under protest until final action on the protest has been completed.

**SUPPLEMENTARY INFORMATION:** The Kemmerer Resource Area includes approximately 1,633,000 acres of public land and approximately 1,837,000 acres of Federal mineral estate administered by BLM.

The EIS analyzes six alternative plans that address issues concerning geophysical exploration, oil and gas exploration and development, reclamation, range management, wildlife and riparian habitat, recreation, land tenure adjustment, access, and utility and communication uses of the BLM administered public lands and mineral estate in the Kemmerer Resource Area.

The draft EIS was filed on April 12, 1985. A 90-day public comment period was provided. As a result of public comments and an internal review, the preferred alternative described in the draft EIS has been modified slightly and selected as the proposed plan.

**FOR FURTHER INFORMATION CONTACT:** Mr. Alan Stein, Team Leader, Rock Springs District, BLM, U.S. Highway 191 North, P.O. Box 1869, Rock Springs, Wyoming 82902–1869.

**Hillary A. Oden,**

*State Director.*

[FR Doc. 85-30482, Filed 12-23-85; 8:45 am]

BILLING CODE 4310-22-M

### National Wildlife Federation v. Burford; Publication of Court Order

**AGENCY:** Bureau of Land Management, Interior.

**ACTION:** Notice of Publication of Court Order.

**SUMMARY:** On December 19, 1985, the United States District Court for the District of Columbia issued an Order in the case of the *National Wildlife Federation* v. *Burford*, Civil Action No. 85–2238, staying the Court's Order of December 4, 1985, published in the **Federal Register** on December 18, 1985 (50 FR 51609), pending the resolution of the defendants' motion to amend, reconsider, and clarify that Order. The Order of December 19, 1985, further required the defendants to publish notice of this stay in the **Federal Register** forthwith. In compliance therewith, the Order of December 19, 1985, is hereby published:

**In the United States District Court for the District of Columbia**

National Wildlife Federation, *Plaintiff*, v. *Robert F. Burford*, et al., *Defendants*.; Civil Action No. 85–2238.

**Order**

Upon consideration of defendants' motion for a stay of this Court's Order of December 4, 1985, it is by the Court this 19th day of December, 198[5].

Ordered, That defendants' motion is granted and this Court's Order of December 4, 1985, is stayed pending the resolution of defendants' motion to amend, reconsider and clarify that order. Notice of this stay shall be published by defendants forthwith in the **Federal Register**.

**J.H. Pratt,**

*United States District Judge.*

**Robert F. Burford,**

*Director.*

[FR Doc. 85-30497 Filed 12-23-85; 8:45 am]

BILLING CODE 4310-84-M

## Fish and Wildlife Service

### Notice of Receipt of Application for Permit

The following applicants have applied for permits to conduct certain activities with endangered species. This notice is provided pursuant to section 10(c) of the Endangered Species Act of 1973, as amended (16 U.S.C. 1531, *et seq.*):

PRT-702036

Applicant: John Sutterlin, Auburn, WA

The applicant requests a permit to import 3.4 white-eared pheasants (*Crossoptilon crossoptilon*) from Harry J.

Hardy, South View Avaries, Burnaby, British Columbia, for the purpose of enhancement of propagation.

PRT-702031

Applicant: San Diego Zoological Society, San Diego, CA

The applicant requests a permit to offer for sale in foreign commerce six Przewalski's horses (*Equus przewalskii*) to the Chinese Forestry Department, People's Republic of China, for the purpose of enhancement of propagation.

PRT-684687

Applicant: Dr. Jerome A. Jackson, Mississippi State, MS

The applicant requests an amendment to his endangered species permit, PRT-684687, to allow for the capture, banding, and color banding of red-cockaded woodpeckers (*Picoides borealis*) in Fork Polk and the D'Arbonne National Wildlife Refuge in Louisiana for the purpose of scientific research.

PRT-701572

Applicant: Peregrine Fund, Inc., Ithaca, NY

The applicant requests a permit to import up to 6 Mauritius Kestrels (*Falco punctatus*) from the Government of Mauritius aviaries, Black River, Mauritius to establish a separate breeding colony for enhancement of population and protection of the species.

PRT-700592

Applicant: Hugh Kauer, Warren, MI

The applicant requests a permit to import the personal sport-hunted trophy of a bontebok (*Damaliscus dorcas dorcas*), culled from the captive herd of Mr. J. D'Alton of Bredasdorp, South Africa, for the purpose of enhancement of propagation.

PRT-701830

Applicant: George E. Norris, Bodfish, CA

The applicant requests a permit to import two white-earned pheasants (*Crossoptilon crossopitilon*) from Harry Hardy, Burnaby, British Columbia, Canada, for the purpose of enhancement of propagation.

PRT-698692

Applicant: Harvard Museum of Comparative Zoology, Cambridge, MA

The applicant requests a permit to export and reimport nonliving museum specimens of endangered or threatened species, accessioned into university collection, for research purposes.

PRT-702299

Applicant: University of North Alabama, Florence, AL

The applicant requests a permit to survey while wading or diving or sample by hand dredging, birdwing pearly mussel (*Conradilla caelata*) and Cumberland monkeyface mussel (*Quadrula intermedia*) in the Duck River, Tennessee; and to use a number of birdwing pearly mussel to parasitize host fish and/or transplant to Cypress Creek, Alabama, and Elk Creek, Tennessee for propagation of the species.

PRT-701648

Applicant: International Animal Exchange, Ferndale, MI

The applicant requests a permit to purchase in interstate commerce a pair of ocelots (*Felis pardalis*) and export said animals to Dianne Best, Anola, Manitoba, Canada, for enhancement of propagation.

PRT-702154

Applicant: Caldwell Schools, Inc., Tyler, TX

The applicant requests a permit to purchase in interstate commerce from the Los Angeles Zoo an ocelot (*Felis pardalis*) for enhancement of propagation.

PRT-702151

Applicant: U.S. Bureau of Land Management and the California Energy Commission, Sacramento, CA

The applicant requests a permit to take (capture, band, attach radio transmitters) bald eagles (*Haliaeetus leucocephalus*) in California for the purpose of scientific research.

PRT-702349

Applicant: Los Angeles Zoo, Los Angeles, CA

The applicant requests a permit to import up to 20 golden-headed tamarins (*Leontopithecus chrysomelas*) from Brazilian Institute of Forestry Development (IBDF), Brazil, for the purpose of enhancement of propagation.

Documents and other information submitted with these applications are available to the public during normal business hours (7:45 am to 4:15 pm) Room 611, 1000 North Glebe Road, Arlington, Virginia 22201, or by writing to the Director, U.S. Fish and Wildlife Service of the above address.

Interested persons may comment on any of these applications within 30 days of the date of this publication by submitting written views, arguments, or data to the Director at the above address. Please refer to the appropriate PRT number when submitting comments.

Dated: December 19, 1985.

**Larry LaRochelle,**

*Acting Chief, Branch of Permits, Federal Wildlife Permit Office.*

[FR Doc. 85-30381 Filed 12-23-85; 8:45 am]

BILLING CODE 4310-55-M

## National Park Service

### National Register of Historic Places; Notification of Pending Nominations

Nominations for the following properties being considered for listing in the National Register were received by the National Park Service before December 18, 1985. Pursuant to § 60.13 of 36 CFR Part 60 written comments concerning the significance of these properties under the National Register criteria for evaluation may be forwarded to the National Register, National Park Service, U.S. Department of the Interior, Washington, DC 20243. Written comments should be submitted by January 8, 1986.

**Carol D. Shull,**

*Chief of Registration, National Register.*

The 15-day commenting period for the following property is to be waived in order to assist the buildings preservation.

**FLORIDA**

**Palm Beach County**

Palm Beach Daily News Building, 204 Brazilian Ave.

[FR Doc. 85-30356 Filed 12-23-85; 8:45 am]

BILLING CODE 4310-70-M

### National Register of Historic Places; Notification of Pending Nominations

Nominations for the following properties being considered for listing in the National Register were received by the National Park Service before December 14, 1985. Pursuant to § 60.13 of 36 CFR Part 60 written comments concerning the significance of these properties under the National Register criteria for evaluation may be forwarded to the National Register, National Park Service, U.S. Department of the Interior, Washington, DC 20243. Written comments should be submitted by January 8, 1986.

**Carol D. Shull,**

*Chief of Registration, National Register.*

**ALABAMA**

**Jefferson County**

Birmingham, *Morris Avenue—First Avenue North Historic District*, 2000—2400 blks.

Morris Ave., and 2100—2500 blks. First Avenue N.

CALIFORNIA

Los Angeles County

*500 Varas Square—Government Reserve*

COLORADO

Arapahoe County

Aurora, *Gully Homestead*, 200 S. Chambers Rd.

Denver County

Denver, *Niblock—Yacovetta Terrace*, 1301—1319 W. 35th Ave.
Denver, *Potter Highlands Historic District*, Roughly bounded by W. 38th, Zuni, & W. 32nd Sts. and Federal Blvd.

Saguache County

Crestone, *Crestone School*, Cottonwood St. and Carbonate Ave.

CONNECTICUT

Fairfield County

Norwalk, *United States Post Office—South Norwalk*, 16 Washington St.

Hampden County

Holyoke, *United States Post Office—Holyoke Main*, 650 Dwight St.

Hartford County

Manchester, *United States Post Office—Manchester Main*, 479 Main—Center St.

New Haven County

Meriden, *United States Post Office—Meriden Main*, 89 N. Colony St.
Naugatuck, *United States Post Office—Naugatuck Main*, Church and Cedar Sts.

New London County

New London, *United States Post Office—New London Main*, 27 Masonic St.

LOUISIANA

East Baton Rouge Parish

Baton Rouge, *Louisiana National Bank Building*, 236 Riverside Mall

MARYLAND

Baltimore (Independent City)

*Lyric Theatre*, 124 W. Mount Royal Ave.

MASSACHUSETTS

Norfolk County

Brookline, *Dutch House (The) (Brookline MRA)*, 20 Netherlands Rd.
Brookline, *Spooner, William, House (Brookline MRA)*, 191 Clyde St.

NEW YORK

St. Lawrence County

Ogdensburg, *Fine, Judge John, House*, 422 State St.

OHIO

Cuyahoga County

Beachwood, *Hanger (The)*, 24400 Cedar Rd.

PENNSYLVANIA

Bucks County

Langhorne, *Langhorne Library*, 160 W. Maple Ave.

Montgomery County

Royersford, *Continental Stove Works*, First St. above Main

SOUTH CAROLINA

Lee County

Bishopville, *Bishopville Commercial Historic District (Bishopville MRA)*, N. Main St. between W. Church and Cedar Lane and along Cedar Lane
Bishopville, *Carnes, James, House (Bishopville MRA)*, 200 S. Main St.
Bishopville, *Fraser, Thomas, House (Bishopville MRA)*, US 15
Bishopville, *Manor (The) (Bishopville MRA)*, 529 N. Main St.
Bishopville, *Rogers, William, House (Bishopville MRA)*, 531 W. Church St.
Bishopville, *South Main Historic District (Bishopville MRA)*, S. Main between E. Harris and W. Ridge Sts.
Bishopville, *Spencer House (Bishopville MRA)*, 817 N. Main St.
Bishopville, *Tall Oaks (Bishopville MRA)*, OH 341

[FR Doc. 85-30352 Filed 12-23-85; 8:45 am]

BILLING CODE 4310-70-M

## INTERSTATE COMMERCE COMMISSION

**[Docket No. AB-6 (Sub-No. 273)]**

### Burlington Northern Railroad Co.—Abandonment—in Johnson and Nemaha Countries, NE;

The Commission has issued a certificate authorizing Burlington Northern Railroad Company to abandon its 13.07-mile rail line between milepost 60.77 near Tecumseh and milepost 47.70 near Johnson in Johnson and Nemaha Counties, NE. The abandonment certificate will become effective 30 days after this publication unless the Commission also finds that: (1) A financially responsible person has offered financial assistance (through subsidy or purchase) to enable the rail service to be continued; and (2) it is likely that the assistance would fully compensate the railroad.

Any financial assistance offer must be filed with the Commission and the applicant no later than 10 days from publication of this Notice. The following notation shall be typed in bold face on the lower left-hand corned of the envelope containing the offer: "Rail Section, AB-OFA". Any offer previously made must be remade within this 10-day period.

Information and procedures regarding financial assistance for continued rail service are contained in 49 U.S.C. 10905 and 49 CFR Part 1152.

**James H. Bayne,**

*Secretary.*

[FR Doc. 85-30334 Filed 12-23-85; 8:45 am]

BILLING CODE 7035-01-M

**[Docket No. AB-43 (Sub-No. 140X)]**

### Illinois Central Gulf Railroad Co.—Abandonment Exemption—in Rockford, IL; Exemption

Applicant, Illinois Central Gulf Railroad Company (ICG), has filed a notice of exemption under 49 CFR Part 1152 Subpart F—*Exempt Abandonments* to abandon a segment of railroad from 6th Street to Kishwaukee Street, a distance of approximately 0.3 miles, in Rockford, IL.

Applicant has certified (1) that no local traffic has moved over the line for at least 2 years and that overhead traffic is not moved over the line, and (2) that no formal complaint filed by a user of rail service on the line (or by a State or local governmental entity acting on behalf of such user) regarding cessation of service over the line either is pending with the Commission or any U.S. District Court, or has been decided in favor of the complainant within the 2-year period. The appropriate State agency has been notified in writing at least 10 days prior to the filing of this notice.

As a condition to use of this exemption, any employee affected by the abandonment shall be protected pursuant to *Oregon Short Line R. Co.-Abandonment-Goshen*, 360 I.C.C. 91 (1979).

The exemption will be effective January 23, 1986 (unless stayed pending reconsideration). Petitions to stay must be filed by January 3, 1986, and petitions for reconsideration, including environmental, energy, and public use concerns, must be filed by January 13, 1986, with: Office of the Secretary, Case Control Branch, Interstate Commerce Commission, Washington, DC 20423.

A copy of any petition filed with the Commission must be sent to applicant's representative: Richard M. Kamowski, 233 North Michigan Avenue, Chicago, IL 60601.

If the notice of exemption contains false or misleading information, use of the exemption is void *ab initio*.

A notice to the parties will be issued if use of the exemption is conditioned upon environmental or public use conditions.

Decided: December 12, 1985.

By the Commission, Heber P. Hardy, Director, Office of Proceedings.

**James H. Bayne,**

*Secretary.*

[FR Doc. 85-30333 Filed 12-23-85; 8:45 am]

BILLING CODE 7035-01-M

---

**[Docket No. AB-1 (Sub-No. 186)]**

## Chicago and North Western Transportation Co.; Abandonment and Discontinuance of Service in Leavenworth and Wyandotte Counties, KS, and Platte and Buchanan Counties, MO; Findings

The Commission has issued a certificate authorizing Chicago and North Western Transportation Company to (1) abandon its 30.7-mile line of railroad between Leavenworth, KS (milepost 25.0) and BC Junction, MO (milepost 52.9), and between milepost 61.7 and milepost 64.0 at St. Joseph, MO; (2) discontinue service over a 23.0-mile line of trackage of the Missouri Pacific Railroad Company between Kansas City (milepost 287.5) and Leavenworth, KS (milepost 309.2) and an additional 7,140 feet of track lacking milepost designation at Kansas City, KS; (3) discontinue service over 7.5-mile line of trackage of the Atchison, Topeka and Santa Fe Railway Company between BC Junction (milepost 65.3) and Terminal Yard (St. Joseph), MO (milepost 72.8); (4) discontinue service over 0.5-mile line of trackage of the St. Joseph Terminal Railroad Company between Station 42+45 and Station 66+27 at St. Joseph, MO; and (5) discontinue service over 0.8-mile line of trackage of the Burlington Northern Railroad Company, between milepost 61.7 and milepost 62.5 at St. Joseph, MO, in Leavenworth and Wyandotte Counties, KS, and Platte and Buchanan Counties, MO.

The abandonment and discontinuance of service certificate will become effective 30 days after this publication unless the Commission also finds that: (1) A financially responsible person has offered financial assistance (through subsidy or purchase) to enable the rail service to be continued; and (2) it is likely that the assistance would fully compensate the railroad.

Any financial assistance offer must be filed with the Commission and the applicant no later than 10 days from publication of this Notice. The following notation shall be typed in bold face on the lower left-hand corner of the envelope containing the offer: "Rail Section, AB-OFA". Any offer previously made must be remade within this 10-day period.

Information and procedures regarding financial assistance for continued rail service are contained in 49 U.S.C. 10905 and 49 CFR Part 1152.

**James H. Bayne,**

*Secretary.*

[FR Doc. 85-30371, Filed 12-23-85; 8:45 am]

BILLING CODE 7035-01-M

---

## DEPARTMENT OF JUSTICE

### Antitrust Division

### Notice Pursuant to the National Cooperative Research Act of 1984; Portland Cement Association

Notice is hereby given that pursuant to section 6(a) of the National Cooperative Research Act of 1984, Pub. L. 98-462 ("the Act"), the Portland Cement Association ("PCA") has filed a written notification simultaneously with the Attorney General and the Federal Trade Commission disclosing a change in its membership. Specifically, Hawaiian Cement is now a member of the PCA. At present the members of the PCA are:

Aetna Cement Corp.
Alaska Basic Industries
Ash Grove Cement Co.
Ash Grove Cement West, Inc.
Blue Circle Atlantic
Blue Circle Inc.
CalMat Co.
Capitol Aggregates, Inc.
Dragon Products Co.
General Portland Inc.
Genstar Cement Co.
Gifford-Hill & Co., Inc.
Hawaiian Cement
Ideal Basic Industries, Cement Division
Independent Cement Corp.
Lehigh Portland Cement Co.
Lone Star Industries, Inc.
The Monarch Cement Co.
Moore McCormack Cement, Inc.
Northwestern States Portland Cement Co.
Rinker Portland Cement Corp.
Rochester Portland Cement Corp.
St. Marys Peerless Cement Co.
St Marys Wisconsin Cement Inc.
The South Dakota Cement Plant
Southwestern Portland Cement Co.
Canada Cement Lafarge Ltd.
Ciment Quebec, Inc.
Federal White Cement Ltd.
Genstar Cement Limited
Lake Ontario Cement Limited
Miron Inc.
North Star Cement Limited St. Lawrence Cement Inc.
St. Marys Cement Limited

In addition, the following equipment suppliers are involved as "Participating Associates," together with PCA members, in the activities of the Manufacturing Process Subcommittee of PCA's General Technical Committee:

Holderbank Consulting, Ltd.
Humboldt Wedag Co.
Centennial Engineering, Inc.
Allis-Chalmers Corp.
F.L. Smidth and Co.
Claudius Peters, Inc.
Polysius Corp.
The Fuller Co.

The notification was filed for the purpose of invoking the Act's provisions limiting the recovery of antitrust plaintiffs to actual damages under specified circumstances. The original notification, identifying the original parties to the venture and describing in general terms the area of planned activities of the venture, is published at 50 FR 5015 (1985).

**Joseph H. Widmar,**

*Director Operations, Antitrust Division.*

[FR Doc. 85-30345 Filed 12-23-85; 8:45 am]

BILLING CODE 4410-01-M

---

### Notice Pursuant to the National Cooperative Research Act of 1984; Semiconductor Research Corp.

Notice is hereby given that pursuant to section 6(a) of the National Cooperative Research Act of 1984, Pub. L. No. 98-462 ("the Act"), Semiconductor Research Corporation ("SRC") has filed a written notification simultaneously with the Attorney General and the Federal Trade Commission disclosing certain changes in the membership of SRC. The changes consist of the addition of the following companies to the Semiconductor Equipment and Materials Institute, Inc. ("SEMI") Chapter of the SRC:

Amedyne
Eagle-Picher Ind. Inc.
E/G Electrograph Inc.
Gryphon Products
Hercules Specialty Chemicals Company
Leighton Electronics Inc.
Machine Intelligence Corporation
Oneac Corporation
Peak Systems, Inc.
The SEMI Group, Inc.
XMR, Inc.

SRC filed its notification of these membership changes for the purpose of extending the Act's provision limiting the recovery of antitrust plaintiffs to actual damages under specified circumstances. Pursuant to Section 6(b) of the Act, the identities of the parties to SRC and SRC's general areas of planned activity are given below.

SRC is a joint venture which, with the addition of the previously identified companies to the SEMI Chapter, consists of the following members:

Advanced MicroDevices, Incorporated
AT&T Technologies, Incorporated

Burroughs Corporation
Control Data Corporation
Digital Equipment Corporation
E.I. du Pont de Nemours & Company
Eastman Kodak Company
Eaton Corporation
GCA Corporation
General Electric Corporation
General Motors Corporation
Goodyear Aerospace Corporation
GTE Laboratories, Incorporated
Harris Corporation
Hewlett-Packard Company
Honeywell, Incorporated
IBM Corporation
Intel Corporation
LSI Logic Corporation
Monolithic Memories, Incorporated
Monsanto Company
Motorola, Incorporated
National Semiconductor Corporation
Perkin-Elmer Corporation
RCA Corporation
SEMI Chapter, consisting of FEP ANALYTIC (division of Verity Instruments, Inc.)
Amedyne
Eagle-Picher Ind. Inc.
Flexible Manufacturing Systems, Inc.
Gryphon Products
Hercules Specialty Chemicals Company
Ion Beam Technologies, Inc.
Isitec Corporation
Micro Mask, Incorporated
Pacific Western Systems, Incorporated
Probe-Rite, Incorporated
Pure Aire Corporation
Mac Dermid, Inc.
Machine Technology, Inc.
Micrion Corporation
Micronix Corporation
Oneac Corporation
Peak Systems, Inc.
Semi-Gas Systems, Incorporated
Silsco, Inc.
The SEMI Group
Universal Energy Systems, Inc.
VLSI Standards, Inc.
XMR, Inc.
Silicon Systems, Incorporated
Sperry Corporation
Texas Instruments, Incorporated
Union Carbide Corporation
Varian Associates, Incorporated
Westinghouse Electric Corporation
Xerox Corporation
Zilog, Incorporated

SRC's purpose is to plan, promote, coordinate, sponsor, and conduct research supportive of the semiconductor industry and directed toward:

1. Increasing knowledge of semiconductory materials and phenomena, and of related scientific and engineering subjects that are required for the useful application of semiconductors;

2. Developing new and more efficient designs and manufacturing technologies for semiconductor devices;

3. Identifying directions, limits, opportunities, and problems in generic semiconductor technologies;

4. Increasing the number of scientists and engineers proficient in research, development, and manufacture of semiconductor devices;

5. Increasing industry-university ties, establishing university semiconductor research centers with major long-term research centers with major long-term research thrusts, and developing university semiconductor research activities with more precisely defined, short-terms objectives;

6. Developing more relevant graduate school education and a larger supply of graduate students in areas related to semiconductor technology;

7. Increasing the ability of universities to attract and retain competent faculty in the semiconductor field;

8. Decreasing fragmentation and redundancy in United States semiconductor research;

9. Establishing advanced research efforts for critical semiconductor technology areas that are beyond the individual resources of many SRC members;

10. Promoting efficient communication of research results to SRC members and to the United States semiconductor community as a whole.

**Joseph H. Widmar,**

*Director of Operations, Antitrust Division.*

[FR Doc. 84-30346 Filed 12-23-85; 8:45 am]

BILLING CODE 4410-01-M

## National Institute of Justice

### Adult Property Offenders Study; Comment Availability

"The Feasibility of an Ethnographic Study of Adult Property Offenders," by Barry Glassner is currently available for comment. This report is a part of the material that the National Institute of Justice staff will be considering in deciding whether or not to recommend initiating a program of grant support for such research. Issues typifying current research and policy interest might include the following:

1. Individual perceptions of the risks involved in the commission of property crimes and measures adopted to minimize these risks.

2. Offenders' perceptions of the criminal justice sanction threat and the prior experience with crime and the criminal justice system that led to this assessment.

3. Variation in individual crime commission frequencies with factors such as age, employment and drug dependence and, in particular, with accumulated experience with crime and criminal justice system processes.

4. Patterns to behavior in commission of property crimes including such things as choice of victims, networks of co-participants and confederates and outlets for disposal of stolen goods.

A program of research that studies active, non-incarcerated property offenders (if such research is feasible) could be a valuable complement to those studies that allow an analysis of information from and about a much larger number of subjects. We are now seeking comments on the general program idea. The Glassner paper should be viewed as a point of departure for your comments. Copies of the paper are available from: The Offender Perceptions Program Manager, Center for Crime Control Research, National Institute of Justice, 633 Indiana Ave., NW. Room 900, Washington, DC 20531.

Comments should be sent before February 15, 1986 to the above address.

Date: December 16, 1985.

**James K. Stewart,**

*Director.*

[FR Doc. 84-30317 Filed 12-23-85; 8:45 am]

BILLING CODE 4410-18-M

## DEPARTMENT OF LABOR

### The Steering Subcommittee of the Labor Advisory Committee for Trade Negotiations and Trade Policy; Meeting

Pursuant to the provisions of the Federal Advisory Committee Act (Pub. L. 92-463 as amended), notice is hereby given of a meeting of the Steering Subcommittee of the Labor Advisory Committee for Trade Negotiations and Trade Policy.

Date, time and place: January 14, 1986; 9:30 a.m., Rm. S4215, A&B Frances Perkins, Department of Labor Building, 200 Constitution Avenue, NW., Washington, DC.

Purpose: To discuss trade negotiations and trade policy of the United States.

This meeting will be closed under the authority of section 10(d) of the Federal Advisory Committee Act. The Committee will hear and discuss sensitive and confidential matters concerning U.S. trade negotiations and trade policy.

For further information, contact: Fernand Lavallee, Executive Secretary, Labor Advisory Committee, Phone: (202) 523-6565.

Signed at Washington, DC this 18th day of December 1985.

Robert W. Searby,

*Deputy Under Secretary, International Affairs.*

[FR Doc. 85-30376 Filed 12-23-85; 8:45 am]

BILLING CODE 4510-28-M

## Mine Safety and Health Administration

[Docket No. M-82-20-M]

### Union Oil Co. of California; Petition for Modification of Application of Mandatory Safety Standard

Union Oil Company of California, 2717 County Road 215, P.O. Box 76, Parachute, Colorado 81635 has filed an amendment to a petition for modification. On May 4, 1982, Union Oil Company of California submitted a petition to modify the application of 30 CFR 57.15-31(a) (self-rescue devices) to its Parachute Creek Mine (I.D. No. 05-03143) located in Garfield County, Colorado. On June 4, 1982, MSHA published notice of the petition in the **Federal Register** (47 FR 24485), allowing interested parties 30 days to submit comments. On October 14, 1982, MSHA granted the petition for specified areas of the mine. On November 1, 1985, the petitioner submitted a request to amend the original petition for modification to extend the proposed alternative method of compliance.

A summary of the petitioner's statement follows:

1. The petition concerns the requirement that self-rescue devices meeting the requirements of 30 CFR 57.15-30 be worn or carried by all persons underground.

2. On October 14, 1982, MSHA granted the petition allowing miners to enter into an underground office building and change room complex without carrying a self-rescuer. The petitioner wants to extend the provisions to include a modular training building adjacent to the underground office and change room complex.

3. Petitioner states that the training building is situated in the same drift that the office and change room complex is located in and is within 34 feet of a door providing ingress and egress into the office and change room complex. The building is equipped with telephones and the audible emergency alarms can be clearly heard when in this building.

4. Petitioner states that the proposed alternate method will provide the same degree of safety for the miners affected as that afforded by the standard.

### Request for Comments

Persons interested in this amendment to the petition for modification may furnish written comments. These comments must be filed with the Office of Standards, Regulations and Variances, Mine Safety and Health Administration, Room 627, 4015 Wilson Boulevard, Arlington, Virginia 22203. All comments must be postmarked or received in that office on or before January 23, 1986. Copies of the amendment and the original petition for modification are available for inspection at that address

Dated: December 4, 1985.

Patricia W. Silvey,

*Director, Office of Standards, Regulations and Variances.*

[FR Doc. 85-30377 Filed 12-23-85; 8:45 am]

BILLING CODE 4510-43-M

## Occupational Safety and Health Administration

### Federal Advisory Council on Occupational Safety and Health; Meeting

Notice is hereby given that the Federal Advisory Council on Occupational Safety and Health, established under Section 1-5 of Executive Order 12196 of February 26, 1980, published in the **Federal Register**, February 27, 1980 (45 FR 12769), will meet on January 8, 1986, starting at 10:00 a.m. in Room N3437 ABCD, of the Frances Perkins Department of Labor Building, 200 Constitution Avenue, NW., Washington, DC. The meeting will be open to the public.

The agenda provides for:

I. Call to Order (Announcements)
II. Introduction of Reappointees
III. Election of Vice Chairman
IV. Approval of Minutes of October 10, 1984 Meeting
V. Applicability of Hazard Communication Standard in the Federal Sector
VI. Reports
A. President's 3% Goal
B. Safety Belt Executive Order
C. Highlights of 40th Annual Federal Safety and Health Conference
D. Status of use of OWCP Statistics
E. Targeted Inspection Program for 1986
F. Reprisals
VII. New Business
Dates of 1986 FACOSH Meetings: January 8, April 9, July 9, October 8
VIII. Adjournment

The Council welcomes written data, views or comments concerning safety and health programs for Federal employees, including comments on the agenda items. All such submissions received by close of business January 3, 1986, will be provided to the members of the Council and included in the record of the meeting.

The Council will consider oral presentations relating to agenda items. Persons wishing to orally address the Council at the meeting should submit a written request to be heard by close of business January 3, 1986. The request must include the name and address of the person wishing to appear, the capacity in which appearance will be made, a short summary of the intended presentation and an estimate of the amount of time needed.

All communications regarding this Advisory Council should be addressed to John E. Plummer, Director, Office of Federal Agency Programs, Department of Labor, OSHA, Frances Perkins Building, 200 Constitution Avenue, NW., Room N3613, Washington, DC 20210, telephone (202) 523-9329.

Signed at Washington, DC, this 19th day of December 1985.

Patrick R. Tyson,

*Acting Assistant Secretary.*

[FR Doc. 85-30375 Filed 12-23-85; 8:45 am]

BILLING CODE 4510-26-M

## NATIONAL COMMISSION FOR EMPLOYMENT POLICY

### Notice of Hearing

*Summary:* Under the provisions of the Federal Advisory Committee Act (Pub. L. 92-463, as amended), notice is hereby given of a public hearing of the National Commission for Employment Policy in the auditorium of the Murry Bergtraum High School for Business Careers, 411 Pearl Street, New York, New York.

*Date:* Thursday, January 9, 1986, 9:00 a.m. to 12:00 p.m.

*Status:* This hearing is open to the public.

*Matters to be discussed:* Commission members will hear testimony from various local government, business, education and community witnesses regarding basic skills remediation and dropout prevention for New York City youth. Witnesses will testify on the importance of basic academic skills to yourg people's success in the job market.

*For further information, contact:* Ms. Nancy ReMine Trego, National Commission for Employment Policy, 1522 K Street, NW., Suite 300, Washington, DC 20005, (202) 724-1545.

*Supplementary Information:* The National Commission for Employment Policy is authorized by the Job Training

Partnership Act (Pub. L. 97–300). The Act gives the Commission the broad responsibility of advising the President and the Congress. Handicapped individuals wishing to attend should contact the Commission so that appropriate accommodations can be made. No public testimony will be authorized except by those asked to do so prior to the hearing date. However, written testimony for the record will be accepted at the Commission office through January 17, 1986.

Copies of the testimony and materials prepared for the hearing will be available for public inspection at the Commission's officies, 1522 K St. NW., Suite 300, Washington, DC 20005.

Signed this 12 day of December, 1985.

**Carol J. Romero,**

*Acting Director.*

[FR Doc. 85–30374 Filed 12–23–85; 8:45 am]

BILLING CODE 4510-30-M

## NATIONAL FOUNDATION ON THE ARTS AND HUMANITIES

### Agency Information Collection Activities Under OMB Review

**AGENCY:** National Endowment for the Humanities, NFAH.

**ACTION:** Notice.

**SUMMARY:** The National Endowment for the Humanities (NEH) has sent to the Office of Management and Budget (OMB) the following proposals for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35).

**DATE:** Comments on this information collection must be submitted on or before January 23, 1986.

**ADDRESS:** Send comments to Ms. Ingrid Foreman, Management Assistant, National Endowment for the Humanities, Administrative Services Office, Room 202, 1110 Pennsylvania Avenue NW., Washington, DC 20506 (202–786–0233) or Mr. Joseph Lackey, Office of Management and Budget, New Executive Office Building, 726 Jackson Place NW, Room 3208, Washington, DC 20503 (202–395–7316).

**FOR FURTHER INFORMATION CONTACT:** Ms. Ingrid Foreman, National Endowment for the Humanities, Administrative Services Office, Room 202, 1100 Pennsylvania Avenue NW, Washington, DC 20506 (202–786–0233) from whom copies of forms and supporting documents are available.

**SUPPLEMENTARY INFORMATION:** All of the entries are grouped into new forms, revisions, or extensions. Each entry is issued by NEH and contains the following information: (1) The title of the form; (2) the agency from number, if applicable; (3) how often the form must be filled out; (4) who will be required or asked to report; (5) what form will be used for; (6) an estimate of the number of responses; (7) an estimate of the total number of hours needed to fill out the form. None of these entries are subject to 44 U.S.C. 3504(h).

Category: Extension
Title: General Programs: General Program Performance Requirements
Frequency of Collection: It varies. It could be quarterly, semi-annually or annually
Respondents: Grantees
Use: Monitoring and evaluating the accomplishment of a grant
Estimated Number of Respondents: 53
Estimated Hours for Respondents to Provide Information: 212

Category: Extension
Title: Reviewer Evaluation
Frequency of Collection: When the application warrants it. On occasion for example, the panel recommends further review; some applications are reviewed if the budget is very large, and some if panel cannot reach an agreement on a proposal or feel that outside expert advice should be sought
Respondents: Experts in specific field of project
Use: To provide more specific information about the quality or rationale of a project in addition to the regular panelist review.
Estimated Number of Respondents: 400 per year
Estimated Hours for Respondents to Provide Information: 800

Category: Extension
Title: General Programs Museums and Historical Organizations Guidelines and Application Instructors
Frequency of Collection: Twice a year at each deadline
Respondents: Museums and historical organizations
Use: Collection of information provides a basis for evaluation of applications in the competitive review process of grant making
Estimated Number of Respondents: 440
Estimated Hours for Respondents to Provide Information: 35,200

Category: Extension
Title: General Programs: Humanities Projects in Libraries/Guidelines and Application Instructions
Frequency of Collection: Twice a year at each deadline
Respondents: Colleges and universities, libraries, private, non-profit organizations, civic and professional groups, or branches of state or local government
Use: Collection of information provides a basis for evaluation of applications in the competitive review process
Estimated Number of Respondents: 35
Estimated Hours for Respondents to Provide Information: 2,800

Category: Extension
Title: General Programs: Humanities Projects in Youth/Guidelines and Application Instructions
Frequency of Collection: Twice a year each deadline
Respondents: Colleges and universities, libraries, private, non-profit organizations, civic and professional groups, or branches of state or local government
Use: Collection of information provides a basis for evaluation of applications in the competitive review process
Estimated Number of Respondents: 11
Estimated Hours for Respondents to Provide Information: 880

Category: Extension
Title: Panelist Evaluation Form
Frequency of Collection: Experts in the field review applications after each application deadline. There are usually two deadlines per program per year
Respondents: Scholars and experts in specific fields
Use: Collection of information serves as a basis for each panelist's evaluation and rating of a proposal. When a panel meets, participants, after discussion based on their notes, then make collectively a final recommendation for each proposal in the competitive process. This information is used extensively as a base from which to respond to applicants on the reasons why they have not received funding.
Estimated Number of Respondents: 270 per year
Estimated Hours for Respondents to Provide Information: 9,945

Category: Extension
Title: General Programs: Humanities Projects in Media/Guidelines and Application Instructions
Frequency of Collection: Twice a year at each deadline
Respondents: Public radio and television stations, private, non-profit organizations, colleges and universities, or branches of state or local government.
Use: Collection of information provides a basis for evaluation of applications in the competitive review process
Estimated Number of Respondents: 355
Estimated Hours for Respondents to Provide Information: 56,800

Category: Extension
Title: General Programs: Humanities Programs for Adults-Guidelines and Application Instructions
Frequency of Collection: Twice a year at each deadline
Respondents: Colleges and universities, libraries, private, non-profit organizations, civic and professional groups, or branches of state or local government
Use: Collection of information provides a basis for evaluation applications in the competitive review process
Estimated Number of Respondents: 56
Estimated Hours for Respondents to Provide Information: 4,480

**Susan Metts,**
*Acting Director of Administration.*
[FR Doc. 85-30379 Filed 12-23-85; 8:45 am]
BILLING CODE 7536-01-M

## NUCLEAR REGULATORY COMMISSION

### Advisory Committee on Reactor Safeguards, Subcommittee on Core Performance; Meeting

The ACRS Subcommittee on Core Performance will hold a meeting on January 29, 1986, Room 1046, 1717 H Street, NW, Washington, DC.

The meeting will be open to public attendance.

The agenda for subject meeting shall be as follows: *Wednesday, January 29, 1986—8:30 a.m. until 11:30 a.m.*

The Subcommittee will review the potential for recriticality of TMI-2 during defueling operations.

Oral statements may be presented by members of the public with the concurrence of the Subcommittee Chairman; written statements will be accepted and made available to the Committee. Recordings will be permitted only during those portions of the meeting when a transcript is being kept, and questions may be asked only by members of the Subcommittee, its consultants, and Staff. Persons desiring to make oral statements should notify the ACRS staff member named below as far in advance as is practicable so that appropriate arrangements can be made.

During the initial portions of the meeting, the Subcommittee, along with any of its consultants who may be present, may exchange preliminary views regarding matters to be considered during the balance of the meeting.

The Subcommittee will then hear presentations by and hold discussions with representatives of the NRC Staff, its consultants, and other interested persons regarding this review.

Further information regarding topics to be discussed, whether the meeting has been cancelled or rescheduled, the Chairman's ruling on requests for the opportunity to present oral statements and the time allotted therefor can be obtained by a prepaid telephone call to the cognizant ACRS staff member, Mr. Dean Houston (telephone 202/634-3267) between 8:15 a.m. and 5:00 p.m. Persons planning to attend this meeting are urged to contact the above named individual one or two days before the scheduled meeting to be advised of any changes in schedule, etc., which may have occurred.

Dated: December 14, 1985.
**Morton W. Libarkin,**
*Assistant Executive Director for Project Review.*
[FR Doc. 85-30391 Filed 12-23-85; 8:45 am]
BILLING CODE 7590-01-M

### Advisory Committee on Reactor Safeguards, Subcommittee on Class 9 (Severe) Accidents; Meeting

The ACRS Subcommittee on Class 9 (Severe) Accidents will hold a meeting on January 29, 1986, Room 1046, 1717 H Street, NW, Washington, DC.

The entire meeting will be open to public attendance.

The agenda for the subject meeting shall be as follows: Wednesday, January 29, 1986—1:00 p.m. until the conclusion of business

The Subcommittee will review the research activities in regard to risk perspective and rebaselining studies intended for NUREG-1150.

Oral statements may be presented by members of the public with the concurrence of the Subcommittee Chairman; written statements will be accepted and made available to the Committee. Recordings will be permitted only during those portions of the meeting when a transcript is being kept, and questions may be asked only by members of the Subcommittee, its consultants, and Staff. Persons desiring to make oral statements should notify the ACRS staff member named below as far in advance as is practicable so that appropriate arrangements can be made.

During the initial portion of the meeting, the Subcommittee, along with any of its consultants who may be present, may exchange preliminary views regarding matters to be considered during the balance of the meeting.

The Subcommittee will then hear presentations by and hold discussions with representatives of the NRC Staff, its consultants, and other interested persons regarding this review.

Further information regarding topics to be discussed, whether the meeting has been cancelled or rescheduled, the Chairman's ruling on requests for the opportunity to present oral statements and the time allotted therefor can be obtained by a prepaid telephone call to the cognizant ACRS staff member, Mr. Dean Houston (telephone 202/634-3467) between 8:15 a.m. and 5:00 p.m. Persons planning to attend this meeting are urged to contact the above named individual one or two days before the scheduled meeting to be advised of any changes in schedule, etc., which may have occurred.

Dated: December 19, 1985.
**Morton W. Libarkin,**
*Assistant Executive Director for Project Review.*
[FR Doc. 85-30392 Filed 12-23-85; 8:45 am]
BILLING CODE 7590-01-M

### Advisory Committee on Reactor Safeguards, Subcommittee on Emergency Core Cooling Systems; Meeting

The ACRS Subcommittee on Emergency Core Cooling Systems will hold a meeting on January 23 and 24, 1986. The Subcommittee will meet at the Electric Power Research Institute (EPRI) Offices, 3420 Hillview Avenue, Palo Alto, CA.

The entire meeting will be open to public attendance.

The agenda for the subject meeting shall be as follows: *Thursday, January 23, 1986—1:00 p.m. until the conclusion of business; Friday, January 24, 1986—8:30 a.m. until the conclusion of business.*

The Subcommittee will continue the review of the joint NRC/B&WOG/EPRI/B&W joint IST Program. A visit is planned to the EPRI-sponsored facilities supporting this Program at the Stanford Research Institute and Science Applications, Inc.

Oral statements may be presented by members of the public with the concurrence of the Subcommittee Chairman; written statements will be accepted and made available to the Committee. Recordings will be permitted only during those portions of the meeting when a transcript is being kept, and questions may be asked only by members of the Subcommittee, its consultants, and Staff. Persons desiring to make oral statements should notify the ACRS staff member named below as far in advance as is practicable so that appropriate arrangements can be made.

During the initial portion of the meeting, the Subcommittee, along with

any of its consultants who may be present, may exchange preliminary views regarding matters to be considered during the balance of the meeting.

The Subcommittee will then hear presentations by and hold discussions with representatives of the NRC Staff, its consultants, and other interested persons regarding this review.

Further information regarding topics to be discussed, whether the meeting has been cancelled or rescheduled, the Chairman's ruling on requests for the opportunity to present oral statements and the time allotted therefor can be obtained by a prepaid telephone call to the cognizant ACRS staff member, Mr. Paul Boehnert (telephone 202/634-3267) between 8:15 a.m. and 5:00 p.m. Persons planning to attend this meeting are urged to contact the above named individual one or two days before the scheduled meeting to be advised of any changes in schedule, etc., which may have occurred.

Dated: December 18, 1985.

Morton W. Libarkin,

*Assistant Executive Director for Project Review.*

[FR Doc. 85-30393 Filed 12-23-85; 8:45 am]

BILLING CODE 7590-01-M

## OFFICE OF PERSONNEL MANAGEMENT

### Excepted Service

**AGENCY:** Office of Personnel Management.

**ACTION:** Notice.

**SUMMARY:** This gives notice of positions placed or revoked under Schedules A, B, and C in the excepted service, as required by civil service rule VI, Exceptions from the Competitive Service.

**FOR FURTHER INFORMATION CONTACT:** Tracy Spencer, (202) 632-6817.

**SUPPLEMENTARY INFORMATION:** The Office of Personnel Management published its last monthly notice updating appointing authorities established or revoked under the Excepted Service provisions of 5 CFR Part 213 on November 26, 1985, (50 FR 48662). Individual authorities established or revoked under Schedules A, B, or C between November 1, 1985 and November 30, 1985, appear in a listing below. Future notices will be published on the fourth Tuesday of each month, or as soon as possible thereafter. A consolidated listing of all authorities will be published as of June 30 of each year.

**Schedule A**

The following exception is established:

*Department of the Air Force*

One Chief of Engineering in Detachment 2, 2762 Logistics Squadron (Special), Air Force Logistics Command, Greenville, Texas. Effective November 18, 1985.

**Schedule B**

No Schedule B exceptions were established or revoked in November.

**Schedule C**

The following exceptions are established:

*Department of Agriculture*

One Confidential Assistant to the Assistant Secretary for Governmental and Public Affairs. Effective November 4, 1985.

One Private Secretary to the Executive Assistant to the Secretary. Effective November 6, 1985.

One Special Assistant to the Secretary. Effective November 6, 1985.

One Staff Assistant to the Assistant Secretary for Governmental and Public Affairs. Effective November 6, 1985.

One Confidential Assistant to the Assistant Secretary for Governmental and Public Affairs. Effective November 7, 1985.

One Confidential Assistant to the Deputy Secretary. Effective November 7, 1985.

One Private Secretary to the Assistant Secretary for Economics. Effective November 12, 1985.

One Confidential Assistant to the Administrator, Rural Electrification Administration. Effective November 22, 1985.

One Confidential Assistant to the Assistant Secretary for Governmental and Public Affairs. Effective November 22, 1985.

One Confidential Assistant to the Chief, Soil Conservation Service. Effective November 22, 1985.

*Department of Commerce*

One Confidential Assistant to the Deputy Secretary. Effective November 8, 1985.

One Confidential Assistant to the Assistant Secretary for Administration. Effective November 15, 1985.

One Congressional Liaison Specialist to the Deputy Assistant Secretary for Congressional Affairs. Effective November 18, 1985.

One Private Secretary to the Chief Economist. Effective November 19, 1985.

One Confidential Assistant to the Director General for the U.S. and Foreign Commercial Services, International Trade Administration. Effective November 22, 1985.

One Confidential Assistant to the Deputy Under Secretary for International Trade. Effective November 25, 1985.

*Department of Defense*

One Secretary (Stenography ) to the Assistant Secretary of the Army (Installations and Logistics). Effective November 4, 1985.

One Counselor and Director, Long-Range Policy, to the Deputy Assistant Secretary of Defense (Negotiations Policy). Effective November 22, 1985.

*Department of Education*

One Special Assistant to the Assistant Secretary for Elementary and Secondary Education. Effective November 1, 1985.

One Special Assistant to the Secretary's Regional Representative, with duty location in Chicago, Illinois. Effective November 5, 1985.

One Special Assistant to the Secretary. Effective November 12, 1985.

One Special Assistant to the Under Secretary. Effective November 27, 1985.

*Department of Energy*

One Executive Assistant to the Secretary. Effective November 4, 1985.

One Confidential Assistant (Secretary) to the Deputy Secretary. Effective November 7, 1985.

One Secretary (Confidential Assistant) to the Associate Director for Geological Repositories. Effective November 7, 1985.

One Staff Assistant to the Deputy Secretary. Effective November 7, 1985.

One Staff Assistant to the Special Assistant to the Secretary. Effective November 7, 1985.

One Staff Assistant to the Assistant Secretary for Environment, Safety and Health. Effective November 8, 1985.

One Staff Assistant to the Deputy Assistant Secretary for Security Affairs. Effective November 8, 1985.

One Director, Office of Domestic Issues, to the Director, Office of Communications, Office of the Assistant Secretary for Congressional, Intergovernmental and Public Affairs. Effective November 21, 1985.

One Staff Assistant to the Administrator, Bonneville Power Administration. Effective November 22, 1985.

One Confidential Assistant to the Administrator, Economic Regulatory

Administration. Effective November 25, 1985.

*Department of Health and Human Services*

One Congressional Liaison Specialist to the Deputy Assistant Secretary for Legislation (Congressional Liaison), Office of the Assistant Secretary for Legislation (Congressional Liaison). Effective November 4, 1985.

*Department of Housing and Urban Development*

One Special Assistant to the Assistant Secretary for Fair Housing and Equal Opportunity. Effective November 5, 1985.

One Special Assistant to the Regional Administrator/Regional Housing Commissioner, with duty location in San Francisco, California. Effective November 12, 1985.

One Executive Assistant to the Deputy Assistant Secretary for Policy, Financial Management and Administration, Office of Housing. Effective November 14, 1985.

One Special Assistant to the President, Government National Mortgage Association. Effective November 25, 1965.

One Intergovernmental Relations Officer to the Deputy Under Secretary for Intergovernmental Relations. Effective November 27, 1985.

*Department of Interior*

One Staff Assistant to the Assistant Secretary for Indian Affairs. Effective November 1, 1985.

One Staff Assistant to the Director, Office of Public Affairs, Office of the Commissioner, Bureau of Reclamation. Effective November 4, 1985.

One Special Assistant for Programs to the Counselor to the Secretary. Effective November 18, 1985.

*Department of Justice*

One Director, Regulatory and Legislative Affairs Staff to the Assistant Attorney General, Civil Division. Effective November 4, 1985.

One Confidential Assistant to the Deputy Assistant Attorney General, Antitrust Division. Effective November 7, 1985.

One Staff Assistant to the Director, Office of Public Affairs. Effective November 25, 1985.

*Department of Labor*

One Special Assistant for Public Affairs to the Deputy Under Secretary, Employment Standards Administration. Effective November 1, 1985.

One Special Assistant to the Director, Office of Federal Contract Compliance Programs, Employment Standards Administration. Effective November 25, 1985.

*Department of State*

One Protocol Clerk to the Chief of Protocol. Effective November 21, 1985.

One Member, Policy Planning Staff, to the Chairman Policy Planning Council. Effective November 27, 1985.

One Protocol Specialist to the Chief of Protocol. Effective November 27, 1985.

One Special Assistant to the Assistant Secretary for the Bureau of Inter-American Affairs. Effective November 27, 1985.

*Department of Transportation*

One Congressional Liaison Officer to the Director, Office of Congressional Affairs, Office of the Assistant Secretary for Governmental Affairs. Effective November 4, 1985.

One Congressional Liaison Specialist to the Director, Office of Congressional Affairs, Office of the Assistant Secretary for Governmental Affairs. Effective November 5, 1985.

One Director, Office of Special Projects, to the Assistant Secretary for Public Affairs. Effective November 5, 1985.

One Intergovernmental Liaison Specialist to the Director, Office of Intergovernmental Affairs, Office of the Assistant Secretary for Governmental Affairs. Effective November 5, 1985.

One Director, Office of Media Relations to the Assistant Secretary for Public Affairs. Effective November 7, 1985.

One Special Assistant to the Administrator, Urban Mass Transportation Administration. Effective November 8, 1985.

One Special Assistant to the Director, Executive Secretariat. Effective November 8, 1985.

*Department of Treasury*

One Travel Assistant to the Deputy Assistant Secretary for Administration. Effective November 12, 1985.

One Legislative Aid to the Assistant Secretary for Legislative Affairs. Effective November 15, 1985.

*ACTION*

One Special Assistant to the Deputy Director. Effective November 18, 1985.

*Agency for International Development*

One Administrative Operations Assistant to the Deputy Assistant Administrator. Effective November 6, 1985.

One Special Assistant to the Deputy Assistant to the Administrator for Management, Bureau for Management. Effective November 14, 1985.

*Consumer Product Safety Commission*

One Special Assistant (Legal) to a Commissioner. Effective November 18, 1985.

One Staff Assistant to a Commissioner. Effective November 18, 1985.

*Equal Employment Opportunity Commission*

One Confidential Assistant to a Commissioner. Effective November 14, 1985.

*Federal Mine Safety and Health Review Commission*

One Special Assistant to the Chairman. Effective November 1, 1985.

*General Services Administration*

One Deputy to the Associate Administrator for Operations (External Affairs). Effective November 25, 1985.

*National Archives and Records Administration*

One Congressional Relations Officer to the Archivist of the United States. Effective November 12, 1985.

*National Endowment for the Humanities*

One Administrative Assistant to the Chairman. Effective November 4, 1985.

*Occupational Safety and Health Review Commission*

One Confidential Assistant to a Commissioner. Effective November 8, 1985.

One Confidential Assistant to a Commissioner. Effective November 13 1985.

*Office of Personnel Management*

One Staff Assistant to the Assistant Director for Executive Administration. Effective November 8, 1985.

One Staff Assistant (Typing) to the Director. Effective November 8, 1985.

*United States Information Agency*

One Special Assistant to the Deputy Director. Effective November 19, 1985.

*United States Tax Court*

One Secretary (Confidential Assistant) to a Judge of the Tax Court. Effective November 26, 1985.

U.S. Office of Personnel Management.

**Constance Horner,**

*Director.*

[FR Doc. 85-30394 Filed 12-23-85; 8:45 am]

BILLING CODE 6325-01-M

## PACIFIC NORTHWEST ELECTRIC POWER AND CONSERVATION PLANNING COUNCIL

### Columbia River Basin Fish and Wildlife Program; Proposed Amendments; Hearing and Opportunity to Comment

**AGENCY:** Pacific Northwest Electirc Power and Conservation Planning Council (Northwest Power Planning Council).

**ACTION:** Notice of proposed amendments, hearings and opportunity to comment.

**SUMMARY:** On November 15, 1982, pursuant to the Pacific Electric Power Planning and Conservation Act (the Northwest Power Act, 16 U.S.C. 839, et seq.) the Pacific Northwest Electric Power and Conservation Planning Council (Council) adopted a Columbia River Basin Fish and Wildlife Program (Program) including certain measures to improve downstream passage of juvenile fish at U.S. Army Corp of Engineers dams on the lower Columbia and Snake River. On October 10, 1984, the Council amended the Program, and adopted interim survival objectives to improve downstream passage of juvenile fish at such Columbia and Snake River dams. On December 12, 1985, the Council voted to initiate rulemaking pursuant to section 4(d)(1) of the Northwest Power Act and section 1404(a)(1) of the Program to amend the program again. This notice describes the proposed amendments (hereafter "proposed interim survival objectives") and explains how to participate in the amendment process. Because the matters being considered would affect the 1986 fish migration season, these proposed interim survival objectives are being considered separately from the 1986–87 general Program amendment process (see 50 FR 28049). Therefore, those interested in commenting on these proposed interim survival objectives should expect to do so only in the comment period and hearings described in this notice. The Council expects to make a decision on these proposed interim survival objectives in February, 1986, well before its decision on the general Program amendments, which is not expected to occur before early 1987. Comments on these proposed interim survival objectives will not be timely in the Council's general Program amendment process.

**DATE AND ADDRESSES:** The public comment period regarding these proposed interim survival objectives closes at 5 p.m. Pacific time on January 24, 1986. Public hearings on the proposed passage amendments will be held in January in Idaho, Montana, Oregon and Washington. The places and times for these hearings will be announced at a later date.

The Council currently expects to take final action on the proposed interim survival objectives at its February, 1986 meeting. The actual date on which the Council will make its final decision will be announced in accordance with applicable law and in accordance with the Council's practice of providing notice of its meeting agendas.

#### Guidelines for Presenting Oral Comments at Hearings

1. To reserve at time period for presenting oral comments at a hearing, contact Ruth Curtis, Information Coordinator, at the Council's central office (850 S.W. Broadway, Suite 1100, Portland, Oregon 97205 or (503) 222–5161, toll free 1–800–222–3355 in Idaho, Montana, and Washington or 1–800–452–2324 in Oregon) no later than two work days before the hearing.

2. Those who do not reserve a time period will be permitted to present oral comments only as time permits.

3. Use the hearing to *summarize* written comments. The comments themselves should not be read.

4. If possible, ten (10) copies of written comments should be submitted to the Council recorder at the hearings. This person will be sitting at a table near the Council members and will be identified at the start of the hearing by the hearing chairman. When preparing these copies, refer to the instructions below for written comments.

5. Comment time may be limited, to allow all commenters a hearing, when the number of people who signed up to testify is sufficiently large. A 15-minute guideline is suggested.

6. Appearance at more than one hearing is unnecessary. At each hearing, scheduling preference will be given to individuals and groups which have not testified at other hearings.

#### Guidelines for Submitting Written Comments

1. All written comments must be received in the Council's central office, 850 S.W. Broadway, Suite 1100, Portland, Oregon, 97205, by 5 p.m. Pacific time on January 24, 1986. Comments should be submitted to the attention of Dulcy Mahar at this address.

2. Comments should be clearly marked "Fish Passage Comments."

3. Written comments should be specific and concise.

4. Please type (double-spaced) comments, if possible. Use only one side of the paper.

5. Provide ten (10) copies of all comments and supporting materials if possible.

**FOR FURTHER INFORMATION CONTACT:** The Council has prepared an issue paper entitled "Alternative Interim Fish Passage Objectives," which discusses the background of this issue and identifies alternatives the Council is considering in connectionwith this proposed rulemaking. Those wishing to receive a copy of the issue paper should contact Judy Allender at the address and telephone numbers listed above.

**SUPPLEMENTARY INFORMATION:** The Northwest Power Act and the Columbia River Basin Fish and Wildlife Program call for improvements in the survival of downstream migrating salmon and steelhead at mainstem hydroelectric projects on the Columbia River system. One method of improving survival, which is reflected in the existing program, is to "spill" water at dams, enabling fish to pass the dam without going through the dam's hydroelectric turbines. Turbines are a significant source of mortality to juvenile fish. This proposed rulemaking concerns interim survival objectives to guide the planning and management of spill to improve fish survival. These interim survival objectives may be included in the Program until permanent mainstem passage improvements are completed.

As adopted in 1982, the Fish and Wildlife Program called on the U.S. Army Corps of Engineers (the Corps), which operates eight dams on the lower Columbia and Snake Rivers, to develop and implement a spill plan to protect juvenile fish. This spill plan was to be developed and implemented by the Corps in consultation with the state fishery agencies and affected Indian tribes. The Program's objectives was to achieve a level of survival comparable to or better than that achievable by the best available bypass and screening systems (mechanical systems for passing fish around dams and turbines).

The Corps and the fishery agencies and tribes failed to develop joint juvenile fish passage plans prior to the 1983 and 1984 outmigrations because they could not agree on the appropriate level of fish protection or spill levels.

The Council amended the Program in 1984 to call on the Corps to provide sufficient spills to enable 90 percent of the fish to survive its projects and to develop and implement an annual juvenile fish passage plan to accomplish that objective. At Bonneville Dam a more stringent 85 percent passage efficiency objective was adopted. These provisions are set out in sections 404

and 1504 of the Program as amended in 1984.

In early 1985 the Corps and the fishery agencies and tribes again were unable to develop a joint juvenile fish passage plan as specified by the Program.

At a March 15, 1985 Council meeting, the directors of various fishery agencies and Indian tribes asked the Council to reconsider the interim 90 percent survival objective. At that time the Council agreed to reconsider the interim survival objective prior to the 1986 fish migration, which begins in the Spring. On August 2, 1985, the Council requested that the agencies and tribes submit to the Council an alternative to the 90 percent survival objective, with scientific information sufficient to justify an alternative. The agencies' and tribes' alternative was submitted to the Council on August 15, 1985.

At the August 8, 1985 Council meeting in Portland, the Council chartered the Mainstem Passage Advisory Committee. The Committee is comprised of members of the region's state and federal fishery agencies, Indian tribes, federal operating agencies (the Corps and the Bonneville Power Administration) and utility groups. One of the committee's primary purposes is to provide technical advice and assistance to the Council staff in examining alternative interim survival objectives for the 1986 fish migration season. Toward that end, the Mainstem Passage Advisory Committee has had seven meetings over the course of four months, and developed much of the information and analysis upon which the proposed rule is based.

On November 22, 1985, the fishery agencies and tribes submitted a request to the Council to enter rulemaking at the December 11–12 Council meeting to amend the mainstem passage provisions contained in sections 304, 404, and 1504 of the Program by mid-February, 1986.

Based on its review of the data and analysis developed in connection with the Mainstem Passage Advisory Committee, the Council determined that a Program amendment may be needed to improve the survival of downstream migrating salmon and steelhead smolts at federal hydroelectric projects, and to provide clearer guidance to the fishery agencies, tribes, and federal operating agencies in formulating and implementing interim spill plans.

The Council now seeks public comment on the proposed amendments described below, and on alternative survival objectives discussed in the issue paper referred to in the "For Further Information" section of this notice, above. The Council particularly encourages submission of comments addressing the following issues:

—What is the most appropriate level of spill for juvenile fish at: (a) non-transport dams; and (b) transport dams?
—Should there be a different survival standard for spring and summer migrants?
—Should the spill program affect firm energy or only nonfirm energy?
—If the proposed rule were adopted in February, 1986, would there be any conflict with BPA short-term firm power contracts?
—Is a different process needed to ensure joint development and mutual acceptance of spill plans?
—What period of time should a spill program be in effect?
—Should spill be defined in terms of spill volume or a percentage of average daily flow over a specified period of time?

**Proposed Amendments**

If adopted by the Council, the proposed amendments would amend section 304, 404 and 1504 of the Columbia River Basin Fish and Wildlife Program.

*Interim Survival Objectives for U.S. Army Corps of Engineers Hydroelectric Projects on the Lower Columbia and Snake Rivers*

The proposed rule addresses three related issues. First, it addresses the broad issue of what survival objective(s) would provide adequate interim protection for juvenile fish. Second, it responds to the narrower issue of whether it is appropriate to specify a survival objective for fish that are collected and transported around the dam by truck or barge. Third, the rule assigns responsibility for coordinating spill requests.

Regarding the first question, the proposed rule would establish an interim survival objective of 94 percent in average and higher water conditions. In lower-than-average water conditions, the survival objective would be 92 percent.

Regarding the second question, the proposed rule would apply to all first stocks at non-transportation dams (i.e., Lower Monumental, Ice Harbor, John Day, and The Dalles dams, where no fish are collected and transported). At transportation dams (i.e., Lower Granite, Little Goose and McNary dams, where fish are collected and transported), the proposed interim survival objectives would apply only to those stocks that are not not collected and transported. In practical terms, the Council anticipates that at transportation dams the proposed survival objectives would apply only to juvenile spring chinook salmon, consistent with recent transportation policies formulated by the Columbia River Basin Fish and Wildlife Council and the Columbia River Inter-Tribal Fish Commission. Under those transportation guidelines steelhead and fall/summer chinook are, as much as possible, to be collected and transported downstream. In contrast, transportation is not the preferred alternative for protecting juvenile spring chinook. If the transportation guidelines change to emphasize transportation of all fish stocks, then the proposed rule would not apply to the three transportation dams. The proposed rule still would apply to all stocks at the four non-transportation dams.

As to the third question, the rule assigns to the Water Budget managers under section 304(b) of the Program the responsibility to coordinate fishery agency and tribal requests for spill during the passage season.

The proposed rule does not address the merits of the Corps' transportation program, nor does it address the problem of reservoir mortalities. It is the Council's preliminary judgment that those issues should not be resolved in this rulemaking.

The proposed rule also does not address certain management and institutional issues raised by the fishery agencies and tribes, which are detailed in a November 22, 1985 letter to the Council. The Council wishes to consider primarily survival objectives in this rulemaking, and therefore has not included management and institutional issues in the proposed rule. However, the Council recognizes that the management and institutional issues raised by the tribes and agencies are serious. Accordingly, comment is invited on whether it is advisable for the Council to address these issues in this rulemaking, and if so in what manner.

Council staff has estimated the system costs and firm energy (refill) impacts of providing varying amounts of spill to achieve different survival objectives. The analysis shows that, when compared to no spill, the total expected costs of the proposed interim survival objectives, including replacement energy purchases to alleviate refill impacts, range from a low of $3.1 million to a high of $9.7 million. The proposed interim survival can be expected to increase Bonneville's preference rate by about .2 mill, or, when compared to the status quo, by about .07 mill. In the Council's preliminary judgment, these costs and power impacts are consistent with an adquate, efficient, economical and reliable power supply for the region. Details of the economic analyses

conducted to evaluate the costs of alternative spill scenarios are included in the issue paper referred to in the "For Further Information" section of this notice.

Copies of the staff issue paper referred to in the "For Further Information" section of this notice have been mailed to those included on the Council's fish and wildlife mailing list. Others may request copies as directed in the "for Further Information" section of this notice.

**Edward Sheets,**

*Executive Director.*

[FR Doc. 85-30312 Filed 12-23-85; 8:45 am]

BILLING CODE 0000-00-M

## SMALL BUSINESS ADMINISTRATION

**[Declaration of Disaster Loan Area No. 2223]**

### Declaration of Disaster Loan Area; Arkansas

The County of Baxter and the adjacent County of Marion in the State of Arkansas constitute a disaster area because of damage caused by tornadoes which occurred on November 18, 1985. Applications for loans for physical damage may be filed until the close of business on February 10, 1986, and for economic injury until the close of business on September 10, 1986, at the address listed below:

Disaster Area 3 Office, Small Business Administration, 2306 Oak Lane, Suite 110, Grand Prairie, Texas 75051.

or other locally announced locations.

The interest rates are:

| | Percent |
|---|---|
| Homeowners with credit available elsewhere | 8.000 |
| Homeowners without credit available elsewhere | 4.000 |
| Businesses with credit available elsewhere | 8.000 |
| Businesses without credit available elsewhere | 4.000 |
| Businesses (EIDL) without credit available elsewhere | 4.000 |
| Other (non-profit organizations including charitable and religious organizations) | 10.500 |

The number assigned to this disaster is 222312 for physical damage and for economic injury the number is 635500.

(Catalog of Federal Domestic Assistance Program Nos. 59002 and 59008)

Dated: December 10, 1985.

**James C. Sanders,**

*Administrator.*

[FR Doc. 85-30336 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

### Magna Pacific Investments; Issuance of a Small Business Investment Company License

**[License No. 09/09-5362]**

On July 26, 1985, a notice was published in the **Federal Register** (30556) stating that an application has been filed by Magna Pacific Investments, with the Small Business Administration (SBA) pursuant to § 107.102 of the Regulations governing small business investment companies (13 CFR 107.102 (1985)) for a license as a small business investment company.

Interested parties were given until close of business August 25, 1985, to submit their comments to SBA. No comments were received.

Notice is hereby given that, pursuant to section 301(d) of the Small Business Investment Act of 1958, as amended, after having considered the application and all other pertinent information, SBA issued License No. 09/09-5362 on December 3, 1985, to Magna Pacific Investments to operate as a small business investment company.

Dated: December 12, 1985.

(Catalog of Federal Domestic Assistance Program No. 59.011, Small Business Investment Companies)

**Robert G. Lineberry,**

*Deputy Associate Administrator for Investment.*

[FR Doc. 85-30360 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

**[Declaration of Disaster Loan Area No. 2222]**

### Florida; Declaration of Disaster Loan Area; Correction

The above numbered Declaration (50 FR 50697), and Amendments thereto, which were issued in accordance with the President's declaration of December 3, 1985, is hereby corrected to read:

The interest rates are:

Business (EIDL) without credit available elsewhere.....4.000%

All other information remains the same.

(Catalog of Federal Domestic Assistance Program Nos. 59002 and 59008).

Dated: December 16, 1985.

**Alfred E. Judd,**

*Acting Deputy Associate Administrator for Disaster Assistance.*

[FR Doc. 85-30361 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

**[Declaration of Disaster Loan Area No. 2222; Amendment No. 2]**

### Florida; Declaration of Disaster Loan Area

The above-numbered Declaration (50 FR 50697), which are issued in accordance with the President's declaration of December 3, 1985, is hereby amended in accordance with the amendment dated December 13, 1985, to include Leon County because of damage from Hurricane Kate and flooding beginning on or about November 20, 1985. All other information remains the same; i.e., the termination date for filing applications for physical damage is the close of business on February 3, 1986, and for economic injury until the close of business on September 3, 1986.

Dated: December 16, 1985.

(Catalog of Federal Domestic Assistance Programs Nos. 59002 and 59008).

**Alfred E. Judd,**

*Acting Associate Administrator for Disaster Assistance.*

[FR Doc. 85-30362 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

**[Declaration of Disaster Loan Area #2225]**

### New York; Declaration of Disaster Loan Area

The County of Erie and the adjacent County of Chatuaqua in the State of New York constitute a disaster area because of damage caused by a winter storm occurring December 1, 1985, accompanied by high winds causing coastal and inland tidal surges. Applications for loans for physical damage may be filed until the close of business on February 11, 1986, and for economic injury until the close of business on September 15, 1986, at the address listed below: Disaster Area 1 Office, Small Business Administration, 15-01 Broadway, Fair Lawn, New Jersey 07410; or other locally announced locations.

The interest rates are:

| | Percent |
|---|---|
| Homeowners with credit available elsewhere | 8.000 |
| Homeowners without credit available elsewhere | 4.000 |
| Businesses with credit available elsewhere | 8.000 |
| Businesses without credit available elsewhere | 4.000 |
| Businesses (EIDL) without credit available elsewhere | 4.000 |
| Other (non-profit organizations including charitable and religious organizations) | 10.500 |

The number assigned to this disaster is 222506 for physical damage and for economic injury the number is 635800.

Dated: December 13, 1985

(Catalog of Federal Domestic Assistance Program Nos. 59002 and 59008).

James C. Sanders,

*Administrator.*

[FR Doc. 85-30359 Filed 12-23-85; 8:45 am]

BILLING CODE 8025-01-M

## DEPARTMENT OF STATE

[Public Notice CM-8/9 18]

### Study Group 5 of the U.S. Organization for the International Radio Consultative Committee (CCIR); Meeting

The Department of State announces that Study Group 5 of the U.S. Organization for the International Radio Consultative Committee (CCIR) will meet on January 17, 1986 in Room CR 1-42, Engineering Center, University of Colorado, Boulder, Colorado. The meeting will begin at 1:00 p.m.

Study Group 5 deals with propagation of radio waves (including radio noise) at the surface of the earth, through the non-ionized regions of the earth's atmosphere, and in space where the effect of ionization is negligible. The purpose of the meeting will be to review the results of the international meeting of Study Group 5 in September, 1985 and discuss preparations for the XVIth CCIR Plenary Assembly in May, 1986.

Members of the general public may attend the meeting and join in the discussions subject to intructions of the Chairman. Admittance of public members will be limited to the seating available. Requests for further information should be directed to Mr. Richard Shrum, State Department, Washington, DC 20520; telephone (202) 632-2592.

Dated: December 13, 1985.

Richard E. Shrum,

*Chairman, U.S. CCIR National Committee.*

[FR Doc. 85-30315 Filed 12-23-85; 8:45 am]

BILLING CODE 4710-07-M

## DEPARTMENT OF TRANSPORTATION

### Order Adjusting the Standard Foreign Fare Level Index

The International Air Transportation Competition Act (IATCA), Pub. L. 96-192, requires that the Department, as successor to the Civil Aeronautics Board, establish a Standard Foreign Fare Level (SFFL) by adjusting the SFFL base periodically by percentage changes in actual operating costs per available seat-mile. Order 80-2-69 established the first interim SFFL and Order 85-10-31 established the currently effective two-month SFFL applicable through November 30, 1985.

In establishing the SFFL for the two-month period starting December 1, 1985, we have projected nonfuel costs based on the year ended September 30, 1985 data, and have determined fuel prices on the basis of experienced monthly fuel cost levels as reported to the Department.

By Order 85-12-54 fares may be increased by the following adjustment factors over the October 1, 1979, level:

Atlantic—1.1051
Latin America—1.3472
Pacific—1.2573
Canada—1.2468

For Further Information Contact: Julien R. Schrenk (202) 472-5126.

By the Department of Transportation.

Dated: December 18, 1985.

Matthew V. Scocozza

*Assistant Secretary for Policy and International Affairs.*

[FR Doc. 85-30386 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-62-M

## Federal Aviation Administration

### Jackson Hole Airport, Jackson, WY; FAA Approval of Noise Compatibility Program

**AGENCY:** Federal Aviation Administration, DOT.

**ACTION:** Notice.

**SUMMARY:** The Federal Aviation Administration (FAA) announced its findings on the noise compatibility program submitted by the Jackson Hole Airport Board under the provisions of Title I of the Aviation Safety and Noise Abatement Act (ASNA) of 1979 (Pub. L. 96-193) and 14 CFR Part 150. These findings are made in recognization of the description of Federal and non-Federal responsibilities in Senate Report No. 96-52 (1980). On May 15, 1985, the FAA determined that the noise exposure maps submitted by the Airport Board under Part 150 were in compliance with applicable requirements. On November 8, 1985, the Administrator approved the Jackson Hole Airport noise compatibility program.

**EFFECTIVE DATE:** The effective date of the FAA's approval of the Jackson Hole Airport noise compatibility program is November 8, 1985.

**FOR FURTHER INFORMATION CONTACT:** Dennis G. Ossenkop; Federal Aviation Administration: Northwest Mountain Region; Airports Division, ANM-611; 17900 Pacific Highway South; C-68966; Seattle, Washington 98168. Documents reflecting this FAA action may be obtained from the same individual.

**SUPPLEMENTARY INFORMATION:** This notice announces that the FAA has given its overall approval to the noise compatibility program for Jackson Hole Airport, effective November 8, 1985.

Under section 104(a) of the Aviation Safety and Noise Abatement Act (ASNA) of 1979, an airport operator who has previously submitted a noise exposure map may submit to the FAA a noise compatability program which sets forth the measures taken or proposed by the airport operator for the reduction of existing noncompatible land uses and prevention of additional noncompatible land uses within the area covered by the noise exposure maps. The Act requires such a program to be developed in consultation with interested and affected parties including the state, local communities, government agencies, airport users, and FAA personnel.

Each airport noise compatibility program developed in accordance with FAR Part 150 is a local program, not a Federal program. The FAA does not substitute its judgment for that of the airport proprietor with respect to which measures should be recommended for action. The FAA's approval or disapproval of FAR Part 150 program recommendations is measured according to the standards expressed in Part 150 and the Aviation Safety and Noise Abatement Act of 1979, and is limited to the following determinations:

The noise compatibility program was developed in accordance with the provisions and procedures of FAR Part 150;

Program measures are reasonably consistent with achieving the goals of reducing existing noncompatible land uses around the airport and preventing the introduction of additional noncompatible land uses;

Program measures would not create an undue burden on interstate or foreign commerce, unjustly discriminate against types or classes of aeronautical uses, violate the terms of airport grant agreements, or intrude into areas preempted by the Federal Government.

Program measures relating to the use of flight procedures can be implemented within the period covered by the program without derogating safety, advesely affecting the efficient use and management of the navigable Airspace and Air Traffic Control Systems, or adversely affecting other powers and responsibilities of the Administrator prescribed by law.

Specific limitations with respect to FAA's approval of an airport noise compatibility program are delineated in FAR part 150, Section 150.5. Approval is not a determination concerning the

acceptability of land uses under Federal, state, or local law. Approval does not by itself constitute an FAA implementing action. A request for Federal action or approval to implement specific noise compatibility measures may be required, and an FAA decision on the request may require an environmental assessment of the proposed action. Approval does not constitute a commitment by the FAA to financially assist in the implementation of the program nor a determination that all measures covered by the program are eligible for grant-in-aid funding from the FAA under the Airport and Airway Improvement Act of 1982. Where Federal funding is sought, requests for project grants must be submitted to the FAA Airports District Office in Denver, Colorado.

The Airport Board submitted to the FAA on April 22, 1985, the noise exposure maps, descriptions, and other documentation produced durding the noise compatibility planning study conducted at Jackson Hole Airport. The Jackson Hole Airport noise exposure maps were determined by FAA to be in compliance with applicable requirements on May 15, 1985. Notice of this determination was published in the Federal Register on May 28, 1985.

The Jackson Hole Airport noise compatibility study contains a proposed noise compatibility program comprised of actions designed for phased implementation by airport management and adjacent jurisdictions. It was requested that the FAA evaluate and approve this material as a noise compatibility program as described in section 104(b) of the Act. The FAA began its review of the program on May 15, 1985, and was required by a provision of the Act to approve or disapprove the program within 180 days (other than the use of new flight procedures for noise control). Failure to approve or disapprove such program within the 180-day period shall be deemed to be an approval of such program.

The submitted program contained 20 proposed actions for noise mitigation on and off the airport and for review and monitoring of the program. The FAA completed its review and determined that the procedural and substantive requirements of the Act and FAR Part 150 have been satisfied. The overall program, therefore, was approved by the Administrator effective November 8, 1985.

Outright approval was granted for 19 specific program elements and part of the 20th. On-airport actions include an access plan to encourage use of quiet aircraft, continued use of the existing curfew and single event noise approach noise limit, a new departure route, preferential runway use, an Automatic Weather Observation System and continuance of pilot education program. Off-airport elements include zoning changes, voluntary noise abatement procedures, avigation easements, transfer of development rights, new subdivision regulations, and preventive land use planning and policies. The program also expands the existing notice complaint system and provides for noise monitoring and program updates.

Part of one program element relating to imposing a nightime curfew on any new airlines was disapproved pending submission to the FAA of additional details to permit an informed analysis under section 104(b) of the ASNA Act. This disapproval does not reflect FAA opposition to the noise mitigation objectives of the proposal or of the concept on which it is based. Rather, as described above, the ASNA Act contemplates approval or disapproval within the 180-day review period. Lacking adequate detail for a proper evaluation, the FAA has disapproved this action. This does not foreclose additional FAA review if additional information is submitted by the airport operator.

These determinations are set forth in detail in a Record of Approval endorsed by the Administrator on November 8, 1985. The Record of Approval as well as other evaluation materials and the documents comprising the submittal, are available for review at the FAA office listed above and at the administrative offices of the Jackson Hole Airport.

Approval by the Administrator of the Part 150 noise compatibility program constitutes approval of the revised noise abatement plan by the Department of Transportation contemplated in the Agreement between the United States Department of the Interior and the Jackson Hole Airport Board of April 27, 1983.

Issued in Seattle, Washington on December 3, 1983.

Wayne Barlow,

*Director, Northwest Mountain Region.*

[FR Doc. 85-30309 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-13-M

## Federal Railroad Administration

[RS&I-Ap-No. 1015]

### The Atchison, Topeka and Santa Fe Railway Co; Petition

The Atchison, Topeka, and Santa Fe Railway Company has petitoned the Federal Railroad Administration (FRA) seeking an exemption from the requirements of the last sentence of § 236.204 of the Rules, Standards and Instructions which reads, "* * * In absolute permissive block signaling, when a train passes a head block signal it shall cause the opposing head block signal to display an aspect with an indication not more favorable than 'STOP'." This proceeding is identified as FRA Rules, Standards and Instructions Application No. 1015.

After examining the carrier's proposal and the available facts, the FRA has determined that a public hearing is necessary before a final decision is made on this proposal.

Accordingly, a public hearing is hereby set for 10 a.m. on February 25, 1986, in Hearing Room B, Fourth Floor of the Kansas State Office Building at 915 SW., Harrison Street in Topeka, Kansas.

The hearing will be an informal one, and will be conducted in accordance with Rule 25 of the FRA Rules of Practice (49 CFR 211.25), by a representative designated by the FRA.

The hearing will be a nonadversary proceeding and, therefore, there will be no cross-examination of persons presenting statements. The FRA representative will make an opening statement outlining the scope of the hearing. After all initial statements have been completed, those persons who wish to make brief rebuttal statements will be given the opportunity to do so in the same order in which they made their initial statments. Additional procedures, if necessary for the conduct of the hearing, will be announced at the hearing.

Issued in Washington, DC on December 19, 1985.

J.W. Walsh,

*Associate Administrator for Safety.*

[FR Doc. 85-30364 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-06-M

[RS-Ap-No. 2402]

### Canadian Pacific, Ltd.; Petition

The Canadian Pacific, Ltd. has petitioned the Federal Railroad Administration (FRA) seeking approval to discontinue the automatic block signal system between Newport, Vermont, and Wells River, Vermont, a distance of approximately 64 miles, and between Newport, Vermont, and Magowan, Vermont, a distance of approximately 4 miles. This proceeding is identified as FRA Block Signal Application No. 2402.

After examining the carrier's proposal and the available facts, the FRA has determined that a public hearing is necessary before a final decision is made on this proposal.

Accordingly, a public hearing is hereby set for 10 a.m. on February 12, 1986, in The Lincoln Inn at 20 Hastings Street in St. Johnsbury, Vermont.

The hearing will be an informal one, and will be conducted in accordance with Rule 25 of the FRA Rules of Practice (49 CFR 211.25), by a representative designated by the FRA.

The hearing will be a nonadversary proceeding and, therefore, there will be no cross-examination of persons presenting statements. The FRA representative will make an opening statement outlining the scope of the hearing. After all initial statements have been completed, those persons who wish to make brief rebuttal statements will be given the opportunity to do so in the same order in which they made their initial statements. Additional procedures, if necessary for the conduct of the hearing, will be announced at the hearing.

Issued in Washington, DC, on December 16, 1985.

**J.W. Walsh,**

*Associate Administrator for Safety.*

[FR Doc. 85-30365 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-06-M

---

**[BS-Ap-No. 2482]**

### Chicago and North Western Transportation Co.

The Chicago and North Western Transportation Company has petitioned the Federal Railroad Administration (FRA) seeking approval of the proposed discontinuance of the automatic block signal system between Janesville, Wisconsin, and Madison, Wisconsin, on its Wisconsin Division, a distance of about 51 miles. This proceeding is identified as FRA Block Signal Application No. 2482.

After examining the carrier's proposal and the available facts, the FRA has determined that a public hearing is necessary before a final decision is made on this proposal.

Accordingly, a public hearing is hereby set for 10 a.m. on February 27, 1986, in Room 460 of the U.S. Court House at 120 North Heary Street in Madison, Wisconsin.

The hearing will be an informal one, and will be conducted in accordance with Rule 25 of the FRA Rules of Practice (49 CFR 211.25), by a representative designated by the FRA.

The hearing will be a nonadversary proceeding and, therefore, there will be no cross-examination of persons presenting statements. The FRA representative will make an opening statement outlining the scope of the hearing. After all initial statements have been completed, those persons who wish to make brief rebuttal statements will be given the opportunity to do so in the same order in which they made their initial statements. Additional procedures, if necessary for the conduct of the hearing, will be announced at the hearing.

Issued in Washington, DC, on December 19, 1985.

**J.W. Walsh,**

*Associate Administrator for Safety.*

[FR Doc. 85-30366 Filed 12-23-85; 8:45 am]

BILLING CODE 4910-06-M

---

### Natchez Trace Railroad (NTR) et al.

In accordance with 49 CFR 211.9 and 211.41, notice is hereby given that four railroads have petitioned the Federal Railroad Administration (FRA) for a waiver of compliance with the provisions of the Hours of Service Act (83 Stat. 464, Pub. L. 91-169, 45 U.S.C. 64a(e)).

The Hours of Service Act currently makes it unlawful for a railroad to require specified employees to remain on duty for a period in excess of twelve hours. However, the Hours of Service Act contains a provision that permits a railroad which employs not more than fifteen employees who are subject to the statute to seek an exemption from the twelve-hour limitation.

Natchez Trace Railroad (NTR); FRA Waiver Petition Docket No. HS-85-23

The NTR seeks a continuation of a previously issued exemption so that it can permit certain employees to remain on duty not more than sixteen hours in any twenty-four hour period.

The NTR states that it is not their intention to employ a train crew over twelve (12) hours per day under normal operating conditions, but that this exemption, if granted, would help their operation if they encountered unusual operating conditions or circumstances.

The petitioner indicates that granting the exemption is in the public interest and will not adversely affect safety. Additionally, the petitioner asserts that it employs not more than fifteen employees and has demonstrated good cause for granting this exemption.

Lackawanna Valley Railroad (LVAL); FRA Waiver Petition Docket No. HS-85-24

The LVAL provides service between Carbon Junction (Moosic), Pennsylvania, and Carbondale, Pennsylvania, a distance of 25 miles. The normal operation of the railroad calls for only one (1) train per day, with work completed within the twelve hour limitation. This exemption, if granted, would allow the carrier to function if they encountered unusual operating conditions or circumstances.

The petitioner indicates that granting the exemption is in the public interest and will not adversely affect safety. Additionally, the petitioner asserts that it employs not more than fifteen employees and has demonstrated good cause for granting this exemption.

Bay Colony Railroad Corporation (BCLR); FRA Waiver Petition Docket No. HS-85-25

The BCLR seeks a continuation of a previously issued exemption so that it can permit certain employees to remain on duty not more than sixteen hours in any twenty-four hour period.

The BCLR states that it is not their intention to employ a train crew other twelve (12) hours per day under normal operating conditions, but that this exemption, if granted, would help their operation if they encountered unusual operating conditions or circumstances.

The petitioner indicates that granting the exemption is in the public interest and will not adversely affect safety. Additionally, the petitioner asserts that it employs not more than fifteen employees and has demonstrated good cause for granting this exemption.

Oregon, California and Eastern Railway Company (OCE); FRA Waiver Petition Docket No. HS-85-26

The OCE seeks this exemption so that it can permit certain employees to remain on duty not more than sixteen hours in any twenty-four hour period.

The OCE provides service over a 64-mile long system that primarily hauls logs from the woods to a conversion facility in Klamath Falls, Oregon.

The OCE states that it is not their intention to employ a train crew over twelve (12) hours per day under normal operating conditions, but that this exemption, if granted, would help their operation if they encountered unusual operating conditions or circumstances.

The petitioner indicates that granting the exemption is in the public interest and will not adversely affect safety. Additionally, the petitioner asserts that it employs not more than fifteen employees and has demonstrated good cause for granting this exemption.

Interested persons are invited to participate in these proceedings by submitting written views and comments. FRA has not scheduled a hearing or

other opportunity for oral comments since the facts do not appear to warrant it. Communications concerning the proceedings should identify the docket number and must be submitted in triplicate to the Docket Clerk, Office of Chief Counsel, Federal Railroad Administration, Nassif Building, 400 Seventh Street, SW., Washington, DC 20590.

Communications received before February 19, 1986, will be considered by FRA before final action is taken. Comments received after that will be considered as far as practicable. All comments received will be available for examination both before and after the closing date for comments during regular business hours (9 a.m.–5 p.m.) in Room 8201, Nassif Building, 400 Seventh Street, SW., Washington, DC 20590.

Issued in Washington, DC on December 16, 1985.

J.W. Walsh,

*Associate Administrator for Safety.*

[FR Doc. 85–30367 Filed 12–23–85; 8:45 am]

BILLING CODE 4910–06–M

[BS-Ap-No. 2424]

## Seaboard System Railroad; Postponement of Public Hearing

The public hearing in the captioned block signal application has been postponed by the Federal Railroad Administration (FRA), at the request of the railroad, from January 8, 1986, until March 26, 1986. Because of the change of hearing date, it has also been necessary to move the hearing to a different room in the same building. (See original hearing notice in 50 FR 47319, November 15, 1985.)

In particular, the hearing has been rescheduled for 10 a.m. on Wednesday, March 26, 1986, in Room 199 of the South Tower at 1718 Peachtree Road, N.W., in Atlanta, Georgia.

The FRA regrets an inconvenience occasioned by this change.

In the application that is the subject of this hearing, the Seaboard System Railroad (Seaboard) petitioned the FRA seeking approval of the proposed discontinuance of the automatic block signal system between Augusta, Georgia, and Atlanta, Georgia. This proceeding is identified as FRA Block Signal Application No. 2424.

After examining Seaboard's proposal and the available facts, the FRA determined that a public hearing is necessary before a final decision is made on this proposal. Accordingly, a hearing was scheduled and has now been postponed.

As stated in the original notice, the hearing will be informal and will be conducted in accordance with Rule 25 of the FRA Rules of Practice (49 CFR 211.25), by a representative designated by the FRA.

The hearing will be a nonadversary proceeding and, therefore, there will be no cross-examination of persons presenting statements. The FRA representative will make an opening statement outlining the scope of the hearing. After all initial statements have been completed, those persons who wish to make brief rebuttal statements will be given the opportunity to do so, in the same order in which they made their initial statements. Additional procedures, if necessary for the conduct of the hearing, will be announced at the hearing.

Issued in Washington, DC on December 19, 1985.

J.W. Walsh,

*Associate Administrator for Safety.*

[FR Doc. 85–30368 Filed 12–23–85; 8:45 am]

BILLING CODE 4910–06–M

## National Highway Traffic Safety Administration

[Docket No. IP85–20; Notice 1]

## Alfa Romeo, Inc.; Receipt of Petition for Determination of Inconsequential Noncompliance

Alfa Romeo, Inc. of Englewood Cliffs, New Jersey, has petitioned to be exempted from the notification and remedy requirements of the National Traffic and Motor Vehicle Safety Act (15 U.S.C. 1381 *et seq.*) for an apparent noncompliance with 49 CFR 571.101 and 571.105, Motor Vehicle Safety Standards No. 101, *Controls and Displays*, and No. 105, *Hydraulic Brake Systems*, on the basis that it is inconsequential as it relates to motor vehicle safety.

This notice of receipt of a petition is published under section 157 of the National Traffic and Motor Vehicle Safety Act (15 U.S.C. 1417) and does not represent any agency decision or other exercise of judgment concerning the merits of the petition.

According to paragraph S5 and Table 2 of Standard No. 101, the brake system telltale shall be identified with the word "Brake". Paragraphs S5.3 (a) and (b) of Standard No. 105, require that:

S5.3.5(a) "Each indicator lamp shall display word or words, in accordance with the requirements of Standard No. 101 (49 CFR 571.101) and/or this section, which shall be legible to the driver in daylight when lighted * * *."

(b) If a single common indicator is used, the lamp shall display the word "Brake" * * *."

The petitioner, Alfa Romeo, Inc., produced some 1,150 1986 Spider models with the ISO (International Standards Organization) symbol for "Brake" instead of the word. This was done in anticipation of the ISO symbol being selected over the other methods of identification in proposed changes to the standard pending at the time.

Alfa Romeo indicated that production orders have been given to the instrument cluster supplier to retool and produce the warning lamp lens with the word "Brake", but before the running change can be effected, some 1,150 vehicles will have been manufactured and sold.

Because of the disproportionate high cost due to the small number of vehicles, $520 per vehicle claimed by Alfa Romeo, the petitioner proposes that the following be allowed in lieu of total replacement of the instrument panel:

a. A special label attached to the outside of the instrument cluster, which would clearly tell the driver that the ISO symbol means "Brake".

b. An Owner's Manual insert explaining clearly that the ISO symbol means "Brake".

All vehicles in Alfa Romeo stock would be identified as outlined above. In addition, Alfa Romeo dealers stock would be identified prior to sale to the user. Those vehicles now in the hands of users would be identified by recalling them for application of an instrument cluster label and updating their Owner's Manuals. This would be performed within Alfa Romeo's standard recall procedure, but not according to the requirements of 49 CFR Parts 577 and 579, due to the small quantity involved.

Interested persons are invited to submit written data, views and arguments on the petition of Alfa Romeo, Inc., described above. Comments should refer to the docket number and be submitted to: Docket Section, National Highway Traffic Safety Administration, Room 5109, 400 Seventh Street, SW., Washington, DC 20590. It is requested but not required that five copies be submitted.

All comments received before the close of business on the closing date indicated below will be considered. The application and supporting materials, and all comments received after the closing date will also be filed and will be considered to the extent possible. When the petition is granted or denied, notice will be published in the **Federal Register** pursuant to the authority indicated below.

*Comment closing date:* January 23, 1986.

(Sec. 102, Pub. L. 93–492, 88 Stat. 1470 (15 U.S.C. 1417); delegations of authority at 49 CFR 1.50 and 49 CFR 501.8)

Issued on December 19, 1985.

**Barry Felrice,**

*Associate Administrator for Rulemaking.*

[FR Doc. 85–30384 Filed 12–23–85; 8:45 am]

BILLING CODE 4910–59–M

## VETERANS ADMINISTRATION

### Agency Forms Under OMB Review

**AGENCY:** Veterans Administration.

**ACTION:** Notice.

**SUMMARY:** The Veterans Administration has submitted to OMB for review the following proposals for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35). This document contains an extension and new collections and lists the following information: (1) The department or staff office issuing the form, (2) the title of the form, (3) the agency form number, if applicable, (4) how often the form must be filled out, (5) who will be required or asked to report, (6) an estimate of the number of responses, (7) an estimate of the total number of hours needed to fill out the form, and (8) an indication of whether section 3504(h) of Pub. L. 96–511 applies.

**ADDRESSES:** Copies of the forms and supporting documents may be obtained from Nancy C. McCoy, Agency Clearance Officer (732), Veterans Administration, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 389–2146. Comments and questions about the items on the list should be directed to the VA's OMB Desk Officer, Dick Eisinger, Office of Management and Budget, 726 Jackson Place, NW., Washington, DC 20503, (202) 395–7316.

**DATES:** Comments on the information collection should be directed to the OMB Desk Officer within 60 days of this notice.

Dated: December 18, 1985.

By direction of the Administrator:

**Everett Alvarez, Jr.,**

*Deputy Administrator.*

### Extension

1. Department of Veterans Benefits.
2. Designation of Certifying Official(s).
3. VA Form 22–8794.
4. On occasion.
5. State or local governments; Businesses or other for-profit; Non-profit institutions; Small businesses or organizations.
6. 3,200 responses.
7. 534 hours.
8. Not applicable.

### New Collections

1. Department of Veterans Benefits.
2. Certification of Attendance for a Course Leading to a Standard College Degree (Under Chapter 30, Title 38, U.S.C.).
3. VA Form 22–8979.
4. On occasion; monthly.
5. Individuals or households; State or local governments.
6. 600 responses.
7. 100 hours.
8. Not applicable.

* * * * *

1. Department of Veterans Benefits.
2. Certificate of Balance on Deposit.
3. VA Form 22–4718a.
4. On occasion; annually; biennially; triennially.
5. Individuals or households; State or local governments; Federal agencies or employees; non-profit institutions.
6. 20,000 responses.
7. 1,000 hours.
8. Not applicable.

[FR Doc. 85–30363 Filed 12–23–85; 8:45 am]

BILLING CODE 8320–01–M

# Sunshine Act Meetings

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

This section of the FEDERAL REGISTER contains notices of meetings published under the "Government in the Sunshine Act" (Pub. L. 94-409) 5 U.S.C. 552b(e)(3).

## CONTENTS

| | Item |
|---|---|
| Commodity Futures Trading Commission | 1-6 |
| Federal Reserve System | 7,8 |
| National Transportation Safety Board | 9 |

1

**COMMODITY FUTURES TRADING COMMISSION**

**"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT:** 50 FR 51503.

**PREVIOUSLY ANNOUNCED TIME AND DATE OF THE MEETING:** 10:00 a.m., December 19, 1985.

**CHANGES IN THE MEETING:** This meeting is rescheduled for Monday, January 6, 1986.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30501 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

2

**COMMODITY FUTURES TRADING COMMISSION**

**TIME AND DATE:** 11:00 a.m., January 3, 1986.

**PLACE:** 2033 K Street, NW., Washington DC., 8th Floor Conference Room.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:** Market Surveillance.

**CONTACT PERSON FOR MORE INFORMATION:** Jean A. Webb, 254-6314.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30502 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

3

**COMMODITY FUTURES TRADING COMMISSION**

**TIME AND DATE:** 11:00 a.m., January 10, 1986.

**PLACE:** 2033 K Street, NW., Washington, DC., 8th Floor Conference Room.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:** Market Surveillance.

**CONTACT PERSON FOR MORE INFORMATION:** Jean A. Webb, 254-6314.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30503 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

4

**COMMODITY FUTURES TRADING COMMISSION**

**TIME AND DATE:** 11:00 a.m., January 17, 1986.

**PLACE:** 2033 K Street, NW., Washington, DC, 8th Floor Conference Room.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:** Market Surveillance.

**CONTACT PERSON FOR MORE INFORMATION:** Jean A. Webb, 254-6314.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30504 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

5

**COMMODITY FUTURES TRADING COMMISSION**

**TIME AND DATE:** 11:00 a.m., January 24, 1986.

**PLACE:** 2033 K Street, NW., Washington, DC, 8th Floor Conference Room.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:** Market Surveillance.

**CONTACT PERSON FOR MORE INFORMATION:** Jean A. Webb, 254-6314.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30505 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

6

**COMMODITY FUTURES TRADING COMMISSION**

**TIME AND DATE:** 11:00 a.m., January 31, 1986.

**PLACE:** 2033 K Street, NW., Washington, DC, 8th Floor Conference Room.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:** Market Surveillance.

**CONTACT PERSON FOR MORE INFORMATION:** Jean A. Webb, 254-6314.

Jean A. Webb,
*Secretary of the Commission.*
[FR Doc. 85-30506 Filed 12-20-85; 3:08 pm]
BILLING CODE 6351-01-M

7

**FEDERAL RESERVE SYSTEM BOARD OF GOVERNORS**

**"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT:** Notice forwarded to the Federal Register on December 12, 1985.

**PREVIOUSLY ANNOUNCED TIME AND DATE OF THE MEETING:** Approximately 11:30 a.m., Thursday, December 19, 1985, following a recess at the conclusion of the open meeting.

**CHANGES IN THE MEETING:** Addition of the following closed item(s) to the meeting with less than one week's advance notice to the public:

1. Issues relating to cost of Federal Reserve notes.
2. Proposed procedures for handling Board voting during the holiday period.

**CONTACT PERSON FOR MORE INFORMATION:** Mr. Joseph R. Coyne, Assistant to the Board; (202) 452-3204.

Dated: December 19, 1985.

James McAfee,
*Associate Secretary of the Board.*
[FR Doc. 85-30422 Filed 12-20-85; 10:39 am]
BILLING CODE 6210-01-M

8

**FEDERAL RESERVE SYSTEM BOARD OF GOVERNORS**

**TIME AND DATE:** 3:00 p.m., Thursday, December 19, 1985.

The business of the Board required that this meeting be held with less than one week's advance notice to the public, and no earlier announcement of the meeting was practicable.

**PLACE:** 20th Street and Constitution Avenue, NW., Washington, DC 20551.

**STATUS:** Closed.

**MATTERS TO BE CONSIDERED:**

1. Personnel actions (appointments, promotions, assignments, reassignments, and salary actions) involving individual Federal Reserve System employees.

**CONTACT PERSON FOR MORE INFORMATION:** Mr. Joseph R. Coyne, Assistant to the Board: (202) 452-3204.

Dated: December 19, 1985.

James McAfee,

*Associate Secretary of the Board.*

[FR Doc. 85-30436 Filed 12-20-85; 11:29 am]

BILLING CODE 6210-01-M

---

9

**NATIONAL TRANSPORTATION SAFETY BOARD**

**TIME AND DATE:** 9:00 a.m., Tuesday, January 7, 1985.

**PLACE:** NTSB Conference Rooms 8A, B C, Eighth Floor, 800 Independence Avenue, SW., Washington, DC 20594.

**STATUS:** The first three items on the agenda will be open to the public; the last two items will be closed under Exemption 10 of the Government in the Sunshine Act.

**MATTERS TO BE CONSIDERED:**

1. *Aircraft Accident Report:* Galaxy Airlines, Inc., Lockleed L-188C, N5532, Reno Cannon International Airport, Reno, Nevada, January 21, 1985.

2. *Marine Accident Report and Letters of Recommendation:* Capsizing of the U.S. Fishing Vessel AMERICUS and disappearance of the U.S. Fishing Vessel ALTAIR, Bering Sea North of Dutch Harbor, Alaska, Febrary 14, 1983.

3. *Marine Accident Report:* Grounding of the Panamanian-Flag Passenger Carferry M/V A. REGINA at Mona Island, Puerto Rico on Febrary 15, 1985.

4. *Opinion and Order:* Administrator v. Woodward Docket SE-6620; disposition of respondent's appeal.

5. *Opinion and Order:* Administrator v. Heinberg, Docket SE-6733; disposition of appeal from order of dismissal.

**CONTACT PERSON FOR MORE INFORMATION:** Catherine T. Kaputa (202) 382-6525

Catherine T. Kaputa,

*Federal Register Liaison Officer.*

December 20, 1985.

[FR Doc. 85-30430 Filed 12-20-85; 10:55 am]

BILLING CODE 7533-01-M

Federal Register

Tuesday
December 24, 1985

Part II

# Department of Health and Human Services

Food and Drug Administration

21 CFR Parts 606, 610, and 640

Biological Products; Blood and Blood Derivatives; Implementation of Efficacy Review; Proposed Rule

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Parts 606, 610, and 640**

**[Docket No. 82N-0163]**

## Biological Products; Blood and Blood Derivatives; Implementation of Efficacy Review

**AGENCY:** Food and Drug Administration.

**ACTION:** Proposed rule.

**SUMMARY:** The Food and Drug Administration (FDA) is proposing to amend the biologics regulations in response to the report and recommendations of the Panel of Review of Blood and Blood Derivatives (the Panel). The proposed rules would affect blood banks, plasmapheresis establishments, and plasma derivative manufacturers. The Panel reviewed the safety, efficacy, and labeling of blood, blood components, blood derivatives, and related products. On the basis of the Panel's findings and recommendations, FDA is proposing to classify products in Category I (safe, effective, and not misbranded), Category II (unsafe, ineffective, or misbranded), and Category IIIB (off the market pending completion of studies permitting a determination of effectiveness). Products recommended for Category IIIA (formerly defined as on the market during further studies in support of effectiveness) will be reviewed by the Blood Products Advisory Committee for reclassification into Categories I or II.

**DATES:** Comments on the proposed classification of products into Category I and on proposed amendments to the biologics regulations should be submitted by March 24, 1986. Comments on the confidentiality of data submitted for review by the Panel should be submitted by January 23, 1986.

FDA proposes the following: (1) That any final rule based on this proposal become effective 60 days after the date the final rule is published in the **Federal Register**; (2) that amendments to a license application, other than labeling amendments, be submitted to FDA within 180 days after the date the final rule is published in the **Federal Register**; (3) that labeling requirements, other than the requirements in §§ 201.56 and 201.57 (21 CFR 201.56 and 201.57), become effective 12 months after the date the final rule is published in the **Federal Register**; and (4) that the labeling requirements in §§ 201.56 and 201.57 become effective 30 months after the date the final rule is published in the **Federal Register** (see § 201.59).

**SUPPLEMENTARY INFORMATION:**

**Table of Contents**

1. Background
2. Introduction of Panel Report
3. Stored Red Blood Cell Products; History of Blood Transfusion; Donor Standards; Testing Donor Blood; and Labeling
4. Whole Blood (Human) Heparin
5. Whole Blood (Human) Modified-Antihemophilic Factor Removed and Whole Blood (Human) Modified-Platelets Removed
6. Red Blood Cells (Human)
7. Frozen Red Blood Cells (Human)
8. Cryoprecipitated Antihemophilic Factor
9. Single Donor Plasma (Human)
10. Normal Serum Albumin (Human)
11. Plasma Protein Fraction (Human)
12. Antihemophilic Fraction (Human)
13. Factor IX Complex (Human)
14. Fibrinogen (Human)
15. Fibrinolysin (Human)
16. $Rh_o$ (D) Immune Globulin (Human)
17. Thrombin
18. Fibrinolysin and Desoxyribonuclease, Combined (Bovine) and Fibrinolysin and Desoxyribonuclease, Combined (Bovine) with Chloramphenicol
19. Blood Grouping Diagnostics
20. Hepatitis B Testing
21. Antivenins
22. Normal Horse Serum
23. Blood Group Substances A, B, and AB
24. Cobra Venom Products
25. Human Plasma as a Source for Fractionation Products
26. Donor Immunization and Hyperimmunization
27. FDA's Response to the Panel's Recommendations

**ADDRESS:** Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** Steven F. Falter, Office of Biologics Research and Review, Center for Drugs and Biologics (HFN-364), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8046.

### 1. Background

In the **Federal Register** of February 13, 1973 (38 FR 4319), FDA issued § 601.25 (21 CFR 601.25) concerning procedures for the review of the safety, effectiveness, and labeling of biological products licensed prior to July 1, 1972. Under the panel assignments publish in the **Federal Register** of June 19, 1974 (39 FR 21176), the biological products reviewed were assigned to one of the following categories: (1) Bacterial vaccines and bacterial antigens with "no U.S. standard of potency," (2) bacterial vaccines and toxoids with standards of potency, (3) viral vaccines and rickettsial vaccines, (4) allergenic extracts, (5) skin test antigens, or (6) blood and blood derivatives.

Under § 601.25, FDA assigned responsibility for the initial review of each of the biological product categories to a separate independent advisory review panel consisting of qualified experts to ensure objectivity of the review and public confidence in the use of these products. Each panel was charged with preparing an advisory report to the Commissioner of Food and Drugs which was to: (1) Evaluate the safety and effectiveness of the biological product, (2) review the labeling of the biological product, and (3) advise the Commissioner on which biological products under review are safe, effective, and not misbranded. The advisory report includes a statement classifying products into one of three categories.

Category I designates those biological products determined by the Panel to be safe, effective, and not misbranded. The Panel's statement may include any condition relating to active components, labeling, tests required prior to release of batches, product standards, or other conditions necessary or appropriate for their safety and effectiveness.

Category II designates those biological products determined by the Panel to be unsafe, ineffective, or misbranded.

Category III designates those biological products determined by the Panel not to fall within either Category I or II on the basis of its conclusion that the available data are insufficient for classification and for which further testing is therefore required. Those biological products in Category III for which continued licensing, manufacturing, and marketing, during the period of further testing are recommended, are designated as Category IIIA. Those biological products in Category III for which the suspension of their license, pending submission of additional data, is recommended are designated as Category IIIB. The recommendations for either Category IIIA or IIIB are based on assessment of the present evidence of safety and effectiveness of the product and the potential benefits and risks likely to result from the continued use of the product for a limited period of time, while questions raised concerning the products are being resolved by further study.

In the **Federal Register** of December 13, 1974 (39 FR 43413), FDA requested data and information regarding blood, blood components, and blood derivatives.

Some concern has been expressed that confidential information submitted to FDA under § 601.25 will become

public information. Data and information submitted in response to the February 28, 1973, June 19, 1974, and December 13, 1974 notices and falling within the provisions of 5 U.S.C. 552(b), 18 U.S.C. 1905, or 21 U.S.C. 331(j) have been handled as confidential. However, with the publication of this proposed implementation and the Panel's findings, such data and information will, under § 601.25(b)(2), be made publicly available after January 24, 1986 and may be viewed at the Dockets Management Branch (address above), except to the extent that the person submitting the data and information demonstrates that it still falls within the confidentiality provisions of one or more of the above statutes. Accordingly, comments concerning confidentiality should be submitted by January 23, 1986.

The Panel appointed by FDA to review the data and information submitted and to prepare a report on the safety, effectiveness, and labeling of blood, blood components, blood derivatives, and related products included the following individuals:

Panel Chairman, Scott N. Swisher, M.D., Professor, Department of Medicine, Michigan State University, East Lansing, MI 48823;
Joseph R. Bove, M.D., Director, Blood Transfusion Service, Yale-New Haven Hospital, New Haven, CT 06510;
John A. Collins, M.D., Chairman, Department of Surgery, University Medical Center, Stanford, CA 94305;
William S. Howland, M.D., Chairman, Department of Anesthesiology, Memorial Hospital, New York, NY 10021;
Robert D. Langdell, M.D., Professor of Pathology, School of Medicine, University of North Carolina, Chapel Hill, NC 27514;
Jacob Nusbacher, M.D., Director, Rochester Regional Red Cross Program, Rochester, NY 14607;
Sherrill J. Slichter, M.D., Associate Director, Puget Sound Blood Center, University of Washington, Seattle, WA 98104.

The Panel was convened on June 26, 1975, in an organizational meeting. Working meetings were held: August 22–23, October 31–November 1, 1975; January 9–10, March 19–20, May 5–6, June 25, October 1–2, November 12–13, 1976; January 14–15, March 11–12, June 17–19, October 7–8, November 18–19, 1977; January 6–7, March 10–11, May 12–13, July 17–18, December 15–16, 1978; and November 15–16, 1979.

Two nonvoting liaison representatives served on the Panel. Louis M. Aledort, M.D., nominated by the National Hemophilia Foundation, served as the consumer representative. Margaret Hilgartner, M.D., or Robert Schwartz substituted for Dr. Aledort during his absences. John Adams, Ph.D., of the Pharmaceutical Manufacturers Association, nominated by a number of producers with products under review by the Panel, served as the industry representative. Karl Bambach, Ph.D., or Charles B. Cleveland substituted for Dr. Adams during his absences. Morris Schaeffer, M.D., Ph.D., participated in the Panel meetings in his capacity as Director of the Office of Scientific Advisors and Consultants, FDA. Clay Sisk, in the Office of Scientific Advisors and Consultants, FDA, served as Executive Secretary of the Panel.

In addition, the Panel considered the advice of the following consultants:

Edward H. Mealey, Ph.D.
Findlay E. Russell, M.D., Ph.D.
James T. Sgouris, Ph.D.

Over 290 persons attended one or more meetings of the Panel and many participated in the open discussions. Every person who requested an opportunity was heard by the Panel. The names of these persons are on file with the Dockets Management Branch as listed in the Summary Minutes of each meeting.

The Panel on Review of Blood and Blood Derivatives evaluated all data submitted for the following blood, blood derivatives, and other related products:

*Licensed Biological Products Considered by the Panel* [1]

Blood Bank Products

Stored Red Blood Cell Products (Includes Whole Blood (Human) ACD and CPD)
Whole Blood (Human) Heparin
Whole Blood (Human) Modified
Red Blood Cells (Human)
Red Blood Cells (Human) Frozen
Cryoprecipitated Antihemophilic Factor (Human)
Single Donor Plasma (Human)

*Plasma Fractionation Products*

Normal Serum Albumin (Human)
Plasma Protein Fraction (Human)
Antihemophilic Factor (Human)
Factor IX Complex (Human)
Fibrinogen (Human)
Fibrinolysin (Human)
$Rh_o$(D) Immune Globulin (Human)
Thrombin
Fibrinolysin and Desoxyribonuclease Combined (Bovine) (with and without Chloramphenicol)

*In Vitro Diagnostics*

Blood Group Diagnostics
Blood Grouping Serums
Reagent Red Cells
Anti-Human Serum
Hepatitis B Testing Reagents

*Miscellaneous Products*

Antivenins (three products)
Normal Horse Serum
Blood Group Substances A & B
Cobra Venom Products

Data submitted for these products are cited by Biologics Efficacy Review (BER) volume numbers. The volumes will be available in accordance with the provisions of 21 CFR 601.25(b)(2) at the Docket Management Branch (address above).

The following products were originally listed for Panel review in the December 13, 1974 notice, but are no longer licensed as biological products and are not reviewed in the Panel's Report:

Albumin Microspheres (Human)
Anti-Human Chorionic Gonadotropic Serum
Modified Plasma (Bovine)
Radioactive Albumin products
Russell Viper Venom

The advisory panel appointed to review data and information concerning the safety, effectiveness, and labeling of blood and blood products has completed its review and has submitted its report to the Commissioner. FDA announced the availability the Panel's report to the public in the **Federal Register** of November 21, 1980 (45 FR 77134). The Final Report of the Panel on Review of Blood and Blood Derivatives follows.

**2. Introduction to Panel Report**

The last decade has seen rapid progess in those areas of science basic to blood transfusion therapy. This has also been a decade of significant change in clinical practice; many changes have occurred as a result in the ways in which blood and blood products are employed as therapeutic agents.

A few examples can be cited. Our knowledge about the problem of post-transfusion hepatitis has broadened greatly. Testing donors for the presence of the hepatitis B associated antigen has effected significant reduction of the incidence of this disorder following infusion of materials that potentially carry this agent. In turn, this has focused attention on the problem of so-called "non-A, non-B" hepatitis for which adequate testing procedures do not exist. The blood coagulation system and its complex interrelationships with the complement system and the kinin system has been further elucidated. Similiarly, clinical experiences with

[1] Only biological products that have been licensed prior to July 1, 1972, are reviewed in this report.

therapeutic preparations of procoagulant proteins has increase our understanding of their utility as well as limitations on that utility. We not have a much better understanding of the physiological role of albumin, coupled with greatly improved clinical management of shock and massive blood loss. Factors affecting oxygen transport by intact red cells have become known, and their clinical significance explored.

These and other developments indicate that a review of blood and blood products licensed in earlier times before our new knowledge was available is timely and in the public interest in assuring the safety and effectiveness of these materials. This review is the product of one of six advisory panels of FDA's Bureau of Biologics and is part of the general review of biological products licensed prior to July 1972 (see 21 CFR 601.25). (Note: Since the time of that Panel's submission of his report, FDA has been reorganized. The Bureau of Biologics is now the Office of Biologics Research and Review (OBRR), Center for Drugs and Biologics.)

The work of the Panel on Review of Blood and Blood Derivatives has occupied a stipulating and informative 3 years. At the outset, it seemed that the Panel's task would be an easy one. The Panel was to deal with a well developed, widely distributed, and accepted group of technologies, a number of familiar products and therapeutic materials in widespread use by most physicians in practice. As the work of the Panel progressed, a significantly different picture emerged. In some areas, particularly with older products, it appeared that highly defensible scientific information about safety and efficacy was scarce. In dealing with some of these problems, it became necessary to rely upon consensus based upon common experience. This experience does, however, point out that the standards which are now applied to justify the introduction of new products have evolved along with the scientific knowledge which makes new products possible. It would seem that the complexity of the regulatory process has grown no faster than has understanding of the biological and clinical ramifications related to the introduction of new products.

A second observation was quickly made by the Panel: There are many eminently researchable problems which relate to a wide variety of blood products that present the opportunity for further improvement and refinement of these products and their clinical utility. Much of the effort of the Panel has gone into attempts to define these problems in researchable terms and to direct them, where possible, to appropriate investigators and sources of support for the work. It is the strong feeling of the Panel that this aspect of its work may, in the long run, be the most rewarding in terms of improved safety and effectiveness of the products review.

This Panel has had to deal with a situation rather different from that which has confronted previous panels which have reviewed other biological therapeutic materials. The bulk of the products reviewed are actually produced widely throughout the country in installations which range from large centralized blood banks, through smaller units, down to the size of a blood bank supported by an individual hospital. There are no large industrial "manufacturers" whose submissions and protocols can be reviewed as the basis for safety and efficacy determinations for therapeutic materials produced by blood banks. Thus, in this area, a manufacturer-by-manufacturer review of the Panel of every blood bank product is manifestly impossible. Rather, the Panel has had to rely upon years of experience with these materials, publications in the literature, submissions of procedures and standards of large blood bank organizations, data available in license applications, generic procedures specified by good manufacturing practices and standards of accreditation as the basis upon which to make judgments about safety and effectiveness of those products. In those areas in which commercial manufacturers do operate, as in the case of plasma derivatives, the more typical review of submitted information has been carried out. Some products were therefore reviewed only generically and recommendations made accordingly, leaving the determination of compliance for each manufactured product to the Bureau of Biologics which evaluates each installation.

The Panel has also been impressed with the difficulties encountered in obtaining adequate clinical investigational data upon which certain decisions about safety and effectiveness depend. Frequently the inadequacy of data is quantitative; not enough observations have been made to permit an adequate judgment, although there may be nothing wrong with the data that have been obtained. This problem arises in evaluating materials which have limited or no commercial sponsorship. It is also encountered in circumstances where a commercial manufacturer is unable to recruit enough clinical investigational resources within reasonable cost boundaries to complete a clinical evaluation which has been started. These difficulties are at the heart of the problem of shortening the time required for approval of new products or modification of old ones. Thought should be given to organizing a national clinical investigation resource to solve this problem in a cost-effective way. The Panel has no recommendations in this regard, but it is impressed with the significance of this problem in the effort to provide timely responsive regulatory actions.

The Panel wishes to thank the many people who have supplied it with consultation, expert opinion, data, and statements of interest for its consideration of a wide range of problems. These people have been related to the major blood-banking organizations of this country, academic institutions, industry, and the staff of the Division of Blood and Blood Products in OBRR. Without the help of these people and organizations, the work of the Panel could not have been completed.

Finally, the Panel wishes to express its strong feeling that this one-time review, whereas it has certain values as it stands, will be primarily of value if it is kept current by an on-going dynamic process. The science which underlies blood transfusion is rapidly changing. The potential exists now for development of many new products from blood. Rapid changes in health care delivery practices will occur in the near future. These factors will make a continuing review of this area over some reasonably short cycle of great value in assuring that the regulatory process enhances and supports the delivery of health care by providing safe and effective blood and blood products in a timely fashion to those who use them. The Panel has viewed its responsibilities from this perspective and has diligently attempted to provide a starting point for future activities in this direction. There are a number of the major unresolved issues which the Panel has identified. In most instances, additional information, the product of specific research, will be needed to resolve the problems which remain. Where it has been necessary to make a decision to deal with a specific problem until adequate data become available, conservative positions have been taken which have a "fail safe" character with regard to at least the issue of safety. With regard to effectiveness of products in this category, it should be noted that the materials reviewed have been in

widespread use over a period of years, and effectiveness has been documented at least by common experience. Thus the issue of effectiveness has been a lesser consideration when adequate data are lacking for decisionmaking in these cases.

**3. Stored Red Blood Cell Products, History of Blood Transfusion, Donor Standards, Testing Donor Blood, and Labeling**

*Generic Statement*

1. *Introduction*—a. *History of blood transfusion.* Although occasional successful blood transfusions were given in the 19th century, little real progress could be made until two major problems, immunological donor-recipient incompatibility and blood storage without clotting, were solved. In 1900, Landsteiner (Refs. 1 and 2) described what we now know as the ABO blood groups, and in 1911 Ottenberg (Ref. 3) applied this discovery to the selection of blood for transfusion. Progress in delineating other erythrocyte antigens was slow. Although in 1927 Landsteiner and Levine described the MN and P systems (Ref. 4), it was not until the discovery of the Rh system by Landsteiner and Weiner (Ref. 5) and Levine and Stetson (Ref. 6) in the early 1940's that immunologically safe blood transfusion could be practiced. Equally important at this time was the development of the antiglobulin test by Coombs et al. (Ref. 7) for the detection of nonagglutinating red cell antibodies. In subsequent years, new erythrocyte antigens were discovered at a remarkable rate; more than 400 antigenic specificities have now been described.

After the discovery of the ABO blood group, direct transfusion, a surgical procedure in which the donor's artery and recipient's vein were temporarily anastomosed, became popular. This was followed by the introduction of syringes or pumps to convey blood from donor to recipient. Direct donor-recipient transfusion became the standard practice for many years. A major difficulty was the tendency of the blood to clot, and the only logical solution was to find a safe anticoagulant to prevent this complication.

The safety of citrate for intravenous administration was demonstrated by Hustin in 1914 (Ref. 8) and by Agote (Ref. 9) and Lewisohn (Ref. 10) a year later. Rous and Turner (Ref. 11) in 1916 showed the beneficial effect of added dextrose on red blood cell preservation. Many years later, Maizels (Ref. 12) demonstrated that dextrose exerted its favorable effect by providing a source of energy for the synthesis of organic phosphate compounds. The acidification of the anticoagulant-preservative solution was first studied by Loutit, et al. (Ref. 13) in 1943 to prevent caramelization of the dextrose solution during sterilization. Serendipitously, it was found that acidification also gave better red cell preservation as judged by post-transfusion survival. The original Anticoagulant Citrate Dextrose (ACD) solution, suggested by Loutit and Mollison (Ref. 14), in 1943, has been modified primarily to reduce its volume.

Stored blood was first used by Rous and Turner (Ref. 11) in 1916, and in 1917 Robertson (Ref. 15) introduced it for treating battlefield casualties. Transfusion of stored, anticoagulated blood became a reality when the first blood banks were organized in 1937 in Chicago and in 1938 in New York City. Forty-four years later, in 1982, an estimated 9,349,700 units of whole blood were collected in the United States by 5,400 blood banks and transfusion services (Ref. 16).

A major development in blood bank practice occurred in the mid 1960's with the introduction of plastic collection containers which have replaced glass bottles as the standard blood container. This made possible the separation of whole blood into various components in an integral, closed sterile system. An inevitable result of component production from whole blood is the availability of Red Blood Cells (Human) ("packed cells"). This product is now widely used when erythrocyte transfusion is indicated and currently accounts for about 40 percent of all such transfusions in the United States.

b. *Whole Blood (Human) ACD.* Evaluation of the efficacy of ACD anticoagulant-preservative has rested primarily on satisfactory clinical responses following transfusion and on studies of post-transfusion red blood cell viability and survival. The accepted survival standard requires that on the last storage date at least 70 percent of the red blood cells be viable for at least 24 hours after transfusion. Both whole blood and red blood cell concentrates collected into ACD solution and stored at 2 to 6 °C easily meet this standard (Refs. 13, 14, and 28). Post-transfusion survival is related to the maintenance of adenosine triphosphate (ATP) levels in erythrocytes (Refs. 22 and 30).

Optimum storage, however, should encompass both erythrocyte survival and appropriate function. The major erythrocyte function, delivery of oxygen to tissues, is related to many variables, including erythrocyte diphosphoglycerate (DPG) level (Refs. 33 and 34). Red cells depleted of DPG release oxygen to tissues less readily than those which have normal levels. When human blood is collected in ACD, the DPG levels fall precipitously to approximately one-third normal after 1 week of storage (Ref. 35 and 241). However, the clinical significance of transfusion with DPG-depleted red cells is unclear.

c. *Whole Blood (Human) CPD.* In 1957 Gibson et al. (Refs. 36) published studies on modified ACD solutions buffered by phosphate to higher pH levels. This anticoagulant-preservative, citrate-phosphate-dextrose (CPD), was found to be superior to ACD in that 80 percent of the red cells retained viability after 32 days storage. Other studies (Refs. 21, 23, and 28) have confirmed that CPD stored erthrocytes have better survival than those stored in ACD, although not to the extent originally claimed. In addition, DPG levels in CPD-stored blood are better maintained; levels appear to be normal for approximately 1 week of routine blood bank storage (Ref. 35). Appropriate testing also has demonstrated that other blood constituents are not affected deleteriously by this anticoagulant when compared with ACD (Refs. 37 and 39). The formulas for ACD and CPD solution are contained in 21 CFR 640.4(d). In 1971, CPD was licensed as an anticoagulant-preservative by the Bureau of Biologics and has largely replaced ACD in general transfusion practice.

d. *Recommendations for Whole Blood (Human).* The Panel recommends that Whole Blood (Human) ACD and CPD be placed in Category I with changes in collection, processing, and labeling as discussed subsequently in this statement. The designation "Human" should be deleted from the product names.

2. *Possible hazards of red blood cell product transfusion*—a. *Metabolic problems related to transfusion*—(1) *Introduction.* Numerous metabolic changes occur in blood during storage. These are of clinical importance only when transfusion is massive, rapid infusion of large quantities of blood relative to the recipient's blood volume or when the recipient is particularly susceptible to these changes. In all other cases, the metabolic complications resulting from transfusion are minimal. The important changes are discussed in the next 14 sections of this statement.

(2) *Changes in blood during storage in citrate.* Red blood cells stored in ACD or CPD undergo a progressive loss of ATP, loss of membrane lipid, increased rigidity, loss of 2,3-DPG which begins

immediately in ACD and after 1 week of storage in CPD, loss of intracellular potassium, and gain of intracellular sodium. After transfusion, the electrolyte changes reverse, ATP and 2,3-DPG are restored to normal, shape and flexibility return to normal, and the life span for surviving cells is unimpaired. The loss of membrane lipid and increased susceptibility to osmotic hemolysis are not corrected (Refs. 194 through 196).

The plasma of stored whole blood contains a number of potentially significant abnormalities: about 14.5 millimoles of citrate per liter which is in excess of the amount required to bind ionized calcium in the blood collected, a high lactate level and consequently a large metabolic acid load (25 to 40 mEq/L), potassium levels up to 30 mEq/L by the third week of storage, ammonia levels up to 1 mg/dL, a variety of vasoactive agents, and denatured proteins. If given rapidly without warming, blood carries a significant negative thermal load (Refs. 112 and 197).

(3) *Citrate toxicity.* Citrate avidly binds ionized calcium. This is why it is effective as an anticoagulant. To guarantee complete anticoagulation there is a deliberate excess of citrate in each unit of blood. Therefore, recipients of massive transfusion are receiving not just blood that is free of ionized calcium, but also an infusion of free citrate. Theoretically, death can result from the depression of ionized calcium levels below a critical level in the recipient. This can be prevented by the administration of ionized calcium during the infusion of citrate. However, the quantitative aspects of calcium balance change rapidly in vivo, and a great excess of ionized calcium is as lethal as is a severe deficiency. Empirical treatment can thus be quite dangerous.

The patient's defenses against citrate infusion fall into two categories, the removal of the infused citrate and the mobilization of ionized calcium. Citrate is removed primarily by metabolic conversion. Since citrate is a normal intermediary metabolite and part of the tricarboxcylic acid cycle, it is methabolized in every nucleated cell in the body. While citrate levels in the recipient do rise during rapid transfusion, marked elevations are usually found only at transfusion rates of greater than one unit of blood every 5 minutes for the normalsized adult (Ref. 198 through 200). The citrate concentration in recipients falls rapidly upon slowing or stopping the transfusion.

Bunker et al. (Refs. 198) reported impaired rates of metabolism of citrate when the recipient was hypotensive, had diffuse liver disease, or was allowed to become cold. Howland et al. (Refs. 199) found more evidence of impairment with hypotension alone. As hypoperfusion, liver disease, and hypothermia can often be found in massively transfused patients, these critical points need more careful documentation. In massively transfused combat casualties in Vietnam, transfused lactate was found to be removed very rapidly, presumably indicating a similar efficiency in handling transfused citrate because of the similar mechanisms for the metabolic conversion of both organic acids (Ref. 201).

The ability of the transfused patient to mobilize calcium in his or her defense depends on two factors: the release of parathyroid hormone (PTH) and the mobilization of calcium from bone by the effect of the newly released parathormone. The rise in parathormone levels in response to the infusion of citrate is extremely rapid (Refs. 202 and 203). This implies release of preformed PTH and raises the question of whether sustained infusion of citrate, as occurs during extended massive transfusion, can be handled adequately once the stores of PTH have been depleted, and the response then relies on synthesis of new hormone. Blood flow to bone is significantly reduced in hemorrhagic hypotension. This must result in impaired mobilization of calcium, but studies on calcium mobilization following hemorrhage are lacking. Several studies (Refs. 204 and 205) indicate that the relationship between the blood citrate level and the ionized calcium level is not a set one, indicating that the patient's mobilization of calcium can be an effective response even when citrate cannot be removed completely.

These relationships are further complicated by the effect of blood pH. Alkalosis increases the binding of ionized calcium by plasma proteins and, at least in some animals, appears to produce a decrease in the concentration of total calcium in the blood (Refs. 206 through 208). Alkalosis also leads to higher blood levels of citrate and higher tissue levels, especially in the renal cortex and less so in the liver, implying impaired metabolism of citrate (Ref. 209). There have been no studies, however, on the effect of alkalosis on the ability to metabolize infused citrate. In the often-quoted study of Bunker (Ref. 198), clinical signs and symptoms of hypocalcemia were related blood levels of citrate, but estimations of the ionized calcium were made without regard to changes in pH. Sodium citrate was used as the anticoagulant in these studies and produced a marked alkalemia in the recipients, some of whom exhibited a decline in serum total calcium during the citrate infusions rather than the expected rise. Other investigators (Refs. 199 and 210) using standard anticoagulant infusions instead of sodium citrate have noted much less change in human volunteers at similar rates of anticoagulant infusion.

More recently, a number of clinical studies (Refs. 211 through 215), using the calcium ion sensitive electrode, have shown that there is some depression of ionized calcium level in most transfused patients, but the physiologic significance of this degree of depression remains obscure. When studied, the recovery was very rapid after transfusion ceased. An exception is the study of Cooper et al. (Ref. 216) in which rather significant changes in myocardial contractility were related to depression of the ionized calcium level in the blood of patients coming off cardiopulmonary bypass. It is possible, of course, that such patients may be unusually sensitive to alterations of ionized calcium levels as appears to be true for their sensitivity to alternations of acid-base balance. In addition, the rates of transfusion were very rapid. Another, more recent study (Ref. 215), demonstrates no reduction in cardiac output despite lowering of the ionized calcium levels.

Objections to the routine administration of calcium after transfusion have been raised on the basis of sporadic case reports of severe iatrogenic hypercalcemia (Ref. 217). This potentially important problem is still handled in an empirical manner because of the lack of adequate data. The calcium ion sensitive electrode may allow some of these old questions about citrate toxicity to be answered adequately. Perhaps some readily acceptable and practical criteria, such as on-line analysis of electrocardiographic changes as indicators of the need for ionized calcium supplementation can be developed. For the time being, it is probably safe to assume that a normothermic adult with a functioning liver can tolerate a unit of blood every 5 minutes without requiring supplemental calcium. Empirical supplementation with ionic calcium is rarely necessary, but should be considered for those recipients who are doing poorly without apparent cause.

(4) *Coagulation abnormalities.* One complication of massive transfusion is pathological diffuse bleeding. This not only interferes with efforts to control the

original hemorrage, but in turn, leads to the requirement for more blood replacement. Such bleeding abnormalities are often attributed to the dilutional effect on coagulation factors of the transfusions themselves.

Some coagulation factors are absent or deficient in stored blood. Platelets, even if present, do not function normally. Depending upon storage time, concentrations of Factors V and VIII may be as low as 15 to 30 percent, and Factor XI may be 20 percent of normal. Ionized calcium of course is absent, but it is not likely that this has an anticoagulant effect because the cardiac effects of severe hypocalcemia are probably lethal before levels low enough to interfere with coagulation are reached.

Published studies on the coagulation changes in massively transfused patients show a variety of clotting abnormalities such that it is difficult to assign a pattern to the defects (Refs. 218 through 225).

Three groups of observations, however, indicate that the clotting abnormalities in massively transfused patients are due to more than simple dilution from transfusion with stored blood. These observations suggest a superimposed abnormality of clotting factor consumption, presumable disseminated intravascular coagulation (DIC). There is often depression of the various clotting components to levels lower than could be expected from the degree of exchange transfusion that has occurred. In addition, these patients often have hypofibrinogenemia, which cannot be explained by transfusion with stored blood since the fibrinogen content of stored blood is normal. Finally, in some seriously injured patients, marked abnormalities of the coagulation system existed before or very early during the course of transfusion. In these patients, the coagulation abnormalities tended to be corrected during the course of transfusion and reverted to the pretransfusion levels when transfusion was stopped (Ref. 221). Taken together these findings suggest that DIC is one cause of the major coagulation abnormalities found at times in massively transfused patients.

Important confirmation of this concept is found in data presented recently on massively transfused patients (Ref. 226). When a series of coagulation test results were plotted against the amount of blood transfused, there was little evident correlation, but when the patients were grouped according to the amount of time they remained hypotensive, there was a strong correlation. The more prolonged the hypotension, the worse the coagulation abnormalities at the same level of transfusion. This implies that perfusion was the critical variable, not the quantity of blood transfused.

The pathogenesis of DIC with massive transfusion is unclear. Hypoperfusion and extensive tissue damage or necrosis almost certainly contribute. Transfusion itself may also facilitate the development of DIC by a number of mechanisms. There is probably partial activation of some clotting factors during storage, and breakdown of platelets, white cells and some red cells which release thromboplastic material into the stored blood. A hemolytic transfusion reaction is a well-recognized cause of DIC. Whatever the cause for the DIC, the key to management appears to be maintenance of good perfusion for several hours during which the patient will often correct the continuing consumption of clotting factors. This, of course, can be difficult in a massively bleeding patient. There is little indication for heparin therapy in such patients, and enthusiasm for this therapy is waning.

In addition to DIC, impaired platelet function has been associated with massive transfusion. While dilutional thrombocytopenia has been noted repeatedly in these patients, the platelet counts are rarely below 50,000 per cubic millimeter, a level sufficient for adequate hemostasis in most circumstances. A recent study (Ref. 225) on heavily transfused trauma patients suggests an impairment in platelet function but it is not clear if these function tests were corrected for the lower platelet counts seen. DIC itself can cause impaired platelet function. This is an important question because an induced defect in platelet function would complicate management of the bleeding problem and increase the need for further transfusion, but is potentially correctable with platelet concentrates. Platelet function should be a focus of attention in current and subsequent studies on the problems of massive transfusion.

(5) *Acid-base alterations* (Ref. 201). Three-week-old stored citrated blood contains an acid load of up to 30 to 40 mEq per liter, and patients requiring massive transfusion often have a preexisting metabolic acidosis. Studies in animals indicate that the acidity of stored blood may contribute to failure of resuscitation from hemorrhage. It is understandable, therefore, that some authors have proposed the routine administration of alkalinizing solution during massive transfusion, supporting these suggestions with uncontrolled clinical observations.

The situation, however, is more complex than it appears. The excess acidity of stored blood is due mainly to the citric acid in the anticoagulant and the lactic acid generated during storage. Both are organic acids, normal intermediary metabolites, and are rapidly metabolized under normal conditions. The preexisting acidosis is also a lactic acidosis which can be reversed rapidly when perfusion is restored. The impact of the transfusion of stored blood on the acid-base status of the recipient then is not one of simple buffering in a closed system, but is rather complex involving rates of administration, metabolic removal, and the changing status of peripheral perfusion in the recipient which relates both to production and metabolism of lactate.

Studies in Vietnam showed that patients whose blood pressure was restored by the transfusion, and even some who remained hypotensive, easily handled the infused acid load of transfusion and reversed the preexisting metabolic acidosis (Refs. 201 and 227). Those in whom hemorrhage was not controlled during transfusion, most of whom died, exhibited increasing acidosis that was probably due more to persistent and worsening hypoperfusion than to the transfusion itself. Administration of alkalinizing agents to this latter group was futile. Besides being unnecessary, the routine use of alkalinizing solution presents several disadvantages. An induced alkalemia will impair oxygen delivery by shifting the oxyhemoglobin dissociation curve to the left, will increase the sodium load in patients whose ability to excrete salt and water is impaired, and may delay the return of ionized calcium to normal levels following cessation of the infusion.

The results discussed above were obtained in previously healthy young adults whose resuscitation was carried out in a high ambient temperature that prevented the development of hypothermia. In these patients failure to restore perfusion was almost always due to failure to control hemorrhage or to injury to a vital organ, rather than to acidosis per se. The need for alkalinizing agents should be based on objective measurements of blood gases and pH rather than on empirical formulas.

One clinical situation in which acidosis may occur during massive transfusion is exchange transfusion in the newborn. One recent study in infants indicated that transfusion-induced acidosis was not a problem (Ref. 228). The blood used, however,

was 1 to 4 days old and therefore had less lactic acid than is found in blood approaching the third week of storage. Also, none of the infants were less than 5 days old.

(6) *Alterations in oxygen transport.* In the simplest of terms, the oxygen delivering capacity can be thought of as a product of blood flow and oxygen content. Oxygen content, in turn, is a function of hemoglobin concentration and oxygen saturation. Recently, an additional aspect, the affinity of hemoglobin for oxygen, has been of interest. At physiologic gas tensions, a decreased affinity of hemoglobin for oxygen leads to less oxygen uptake in the lungs, but more oxygen release at the periphery, resulting in increased delivery of oxygen, independent of changes in flow or the concentration of hemoglobin (Refs. 229 and 230). A more complete description of the oxygen delivering system then includes blood flow, hemoglobin concentration, oxygen saturation, hemoglobin oxygen transport efficiency, and tissue oxygen tensions which reflect the metabolic need for oxygen. All five of these parameters can be altered by transfusion.

Blood flow can be increased by increasing blood volume in hypovolemic patients. Paradoxically, blood flow can be decreased by transfusing patients to the point of heart failure secondary to hypervolemia. The concentration of hemoglobin is increased by transfusion but the relationship to oxygen delivery is complicated by the fact that an increasing hematocrit is associated with increasing resistance of blood to flow due to increasing viscosity. This relationship is complex, with several variables poorly understood (Refs. 231 through 233). For the severely anemic patient, however, improved delivery of oxygen almost certainly results from transfusion. The saturation of hemoglobin with oxygen will decrease if transfusion leads to circulatory overload and consequent pulmonary edema. Restoring volume and/or hemoglobin concentration toward normal will increase the oxygen tension of mixed venous blood and indirectly will lead to higher arterial oxygen tensions even if the degree of "shunting" in the lung does not change. Finally, the efficiency of hemoglobin as an oxygen delivering agent is also altered by transfusion, and most of the remainder of this section will consider this relationship.

The concentration of 2,3-diphosphoglycerate acid (2,3-DPG) falls essentially to zero by the third week of storage of RBC in either ACD or CPD, although at different rates in the two solutions (Ref. 234). The 2,3-DPG depleted blood has an increased affinity for oxygen, making it a less efficient oxygen delivering agent at physiologic gas tensions. In most clinical situations of stress on the oxygen-delivering system, the affinity of hemoglobin for oxygen changes toward reduced affinity resulting in increased effectiveness of delivery. Patients massively transfused with old stored blood have an alteration in hemoglobin oxygen affinity opposite in direction to what would presumably occur in the absence of massive transfusion (Ref. 235). Several clinical studies have shown that a marked change in the affinity of hemoglobin for oxygen can result from massive transfusion (Refs. 236 through 243). Recovery of 2,3-DPG content and of normal oxygen transport function occur within approximately 1 to 2 days after transfusion of depleted red cells.

In spite of the obvious theoretical considerations, the detrimental effects of an increase in oxygen affinity in stored transfused cells have been difficult to demonstrate. Studies on massively transfused combat casualties in Vietnam (Ref. 201), who routinely received ACD blood in the second or third week of storage, indicated not only good resuscitative effectiveness, but immediate restoration of aerobic metabolism as indicated by rapid clearing of elevated pretransfusion blood lactate levels and intraresuscitative lactate loads.

Studies in rats (Ref. 244) and in humans (Ref. 245) have shown that lowering the 2,3-DPG content and increasing the affinity of hemoglobin for oxygen produces essentially no detectable effects on work performance or maximal oxygen consumption.

Almost all studies showing a detrimental effect of increased affinity of hemoglobin for oxygen have been complicated by the presence of anemia, while the studies showing a minimal physiologic effect were carried out at normal hemoglobin concentrations. The interaction of anemia and 2,3-DPG has been studied (Ref. 246) as related to the ability of rats to survive hemorrhage. At nearly normal hemoglobin concentrations, transfusion with red cells depleted in 2,3-DPG did not impair the ability of the animals to survive two different levels of hemorrhagic challenge. When the animals were studied at acutely anemic levels, however, transfusion with red cells depleted of 2,3-DPG was associated with a much higher mortality. These findings indicate that in stressful circumstances the resiliency and integrity of the oxygen delivering system is such that the degree of impairment produced by depleting red cells of 2,3-DPG is, by itself, insufficient to endanger survival, but that when combined with other circumstances such as acute reductions in red cell mass these shifts may become important.

There may be other circumstances where special attention must be paid to hemoglobin function. It is likely that a fixed and relatively low limit on cardiac output will also impair the patient's ability to compensate for impaired hemoglobin function so that these two together may assume new importance. Indirect evidence indicates that the newborn infant has a less well protected oxygen delivering system and is susceptible to conditions which would be tolerated by the adult.

Recently, Dennis et al. (Ref. 247) reported an increase in cardiac output when red cells rich in 2,3-DPG were used during cardiopulmonary bypass, using patients treated with red cells with lower concentrations of 2,3-DPG as controls. The differences in myocardial performance were greater than predicted from the small differences in hemoglobin oxygen affinity between the two groups, indicating that other variables must have been present. The same group (Ref. 278) subsequently reported better left ventricular performance in patients with abdominal aortic aneurysms operated upon electively and given relatively normal red cells compared with patients with ruptured abdominal aneurysms given old stored red cells. Obviously, hemorrhage was worse in the patient with ruptured aneurysm so it is difficult to see how any legitimate comparison can be made. Better controlled studies are needed on this important point.

(7) *Hypothermia.* Many studies (Refs. 248 and 249) have demonstrated that a massively transfused patient will become cold if the transfused blood is not warmed, especially if transfusion occurs in an air-conditioned operating room and is given to a paralyzed patient who may have one or more body cavities open to the air. It requires nearly 150 Kilocalories to warm five liters of blood from 4 to 37 ° C. This is equivalent to the heat produced by 30 minutes of moderately heavy work and represents a requirement for an additional 30 liters of oxygen. This added requirement for oxygen for the production of heat may come at the time when the patient's survival is being threatened by a challenge to the oxygen delivering system.

It is widely assumed that hypothermia impairs the metabolism of citrate and of lactate, thus increasing the chances for developing hypocalcemia and metabolic

acidosis during transfusion. Cold increases the affinity of hemoglobin for oxygen, thereby worsening the impairment of hemoglobin function. Cold also promotes the release of potassium from the intracellular compartment which, when added to the increased chance for acidosis, might result in hyperkalemia that would not otherwise exist. Rapid transfusion through central venous catheters could differentially cool areas of the heart and may cause arrhythmias. Hypothermia, then, is potentially disastrous in the massively transfused patient, but many of these possible complications have not been documented.

At least two reported clinical experiences reported better patient survival during massive transfusion when the blood was warmed, but neither was adequately controlled. A recent study on exchange transfusion in the newborn could not document any detrimental effect from cold blood (Ref. 251), although the degree of hypothermia produced in adults in an operating room with an open abdomen is often much greater.

The potential for detrimental effect is apparent, and efforts should be made to warm the transfused blood in an exsanguinating patient. Unfortunately, blood can be hemolyzed by temperatures not far above normal body temperature; at the same time, rapid warming is needed so as not to delay the transfusion. All available devices exhibit some drawbacks (Ref. 252). The microwave equipment, in particular, has a small margin for error (Ref. 253). New devices are being constantly introduced and require careful evaluation.

(8) *Infusion of denatured proteins.* There is preliminary evidence that certain forms of storage may render blood, and particularly plasma, more harmful then beneficial to the acutely hemorrhaged animal. Controlled studies in rats (Ref. 254) indicate that plasma is inferior to almost any reasonable alternative as a treatment for hemorrhage. Denaturation is recognized as a serious problem in cardiopulmonary bypass. Even without cardiopulmonary bypass, foreign surface contact may alter the efficacy of shed blood when reinfused to treat hemorrhage (Refs. 255 and 256). Other studies reporting poor results when comparing the reinfusion of shed blood to other forms of treatment are characterized by harsh handling of the blood ex vivo. Both length of storage and specific plasma protein fractions have been found to make significant differences in the survival of animals treated for hemorrhage (Refs. 257 and 258). These findings indicate that biological effects can be related to the manner in which blood is handled during storage.

(9) *Infusion of vasoactive substances.* Much of the experimental work dealing with the release of vasoactive substances during storage has dealt with single donor or pooled plasma stored under conditions not necessarily applicable to the usual blood banking practices (Ref. 259). There has, in fact, been little study of the release of vasoactive substances into the plasma of stored whole blood. Serotonin levels increase as would be expected from the breakdown of stored platelets (Ref. 260). There is evidence that the kinin system is activated during storage, but much of this work was done on blood stored in glass rather than in plastic containers. It is likely that there is partial activation of Factor XII during storage, which in turn might lead to partial activation of the kininogen systems. The status of the prostaglandins, angiotensin and other as yet undefined vasoactive materials remains to be established. In the massive transfusion situation this array of vasoactive substances, many of which are associated with the production of increased capillary permeability and vasoconstriction, might explain some of the pulmonary problems occasionally encountered in massively transfused patients.

(10) *Impaired bacterial defenses.* There is suggestive evidence that massive transfusion with stored blood may impair antibacterial defenses (Ref. 261), probably through two mechanisms. First, blood that has been run through an extracorporeal circulatory device and then administered to animals produces an impairment of reticuloendothelial function (Ref. 262). More recently the same effects have been shown (Ref. 263) from simple storage of blood. The added observation has been made that less impairment of phagocytic function follows the transfusion of washed erythrocytes when compared with stored whole blood. The second possible mechanism relates to older observations (Ref. 264) that citrated whole blood decreases the phagocytic ability of polymorphonuclear leukocytes.

(11) *Hyperkalemia.* The potassium level in the plasma of stored whole blood rises to approximately 30 mEq/L by the end of three weeks, a 25 mEq/L excess over normal. Therefore, 10 units of blood may contain an excess of up to 75 mEq over the normal expected potassium content in plasma. This suggests that hyperkalemia might be a serious problem in massive transfusion, but the practical problem is less than it might seem. Most of the excess potassium represents leakage from intact viable red cells. Upon transfusion, these viable red cells reverse the lesion that occurred during storage and take up potassium (Ref. 195). Almost every study on massively transfused patients has shown hypokalemia rather than hyperkalemia, reflecting the metabolic and respiratory alkalosis which is so common in these patients (Refs. 222, 265, and 266). There is evidence, however, that even transient hyperkalemia may worsen the effects of hypocalcemia, in vivo as well as in vitro (Refs. 267 and 268). As this situation may occur at the peak rates of massive transfusion, it is possible that potassium may in fact cause trouble for patients in certain circumstances.

(12) *Impaired red cell deformability.* Concomitant with the fall in red cell ATP levels during storage, red cell membrane elasticity decreases so that stored red cells are less deformable than normal (Refs. 22 and 29). This has significance in terms of the function of transfused blood in the microcirculation because red cells have a greater diameter than many of the capillaries of the body which they must traverse and must deform to circulate. Nevertheless, the fact that such cells survive and function indicates that, by some mechanism or another, deformability is rapidly restored.

(13) *Elevated phosphate and ammonia levels.* Plasma phosphate and ammonia levels rise during storage. Even with CPD, however, the phosphate levels represent little threat in terms of the total body phosphate. Similarly, the ammonia in stored blood, as high as 1 mg/dL, is easily handled by a functioning liver and represents a problem only in patients with significant hepatic insufficiency.

(14) *Miscellaneous.* In the newborn, hypoglycemia has been reported as a consequence of exchange transfusion with CPD blood (Ref. 279), probably reflecting the release of insulin triggered by the high glucose levels of the stored blood.

3. *Plastic transfusion equipment*—a. *Introduction.* Compared with glass bottles, the advantages of plastic bags are: (1) Decrease in weight, (2) reduction in storage space, (3) reduction in breakage, (4) ability to prepare components in a sterile closed system, (5) ability to infuse blood under pressure without risk of air embolism, (6) elimination of risk of trauma to the recipient if the container should fall, and (7) easiness of handling.

Most plastic transfusion equipment consists of polyvinyl chloride (PVC),

plasticizers, a mold-release agent, and a variety of other compounds. Although it was recognized that constituents of PVC leach into the stored blood (Ref. 40), it was Jaeger and Rubin (Ref. 41), in 1972, who showed tissue deposition of phthalate ester plasticizers, specifically di-2-ethylhexyl phthalate (DEHP). This report led to renewed concern about the safety of plastic bags and the effects of the plastic, not only on red cells and other blood components, but on organ function as well.

b. *Factors affecting blood during storage in plastic bags.* (1) *Plasticizers.* Polyvinyl chloride, developed in 1933, is a rigid plastic, but the synthesis of DEHP in 1933 permitted interfusion of these two components to yield a plastic with flexibility, extensability, and workability (Ref. 42). Phthalate plasticizers are used extensively in commerce (Ref. 42). Approximately 1 billion pounds of 20 different phthalate compounds were manufactured in 1972 representing about 2 to 3 kg of esters produced for every citizen in the USA per year (Ref. 43). The food and medical products industry accounted for only about 5 percent of the total produced with the building and construction industry using 38 percent, home furnishings 19 percent, transportation 11 percent, and apparel 7 percent.

Diffusion of the plasticizer depends on its molecular weight, compatibility with the plastic, viscosity, affinity of the environment for the plasticizer, and temperature at which the plastic is used (Ref. 42). The plasticizer DEHP represents about 30 to 40 percent of the dry weight of plastic blood bags (Fenwal JA-2 blood pack) and is not firmly bound. DEHP is soluble in blood plasma, accumulating at about 0.25 to 0.361 mg/100mL/day during whole blood storage at 4 °C with ACD or CPD solutions (Refs. 41, 44, and 45). There is no accumulation of DEHP in blood frozen at −80 °C or −150 °C for up to 2 years (Ref. 44).

There is essentially no DEHP in the anticoagulant during storage of the bag at room temperature (Refs. 44 and 46), and DEHP is not extracted by saline (Refs. 44 and 47). About 20 percent of the DEHP in stored blood is in the high-density (greater than 1.21) fraction of plasma, while 60 percent was found in the low-density lipoprotein fraction (less than 1.21) suggesting lipoproteins may solubilize DEHP (Ref. 47); washed red cells contain 4 percent to 6 percent of the DEHP found in the blood (Refs. 44 and 47). Compared with the progressive accumulation of DEHP in blood stored for 21 days, DEHP levels in plasma stored in plastic stabilize after 7 days with a peak of 120 μg/mL (Ref. 48). Even frozen plasma (−20 °C) accumulates levels of DEHP about half that of 4 °C stored plasma (Ref. 48). Among plasma derivatives, the fibrinogen fraction contains 18 to 39 μg/mL, albumin 5 to 25 μg/mL and immunoglobulins 63 to 160 μg/mL (Ref. 48). Of all blood components the highest accumulation of DEHP occurs in the supernatant plasma of platelet concentrates stored at 22 °C (Refs. 44 and 49). Levels of DEHP are 16.7 mg/100 mL after 48 hours of storage and 44 mg/100 mL at 72 hours. In contrast, stored platelet concentrates at 4 °C accumulate only 11 mg of DEHP per 100 mL at 72 hours.

DEHP is the only plasticizer known to leach from plastic blood bags, although other plasticizers are found in blood passed through commonly used biomedical tubing. Studies of tissue, blood, and urine levels of DEHP in man (Refs. 41, 45, 47 and 50) show no correlation between transfusion history and DEHP accumulation. DEHP can be isolated from tissues and urine of nontransfused persons suggesting the importance of other environmental sources of DEHP.

Storage studies with human blood in PVC bags compared to polyolefin from which no measurable DEHP is leached showed that microaggregate formation is not related to DEHP accumulation (Ref. 44). Also, DEHP could not be removed by the usual blood filters which remove microaggregates or by millipore filtration.

Neonates who had umbilical catheters used to administer fluids or blood and then died had higher levels of cardiac DEHP than control stillborns (Ref. 52). Higher levels were also found in the blood of infants dying of necrotizing enterocolitis. It is not clear whether DEHP accumulation is a cause of tissue damage or whether ischemic tissue accumulates DEHP more avidly.

One report has shown a decreased growth of human fibroblasts in tissue culture when the serum of the culture medium was obtained from 21 day old blood stored in plastic compared with blood stored in glass. Even more depression of growth was seen with serum obtained from the supernatant of 48-hour room temperature stored platelets (Ref. 53).

Other studies suggesting various toxic effects on drug metabolism and pulmonary, reticuloendothelial, and cardiac function have been done in animal systems using unphysiologic forms of DEHP, i.e., an emulsion or a poorly solubilized liquid solution (Refs. 51 and 54). Extensive studies by a manufacturer (Fenwal) in both animals and man using plasma extracted DEHP have shown no toxic effects (Ref. 45).

(2) *Bag thickness.* Viability of both red cells (Ref. 55) and platelets (Ref. 56) is influenced during storage by the ability of $CO_2$ and oxygen to pass through the plastic bag. Gas exchange is a function of bag wall thickness, agitation during storage, and storage surface area per unit volume of the blood product.

c. *Effects on cell viability and AHF activity.* Post-transfusion red cell survival varies among lots of plastic bags (Refs. 40 and 57). Whether this represents a result of plasticizers that leach during storage or some other variable is not known. Platelet viability is also related to the plastic bag (Refs. 58 and 60). Since viability appears to be better maintained at 22 °C than at 4 °C and the amount of DEHP leached is higher during 22 °C storage (Ref. 59), differences in platelet viability are unlikely to be due to plasticizers.

Studies by Kevy (Ref. 61) show a variable cryoprecipitate yield in vivo depending on the plastic bag used. However, no difference has been found in a subsequent report (Ref. 62).

d. *Summary.* The composition of the plastic bag used for blood storage influences the post-transfusion viability of red cells and platelets. Measureable quantities of the plasticizer DEHP accumulate during the blood storage but whether this is related to red blood cell viability derangements during storage is not known. Other potential toxic effects of DEHP on blood products or organ dysfunction following massive blood transfusion have not been well documented.

The production of blood bags and transfusion tubing needs to be standardized so that significant differences between lots do not occur. Furthermore, toxicology studies should be done only with plasma extracted DEHP rather than with other methods of administering the compound.

e. *Recommendations relating to plastic transfusion equipment.* (1) The evidence that leachables from plastic result in toxicity in vivo is not convincing and no action is recommended at this time.

(2) Research support should be provided for further investigation of possible toxicity of leachables in vivo, the interaction between plastics and blood components in vitro, and for the development of plastic bags and tubing which do not interact with blood.

(3) The production of blood bags and transfusion tubing needs to be standardized so that important differences do not occur between lots.

4. *Microaggregates*—a. *Introduction.* During storage of whole blood or red blood cells microaggregates consisting of platelets, granulocytes and possibly fibrin are formed. The number of microaggregates is proportional to the concentration of leukocytes and platelets in blood prior to storage and the progressive accumulation of aggregates is associated with decreasing levels of platelets and granulocytes (Ref. 63). The quantity of aggregates is higher in CPD than ACD blood during the first 24 hours but between 7 and 21 days the amount is the same (Ref. 63). Few aggregates form during the first 2 days of storage. The amount then increases slowly between 2 to 10 days (0.01 to 0.02 mg/mL) and then increases logarithmically during the remaining 21 days of storage (0.1 mg/mL) (Ref. 64). This rapid accumulation of aggregates after 10 days is associated with accumulation of fibrinogen in the aggregates (Ref. 64).

b. *Physiologic effect of aggregate infusion.* Microaggregates in stored blood have been suggested as a cause of pulmonary insufficiency following massive blood transfusion. To determine whether aggregates in stored blood cause or contribute to pulmonary insufficiency in the clinical setting has been a major problem, particularly since platelet microaggregates may be formed intravascularly in response to tissue injury (Ref. 65). Studies in dogs show that pulmonary damage associated with massive blood transfusion can be prevented by dacron wool filtration of stored blood (Ref. 66). Subsequent studies in the baboon also show pulmonary damage on histologic examination (Ref. 67), but this is not prevented by filtering the blood (Ref. 68). Whether these animal studies are applicable to man requires clarification.

One clinical study in man has suggested that pulmonary insufficiency can be reduced by blood filtration, but this was not adequately controlled (Ref. 69). A similar but more tightly controlled study in older patients transfused during elective operations on the abdominal aorta revealed little evidence of pulmonary dysfunction, and no difference between the group receiving blood through the standard filter and a similar group transfused through fine filters (Ref. 31). It has been suggested that pulmonary insufficiency may be more closely related to the type of patient injury than to blood transfusion. Studies on large numbers of transfused casualties in Vietnam yielded no convincing data suggesting that transfusion without special filtering produced pulmonary dysfunction (Ref. 32).

c. *Methods of aggregate removal*—(1) *Filtration.* Standard blood bank filters have a pore size of 170 microns and remove large debris. Filters available to remove microaggregates (16 to 170 microns) are made of: (a) Dacron wool, (b) polyester mesh (40 X 40 micron pore), (c) polyurethane foam, and (d) polyurethane foam-nylon wool. All remove particles greater than 40 microns, but filtration efficiency for smaller particles varies inversely with their resistance to gravity flow (Refs. 70 and 73), i.e., dacron wool, foam-nylon wool, foam and 40-micron mesh. The 40-micron mesh filter is efficient for volumes of 1,600 to 2,000 mL (Refs. 71 and 73), while the others have a limited efficiency for filtering more than 1 unit of blood (Refs. 72 and 73). Pressure filtration (150 to 200 mg Hg applied with an infusion cuff) removes particles with the same degree of efficiency with all filters except the 40 micron pore where pressure decreases the number of particles trapped (Refs. 71 and 73). Filtration of microaggregates is an efficient but costly method of removing microaggregates. Recent work using laser methods to measure microaggregates indicates that there may in fact be a paradoxical increase in the total number of particles with at least some of the fine filters used (Ref. 84). The advisability of using such filters might therefore be open to considerable question.

(2) *Other*—(a) *Age of blood.* Blood less than 2 days old has very few aggregates, and at less than 10-days old the quantity is still very small (Ref. 64).

(b) *Centrifugation.* (i) Centrifuging whole blood causes macroaggregates to form. These can be removed by a standard blood filter (Refs. 63 and 74).

(ii) Preparation of platelet and/or white-cell-poor before storage eliminates microaggregates (Ref. 74).

(c) *Washing with or without freezing.* Saline washing of red cells or freezing followed by deglycerolization and washing effectively removes aggregates (Ref. 74).

(d) *Agitation.* Continuous agitation during storage for 24 days decreases aggregate formation (Ref. 75).

(e) *Aspirin.* Addition of aspirin to blood prior to storage (Refs. 74 and 76) or ingestion of aspirin by donors (Ref. 76) is associated with lower quantities of aggregate formation.

d. *Summary.* Microaggregates progressively form during the storage of whole blood. The final volume of aggregates produced does not depend on the anticoagulant used (ACD vs. CPD). These aggregates might be partially removed by special filtration or by other means. Disadvantages in using microaggregate filters include reduced rate of infusion, added costs, and recent questions regarding overall efficacy. The value of removing these aggregates in preventing pulmonary insufficiency remains to be determined. In view of lack of evidence, there is no basis on which to recommend routine use of microaggregate filter at this time except in cardiopulmonary bypass where the filtering function of the lungs is absent.

e. *Recommendations regarding microaggregate filtration.* (1) Filters that remove microaggregates should be used in patients undergoing cardiopulmonary bypass.

(2) At this time there is insufficient evidence on which to recommend the use of microaggregate filters in other specific transfusion settings.

(3) Investigative efforts in this area should address the question of the optimal characteristics of a single filtering device to be used during transfusion and to be incorporated into the commonly used transfusion sets.

5. *Diseases transmitted by blood transfusion*—a. *Introduction.* A number of diseases, some of serious clinical importance, can be transmitted by transfusion. Since pathogenic organisms are found in different portions of whole blood, risks of post-transfusion diseases vary depending on the blood product or component used. In general, the risk for any disease is directly proportional to the volume of blood transfused.

b. *Viral hepatitis.* Since the first report in 1938 (Ref. 77), there has been increasing awareness of relationship between blood transfusion and some cases of viral hepatitis. Two distinct viruses have been identified as causing post-transfusion hepatitis (Refs. 78 and 79), and there is considerable evidence that additional, as yet unidentified, agents exist (Refs. 80 and 81). Until recently, the inability to transmit the disease to most laboratory animals made research difficult and slow. There is now, however, a practical laboratory test which detects a surface antigen (HBsAg) of one causative agent, hepatitis virus B (HVB). The incidence of post-transfusion hepatitis has been estimated at 4.6 cases per 1,000 units of blood transfused, with one third of these being icteric (Ref. 82). More recent studies indicate a higher risk of between 7 to 10 percent of all blood recipients. The risk of post-transfusion hepatitis is increased when blood from commercial donors is used (Refs. 82, 83, and 85). Elimination of these donors along with routine testing of all donor blood by

sensitive tests for HBsAg, if performed by the most sensitive radioimmunoassay method, will reduce the occurrence of post-transfusion hepatitis. It is becoming apparent, however, that all cases may not be related to HBV (Refs. 80 and 81) or even the recently characterized hepatitis A virus (Ref. 80). Studies (Refs. 87 and 89) attempting to implicate cytomegalovirus (CMV) and Epstein-Barr virus (EBV) have been fruitless, suggesting that most cases of post-transfusion hepatitis result from infections with virus(es) not previously implicated.

Testing of large United States donor populations with sensitive third generation tests for HBsAg shows a carrier rate of 0.33 per hundred (Ref. 90). There is no evidence that recipients of blood containing anti-HBsAg have an increased risk of hepatitis B and no reason to test donors routinely for this antibody (Ref. 91).

c. *Transmission of other infectious diseases.* A syndrome of fever, lymphocytosis with atypical cells, negative heterophile test, inconstant splenomegaly, and mild hepatic dysfunction has been reported 2 to 6 weeks after transfusion (Refs. 92 and 94). Although originally labeled as the "post perfusion" or "post pump syndrome" it can occur after any transfusion of whole blood (Ref. 95). Studies have shown rises in anticytomegalovirus (CMV) titers in these patients supporting the hypothesis that CMV infections transmitted by blood transfusion may be the cause. One large study has shown serologic evidence of CMV infection in 35 percent of patients who had been infused with fresh whole blood (Ref. 96).

Heterophile-positive infectious mononucelosis, the clinical syndrome associated with the Epstein-Barr virus infection, has been transmitted by blood transfusion (Ref. 97). Anti-EBV responses have been reported in 8 percent of patients undergoing transfusions or extracorporeal circulation (Ref. 96). Both CMV and EBV appear to reside in leukocytes.

Transfusion-induced malaria in seen infrequently, although the incidence recently increased (Ref. 98). *P. malariae, P. vivax,* and *P. falciparum* all have been implicated, and a rise in the number of cases due to *P. falciparum* was noted coincident with the return of service personnel from Vietnam (Ref. 98). Current standards for donor acceptance, if followed rigidly, are adequate to eliminate nearly all potentially malaria infectious donors. The malarial parasites reside exclusively in erythrocytes and are transmitted only with transfusion of RBC-containing products.

Chaga's disease, African trypanosomiasis, kala-azar, toxoplasmosis, and infections with micro filaria can be transmitted by whole blood, but these complications are almost unknown in the United States.

Transfusion-induced syphilis, while it does occur, is not an important hazard today. This topic is discussed below regarding the serological test for syphilis.

6. *Hazards related to transfusion of blood elements other than RBC*—a. *Introduction.* Noneythrocytic blood elements—plasma, platelets, and leukocytes—are responsible for a variety of common transfusion problems. Although it would seem logical that red blood cells ("packed cells") which contain smaller quantities of these blood elements would have less risk than whole blood, there is no evidence to substantiate this notion. Problems related to plasma, granulocytes, or platelets are largely, but not completely, obviated by either simple washing or the washing associated with deglycerolization of frozen red cells. Lymphocyte-related problems may, however, still be present. Recent studies indicate that even after freeze-deglycerolization, there are significant numbers of viable lymphocytes in the final product (Ref. 102).

b. *Anaphylactoid reactions to IgA.* Severe transfusion reactions characterized by flushing, abdominal pain, diarrhea, chills, fever, edema bronchospasm, hypotension, and shock have been seen when IgA-deficient patients with antibodies to IgA are transfused with whole blood (Refs. 103 through 105 and 107). Although the incidence of absent IgA is about 0.1 percent (Ref. 106) and about 15 percent of these IgA-deficient persons have high titer antibodies to IgA (Ref. 108), anaphlactoid reactions from this cause are extremely infrequent.

c. *Pulmonary "hypersensitivity" reactions.* There have been several reports of normovolemic pulmonary edema after blood transfusion. In most cases they have been associated with leukocyte antibodies in donor or recipient (Refs. 108 and 109).

d. *Post-transfusion purpura.* A number of cases of acute, severe, thrombocytopenic purpura occurring approximately 1 week after transfusion of whole blood have been described (Refs. 110 and 111). In most cases the antibody in the recipient's plasma has been anti-$PL^{A1}$, and the patient's own platelets are $PL^{A1}$-negative. The donor platelets have been $PL^{A1}$-positive and incompatible with this recipient's antibody. The mechanism suggested in immune destruction of donor platelets by recipient antibody with concurrent immune complex-mediated autoimmune thrombocytopenia (Ref. 110).

e. *Graft vs. host reactions.* A disease process identical with the graft vs. host reaction has been reported in transfused children with immunologic deficiency (Ref. 113). Evidence obtained in vitro has shown that lymphocytes are viable in stored blood for 15 to 20 days (Ref. 115) and that patients who receive fresh or stored whole blood show evidence of cellular activation as manifested by a rise in atypical lymphocytes, or incorporation in vitro of $^3H$-thymidine by autologous lymphocytes (Ref. 114). The relationship of these findings to the graft vs. host reaction is unclear, but is in keeping with the concept of lymphocyte stimulation by transfusion.

f. *Allergic reactions.* Allergic reactions, as manifested by pruritis or hives, are seen in about 1 percent of transfusions (Ref. 116). These reactions are usually mild and respond quickly to appropriate treatment, although occasionally an allergic reaction can be more serious. These reactions are presumably related to allergy to plasma factors.

g. *Reactions due to leukocyte antibodies.* The relationship between leukocyte antibodies and febrile transfusion reactions has been clear since 1957 (Refs. 117 and 118). The antibodies, formed as a result of alloimmunization during pregnancy or transfusion, react in vivo with donor leukocytes to produce a reaction marked by an initial flush, a latent period of about 60 minutes followed by a shaking chill, high fever, apathy, and generalized malaise. The development of these reactions in patients with appropriate antibodies is influenced mainly by the dose of white cells administered (Refs. 119 and 120). Fatalities have been reported.

7. *Other hazards of red blood cell product transfusion*—a. *Hemolytic transfusion reactions.* The reaction in vivo between blood group alloantibodies and red blood cells carrying the appropriate antigen is usually marked by an accelerated destruction of the red blood cells. The rate and site of this hemolysis and the severity of the clinical signs and symptoms accompanying it are dependent upon many variables, including class, titer, avidity, specificity, IgG subclass and complement-binding activity of the antibody, strength of the

blood group antigen, clinical condition of the patient, amount of blood administered, general anesthesia, and other drug therapy. Most hemolytic transfusion reactions result from clerical rather than laboratory errors. Misidentification of patients, blood samples, or blood containers is far more frequent and serious than the failure of appropriate laboratory tests to detect the incompatibility before the transfusion is administered. Cross-matching procedures, including the antiglobulin (Coombs) test, are required before transfusion in all but the most urgent cases and, if properly done, detect almost all potential incompatibilities. Prompt recognition and treatment of hemolytic transfusion reactions usually prevents the renal failure which is often seen after acute intravascular hemolysis. Disseminated intravascular coagulation has been reported in patients with hemolytic transfusion reactions (Refs. 121 through 123).

b. *Hemolytic transfusion reactions without demonstrable antibody.* Diminished survival of transfused red blood cells can occur without demonstrable antibody (Ref. 124). The hemolytic rate is generally moderate, although rapid hemolysis with clinical transfusion reactions has been reported. More sensitive methods for detection of antibodies in vitro may reveal some examples of antibodies that do not react by routine cross-matching procedures.

c. *Alloimmunization.* Blood transfusion is, of necessity, associated with the injection of many antigens into a recipient lacking of these antigens. Because of extreme complexity of the blood group systems, the HLA antigens of white blood cells and platelets, and the various polymorphisms of plasma proteins, it is impossible to give transfusions that are antigentically identical—or even similar—to the recipient. The red blood cell antigens A, B and $RH_o$ (D) are of sufficient immunizing potential that pretransfusion tests for them are routine so that these incompatibilities can be eliminated by donor selection. Transfusion to recipients who lack any of these antigens should be from donors who are also negative for the antigen in question. No such routine testing is required or recommended for other red blood cell antigens and, as a consequence of this practice, the risk of alloimmunization in recipients is 1 percent per unit of blood transfused (Ref. 125). Alloimmunized recipients are at increased risk when additional transfusions are required since the alloantibody may be directed against a high-frequency red blood cell antigen making it difficult or impossible to find compatible blood. In addition, the antibody may not be detectable at the time of pretransfusion testing so that apparently compatible blood will lead to an anamnestic response and a delayed hemolytic transfusion reaction. Such reactions are serious and, at times, fatal.

Alloimmunization to white cell and platelet antigens is directed predominately against antigens in the HLA system. HLA immunized recipients may have clinical reactions or, if candidates for granulocyte (Refs. 130 through 132) or platelet (Refs. 126 through 129) transfusions, may show decreased effectiveness of the transfusion.

Alloimmunization to plasma protein antigens is seen in the IgG, IgM, IgA, and lipoprotein systems. Anaphylactic transfusion reactions in such alloimmunized patients have been reported.

d. *Hemolysis from a mixture of blood with dextrose containing solutions* (Ref. 133). Transfusion reactions with intravascular hemolysis have occurred when whole blood was administered through a secondary recipient set containing solutions of dextrose alone. The mechanism of these reactions is related to osmotic swelling of red blood cells that are in contact with the glucose solution followed by lysis when the swollen cells are infused into normal recipients (Ref. 134).

e. *Bacteriologic contamination.* Transfusion reactions from bacterial contamination of blood are rare but serious occurrences. The high contamination rate (about 2 percent) (Ref. 135) seen in blood shortly after collection is not accompanied by clinical signs or symptoms at the time of transfusion because of the small number of bacteria present and their failure to survive or multiply during storage of the blood at refrigerator temperatures (Ref. 136). Those reactions that do occur are usually caused by gram-negative bacilli capable of growing in the cold (Ref. 137). Many of these organisms possess powerful endotoxins and, if transfused, bring about serious rections with a fatality rate of about 50 percent (Ref. 138). This problem has diminished dramatically with development of closed system processing and transfusion using plastic containers.

f. *Circulatory overload.* Circulatory overload is a common complication of whole blood transfusion especially when treating infants, patients with heart failure, and patients with chronic anemia. In the latter groups, cardiovascular compensation may be very precarious and the administration of unnecessary plasma in whole blood may precipitate left ventricular failure and pulmonary edema. Without monitoring pulmonary capillary wedge pressure, which is rarely indicated for the administration of blood, it may be impossible to detect early left ventricular decompensation before the onset of pulmonary edema. The resultant hypoxemia combined with the anemia and acute ventricular failure can be disastrous.

8. *Indications for transfusion of red blood cell products*—a. *Introduction.* Despite a large and long-standing experience, the indications for blood transfusion are not always easy to delineate. This is to be expected because of the complexity of transfusion products, wide variations in the homeostatic capabilities of patients, and the multiplicity of clinical situations that may be encountered. Thus, rules of thumb about when to transfuse, optimal hematocrit levels, and other such notions are unrealistic. The following discussion analyzes the recognized indications for blood transfusion, particularly in regard to the treatment of acute and chronic red cell deficits.

b. *Anemia.* The correction of a red cell deficit is probably the commonest reason for transfusing blood. In considering the indications for transfusing one must consider risk, benefit, and need. Risk is discussed elsewhere. As noted, it may be lower with some types of red cell preparations than with others.

The benefits of red cell transfusions are not as clear as they may seem. The red cell mass in any patient represents a dynamic equilibrium between production and loss. Any disorders of production or loss that can be corrected, should be. This will be more effective than the temporary benefit of transfusing red cells. If the hematocrit remains elevated after transfusion it is because the balance between production and loss has changed favorably, not because the transfused cells are somehow persisting indefinitely.

Given that transfusion brings about only a temporary increase in red cell mass accompanied by significant risk, there are situations where such temporary benefits outweigh the risks. Increasing the hematocrit increases oxygen availability by increasing the oxygen content of blood, while at the same time decreasing oxygen delivery by increasing the intrinsic resistance to blood flow. In order to predict the optimal hematocrit under varying conditions, detailed and accurate quantitative data on blood viscosity are

required. The few studies in vivo that have been attempted indicate that the resistance of blood to flow is probably an exponential function of hematocrit, but with different relative changes in different vascular beds (Refs. 271 and 272). Factors other than hematocrit are also demonstrably important (Refs. 273 through 275).

Most authors agree that under the conditions that apply in the normal state, there is maximal oxygen delivery at normal hematocrits (Refs. 231 through 233 and 276). As flow rate decreases, there may be an advantage in moderate hemodilution, but more studies of this problem are needed under conditions that more nearly approximate those in vivo.

The hemodynamic changes in acutely anemic patients and animals have been reviewed recently (Refs. 280 and 281). Perhaps the most fundamental observation is that when other variables are kept constant, increased cardiac output is a most important compensatory mechanism to maintain nearly normal oxygen delivery. There are probably elements of both increased left ventricular work and decreased viscosity in the compensatory increase in cardiac output. Such changes in cardiac output can only occur if blood volume is maintained near normal. Therefore, it is mandatory that hypovolemia be avoided in the acutely anemic patient. Indeed, loss of blood volume is more detrimental to oxygen delivery than is loss of blood oxygen-carrying capacity except at extreme levels of anemia. The primacy of volume over red cell mass is a well recognized principle of resuscitation from hemorrhage.

In studies in patients with chronic anemias it has been difficult to detect a deficit in work capacity with hemoglobin concentrations as low as 7 grams per dL (Refs. 282 through 291). Other investigators have found evidence of only moderately impaired function (Refs. 292 through 296). This correlates with the failure to detect much increase in cardiac output at rest with similar hemoglobin levels (Ref. 297). Unfortunately, many of these studies were carried out before the awareness of the liability and responses of oxyhemoglobin affinity in vivo to stresses on oxygen delivery. By changing levels of 2,3-diphosphoglyceric acid (2,3-DPG) in red cells, these shifts could compensate for losses of red cell mass by proportionally increasing the efficiency of hemoglobin as an oxygen-delivering agent at physiologic gas tensions. In view of the importance of the affinity of hemoglobin for oxygen in the oxygen-delivering system, it is surprising how little has been done to investigate the interaction between hemoglobin function and hemoglobin concentration in the response to stress. This question is discussed in the section on Oxygen Transport.

The heart occupies a unique position in the oxygen-delivering system apart from its central role as pump. With loss of volume and/or loss of red cell mass as well as with most other acute stresses to the oxygen delivering system, the heart works harder to increase total flow or to minimize any decrease in flow at lower filling pressures. The oxygen requirements of the heart increase, either absolutely or relatively, at a time when systemic oxygen delivery is decreasing. Oxygen delivery to the heart itself occurs largely during diastole, and is threatened in the bleeding patient by lower diastolic pressure as central aortic pressure declines and less time in diastole as heart rate increases. Most other organs can greatly increase oxygen extraction by working at a lower partial pressure of oxygen, but in man this important mechanism is almost completely unavailable to the heart, which works at all times near the minimum functioning $PO_2$. This unusual constellation of circumstances, increased oxygen requirements, a tendency to decreased blood supply from purely physical factors, and inability to extract more oxygen from available blood, place extraordinary importance on the ability of the coronary vessels to dilate in order for the heart to perform satisfactorily and the patient to survive during hemorrhage. Against this background, factors such as hemoglobin function and hematocrit could conceivably become survival-limiting variables in patients with coronary vessel disease. There are a number of studies relevant to these questions which are beyond the scope of the current discussion, but some of these studies suggest that the heart with limited coronary perfusion may be very sensitive to the oxygen-delivering properties of the blood perfusing it (Ref. 86).

With respect to oxygen delivery as an integrated system, the body has regulatory mechanisms controlling a number of important components: cardiac output, blood volume, hematocrit, and 2,3-DPG levels. Presumably other variables are manipulated to give high efficiency to the cardiac mechanism, that is, maximum peripheral oxygen delivery per unit of energy consumed in pumping.

For the clinician faced with the problem of what is best for the anemic patient, it is important to keep in mind the risks of transfusion and the transitory nature of the improvement that results from transfusion. Chronic anemia down to hemoglobin concentrations that are half normal is tolerated even by patients who must perform physical work. Even acute anemia can be well tolerated at similar hemoglobin levels if demands on the oxygen delivering system are minimal. On the other hand, factors such as coronary insufficiency, fever, hypovolemia, and likely further acute loss of blood, greatly increase the risks of anemia.

There are no simple guidelines or rules for establishing the need for transfusion to correct anemia. Need will vary with circumstances, and the decision to transfuse must be made on an individual basis considering both the current status and projected future course of the patient and the risks of all courses of action.

c. *Hemorrhage.* Hemorrhage is a clear and logical indication for transfusion when a significant percentage of the patient's blood volume has been lost. Limited hemorrhage can be treated with simple salt solutions or natural or artificial colloidal solutions (Refs. 298 through 300). The use of such solutions results in hemodilutional anemia, and the considerations discussed in the previous section on anemia apply. These solutions can be used as the sole replacement for limited hemorrhages, to keep the patient alive until blood is available, or in combination with blood to lessen the total amount needed.

The important consideration in the management of hemorrhage is that blood volume must be maintained. Most patients can tolerate acute loss of half their red cell mass, but acute untreated loss of half a blood volume is usually fatal. Therefore, volume replacement, not necessarily in the form of blood, must be begun as soon as possible.

Simple electrolyte solutions are effective, safe, and practical for initial resuscitation from hemorrhage. Experience in Vietnam (Refs. 301 and 302) and detailed studies in the United States (Refs. 297 and 298) indicate that blood volume can be restored by electrolyte solutions after hemorrhage. With electrolyte solutions alone, however, each volume of lost blood must be replaced by three volumes of solution. Disadvantages are over-expansion of extracellular fluid requiring subsequent excretion by the patient, failure of the central venous pressure to reflect dangerous degrees of overloading loss of efficacy of the solution in terms of the fraction retained

in the vascular space as hemorrhage progresses, and lowering of plasma colloid osmotic pressure. Advantages are as follows: Administration of electrolyte solutions can be quickly and safely begun even outside the hospital; there are no adverse reactions except for overloading; the risk of post-hemorrhagic renal failure is reduced; losses through sequestration (third space losses) can be treated as they occur. Artificial colloids preserve plasma osmotic activity, but those now available in the United States, dextran and hydroxyethyl starch, may interfere with clotting (Ref. 184). The natural colloids, albumin or albumin plus other plasma protein preparations, do not interfere with clotting and carry little risk of hepatitis, but they are expensive and occasionally of limited availability.

Whatever is used initially, as the hemorrhage approaches half the blood volume, replacement with blood will be necessary. The more rapid the rate of bleeding and the more significant the associated diseases or disorders, the earlier blood must be used. Nonblood replacement of blood loss should be continued only if the anticipated loss is limited, the patient is doing well, and their are no associated conditions that make acute anemia less tolerable.

In severe situations in which exsanguination is imminent, it may be necessary to use uncrossmatched blood in order to save the patient's life. If possible, this will be type and Rh specific. The military experience with the use of uncrossmatched blood has been excellent (Ref. 185), but few of those recipients had been transfused or pregnant previously, and the blood was tested for high-titer anti-A and anti-B. In extensive bleeding the cause of hemorrhage must be identified and corrected as soon as possible. Evaluation of the clotting system early in the course of the hemorrhage occasionally yields evidence of a treatable clotting defect. Some patients with rapid exsanguination must be operated on to control bleeding before resuscitation is complete, as the maximum possible rate of administration of fluid and blood may not equal the rate of loss.

Monitoring central venous pressure can be helpful in the extensively hemorrhaging patient, but may not reflect overloading with simple salt solutions or, occasionally, acute left ventricular failure. Pulmonary capillary wedge pressure is more informative, but carries added risks and should be reserved for difficult situations. Blood pressure, pulse rate, respiratory rate, state of consciousness, urinary output, and skin temperature and color all can be valuable indicators of the adequacy of perfusion, but any of them alone can be misleading. Hematocrit, is a measure of red cell concentration and reflects changes in whole blood volume only over a longer range of time than is appropriate for resuscitation. Hematocrit, therefore, does not accurately reflect acute blood loss. Similarly, the central venous pressure does not always bear a linear relationship to blood volume. The rate of change with fluid administration is often more informative than the absolute level itself. Central venous pressure monitoring is most valuable as an aid to the early detection of fluid overload when administering blood or other fluids with plasma specific colloid activity.

d. *Clotting abnormalties associated with massive transfusion.* Component therapy guided by appropriate laboratory studies is the rational way to manage clotting abnormalities. The use of platelet concentrates, fresh frozen plasma, cryoprecipitate, and cryoprecipitate-poor plasma are indicated in the appropriate clinical setting. The use of clotting fractor concentrates, which are prepared from large plasma pools, are not indicated in the usual massive transfusion setting because of the high risk of hepatitis and other hazards.

The use of blood transfusions to correct coagulation abnormalities implies the use of fresh whole blood. This becomes rational only when multiple clotting deficiencies are to be treated simultaneously, appropriate components are not on hand, there is a concomitant need for red blood cells, and fresh blood is easily available. Such circumstances are most likely to occur in a small hospital when the need arises for platelet replacement in an actively bleeding patient. Even here, the use of fresh whole blood should be considered a temporary measure until platelet concentrates can be obtained. For replacement of plasma clotting factors, except factor VIII and factor V, blood 24 to 48 hours old is adequate.

e. *Exchange transfusion.* Exchange transfusion is an established therapeutic procedure for hemolytic disease of the newborn (Ref. 277). Special precautions are necessary for this particular version of massive transfusion as the metabolic defense of these sick newborn infants are not as efficient as in adults, especially if the infant is premature. The blood must be warmed, generally should be less than 5 days old, and adjunct therapy with calcium chloride and sodium bicarbonate may be necessary. The exchange rate must be carefully controlled, intake and output balanced, and the infant monitored closely. Mortality rates of 1 to 5 percent have been reported, although most deaths were probably due to underlying disease.

In performing exchange transfusion in the neonatal period, whole blood (CPD), heparinized whole blood, and frozen red cells reconstituted with fresh-frozen plasma are used, each having a number of real and theoretical advantages. It has been suggested, when using citrate-anti-coagulated blood, that half the plasma should be removed (Ref. 269). This will reduce the risk of citrate toxicity and leave the infant with a higher hematocrit at the end of the procedure.

Exchange transfusion has been extended to several other conditions, usually various forms of poisoning or intoxication. Recently, exchange transfusion has been used in the treatment of disseminated intravascular coagulation in infants, but there are no controlled studies. Exchange transfusion is being evaluated in the high-risk infants and in infants with respiratory distress syndrome (Ref. 270). Preliminary results are encouraging. A modification of exchange transfusion has been used for hepatic coma in adults. Total body washout is achieved by rapid exchange with cold asanguineous fluid followed by a short run on cardiopulmonary bypass to support the circulation, restore temperature, and restore red cell mass. The most notable successes have been in patients with Reye's syndrome and not in those with hepatitis A or B. Again, proof of benefit by controlled clinical trials is needed.

f. *Nutritional deficiencies.* Whole blood is occasionally given to provide a "general support," or to treat hypoproteinemia with some degree of concomitant anemia, or even to prepare a nutritionally depleted patient for some form of stressful treatment. All of these approaches and concepts represents serious misconceptions about the efficacy of blood transfusion, the dynamics of blood cell protein turnover in disease and malnutrition, the optimal management of the undernourished patient, and even more serious misconceptions about the risks of transfusion. General support and the correction of malnutrition are not legitimate indications for transfusion.

g. *Wound healing.* Wound healing is impaired by protein deficiency and hypoproteinemia, but is not impaired by anemia. Transfusion to promote wound dealing is not indicated; quite the

contrary, this is usually a florid example of poor medical practice.

h. *Extracorporeal circulation.* Some blood is necessary for cardiopulmonary bypass, but most such operations are now done using very little blood in the priming solution, allowing hemodilution during bypass and slowly replacing red cell mass after bypass. It is difficult to justify the persistent use of large amounts of blood in the priming solution in some institutions or to understand the marked interinstitutional discrepancies in utilization of blood for similar bypass procedures.

i. *Recommendations regarding red blood cell product indications.* (1) Red blood cell products should be administered only after a responsible physician has evaluated the potential benefit in light of the known risks and hazards.

(2) Red blood cell products are indicated to correct a red cell deficit, chronic or acute, when the deficit is severe enough to cause signs or symptoms resulting from oxygen deprivation.

(3) Red blood cell products are indicated to correct a red cell deficit in the absence of signs or symptoms when there is a reasonable expectation that serious signs or symptoms may soon occur if transfusion is not given.

(4) Whole Blood transfusion indications:

(a) Whole Blood is indicated for the replacement of actual or anticipated blood loss, e.g., during the course of major surgery, when the loss is massive, or, if the loss is moderate, when accompanied by signs and symptoms of oxygen deficiency or shock and when simultaneous restoration of red blood cells and volume is necessary.

(b) Extensive blood loss is also an indication for the use of Whole Blood when recognized single or multiple coagulation defects are present. The use of specific blood components is preferable, but in an emergency, or when these are unavailable and there is no reasonable alternative, fresh Whole Blood may be used. In general, this approach is not as efficacious as the judicious use of specific components.

(c) Whole Blood may be used when exchange transfusion is indicated in hemolytic disease of the newborn, and, perhaps, in selected cases of hepatic encephalopathy, acute massive hepatic failure, sickle cell crisis, post-transfusion purpura, drug intoxication, and respiratory distress syndrome in the newborn.

(d) Whole Blood is indicated to prime the pump-oxygenator for extracorporeal circulation in those special circumstances where crystalloid priming fluid alone cannot be used.

(5) Red Blood Cells (Human) (red cell concentrate, "packed cells") is the product of choice to increase the oxygen carrying capacity of blood in most situations requiring transfusion. It can be used in place of Whole Blood if administered in combination with specific components, crystalloid solutions, derivatives, or volume expanders as indicated by the patient's clinical condition.

9. *The donor*—a. *Donor standards*—(1) *Introduction.* A person's suitability to donate blood depends on two general considerations: The donation will not be injurious to the donor and the donated blood will not be unnecessarily hazardous to the recipient. Overly restrictive criteria for donor suitability are harmful because they unnecessarily reduce the number of eligible blood donors, thereby creating difficulty in maintaining adequate blood supplies. It is commonly asssumed that only 3 to 4 percent of the eligible population donates in any year; however, this figure is probably inaccurate. The correct figure is probably about 8 to 9 percent, and up to 25 percent of the eligible population have donated at least once within a 10-year period (Ref. 139).

(2) *The physician's role in donor selection.* The Code of Federal Regulations (21 CFR 640.3) requires that a physician take responsibility for developing criteria for suitability as a donor, although he or she may delegate the day-to-day selection of donors to trained responsible individuals. The Code of Federal Regulations further mandates that a procedure manual describing these criteria be available in the blood bank. A physician need not be at a collection site. The American National Red Cross (ANRC) requires that donor selection be delegated to a person "no less professionally qualified than a Registered Professional Nurse" and that a physician or emergency medical facilities must be "available" and "no longer than 15 minutes away by automobile" from the blood-collecting team. Since there are few published data regarding how often serious reactions occur and whether they require the immediate availability of a physician, it is difficult to analyze this problem completely. A study by the United States Army found that 6.7 percent of their donors had reactions on the phlebotomy bed and another 3.8 percent after leaving the bed but before leaving the donor area (Ref. 140). In an unpublished study (Ref. 141) of 65,182 consecutive blood donations during a 12-month period, donor reactions occurred in 3.9 percent. Reactions classified as moderate or severe occurred in only 0.25 percent and only eight donors (0.012 percent) required medical consultation away from the donor site. Moderate or severe reactions include all instances where the donor lost consciousness no matter how transiently. There were no fatalities and no morbidity beyond the day of donation.

(3) *Donor safety.* 21 CFR 640.3 requires only that the donor shall be in good health, have a "normal" temperature and blood pressure, a hemoglobin level of more than 12.5 gm per dL (no distinction is made between males and females) and be free of any acute respiratory disease. Donations of a unit of whole blood may occur no more frequently than every 8 weeks, although this requirement and the blood pressure constraints may be waived in an otherwise acceptable donor at the discretion of an examining physician. All other donor standards listed in the CFR are clearly for the recipient's benefit.

(a) *Criteria to prevent anemia in the donor.* It is well recognized that normal hemoglobin levels are higher in men than in women. Thus, although not required by the CFR, most blood donor centers use a higher minimal level for men, 13.5 gm per dL, than for women, 12.5 gm per dL. The copper sulfate method for estimating safe minimal hemoglobin levels is in wide use today and uses two solutions of differing specific gravities, one for men, the other for women.

It has been suggested (Ref. 145) that the specific gravities of the copper sulfate solutions be increased to avoid phlebotomy of iron-deficient donors. To counterbalance an increased deferral rate of normal donors with this approach, it was also recommended that finger stick microhematocrits be performed on all those who "fail" the copper sulfate test. Spurious results, both high and low, may be obtained with the copper sulfate technique (Ref. 142) owing to technical errors, donor-sampling variables such as use of venous blood, ear or finger prick (Ref. 145), or donor variables such as hyperproteinemia (Ref. 143). Also, quality control on the copper sulfate solutions may not be adequate (Ref. 154).

Of major significance is the site of blood sampling for hemoglobin determination. It has been shown that samples obtained by ear prick give less consistent and generally higher hemoglobin values than samples obtained by finger prick or from venous blood (Refs. 189 through 191). In one

study, the donor rejection rate was 7.96 percent by finger prick and only 1.94 percent by ear prick (Ref. 189).

In healthy individuals with adequate dietary intake, the daily iron requirement depends primarily on age and sex. Within the usual age for donating blood, the donor's sex is the primary variable. Men lose about 1 mg of iron daily and absorb the same amount from the average daily dietary intake of about 10 mg. Menstruating women lose about 2 mg of iron per day and, without dietary supplementation, may or may not increase absorption sufficiently to prevent iron deficiency. Childbearing adds a significant additional requirement for iron in that a net loss of 400 mg occurs during pregnancy. Once iron deficiency anemia occurs, it is generally recognized that increased absorption of normal dietary iron cannot adequately compensate for the deficiency and drug iron supplementation is necessary.

Phlebotomy of 8 percent of the total blood volume, removal of approximately a unit of blood from an average person, causes a 6 percent drop in the donor's hemoglobin level within 1 week. Hemoglobin levels return to normal after another 2 weeks (Ref. 144). However, each 450 mL of donated blood contains about 250 mg of iron or about 5 percent of the total body iron. Thus, a frequent blood donor in good health can become iron depleted in a few years if there is inadequately increased absorption of dietary iron. In donors, particularly women, who have compromised iron reserves, inadequate intake, or impaired absorption, the occurrence of iron deficiency is inevitable.

The prevalence of iron deficiency and/or iron deficiency anemia in the normal adult population has been the subject of a number of studies (Refs. 146 through 150). Broad generalizations are risky because of a number of variables among these studies, particularly those related to dietary iron intake and to criteria for establishing iron deficiency and iron deficiency anemia. A recent study (Ref. 148) of a northwest United States population, using 3 parameters for evaluating iron status, found iron deficiency in 20 percent of menstruating women and in 3 percent of men. The data also suggest that about 10 percent of all persons who might be blood donors are iron deficient, and the current tests for anemia in the donor population would detect fewer than half of them.

The iron status of blood donors has been studied extensively. Decreased serum iron and/or increased iron-binding capacity (Refs. 147 and 152) or diminished stores (Refs. 146, 147, 151, and 152) have usually been found. As early as 1944, anemia was found to correlate with the number of previous blood donations (Ref. 153) and reduced serum ferritin levels have been correlated with donation frequency as well (Ref. 187). The inescapable conclusion of all these considerations is that iron depletion and occasionally iron deficiency anemia will occur with measurable frequency in the blood donor population that donates blood regularly, particularly in women donors.

Iron depletion without anemia does not seem to be associated with any morbidity in man. Mild degrees of iron deficiency anemia are also generally well-tolerated. However, it seems desirable to prevent the occurence of iron deficiency aneima among blood donors so that they would not be subject to unnecessary medical evaluations and would have adequate compensatory capabilities if unexpected hemorrhage should occur.

There are a number of ways of dealing with this problem. One approach is to reduce the permissible frequency of blood donation, particularly among at-higher-risk women donors. A second approach is to recommend iron supplementation after blood donation as is currently being done by the British National Blood Transfusion Service. Even this approach will not be entirely effective in preventing iron depletion in very frequent donors (Ref. 152). A third approach may be to increase the acceptable level of hemoglobin for determining donor suitability.

The presumed benefits of reducing the frequency of blood donation must be weighed against the possibility that such a regulation would reduce the blood supply in this country. While there are undoubtedly a number of donors who donate regularly every 8 weeks, these may represent a small percentage (1.7 percent) of all blood donated (Ref. 188). Irrespective of this, the issue appears to be one of balancing societal interests in the blood supply against those of the individual donor. Similarly, the benefits of iron supplementation to donors must be weighed against the occurrence of gastrointestinal distress from the medications and the possibility of masking iron deficiency from a pathological cause and thereby delaying detection and early treatment of disease.

(b) *The donor must have a normal temperature.* This standard seems directed primarily at protecting the recipient from possible infection from blood obtained from a febrile infected donor. Fever is a clinical sign usually indicating an underlying pathological process and this standard might protect the donor as well. The delineation of normal temperature is more difficult, however. The mean normal oral temperature in a number of studies was 98.34 °F with a standard deviation of 0.47. It has been calculated that the normal range of temperature would then be between 97° to 100.4 °F. Furthermore, there is a diurnal variation in temperature which may be as much as 3 °F (Ref. 99). Fortunately, the peak temperature usually occurs between 8 and 11 p.m., while the nadir occurs at between 4 and 6 a.m., both times not usual for blood donations. These data apply to the resting state; in more usual circumstances other factors, such as degree of activity, play significant roles. Pathological conditions also affect the temperature level significantly, usually by producing an elevation. Conditions which cause low temperature levels, such as hypothyroidism, are distinctly uncommon. Both AABB and ANRC standards require only that the donor's temperature be below 99.6 °F. The rationale behind this limit is not known. Whether increasing the upper temperature limit would increase the donor pool significantly without compromising the quality of the product is unclear.

(c) *Weight.* Although not required in the Code of Federal Regulations, both AABB and ANRC standards require donors to weigh at least 110 pounds if they are to donate one unit (450 mL) of blood. Although apparently an arbitrary standard, it seems a reasonable protection against acute hypovolemic hypotension which might occur in a donor below the weight standards. For example, a 110-pound, five-foot tall woman has a blood volume of about 3 liters. Phlebotomy of one unit of blood amounts to an acute hemorrhage of about 15 percent of her total blood volume, probably the upper limit of acute hemorrhage that is not associated with frequent postural hypotension. While it is recognized that blood volume estimation based on weight alone is inaccurate, the minimum weight criterion seems effective and not unnecessarily exclusive.

(d) *Pulse rate.* Although not required in the Code of Federal Regulations, both the AABB and ANRC have pulse rate standards (AABB 50 to 100 per minute; ANRC 60 to 100 per minute). Bradycardia and tachycardia may occur in normal persons. Here again, while arbitrary and occasionally excluding healthy donors, these standards are reasonable to protect prospective donors who might have heart disease.

As a general practice, donors with irregularities of pulse are referred to

supervisory personnel for evaluation. Donors with sinus arrhythmia or atrial premature contractions are usually acceptable. Similarly, healthy donors with physiological bradycardia, such as can be seen with trained athletes, may be accepted.

(e) *Age limits.* Although age limits are arbitrary, upper limits are based upon well established correlates of the probability of cardiovascular disease as a function of increasing age. The present regulations provide for individual judgments to be made beyond the usually accepted age range for donations.

(4) *Recommendations regarding donor standards.* (a) Acceptable minimum hemoglobin level for males should be increased to 13.5 gm/dL.

(b) Donors may not donate more than four times per year and no more frequently than every 8 weeks. Procedures to bleed donors more frequently may be established with the concurrence of the Bureau of Biologics if adequate means are employed to protect donors from the development of iron deficiency.

(c) Hemoglobin levels must be determined in a manner that correlates with concentration in venous blood.

(d) Research should be encouraged into the feasibility, acceptability and efficacy of administering iron supplements to blood donors.

10. *Testing of donor blood*—a. *Blood typing.* Characterization of the ABO and Rh types of all donor bloods is universally practiced and mandated in the Code of Federal Regulations (21 CFR 640.5). Although there are hundreds of blood group antigens on the red cell surface, those in the ABO and Rh systems are critical because of their immunogenicity, frequency distribution, and the dire consequences of transfusion when incompatibilities exist. The reliability of ABO and Rh typing depends largely on (1) the quality of reagents used for testing, (2) the tests that are performed, (3) the controls used in tests, (4) the competence of the technologist, and (5) the recordkeeping and organizational and operational abilities of the blood collection center.

b. *ABO typing.* The most important test is determination of the ABO type. The serious complication of transfusing ABO incompatible blood, frequently fatal when it occurs, demands that this test be performed by a dedicated technologist using the utmost care, highest quality reagents, and well-controlled labeling procedures.

ABO typing (also called grouping) is usually done with monospecific anti-A and anti-B reagents. In many laboratories, an additional test using anti-A, B (group O serum) is also done to check on the monospecific tests and to detect variants of A or B red cells. Most laboratories also perform so-called reverse grouping (serum typing or "back typing") in which the donor's plasma is tested with known type A and B RBC. This confirms the cell typing since normal persons have serum antibody specificity antithetical to the cell type.

Current standards for antisera used in ABO typing are the subject of another review in this document. These reagents are designed to give strong reactions when tested against cells specific for the labeled antigentic type and are more than adequate to facilitate accurate serological determination by even relatively unskilled technologists. There are, however, situations in which routine testing with anti-A or anti-B is not entirely adequate in that erroneous results will be obtained unless additional tests and/or control observations are made. These include:

(1) *Weak sub-groups of A or B antigens.* Numerous variants of the A antigen give weak or no agglutination when tested with usual blood-typing reagents. In some persons of group AB, the B antigen weakens the reactivity of the associated A leading to weakened agglutination when testing is done with anti-A reagents.

(2) *Positive direct antiglobulin tests.* Blood donors who have positive direct antiglobulin tests may be erroneously type as positive for certain red cell antigens as a result of excessive globulins bound to the red cell surface. This is true particularly with blood-typing reagents diluted in high-protein media or automated blood-typing systems.

(3) *Other conditions.* There are a variety of other conditions that may affect the accuracy of blood-typing reactions. These include acquired B antigens, hypoglobulinemia, hyperglobulinemia, polyagglutinable red cells, and recent previous transfusion with blood of a different type.

c. *Recommendations regarding ABO typing.* According to the Code of Federal Regulations (21 CFR 640.5(b)), blood shall be classified as to ABO blood group by at least two separate blood group tests, and blood-grouping results obtained by the different methods and with different lots of reagents must be in agreement. The Code is not specific about the tests required. In the interest of accurate ABO blood type determinations, the Code of Federal Regulations should be modified to be more specific as follows:

(1) Licensed anti-A and anti-B reagents or equivalent must both be used for determining blood type.

(2) Reverse grouping of donor plasma or serum against red blood cells of known ABO type (A and B) must be part of the routine testing.

(3) Cell and serum grouping must be in agreement before a final label is placed on the blood.

d. *Rh typing.* Typing for the $Rh_o$(D) antigen is routine on all donor bloods. Because the majority of Rh antibodies are of the coating ("incomplete") type, Rh typing usually is done in the presence of added protein and/or other diluent materials and a control test is required using a high protein solution and/or other diluent solutions without any anti-$Rh_o$(D) antibody. A positive control test suggests that the Rh typing may be erroneous.

If the test with Rh antisera is positive, the donor is considered to be "Rh positive." If there is no agglutination the donor may ge Rh negative, although some of the persons whose cells fail to react are, in truth, $Rh_o$ positive. These persons are of the $D^u$ phenotype and can be detected by incubating donor erythrocytes with Rh antibody, washing them, and then performing an indirect antiglobulin test. Only persons negative by direct typing and $D^u$ testing are truly $Rh_o$ negative.

Some laboratories further test $Rh_o$ negative blood for other Rh antigens, particularly C and E. Approximately 97 percent of $Rh_o$(D) negative individuals have the Rh genotype *rr* (*cde/cde*) and thus also lack C and E antigens. In some laboratories the 5 percent of $Rh_o$(D) negative individuals who are positive for either the C or E antigen are generally not used as donors for $Rh_o$(D) negative (*rr*) recipients because of the possible immunization of the recipient to the C or E antigens. This practice is unnecessary and inconsistent because: (1) C and E are relatively weakly immunogenic, and (2) there are situations of Rh positive donor-recipient pairs where the donor has C or E while the recipient is negative for these antigens.

Rh typing is second in importance only to ABO typing. The $Rh_o$(D) antigen is probably the most immunogenic red cell antigen outside the ABO system. Thus, the likelihood of immunization when an $Rh_o$(D) negative recipient is transfused with $Rh_o$(D) positive blood is high, although by no means certain. Development of antibodies to the $Rh_o$(D) antigen compromises the safety of future transfusions should $Rh_o$(D) blood be used. It also has significance in women recipients with a change of childbearing because of the possible induction of maternal $Rh_o$ antibodies that are crucial in the pathogenesis of hemolytic disease

of the newborn. These considerations make the requirement for $Rh_o$ (D) typing of considerable importance.

The necessity of $D^u$ typing has been questioned. If $D^u$ testing were not done, these units would be labeled as $Rh_o$ negative and transfused into $Rh_o$ negative recipients. In one study of 45 donor recipient pairs (Ref. 155), there were no instances of immunization of $Rh_o$(D) negative recipients to the $Rh_o$(D) antigen after transfusion with $D^u$ positive blood. Immunization with $D^u$ blood has been reported rarely (Refs. 156 and 157), but in one case the specificity of the resulting antibody is in question (Ref. 158). Thus, the immunogenicity of the $D^u$ antigen is low. However, $D^u$ testing does afford an extra measure of protection, perhaps only theoretical, against immunizing women with a potential for childbearing.

e. *Recommendations regarding Rh typing.* (1) Testing for the $Rh_o$ variant $D^u$ is required. Blood that is $D^u$ positive should be labeled $Rh_o$(D) positive.

(2) Routine testing for C and E or other antigens should not be required.

f. *Antibody detection tests.* Although not required by the Code of Federal Regulations, antibody detection testing on donor serum is common in most blood collection facilities. If the test is negative, the blood is labeled "no unexpected antibodies detected when tested by * * *." Unexpected antibodies are found exclusive of the normally occurring anti-A or anti-B alloantibodies. Unexpected antibodies found may or may not be identified, depending on the practice of the particular blood collection facility. The label must indicate that antibody is present, and if identified, the specificity must be noted. Such units may be transfused at the discretion of the transfusion service director and attending physician. The incidence of significant antibodies is low in healthy individuals who have never been pregnant or transfused with red blood cell products. It has been found (Ref. 192) that 0.322 percent of all donor bloods contain unexpected antibodies, 80 percent of these in women. Antibody screening eliminates the need for minor cross-matching prior to transfusion.

Considerable controversy exists over many facets of antibody screening. Should antibody screening be mandatory for all units of blood collected? If so, which test(s) is (are) most suitable? Should antibody identification be mandatory for those units in which antibody is detected. Which antibodies are clinically significant when transfused into a recipient? The question of clinical significance must be addressed in relation to the transfusion in prospect. For example, the presence of anti-$Rh_o$ (D) in Rh negative donor blood may be significant if transfused into an $Rh_o$(D) positive recipient, but is insignificant if the recipient is $Rh_o$(D) negative.

It is advisable to do whatever antibody testing is required as part of the routine processing of donor blood. This permits detection of antibody-positive units at the time of collection rather than in the transfusion service where unexpected findings can delay transfusion to a patient. Serum from donors without antibody need not be tested against recipient cells (minor cross-match) eliminating that time consuming and, at times, confusing procedure in the pretransfusion evaluation.

Antibody screening at the collection center also leads to detection of rare donor units because the presence of antibody implies that the donor is negative for the corresponding antigen. These rare donors should be registered for future recruitment should there be a need for their blood. In addition, the red blood cells may be frozen for use when rare blood is required.

There are numerous procedures, both manual and automated, for antibody detection testing. The goal is to detect all clinically significant antibodies, but not necessarily all antibodies. While the question of which antibodies are clinically significant is thorny, there appears to be agreement that antibodies reacting only in vitrol at 5° C, and/or room temperature, but not at 37° C, usually are of little clinical importance. Most clinically significant antibodies belong to the IgG immunoglobulin class and a test to detect these is necessary. Within these constraints, there are numerous acceptable procedures for antibody screening.

Determination of specificity on antibody detected in donor plasma is desirable to identify special donors who might be needed in the future and to allow development of a frozen red cell inventory. Antibody identification could be done at the blood collection facility or the transfusion service, whichever has greater competence.

An alternative to testing all donor bloods for unexpected antibodies has been developed, which appears efficacious in ascertaining those units which contain antibody (Ref. 192). With this approach, only donors giving a history of previous pregnancy or blood transfusion and all Rh negative donors are tested for irregular antibodies. The incidence of undetected sensitized donors with this approach was estimated at 1 in 10,000.

While it is generally conceded that transfusion of antibody (outside of anti-A, anti-B, and anti-D) in donor plasma is of little clinical significance and there has probably never been a well-documented case of this hazard (Refs. 192 and 193), there appears to be no good way of ensuring this in every case. Undoubtedly, in some cases the passive transfusion of antibody results in a positive direct antigobulin test in the recipient and may create unnecessary laboratory confusion and testing if post-transfusion samples are evaluated. Furthermore, the amount of antibody transfused must be considered relative to the recipient's blood volume. Also, the amount varies with the blood product; whole blood contains about three times as much plasma as red blood cells, while deglycerolized red blood cells contain almost none. Problems with infusion of antibody are thus more likely to be seen with whole blood transfusion. The major drawback in labeling units of blood containing antibody is that some physicians will not use this blood in appropriate and safe settings because they do not understand the issues involved. This problem in medical education does not seem amenable to correction by compromising the quality of testing or by failing to disclose what the blood contains.

In summary, antibody detection and identification procedures on donor blood are valuable: (1) In identifying blood that might be harmful if transfused, (2) in identifying blood that might confuse future serological evaluation of the recipient, (3) in selecting donors who might be called when specific phenotypes are needed, (4) in permitting frozen storage of blood of known phenotypes, and (5) in identifying donors who could be used as a source of blood-typing reagents. Proper selection of test conditions and reagents is vital for adequate antibody screening and idenfitication. Routine testing is not generally useful at a temperature less than 20 °C, and conditions should be appropriate for detecting IgG coating antibodies. While the clinical importance of passive antibody transfusion is slight and is related to the product transfused, the size of the recipient, the specificity and immunoglobulin class and subclass of the antibody, and the presence of the corresponding antigen in the recipient, the designation on the label of any antibody specificity present permits the transfusion therapist and clinician to make sound clinical decisions with all the available facts. For frozen deglycerolized red blood cells, however,

such a designation is unnecessary, inaccurate and, perhaps, confusing.

g. *Recommendation regarding antibody detection tests.* (1) In general, each unit of donor blood should be screened for unexpected antibodies either using Reagent Red Cells intended for this purpose or by an equally effective method. Thus, in carefully selected populations an adequate medical history may be utilized in lieu of laboratory tests for unexpected antibodies provided the procedure meets FDA requirements.

(2) Donor blood found to contain significant antibodies should not be used for transfusion purposes unless the plasma has been removed.

(3) Tests utilizing donor serum and recipient cells should not be required as part of pretransfusion testing.

(4) If the unit of blood is to be transfused without significant levels of donor plasma, antibody screening and identification are not necessary.

(5) Research should be encouraged to develop alternative methods to detect and define antibodies that are of clinical significance.

11. *Testing for serological incompatibility (cross-matching).* The test for serological incompatibility (cross-matching) occupies a central role in determining safety of blood transfusions. It is the final laboratory test performed prior to transfusion and is an attempt to ascertain whether the donor red blood cells to be transfused will have a normal life span in the recipient. This procedure must be performed prior to transfusion except in situations where the time required for such tests would compromise the recipient's chances for survival.

Cross-matching is necessary for two primary reasons. The human red cell contains numerous antigens, each potentially immunogenic. It is impossible and undesirable to phenotype all potential blood donors and recipients in an attempt to transfuse completely matched blood; it is routine to type only for the A, B, and the Rh°(D) antigen. This practice is based on both the known disastrous consequences of transfusion of ABO incompatible blood and on the immunogenicity and relative frequency of the Rh antigen within the population. Furthermore, most transfusion services now routinely test potential recipient's plasma for unexpected antibodies by using specially prepared test cells which bear a large number of erythrocyte antigens. Antibodies in the recipient directed against antigens on donor RBC but not on the test cells are detected by the cross-match. Thus, the cross-match tests recipient's plasma for antibodies against donor RBC antigens (other than ABO and Rh) which may have been missed by routine plasma antibody screening procedures. A second, and no less important, role of the compatibility test is that it helps in discovering errors in ABO and Rh typing or labeling.

a. *Limitations of cross-matching.* Despite its importance, cross-matching has certain limitation:

(1) Not all errors in labeling or typing will be detected by this test.

(2) In vitro testing for serological incompatibility is not always predictive of survival in vivo. Recipient antibody against donor red cells does not always mean that, if transfused, the cells will have a shortened survival. Conversely, the absence of antibody as determined by the cross-match cannot ensure in vivo red cell survival.

(3) Cross-matching will not prevent the immunization of a recipient since it only detects performed antibody.

b. *Technical considerations regarding cross-matching.* The major cross-match tests donor erythrocytes against recipient serum and the minor cross-match tests recipient erythrocytes against donor serum. The importance of the major cross-match has never been questioned seriously because it is designed to detect the presence of antibody in the entire plasma volume of the recipient which is directed against donor erythrocytes. Whether antibody screening alone of recipients would suffice in certain transfusion settings is the subject of considerable recent discussion but beyond the scope of the Panel's work.

The minor cross-match is designed to detect a finite and relatively small quantity of antibody in donor plasma directed against the entire erythrocyte mass of the recipient. This latter test, widely used in the past, is unnecessary because:

(1) The majority of donor processing laboratories now do antibody screening on all donor bloods.

(2) Infusion of plasma containing antibody in the course of a transfusion results in an immediate dilution of that antibody approximately tenfold in the average adult, thus rendering the antibody harmless for the recipient in most cases.

(3) Unexpected donor antibodies almost never cause hemolytic reactions. For more discussion of this issue see section on Antibody Screening.

c. *Recommendations regarding cross-matching.* Tests for incompatibility shall employ methods that demonstrate significant hemolyzing, agglutinating, and coating antibodies which are active at 37° C and shall include antiglobulin tests or their equivalent.

12. *Serological testing for syphilis in blood donors.* The routine testing of blood donors for evidence of syphilitic infection became common practice in the era when blood was transfused in the fresh state and when there was only questionably effective treatment for syphilis. The transmission of syphilis by blood transfusion was a documented hazard with potentially severe consequences for the recipient. Testing of the donors at the time of collection seemed to be a logical and possibly effective control measure (Ref. 159).

Transfusion-related syphilis has not been reported in the United States for over 20 years. There is reason to believe that this success is not due solely or even primarily to routine serological testing of the donor. This practice, which has now become codified (21 CFR 640.5(a)), should be reexamined.

There are three hypothetical reasons for performing serological tests for syphilis (STS) in all blood donors: Prevention of syphilis in the recipient, detection of syphilis in an asymptomatic donor, and detection of "biological false positive" (BFP) reactors and removal of this blood from the blood banking system.

Routine STS probably has little to do with prevention of syphilis in recipients because the STS is often negative during the early period of infectivity. Further, most blood is now usually transfused after at least 4 days of liquid storage (exact figures are not available), which alone is sufficient to eliminate infectivity for syphilis (Refs. 100 and 160 through 163). It is quite likely that the great majority of the recipients of blood less than 4 days in storage receive antibiotic treatment because of the nature of their illnesses. Syphilis is no longer the dreaded, incurable disease it once was. If the control of syphilis were worth of being singled out for such attention, it would be more efficient to test the recipients 3 weeks to 4 months after transfusion. After 3 weeks, passively transfused regain will probably have fallen below the level detected by currently used STS, and any new syphilitic infection in the recipient would be manifested by a positive STS by 4 months (Ref. 164).

As a case-detecting and venereal disease-controlling strategy, routine STS of all blood donors has some rational basis, but the cost-effectiveness ratio should be carefully examined. In testimony in open session before the Panel, it was estimated that there is one true positive STS per 1,400 donor tests in the United States as a whole. Of 26,128 cases of primary and secondary syphilis reported to the United States Public

Health Service (USPHS) in 1975, only 154 were detected by screening blood donors (0.6 percent). Only 521 cases of syphilis in all stages were detected and reported, from an estimated 8 to 9 million tests. Even with this yield, more rigorous systems of followup on reported reactors and their contacts would be necessary in order for the program to be truly effective. If the act of blood donation is to be used as an opportunity to engage in the random screening of the health of asymptomatic adults, it is not logical to single out syphilis as the disease worth this effort.

The final consideration in STS of blood donors is the Biological False Positive (BFP) reaction. Recent data (Refs. 165 and 166) indicate that the BFP now accounts for 90 percent of the positive reactions to STS in the United States. If ture, this seems to reflect a continuing increase in this fraction, which was reported in the early 1950's as 50 percent in some areas of the United States (Ref. 167). The absolute percent of the total population with BFP (0.47 percent then versus 0.4 percent now) indicates that most of this trend is due to the reduced number of true positive reactors reflecting infection. It is clear that most positive reactors now have BFP reactions.

The BFP reaction seems usefully divided into two categories: acute (reversion to negative within 6 months in the absence of treatment for syphilis) and chronic (continued positive reactions in the continued absence of evidence of syphilis with more specific tests and on physical examination). The acute BFP reactions are associated with a wide variety of conditions, most of them infectious (Ref. 175). Most texts now state that almost any acute febrile disorder or immunization can result in an acute BFP (Ref. 168). Some of the better documented causes, however, are infectious diseases that could be transmited by transfusion where they could induce significant illness in the recipient, e.g., malaria, infectious hapatitis, infectious mononucleosis. The temporal relationship between infectivity as a blood donor and the development of a BFP is not known for these illnesses. Other causes for BFP mentioned are Hodgkin's disease, sarcoidosis and, increasingly, intravenous drug abuse. There is some dispute about the role of repeated blood donation in causing BFP reactions.

The chronic BFP reactors are an interesting group of patients who have been studied in detail and followed carefully in several investigations (Refs. 167 through 169). Up to 80 percent develop manifestations of dysgammaglobulinemia. As many as one-half develop laboratory and clinical signs of a "collagen disease," usually systemic lupus erythematosus (SLE), within 10 years. Only about one quarter remain seemingly healthy 10 years after their detection as a BFP reactor. The disorders associated with BFP reactions are serious, sometimes fatal, diseases without known cause or cure. There is no evidence that these conditions can be transmitted by blood transfusion. Conversely, their very slow onset and gradual development make it unlikely that transmission by transfusion would be readily detected. In fact, it would require very long range, careful followup of a type that is rarely done to detect this result because the latent period can exceed 10 years in the donor.

a. *Summary regarding the STS.* The mandatory STS on all blood donors represents an unusual regulatory situation. The practice was instituted for good reasons and was initially probably beneficial to donors and recipients. Both the potential infectivity of the blood and the treatment of the disease have changed drastically, however, and the STS probably has little value now in preventing the transmission of syphilis by transfusion. It may have some small value in case-detection of syphilis, but this does not seem an appropriate indication to mandate its continued use. There is no evidence that the biological false-positive STS reaction is associated with any known acute or chronic diseases that might be transmissible by transfusion. Nevertheless, because the frequency of the BFP reaction is relatively high, it might indicate the presence of a transmissible disease.

b. *Recommendations regarding the STS.* The STS should be eliminated as a mandated test on donor blood prior to release for transfusion.

13. *Testing for hepatitis.* Estimates of the incidence of post-transfusion hepatitis are difficult to find. In 1970 (Ref. 172), the National Research Council (NRC) estimated that perhaps there were 30,000 cases of clinical hepatitis annually, with a mortality rate of 10 percent. They also suggested that there may be up to five times that many cases when one considers subclinical cases. More recent studies (Ref. 173) estimate the risk of post-transfusion hepatitis at 6.4 cases per 1,000 units of blood transfused; one-third of these are icteric. This estimate is consistent with the earlier one of the NRC. The difficulty in defining the precise risk is related to numerous variables including ineffective reporting and followup, variable criteria for diagnosis, and source of donor blood from both a geographic (Ref. 174) and socioeconomic (Refs. 82, 176 and 177) point of view.

Two risk factors for post-transfusion hepatitis have been clearly identified. Blood obtained from paid blood donors carries a higher risk (Refs. 82, 176 and 177), although payment per se does not make the blood more dangerous. Undoubtedly, socioeconomic factors related to donor recruitment are important. The second risk factor is the presence of the hepatitis B surface antigen (HBsAg) (Refs. 178 through 182). The introduction of universal HBsAg testing on all blood donated in the United States, particularly with sensitive third generation tests, has been associated with a reduced incidence of post-transfusion hepatitis. Eliminating the commercial blood source would be even more effective in this regard (Ref. 82). The recently published Food and Drug Administration regulation requiring designation of whether a unit has been obtained from a paid donor is directed at this risk factor.

In recent years, studies have been increasingly directed at elucidating the etiological agent(s) responsible for post-transfusion hepatitis unrelated to the Hepatitis B agent. While hepatitis A may be involved in some cases, it is clear that there are a large number of "non-A and non-B" cases which currently escape detection for lack of appropriate tests. Development of these test must be encouraged (Refs. 80, 81, 183 and 186).

New lines of investigation hold promise for improved control of Hepatitis B infection. Studies on the core antigen, HBcAg, and its antibody, the e antigen and DNA polymerease hold promise for better understanding of Hepatitis B and perhaps ascertainment of which units are truly infectious.

No changes are recommended at this time regarding hepatitis testing of stored red blood cell products.

14. *Labels for blood bags*—a. *Content and design.* The label affixed to the blood bag must be designed to enhance the safety of the product by providing adequate vital information to all individuals who handle it. Unnecessary information, or information that is readily available elsewhere, when present on the label, may interfere with optimal blood bank practice by distracting the eye from the vital information. As it is generally agreed that most avoidable serious complications of blood transfusion result from "clerical" rather than technical errors, the information present on the label and the manner in which it is displayed assume major significance.

Labels currently affixed to units of whole blood or red blood cells contain much information which is almost never read or used. Much of the information documents that the units have been processed in a manner which meets Federal regulations. As blood may not be collected or transfused otherwise, the presence on the label of such information is unnecessary and detracts from the safe use of the product. However, this information should be available in every blood bank as part of the product labeling.

b. *Color coding of labels.* Currently, color codes for blood typing labels are optional. While there are no data to indicate whether color coding of labels for ABO blood types would help reduce blood transfusion errors, the Panel feels that immediate recognition of blood types by label color would be advantageous, particularly in acute, massive transfusion situations.

c. *Recommendations for blood bag labels.* The following information on labels affixed to units of Whole Blood (Human) or Red Blood Cells (Human) is vital to the safety and effectiveness of the product and must appear on the bag with the first four items in greatest prominence:

(1) Name of the product including designation of the anticoagulant-preservative solution. The designation "(Human)" is unnecessary.

(2) Blood type. ABO and Rh ($Rh_oD$ positive or negative) types of blood are of vital importance and must be displayed most prominently.

(3) Expiration date.

(4) A unique number which will permit tracing the unit of blood back to the donor. The number used to identify the unit of blood must be the only prominent number.

(5) Manufacturer's codes, referring to codes of blood bag manufacturers including lot numbers have no intrinsic value in routine use and should be displayed on the label in an unobtrusive place in small print.

(6) The name of the blood collection facility should be on the label in an as unobtrusive manner as possible.

(7) The designation that the unit was collected from a "Volunteer Donor" should be discontinued. The designation "Paid Donor" should be retained and used when appropriate.

(8) Instructions:

(a) Store between 1 to 6 °C.

(b) Do not add medication other than 0.9 percent NaC1 solution.

(c) Transfuse through a filter.

(9) The following statement, "For additional information refer to circular of information."

(10) Space for additional labeling. If the unit has special properties, e.g., donor antibody or an unusual red cell phenotype, this should be noted on the label in an available space.

(11) License number in a small and unobtrusive manner.

(d) *Other label recommendations.* (1) Blood labeling regulations should be modified to require that those items listed above, and only those items, be present on all units of Whole Blood and Red Blood Cells as delivered by the collecting agency.

(2) Research should be encouraged for analysis of the best eye-readable format for blood bag labeling.

(3) The developing of machine-readable costs on labels must be conducted in a way to assure that the results would not detract from the eye-readable aspects of the label.

**References**

(1) Landsteiner, K., "Zur Kenntnis der Antifermentativen, Lytischen and Agglutinierenden Wirkungen des Blutserums und der Lymphe," *Zentrablat Bakteriologie*, 27:357–362, 1900.

(2) Landsteiner, K., "Ueber Agglutination-Serscheinungen Normalen Menschlichen Blutes," *Wiener Klinische Wochenschrift*, 14:1132–1134, 1901.

(3) Ottenberg, R., "Studies in Isoagglutination. I. Transfusion and the Question of Intravascular Agglutination," *Journal of Experimental Medicine*, 13:425–428, 1911.

(4) Landsteiner, K. and P. Levine, "Further Observations on Individual Differences of Human Blood," *Proceedings Society for Experimental Biology and Medicine*, 24:941–942, 1927.

(5) Landsteiner, K. and A.S. Wiener, "An Aglutinable Factor in Human Blood Recognized by Immune Sera for Rhesus Blood," *Proceedings Society for Experimental Biology and Medicine*, 43:223, 1940.

(6) Levine, P. and R. Stetson, "An Unusual Case of Intra-Group Agglutination," *Journal of the American Medical Association*, 113:126–127, 1939.

(7) Coombs, R.R.A., A.E. Mourant and R.R. Race, "A New Test for the Detection of Weak and 'Incomplete' Rh Agglutinins," *British Journal of Experimental Pathology*, 26:255–266, 1945.

(8) Hustin, A., "Principe d'une Nouvelle Methode de Transfusion Muqueuse," *Journal Med. Brux.*, 2:246, 1914.

(9) Agote, L., "Transfusion de Sangre: Un Curioso Casa de Aparente Coincidencia," *Anales Institute Clinica Medica*, (Buenos Aires), 2:361, 1915.

(10) Lewisohn, R., "Blood Transfusion by the Citrate Method," *Surgery, Gynecology and Obstetrics*, 21:37, 1915.

(11) Rous, P. and J.R. Turner, "Preservation of Living Red Blood Corpuscles *In Vitro*. I. Methods of Preservation," *Journal of Experimental Medicine*, 23:219–237, 1916.

(12) Maizels, M., "Preservation of Organic Phosphorus Compounds in Stored Blood by Glucose," *Lancet*, 7:722–723, 1941.

(13) Loutit, J.F., P.L. Mollison and I.M. Young, "Citric Acid-Sodium Citrate-Glucose Mixtures for Blood Storage," *Quarterly Journal of Experimental Physiology and Cognate Medical Sciences*, 32:183–202, 1943.

(14) Loutit, J.F. and P.L. Mollison, "Advantages of a Disodium-Citrate-Glucose Mixture as a Blood Preservative," *British Medical Journal*, 2:744–745, 1943.

(15) Robertson, O.H., "Transfusion with Preserved Red Blood Cells," *British Medical Journal*, I:691–695, 1918.

(16) National Heart and Lung Institute Blood Resource Studies: Summary Report. *National Institute of Health, Department of Health, Education, and Welfare*, 1972.

(17) Ross, J.F., C.A. Finch, W.C. Peacock and M.E. Sammons, "The *In Vitro* Preservation and Post-Transfusion Survival of Stored Blood," *Journal of Clinical Investigation*, 26:687–703, 1947.

(18) Gibson, J.G., R.D. Evans, J.C. Aub, T. Sack and W.C. Peacock, "The Post-Transfusion Survival of Preserved Human Erythrocytes Stored as Whole Blood or in Resuspension, After Removal of Plasma, by Means of Two Isotopes of Radio-active Iron," *Journal of Clinical Investigation*, 26:715–738, 1947.

(19) Donohue, D.M. and C.A. Finch, "An Animal Assay Method for the Measurement of Post-Transfusion Survival of Stored Blood," *Vox Sanguinis*, 2:369–375, 1957.

(20) Mollison, P.L. and M.A. Robinson, "Observations on the Effects of Purine Nucleosides on Red-Cell Preservation," *British Journal of Haematology*, 5:331–343, 1959.

(21) Dern, R.J., G.J. Brewer and J.J. Wiorkowski, "Studies on the Preservation of Human Blood. II. The Relationship of Erythrocyte Adenosine Triphosphate Levels and Other *In Vitro* Measures to Red Cell Storageability," *Journal of Laboratory and Clinical Medicine*, 69:968–978, 1967.

(22) Haradin, A.R., R.I. Weed and C.F. Reed, "Changes in Physical Properties of Stored Erythrocytes: Relationship to Survival *In Vivo*," *Transfusion*, 9:229–237, 1969.

(23) Orlina, A. and A. Josephson, "Comparative Viability of Blood Stored in ACD and CPD," *Transfusion*, 9:62–69, 1969.

(24) Seidl, S. and W. Spielmann, "Comparative Studies on the Effect of Different Nucleosides in Red Cell Preservation," *in* "Modern Problems of Blood Preservation," Edited by Spielmann, W. and S. Seidl, Gustav Fischer, Stuttgart, Germany, 1970.

(25) Shields, C.E., "Comparison Studies of Whole Blood Stored in ACD and CPD and with Adenine," *Transfusion*, 8:1–8, 1968.

(26) Shields, C.E., "Studies on Stored Whole Blood. II. Use of Packed Red Blood Cells," *Transfusion*, 9:1–4, 1969.

(27) Strumia, M.M., P.V. Strumia and A.J. Eusebi, "The Preservation of Blood for Transfusion. VII. Effect of Adenine and Inosine on the Adenosine Triphosphate and Viability of Red Cells when Added to Blood Stored from Zero to Seventy Days at 1 °C," *Journal of Laboratory and Clinical Medicine*, 75:244–249, 1970.

(28) Warner, W.L., "Red Cell Preservation and Survival Determinations in

Anticoagulant Systems," *in* "Modern Problems of Blood Preservation," Edited by Spielman, W. and S. Seidl, Gustave Fischer, Stuttgart, Germany, 1970.

(29) LaCelle, P.L., "Alteration of Deformability of the Erythrocyte Membrane in Stored Blood, "*Transfusion*, 9:238–245, 1969.

(30) Weed, R.I. and P.L. LaCelle, "ATP Dependence of Erythrocyte Membrane Deformability," *in* "Red Cell Membrane Structure and Function," Edited by Jamieson, G.A. and T.J. Greenwalt, Lippincott, Philadelphia, 1969.

(31) Virgilio, R., "A Prospective Controlled Study on the Effect of Fine Filters on Postoperative Pulmonary Function in Heavily Transfused Patients," Presented at U.S. Army Medical R&D Command Symposium on Microaggregates, Letterman Army Medical Center, June 1977.

(32) Collins, J.A., P.M. James, C.E. Bredenberg, R.W. Anderson, C.A. Heisterkamp and R.L. Simmons, "The Relationship Between Transfusion and Hypoxemia in Combat Casualties," *Annals of Surgery*, 188:513–520, 1978.

(33) Benesch, R. and R.E. Benesch, "The Influence of Organic Phosphates on the Oxygenation of Hemoglobin," *Federation Proceedings*, 26:673, 1967.

(34) Chanutin, A. and R.R. Curnish, "Effect of Organic and Inorganic Phosphates on the Oxygen Equilibrium of Human Erythrocytes," *Archives of Biochemistry and Biophysics*, 121: 96–102, 1967.

(35) Dawson R.B., W.F. Kocholaty and J.L. Gray, "Hemoglobin Function and 2,3-DPG Levels of Blood Stored at 4 °C in ACD and CPD pH Effect," *Transfusion*, 10:299–304, 1970.

(36) Gibson, J.G., S.B. Rees, T.J. McManus and W. Scheitline, "A Citrate-Phosphate-Dextrose Solution for the Preservation of Human Blood," *American Journal of Clinical Pathology*, 28:569–578, 1957.

(37) Mooreside, D.E., F.Q. Graybeal and R.D. Langdell, "Effects of Adenine on Clotting Factors in Fresh Blood, Stored Blood and Stored Fresh Frozen Plasma," *Transfusion*, 9:191–197, 1969.

(38) Graybeal, F.Q., D.E. Mooreside and R.D. Langdell, "Clotting Factor Activity in Cryoprecipitate and Supernatant Plasma Prepared from Blood Collected in ACD, ACD-Adenine, CPD and CPD-Adenine and from Plasma Collected by Plasmapheresis," *Transfusion*, 9:135–140, 1969.

(39) Odake, K. and J.L. Ambrus, "Adenine Nucleotide Metabolism in Stored Human Platelets," *American Journal of Pathology*, 56:393–403, 1969.

(40) Strumia, M., L.S. Colwell and K. Ellenberger, "The Preservation of Blood for Transfusion. I. The Effect of Plastic Containers on Red Cells," *Journal of Laboratory and Clinical Medicine*, 46:225–233, 1955.

(41) Jaeger, R.J. and R.J. Rubin, "Migration of a Phthalate Ester Plasticizer from Polyvinyl Chloride Blood Bags into Stored Human Blood and its Localization in Human Tissues," *New England Journal of Medicine*, 287:1114–1118, 1972.

(42) Graham, P.R., "Phthalate Ester Plasticizers—Why and How They Are Used," *Environmental Health Perspectives*, 3:3–12, 1973.

(43) Rall, D.P., "The Invisible Pollution," *New England Journal of Medicine*, 287:1146–1147, 1972.

(44) Contreras, T.J., R.H. Sheibley and C.R. Valeri, "Accumulation of Di-2-Ethylhexyl Phthalate (DEHP) in Whole Blood, Platelet Concentrates, and Platelet-Poor Plasma," *Transfusion*, 14:34–46, 1974.

(45) Josephson, A.M., "Toxicology of Plastic Having Contact with Blood," Report of Program Progress, Travenol Laboratories, Inc.

(46) Guess, W.L., J. Jacob and J. Autian, "Blood Bag Assemblies. I. Alteration or Contamination of ACD Solutions," *Drug Intelligence*, 1:120–127, 1967.

(47) Jaeger, R. and R.J. Rubin, "Extraction, Localization, and Metabolism of Di-2-ethylhexyl Phthalate from PVC Plastic Medical Devices," *Environmental Health Perspectives*, 3:95–102, 1973.

(48) Vessman, J. and G. Rietz, "Studies on the Contamination of Blood and Plasma Proteins by Phthalate Esters," *Developments in Biological Standardization*, 27:205–208, 1974.

(49) Jaeger, R.J. and R.J. Rubin, "DI-2-ethylhexyl Phthalate, A Plasticizer Contaminant of Platelet Concentrates," *Transfusion*, 13:107–108, 1974.

(50) Rubin, R.J. and P.P. Nair, "Plasticizers in Human Tissues," *New England Journal of Medicine*, 288:915–916, 1973.

(51) Rubin, R.J. and R.J. Jaeger, "Some Pharmacologic and Toxicologic Effects of Di-2-ethylhexyl Phthalate (DEHP) and Other Plasticizers," *Environmental Health Perspectives*, 3:53–59, 1973.

(52) Hillman, L.S., S.L. Goodwin, and W.R. Sherman, "Identification and Measurement of Plasticizer in Neonatal Tissues After Umbilical Catheters and Blood Products," *New England Journal of Medicine*, 292:382–381, 1975

(53) Jacobson, M.S., R. Parkman, L.N. Button, R.J. Jaeger and S.V. Kevy, "The Toxicity of Human Serum Stored in Flexible Polyvinylchloride Containers on Human Fibroblast Cell Cultures: An Effect of Di-2-ethylhexyl Phthalate," *Research Communications in Chemical Pathology and Pharmacology*, 9:315–323, 1974.

(54) "Blood Bag Plasticizer May Damage Lungs," *Chemical and Engineering News*, 5, 1975.

(55) Beutler, E. and L.E. Wood, "Preservation of Red Cell 2,3-DPG and Viability in Bicarbonate-Containing Medium. The Effect of Blood-bag Permeability," *Journal of Laboratory and Clinical Medicine*, 80:723–728, 1972.

(56) Murphy, S. and F.H. Gardner, "Platelet Storage at 22 °C: Role of Gas Transport Across Plastic Containers in Maintenance of Viability," *Blood*, 46:209–218, 1975.

(57) Strumia, M., L.S. Colwell and A. Dugan, "The Preservation of Blood for Transfusion. III. Mechanism of Action of Containers on Red Blood Cells," *Journal of Laboratory and Clinical Medicine*, 53:106–116, 1959.

(58) Slichter, S.J. and L.A. Harker, "Preparation and Storage of Platelet Concentrates. II. Storage Variables Influencing Platelet Viability and Function," *British Journal of Haematology*, 34:403–419, 1976.

(59) Murphy, S. and F.H. Gardner, "Platelet Preservation Effect of Storage Temperature on Maintenance of Platelet Viability—Deleterious Effect of Refrigerated Storage," *New England Journal of Medicine*, 208:1094–1098, 1969.

(60) Murphy, S., S.N. Sayar and F.H. Garner, "Storage of Platelet Concentrates at 22 °C," *Blood*, 35:549–557, 1970.

(61) Kevy, S.V., "Studies on Improving and Standardizing the Process for Preparation of Cryoprecipitated Antihemophiliac Factor," PB 211–926, contract PHS–71–2396, 1972.

(62) Slichter, S.J., R.B. Counts, R. Henderson and L.A. Harker, "Preparation of Cryoprecipitated Factor VIII Concentrates," *Transfusion*, 16:616–628, 1976.

(63) Solis, R.T., D. Goldfinger, M.B. Gibbs and J.A. Zeller, "Physical Characteristics of Microaggregates in Stored Blood," *Transfusion*, 14:538–550, 1974.

(64) Arrington, P. and J.J. McNamara, "Mechanism of Microaggregate Formation in Stored Blood," *Annals of Surgery*, 179:146–148, 1974.

(65) Berman, I.R., V.S. Gutierrez, E.L. Burran and R.D. Boatright, "Intravascular Microaggregation in Young Men with Combat Injuries," *Surgical Forum*, 20:14–16, 1969.

(66) Connell, R.S. and R.L. Swank, "Pulmonary Microembolism After Blood Transfusions," *Annals of Surgery*, 177:40–50, 1973.

(67) Bennett, S.H., G.W. Geelhoed, R.K. Aaron, R.T. Solis and R.C. Hoye, "Pulmonary Injury Resulting From Perfusion with Stored Bank Blood in the Baboon and Dog," *Journal of Surgical Research*, 13:295–306, 1972.

(68) Geelhoed, G.W. and S.H. Bennett, "Modification in Primate Shock Lung Resulting from Perfusion in the Stored Blood by Pretreatment with Steroids and Trasylol," Presented at Association for Academic Surgery 7th Annual Meeting, Rochester, New York, November 1–3, 1973.

(69) Reul, G.J., S.E. Greenberg, E.A. Lefrak, W.B. McCollum, A.C. Beall, Jr., and G.L. Jordan, Jr., "Prevention of Post-traumatic Pulmonary Insufficiency," *Archives of Surgery*, 106:386–394, 1973.

(70) Gervin, A.S., K.G. Mason and C.B. Wright, "Microaggregate Volumes in Stored Human Blood," *Surgery, Gynecology and Obstetrics*, 139:519–524, 1974.

(71) Solis, R.T., G.P. Noon and M.E. DeBakey "Filtration Characteristics of Microemboli in Stored Blood and in Autotransfused Blood," *Transactions of the American Society for Artificial Internal Organs*, XX:499–503, 1974.

(72) Gervin, A.S., K.G. Mason and C.B. Wright "The Filtration Limitations of Ultrapore Filters," *Surgery*, 77:186–193, 1975.

(73) Soeter, J.R., G.T. Suehiro, S. Ferrin, P. Nakagawa and J.J. McNamara, "Comparison of Filtering Efficiency of Four New In-line Blood Transfusion Filters," *Annals of Surgery*, 181:114–117, 1975.

(74) Gervin, A.S., K.G. Mason and R.F. Buckman, "The Source and Removal of Microaggregates in Aged Human Blood and Human Blood Components," *Surgery*,

*Gynecology and Obstetrics*, 141:582–586, 1975.

(75) Arrington, P.J. and J.J. McNamara, "Effect of Agitation on Platelet Aggregation and Microaggregate Formation in Banked Blood," *Annals of Surgery*, 181:243–244, 1975.

(76) Arrington, P.J. and J.J. McNamara, "Effect of Aspirin on Microaggregate Formation in Banked Blood," *Surgery*, 76:295–297, 1974.

(77) Junet, R. and W. Junet, "Ictere Infectieux Transmis par un Donneur de Sang," *Revue Medicale de la Suisse Romande*, 58:537–546, 1938.

(78) MacCallum, F.O., "in Scientific Discussions (Infective Hepatitis)," *Lancet*, ii:435–436, 1947.

(79) Krugman, S., J.P. Giles and J. Hammond, "Infectious Hepatitis. Evidence for Two Distinctive Clinical, Epidemiological and Immunological Types of Infection," *Journal of the American Medical Association*, 200:365–373, 1967.

(80) Feinstone, S.M., A.Z. Kapikian, R.H. Purcell, H.J. Alter and P.V. Holland, "Transfusion Associated Hepatitis Not Due to Viral Hepatitis Type A or B," *New England Journal of Medicine*, 292:767–770, 1975.

(81) Prince, A.M., B. Brotman, G.F. Grady, W.J. Kuhns, C. Hazzi, R.W. Levine and S.J. Millian, "Long-Incubation Post-Transfusion Hepatitis Without Serological Evidence of Exposure to Hepatitis-B Virus," *Lancet*, ii:241–246, 1974.

(82) Alter, H.J., P.V. Holland, R.H. Purcell, J.J. Lander, S.M. Feinstone, A.G. Morrow and P.J. Schmidt, "Posttransfusion Hepatitis After Exclusion of Commercial and Hepatitis-B Antigen-Positive Donors," *Annals of Internal Medicine*, 77:691–699, 1972.

(83) Taswell, H.F., "Incidence of HBAg in Blood Donors: An Overview," *in* "Hepatitis and Blood Transfusion," Edited by Vyas, G.N., H.A. Perkins and R. Schmid, Grune and Stratton, New York, pp. 271–274, 1972.

(84) Haas, S., "The Influence of Microfiltration on Blood Coagulation, Free Hemoglobin, and Blood Cells of Transfused Blood," Presented at Symposium on Microfiltration in Blood Tranfusion, Berne, Switzerland, January, 1979.

(85) Goldfield, M., "Some Epidemiologic Studies of Transfusion-Associated Hepatitis," *in* "Transmissible Disease and Blood Transfusion" Edited by Greenwalt, T.J. and G.A. Jamieson, Grune and Stratton, pp. 141–151, 1974.

(86) Case, R.B., E. Berglund and S.J. Sarnoff, "Ventricular Function. VII. Changes in Coronary Resistance and Ventricular Function Resulting from Acutely Induced Anemia and the Effect Thereon of Coronary Stenosis," *American Journal of Medicine, 18:397–405, 1955.*

(87) Prince, A.M., W. Szmuness, S.J. Millian and D.S. David, "A Serologic Study of Cytomegalovirus Infections Associated with Blood Transfusions," *New England Journal of Medicine*, 284:1125–1131, 1971.

(88) Purcell, R.H., J.H. Walsh, P.V. Holland, A.G. Morrow, S. Wood and R.M. Chanock, "Seroepidemiological Studies of Transfusion-Associated Hepatitis," *Journal of Infectious Diseases*, 123:406–413, 1971.

(89) Stevens, D.P., L.F. Barker, A.S. Ketcham and H.M. Meyer, Jr., "Asymptomatic Cytomegalovirus Infection Following Blood Transfusion in Tumor Surgery," *Journal of American Medical Association*, 211:1341–1344, 1970

(90) Barker, L.F. Nortman, "Viral Hepatitis B: Detection and Prophylaxis," *in* "Transmissible Disease and Blood Transfusion," Edited by Greenwalt, T.J. and G.A. Jamieson, Grune and Stratton, pp. 81–111, 1974.

(91) Hoofnagle, J.H., R.J. Gerety and L.F. Barker, "Antibody to Hepatitis-B Core Antigen, *in* "Transmissible Diseases and Blood Transfusion," Edited by Greenwalt, T.J., and G.A. Jamieson, Grune and Stratton, New York, pp. 43–55, 1974.

(92) Battle, J.D. and J.S. Hewlett, "Hematologic Changes Observed After Extracorporeal Circulation During Open-Heart Operations," *Cleveland Clinic Quarterly*, 25:112–117, 1958.

(93) Kreel, I., L.I. Zaroff, J.W. Canter, I. Krasna and I.D. Baronofsky, "A Syndrome Following Total Body Perfusion," *Surgery, Gynecology and Obstetrics*, 111:317–321, 1960.

(94) Lang, D.J. and J.B. Hanshaw, "Cytomegalovirus Infection and the Postperfusion Syndrome: Recognition of Primary Infections in Four Patients," *New England Journal of Medicine*, 280:1145–1149, 1969.

(95) Kaariainen, L., E. Klemola and J. Paloheimo, "Rise of Cytomegalovirus Antibodies in an Infectious-Mononucleosis-Like Syndrome after Transfusion," *British Medicial Journal*, 1:1270–1272, 1968.

(96) Henle, W., G. Henle, M. Scriba, C.R. Joyner, F.S. Harrison, R. von Essen, J. Palokeimo and E. Klemola, "Antibody Responses to the Epstein-Barr Virus and Cytomegaloviruses after Open-Heart and Other Surgery," *New England Journal of Medicine*, 282:1068–1074, 1970.

(97) Gerber, P., J.H. Walsh, E.N. Rosenblum and R.H. Purcell, "Association of EB-Virus Infection with the Post-Perfusion Syndrome," *Lancet*, i:593–595, 1969.

(98) Dover, A.S. and M.G. Schultz, "Transfusion-Induced Malaria," *Transfusion*, 11:353–357, 1971.

(99) MacBryde, C.M., "Signs and Symptoms," J. B. Lippincott, Philadelphia, pp. 461–462, 1957.

(100) Chambers, R.W., H.T. Foley and P.J. Schmidt, "Transmission of Syphilis by Fresh Blood Components," *Transfusion*, 9:32–34, 1969.

(101) Berman, I.R., H. Iliescu and I. Stachura, "Pulmonary Effects of Blood Container Materials," *Surgical Forum*, 28:182–185, 1977.

(102) Telischi, M., E. Krmpotic and G. Moss, "Viable Lymphocytes in Frozen Washed Blood," *Transfusion*, 15:481–484, 1975.

(103) Pineda, A.A. and H.F. Taswell, "Transfusion Reactions Associated with Anti-IgA Antibodies: Report of Four Cases and Review of the Literature," *Transfusion*, 15:10–15, 1975.

(104) Schmidt, A.P., H.F. Taswell and G.J. Gleich, "Anaphylactic Transfusion Reactions Associated With Anti-IgA Antibody," *New England Journal of Medicine*, 280:188–193, 1969.

(105) Vyas, G.N., H.A. Perkins and H.H. Fudenberg, "Anaphylactoid Transfusion Reactions Caused by Anti-IgA Antibody," Abstract presented at Annual Meeting, American Association of Blood Banks, Washington, DC., October 1968.

(106) Bachmann, R., "Studies on the Serum Gamma A-Globulin Level. III. The Frequency of A-Gamma-A-Globulinemia," *Scandinavian Journal of Clinical and Laboratory Investigation*, 17:316–320, 1965.

(107) Miller, W.V., P.V. Holland, E. Sugarbaker, W. Strober and T. Waldmann, "Anaphylactic Reactions to IgA," *American Journal of Clinical Pathology*, 54:618–621, 1970.

(108) Thompson, J.S., C.D. Severson, M.J. Parmely, B.L. Marmorstein and A. Simmons, "Pulmonary 'Hypersensitivity' Reactions Induced by Transfusion of Non-HL-A Leukoagglutinins," *New England Journal of Medicine*, 284:1120–1125, 1971.

(109) Ward, H.N., "Pulmonary Infiltrates Associated with Leukoagglutinin Transfusion Reactions," *Annals of Internal Medicine*, 73:689–694, 1970.

(110) Shulman, N.R., R.H. Aster, A. Leitner and M.C. Hiller, "Immunoreactions Involving Platelets. V. Post-Transfusion Purpura Due to a Complement-Fixing Antibody Against a Genetically Controlled Platelet Antigen. A Proposed Mechanism for Thrombocytopenia and Its Relevance in 'Autoimmunity'," *Journal of Clinical Investigation*, 40:1597–1620, 1961.

(111) Morrison, F.S. and P.L. Mollison, "Post-Transfusion Purpura," *New England Journal of Medicine*, 275:243–248, 1966.

(112) Russell, W.J., "A Review of Blood Warmers for Massive Transfusion," *Anaesthesia and Intensive Care*, 2:109–130, 1974.

(113) Hong, R., R.A. Gatti and R.A. Good, "Hazards and Potential Benefits of Blood Transfusion in Immunological Deficiency," *Lancet*, ii:388–389, 1968.

(114) Schechter, G.P., F. Soehnlen and W. McFarland, "Lymphocyte Response to Blood Transfusion in Man," *New England Journal of Medicine*, 287:1169–1173, 1972.

(115) Petrakis, N.L. and G. Politis, "Prolonged Survival of Viable, Mitotically Competent Mononuclear Leukocytes in Stored Whole Blood," *New England Journal of Medicine*, 267:286–288, 1962.

(116) Huestis, D.W., J.R. Bove and S. Busch, "Practical Blood Transfusion," 2nd Ed., Little Brown, Boston, p. 261, 1976.

(117) Payne, R., "Leukocyte Agglutinins in Human Sera," *Archives of Internal Medicine*, 99:587–606, 1957.

(118) Brittingham, T.E., and H. Chaplin, "Febrile Transfusion Reactions Caused by Sensitivity to Donor Leukocytes and Platelets," *Journal of the American Medical Association*, 165:819–825, 1957.

(119) Brittingham, T.E. and H. Chaplin, "The Antigenicity of Normal and Leukemic Human Leukocytes," *Blood*, 17:139–165, 1961.

(120) Perkins, H.A., R. Payne, J. Ferguson and M. Wood, "Nonhemolytic Febrile Transfusion Reactions. Quantitative Effects of Blood Components with Emphasis on Isoantigenic Incompatibility of Leukocytes," *Vox Sanguinis*, 11:578–600, 1966.

(121) Krevans, J.R., D.P. Jackson, C.L. Conley and R.C. Hartmann, "The Nature of

the Hemorrhagic Disorder Accompanying Hemolytic Transfusion Reactions in Man," *Blood*, 12:834–843, 1957.

(122) Hardaway, R.M., D. McKay and J.H. Williams, "Lower Nephron Nephrosis (Ischemuric Nephrosis): With Special Reference to Hemorrhagic Diathesis Following Incompatible Blood Transfusion Reaction," *American Journal of Surgery*, 87:41–49, 1954.

(123) Rock, R.C., J.R. Bove and Y. Nemerson, "Heparin Treatment of Intravascular Coagulation Accompanying Hemolytic Transfusion Reactions," *Transfusion*, 9:57–61, 1969.

(124) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publication, Oxford, pp. 514–525, 1972.

(125) Lostumbo, M.M., P.V. Holland and P.J. Schmidt, "Isoimmunization After Multiple Transfusions," *New England Journal of Medicine*, 275:141–144, 1966.

(126) Grumet, F.C. and R.A. Yankee, "Long-term Platelet Support of Patients with Aplastic Anemia," *Annals of Internal Medicine*, 73:1–7, 1970.

(127) Lohrmann, H.P., M.I. Bull, J.A. Decter, R.A. Yankee and R.G. Graw, Jr., "Platelet Transfusions from HL-A Compatible Unrelated Donors to Alloimmunized Patients," *Annals of Internal Medicine*, 80:9–14, 1974.

(128) Mittal, K.K., E.A. Ruder and D. Green, "Matching of Histocompatibility (HL-A) Antigens for Platelet Transfusions," *Blood*, 47:31–41, 1976.

(129) Yankee, R.A., K.S. Graff, R. Dowling and E.S. Henderson, "Selection of Unrelated Compatible Platelet Donors by Lymphocyte HL-A Matching," *New England Journal of Medicine*, 288:760.–764, 1973

(130) Graw, R.G., G. Herzig, S. Perry and E.S. Henderson, "Normal Granulocyte Transfusion Therapy," *New England Journal of Medicine*, 287:367–371, 1972.

(131) Graw, R.G., I.M. Goldstein, H.J. Eyre and P.I. Terasaki, "Histocompatibility Testing for Leukocyte Transfusion," *Lancet*, i:77–78, 1970.

(132) Higby, D.J., J.M. Mishler, E. Cohen, W. Rhomberg, R.W. Nicora and J.F. Holland, "Increased Elevation of Peripheral Leucocyte Counts by Infusion of Histocompatible Granulocytes," *Vox Sanguinis*, 27:186–189, 1974.

(133) Huestis, D.W., J.R. Bove and S. Busch, "Practical Blood Transfusion," 2d Ed., Little Brown, p. 258, 1976.

(134) DeCesare, W.R., J.R. Bove and F.G. Ebaugh, "The Mechanism of the Effect of Iso- and Hyperosmolar Dextrose-Saline Solutions on *In Vivo* Survival of Human Erythrocytes," *Transfusion*, 4:237–250, 1964.

(135) Braude, A.I., J. P. Sanford, J.E. Bartlett and O.T. Mallery Jr., "Effects and Clinical Significance of Bacterial Contaminants in Transfused Blood," *Journal of Laboratory and Clinical Medicine*, 39:902–916, 1952.

(136) Chaplin, H., E. Chang and R.W. Kolb, "Report of Routine Tests for Psychrophilic and Mesophilic Contaminants in Banked Blood," *Applied Microbiology*, 3:213–215, 1955.

(137) Braude, A.I., F.J. Carey and J. Siemienski, "Studies of Bacterial Transfusion Reactions from Refrigerated Blood: The Properties of Cold-Growing Bacteria," *Journal of Clinical Investigation*, 34:311–325, 1955.

(138) Pittman, M., "Study of Bacteria Implicated in Transfusion Reactions and of Bacteria Isolated from Blood Products," *Journal of Laboratory and Clinical Medicine*, 42:273–288, 1953.

(139) Miller, T.R. and M.K. Weikel, "Blood Donor Eligibility, Recruitment and Retention," *Transfusion*, 14:616–622, 1974.

(140) Shields, C.E., "Quality-Control Approach to Improve Donor Care," *Transfusion*, 10:272–278, 1970.

(141) Nusbacher, J., Unpublished Observation.

(142) Pirofsky, B. and H.M. Nelson, "The Determination of Hemoglobin in Blood Banks," *Transfusion*, 4:45–49, 1964.

(143) Mannarino, A.D. and C.R. Macpherson, "Copper Sulfate Screening of Blood Donors: Report of a Donor Passing the Test with Less Than Eight Grams of Hemoglobin," *Transfusion*, 3:398–400, 1963.

(144) Wadsworth, G.R., "Recovery from Acute Haemorrhage in Normal Men and Women," *Journal of Physiology*, 129:583–593, 1955.

(145) Avoy, D.R., M.L. Canuel, B.M. Otton and E.B. Mileski, "Hemoglobin Screening in Prospective Blood Donors: A Comparison of Methods," *Transfusion*, in press.

(146) Olsson, K.S., "Iron Stores in Normal Men and Male Blood Donors," *Acta Medica Scandinavica*, 192:401–407, 1972.

(147) Lieden, G., "Iron State in Regular Blood Donors," *Scandinavian Journal of Haematology*, 11:342–349, 1973.

(148) Cook, J.D., C.A. Finch and N.J. Smith, "Evaluation of the Iron Status of a Population," Blood, 48:449–455, 1976

(149) Garby, L., L. Irnell and I. Werner, "Iron Deficiency in Women of Fertile Age in a Swedish Community. III. Estimation of Prevalence Based on Response to Iron Supplementation," *Acta Medica Scandinavica*, 185: 113–117, 1969.

(150) Cook, J.D., J. Alvarado, A. Gutnisky, M. Jamra, J. Labardini, M. Layrisse, J. Linares, A. Loria, V. Maspes, A. Restrepo, C. Reynafarje, L. Sanchez-Medal, H. Velez and F. Viteri, "Nutritional Deficiency and Anemia in Latin America: A Collaborative Study," Blood, 38:591–603, 1971.

(151) Fielding, J., C. Karabus and G.M. Brunstrom, "Storage Iron Depletion in Male Blood Donors: Its Significance for Iron Status in Women," *Journal of Clinical Pathology*, 21:402.–405 1968.

(152) Magnusson, B., L. Solvell, B. Arvidsson and C. Siosteen, "Iron Absorption During Iron Supplementation in Blood Donors," *Scandinavian Journal of Haematology*, 14:337–346, 1975.

(153) National Research Council, Meeting of the Subcommittee on Blood Substitute, p. 1062, March 2, 1944.

(154) Chapman, R.G., Personal Communication, BER Volume 6144.

(155) Schmidt, P.J., E.G. Morrison and J. Shohl, "The Antigenicity of the $Rh_o(D^u)$ Blood Factor," Blood, 20:196–202, 1962.

(156) Van Loghem, J.J., "Production of Rh Agglutinins Anti-C and Anti-E by Artificial Immunization of Volunteer Donors," *British Medical Journal*, 2:958–959, 1947.

(157) Rosenfield, R.E., P. Vogel, E.B. Miller and G. Haber, "Weakly Reacting Rh Positive ($D^u$) Bloods," Blood, 6:1123–1134, 1951.

(158) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publications, London, p. 293, 1972.

(159) Rein, C.R., F. Wise and A.R. Cukerbaum, "The Control and Prevention of Transfusion Syphilis," *Journal of the American Medical Association*, 110:13–19, 1938.

(160) Turner, T.B. and T.H. Diseker, "Duration of Infectivity of Treponema Pallidum in Citrated Blood Stored Under Conditions Obtaining in Blood Banks," *Bulletin of the Johns Hopkins Hospital*, 68:269–279, 1941.

(161) Block, O., "Loss of Virulence of Treponema Pallidum in Citrated Blood at 5 °C," *Bulletin of the Johns Hopkins Hospital*, 68:412–415, 1941.

(162) Kolmer, J.A., "A Note on the Survival of Treponema Pallidum in Preserved Citrated Human Blood and Plasma," *American Journal of Syphilis, Gonorrhea and Venereal Diseases*, 26:156–158, 1942.

(163) Guthrie, N., "Failure of Stored Syphilitic Blood to Transmit Syphilis," *Journal of Venereal Disease Information*, 23:246–247, 1951.

(164) Walker, R.H., "The Disposition of STS Reactive Blood in a Transfusion Service," *Transfusion*, 5:452–456, 1945.

(165) Panel on Review of Blood and Blood Derivatives Meeting 4, Open Testimony, Bethesda, MD, January 9, 1976.

(166) Bove, J., Personal Communication, BER Volume 6144.

(167) Moore, J.E. and C.F. Mohr, "Biologically False Positive Serologic Tests for Syphilis. Type, Incidence and Cause," *Journal of the American Medical Association*, 150:467–473, 1952.

(168) Johnson, T.W., "Syphilis" *in* "Infectious Disease," Edited by Hoeprich, P.D., Harper and Row, p. 550, 1972.

(169) Moore, J.E. and W.B. Lutz, "The Natural History of Systemic Lupus Erythematosus: An Approach to Its Study Through Chronic Biologic False Positive Reactors," *Journal of Chronic Diseases*, 1:297–316, 1955.

(170) Harvey, A.M. and L.E. Shulman, "Connective Tissue Disease and the Chronic Biologic False-Positive Test for Syphilis (BFP Reaction)," *The Medical Clinics of North America*, 50:1271–1279, 1966.

(171) Catterall, R.D., "Systemic Disease and the Biological False Positive Reaction," *British Journal of Venereal Diseases*, 48:1–12, 1972.

(172) Panel of The Committee on Plasma Substitutes of the Division of Medical Sciences, National Academy of Sciences, National Research Council: "Statement on Laboratory Screening Tests for Identifying Carriers of Viral Hepatitis in Blood-banking and Transfusion Services," *Transfusion*, 10:1–2, 1970.

(173) Alter, H.J., P.V. Holland, A.G. Morrow, R.H. Purcell, S.M. Feinstone and Y. Moritsugu "Clinical and Serological Analysis of Transfusion-Associated Hepatitis," Lancet, ii:838–841, 1975.

(174) Bar-Shany, S. L. Naggan and N. Wolpiansky, "Hepatitis-Associated Antigen in 10,000 Israel Blood Donors," *Israel Journal of Medical Science*, 8:1–6, 1972.

(175) Bennett, C.W., *In* "Clinical Serology." C.L. Thomas, Springfield, p. 53, 1968.

(176) Goldfield, M., Unpublished Observations cited by Barker, L.F., R.J. Gerety, J.H. Hoofnagle and D.F. Nortman, "Viral Hepatitis B: Detection and Prophylaxis," *In* "Transmissible Disease and Blood Transfusion," Edited by Greenwalt, T.J. and G.A. Jamieson, Grune and Stratton, p. 81, 1974.

(177) Kliman, A., "Australia Antigen in Volunteer and Paid Blood Donors," *New England Journal of Medicine*, 284:109, 1971.

(178) Prince, A.M., "An Antigen Detected in the Blood During the Incubation Period of Serum Hepatitis," *Proceedings of the National Academy of Sciences*, 60:814–821, 1968.

(179) Okochi, K. and S. Murakami, "Observations on Australia Antigen in Japanese," *Vox Sanguinis*, 15:374–385, 1968.

(180) Gocke, D.J., H.B. Greenberg and N.B. Kavey, "Hepatitis Antigen. Detection of Infectious Blood Donors," *Lancet*, ii:248–249, 1969.

(181) Giles, J.P., R.W. McCollum, L.W. Berndtson, Jr. and S. Krugman, "Viral Hepatitis: Relation of Australia/SH Antigen to the Willowbrook MS-2 Strain," *New England Journal of Medicine*, 281:119–122, 1969.

(182) Hirschman, R.J., N.R. Shulman, L.F. Barker and K.O. Smith, "Virus-Like Particles in Sera of Patients with Infectious and Serum Hepatitis," *Journal of the American Medical Association*, 208:1667–1670, 1969.

(183) Purcell, R.H., S.M. Feinstone and A.Z. Zapikian, "Recent Advances in Hepatitis A Research," *in* "Transmissible Disease and Blood Transfusion," Edited by Greenwalt, T.J. and G.A. Jamieson, Grune and Stratton, New York, pp. 11–26, 1974.

(184) Alexander, B., "Recent Studies on Plasma Colloid Substitutes: Their Effects on Coagulation and Hemostasis," *in* "Body Fluid Replacement in the Surgical Patient," Edited by Fox, C.L. and G.G. Nahas, Grune and Stratton, New York, p. 157, 1970.

(185) Barnes, A. Jr., Status of the Use of Universal Donor Blood Transfusion," *CRC Critical Reviews in Clinical Laboratory Sciences*, 4:147–160, 1973.

(186) Prince, A.M., B. Brotman, G.F. Grady, W.J. Kuhns, C. Hazzi, R.W. Levine and S.J. Millian, "Posttransfusion Viral Hepatitis Caused by an Agent or Agents Other Than Hepatitis B Virus or Hepatitis A Virus. Impact on Efficiency of Present Screening Methods," *In* "Transmissible Disease and Blood Transfusion," Edited by Greenwalt, T.J. and G.A. Jamieson, Grune and Stratton, pp. 129–140, 1974.

(187)— Finch, C.A., J.D. Cook, R.F. Labbe and M. Culala, "Effect of Blood Donation on Iron Stores as Evaluated by Serum Ferritin," *Blood*, 50:441–447, 1977.

(188) Moss, A.J., "Blood Donor Characteristics and Types of Blood Donations," National Center for Health Statistics, Department of Health, Education and Welfare Publication No. (HRA) 76–1533, 1976.

(189) Coburn, T.J., W.V. Miller and W.D. Parrill, "Unacceptable Variability of Hemoglobin Estimation on Samples Obtained from Ear Punctures," *Transfusion*, 17:265–268, 1977.

(190) Maxwell, N.G., "The Use of Blood From the Ear Lobe for Measuring Hemoglobin by the Copper Sulfate Method," *American Association of Blood Banks Bulletin*, 13:403–405, 1960.

(191) Stuart, J., B.A. Barrett and R. Prangnell, "Capillary Blood Collection in Haematology," *Journal of Clinical Pathology*, 27:869–874, 1974.

(192) Giblett, E.R., "Blood Group Alloantibodies: An Assessment of Some Laboratory Practices," *Transfusion*, 17:299–308, 1977.

(193) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell, London, p. 533, 1972.

(194) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., pp. 51–52, Blackwell, London, 1972.

(195) Valeri, C.R. and N.M. Hirsch, "Restoration *In Vivo* of Erythrocyte Adenosine Triphosphate, 2, 3-Diphosphoglycerate, Potassium Ion, and Sodium Ion Concentrations Following the Transfusion of Acid-Citrate-Dextrose-Stored Human Red Blood Cells," *Journal of Laboratory and Clinical Medicine*, 73:722–733, 1969.

(196) Beutler, E. and L. Wood, "The *In Vivo* Regeneration of Red Cell 2,3-Dephosphoglyceric Acid (DPG) After Transfusion of Stored Blood," *Journal of Laboratory and Clinical Medicine*, 74:300–304, 1969.

(197) Collins, J.A., "Massive Blood Transfusion," *Clinics in Haematology*, 5:201–222, 1967.

(198) Bunker, J.P., H.H. Bendixen and A.J. Murphy, "Hemodynamic Effects of Intravenously Administered Sodium Citrate," *New England Journal of Medicine*, 266:372–377, 1962.

(199) Howland, W.S., J.W. Bellville, M.B. Zucker, P. Boyan and E.E. Cliffton, "Massive Blood Replacement. V. Failure to Observe Citrate Intoxication," *Surgery, Gynecology and Obstetrics*, 105:529–540, 1957.

(200) Ludbrook, J. and V. Wynn, "Citrate Intoxication: A Clinical and Experimental Study," *British Medical Journal*, 2:523–528, 1958.

(201) Collins, J.A., R.L. Simmons, P.M. James, C.E. Brendenberg, R.W. Anderson and C.A. Heisterkamp, "Acid-base Status of Seriously Wounded Combat Casualties. II. Resuscitation with Stored Blood," *Annals of Surgery*, 173:6–18, 1971.

(202) Blum, J.W., G.P. Mayer and J.T. Potts, Jr., "Parathyroid Hormone Responses During Spontaneous Hypocalcemia and Induced Hypercalcemia in Cows," *Endocrinology*, 95:84–92, 1974.

(203) Miller, R.N., R. Engelhardt, J.A. Collins, E. Slatopolsky and J.H. Ladenson, "Observations on the Biochemical Effects of Transfusion of Citrate-Phosphate-Dextrose Stored Blood in Man," *Laryngoscope*, 86:1272–1279, 1976.

(204) Saffran, M. and O.F. Denstedt, "The Effect of Intravenously Injected Citrate on the Serum Ionized Calcium in the Rabbit," *Canadian Journal of Medical Sciences*, 29:245–254, 1951.

(205) Miller, L.W., J.A. Collins, L. Sherman and J. Ladenson, "Massive Transfusion in Swine," *Surgical Forum*, 28:21–23, 1977.

(206) Irvin, G.L., R.F. Gittes and M.F. Gibbs, "Influence of Acid-based Disturbances on Total Plasma Calcium and Evidence for a Homeostatic Role of Thyrocalcitonin," *Annals of Surgery*, 164:1073–1076, 1966.

(207) Kaplan, E.L., B.J. Hill, S. Locke and G.W. Peskin, "Acid-base Balance and Parathyroid Function: Metabolic Alkalosis and Hyperparathyroidism," *Surgery*, 70:198–204, 1971.

(208) Hoffken, B., D.K. Parkinson, P. Storms and I.C. Radde, "Effects of Alterations of Blood pH on Calcium Ion Activity in Rat Plasma," *Clinical Orthopaedics and Related Research*, 78:30–39, 1971.

(209) Adler, S., B. Anderson and L. Zemotel, "Metabolic Acid-base Effects on Tissue Citrate Content and Metabolism in the Rat," *American Journal of Physiology*, 220:986–992, 1971.

(210) Shields, C.E., L.H. Dennis, J.W. Eichelberger and M.E. Conrad, "The Rapid Infusion of Large Quantities of ACD Adenine Solution into Humans," *Transfusion*, 7:133–137, 1967.

(211) Perkins, H.A., M. Snyder, C. Thacher and M.R. Rolfs, "Calcium Ion Activity During Rapid Exchange Transfusion with Citrated Blood," *Transfusion*, 11:204–212, 1971.

(212) Hinkle, J.E. and L.H. Cooperman, "Serum Ionized Calcium Changes Following Citrated Blood Transfusion in Anaesthetized Man," *British Journal of Anesthesia*, 43:1108–1112, 1971.

(213) Gershanik, J.J., A.H. Levkoff and R. Duncan, "Serum Ionized Calcium Values in Relation to Exchange Transfusion," *Journal of Pediatrics*, 82:847–850, 1973.

(214) Pittinger, C., P.M. Chang and W. Faulkner, "Serum Ionized Calcium: Some Factors Influencing its Level," *Southern Medical Journal*, 64:1211–1215, 1971.

(215) Howland, W.S., O. Schweizer, D. Jascott and J. Ragasa, "Factors Influencing the Ionization of Calcium During Major Surgical Procedures," *Surgery, Gynecology and Obstetrics*, 143:895–900, 1976.

(216) Cooper, N., J.R. Brazier, C. Hottenrott, D.G. Mulder, J.V. Maloney, Jr. and G.D. Buckberg, "Myocardial Depression Following Citrated Blood Transfusion," *Archives of Surgery*, 107:756–763, 1973.

(217) Wolf, P.L., L.J. McCarthy and B. Hafleigh, "Extreme Hypercalcemia Following Blood Transfusion Combined with Intravenous Calcium," *Vox Sanguinis*, 19:544–545, 1970.

(218) Scott, R. and W.H. Crosby, "Changes in the Coagulation Mechanism Following Wounding and Resuscitation with Stored Blood," *Blood*, 9:609–621, 1954.

(219) Krevans, J.R. and D.P. Jackson, "Hemorrhagic Disorder Following Massive Whole Blood Transfusions," *Journal of the American Medical Association*, 159:171–177, 1955.

(220) Gollub, S., A.W. Ulin, H.S. Winchell, E. Ehrlich and W. Weiss, "Hemorrhagic Diathesis Associated with Massive Transfusion," *Surgery*, 45:204–222, 1959.

(221) Simmons, R.L., J.A. Collins, C.A. Heisterkamp, III, D.E. Mills, R. Andren and

L.L. Phillips, "Coagulation Disorders in Combat Casualties," *Annals of Surgery*, 169:455–482, 1969.

(222) Wilson, R.F., E. Mammen and A.J. Walt, "Eight Years of Experience with Massive Blood Transfusions," *Journal of Trauma*, 11:275–285, 1971.

(223) Miller, R.D., T.O. Robbins, M.J. Tong and S.L. Barton, "Coagulation Defects Associated with Massive Blood Transfusions," *Annals of Surgery*, 174:794–801, 1971.

(224) McNamara, J.J., E.L. Burran, J.F. Stemple and M.D. Molot, "Coagulopathy After Major Combat Injury: Occurrence, Management, and Pathophysiology," *Annals of Surgery*, 176:243–246, 1972.

(225) Lim, R.C., C. Olcott, A. Robinson and F.W. Blaisdell, "Platelet Response and Coagulation Changes Following Massive Blood Replacement," *Journal of Trauma*, 13:577–582, 1973.

(226) Harke, H. and E.V. Meissner, "Störungen der Haömostase nach Massivtransfusionen." Presented at Annual Congress German Society for Blood Transfusion and Immunohematology, Interlaken, Switzerland, May 27, 1978.

(227) Miller, R.D., M.J. Tong and T.O. Robbins, "Effects of Massive Transfusion of Blood on Acid-based Balance," *Journal of the American Medical Association*, 216:1762–1764, 1971.

(228) Xanthou, M., P. Oeconomopoulos, D. Nicolopoulos, P. Papathanassiou and N. Matsaniotis, "The Acid-base Balance of the Newborn During and After Exchange Transfusion," *Clinical Pediatrics*, 13:759–764, 1974.

(229) Finch, C.A. and C. Lenfant, "Oxygen Transport in Man," *New England Journal of Medicine*, 286:407–415, 1972.

(230) Brewer, G.J. and J.W. Eaton, "Erythrocyte Metabolism: Interaction With Oxygen Transport," *Science*, 171:1205:1211, 1971.

(231) Chien, S., "Present State of Blood Rheology," *In* "Hemodilution, Theoretical Basis and Clinical Application," Edited by Messmer, K. and H. SchmidSchonbein, Karger, Basel, p. 1, 1972.

(232) Crowell, J.W., S.H. Bounds and W.W. Johnson, "Effect of Varying the Hematocrit Ratio on the Susceptibility to Hemorrhagic Shock," *American Journal of Physiology*, 192:171–174, 1958.

(233) Gordon, R.J., G.K. Snyder, H. Tritel and W.J. Taylor, "Potential Significance of Plasma Viscosity and Hematocrit Variations in Myocardial Ischemia," *American Heart Journal*, 87:175–182, 1974.

(234) Bunn, H.F., M.H. May, W.F. Kocholaty and C.E. Shields, "Hemoglobin Function in Stored Blood," *Journal of Clinical Investigation*, 48:311:321, 1969.

(235) Valeri, C.R., "Viability and Function of Preserved Red Cells," *New England Journal of Medicine*, 284:81–88, 1971.

(236) Valtis, D.J. and A.C. Kennedy, "Defective Gas-Transport Function of Stored Red Blood-Cells," *Lancet*, 1:119–124, 1954.

(237) Gullbring, B. and G. Storm, "Changes in Oxygen-Carrying Function of Human Hemoglobin During Storage in Cold Acid-Citrate-Dextrose Solution," *Acta Medica Scandinavica*, 155:413–430, 1956.

(238) O'Brien, T.G. and E. Watkins, "Gas-exchange Dynamics of Glycerolized Frozen Blood," *Journal of Thoracic and Cardiovascular Surgery*, 40:611–624, 1960.

(239) Sugeman, H.J., D.T. Davidson, S. Vibul, M. Delivoria-Papadopoulos, L.D. Miller and F.A. Oski, "The Basis of Defective Oxygen Delivery from Stored Blood," *Surgery, Gynecology and Obstetrics*, 131:733–741, 1970.

(240) Broennle, A.M., C.K. Tung, B. Buchman and M.B. Laver, "Ocyhemoglobin Dissociation Following Massive Transfusion in Man," *Federation Proceedings*, 29:329, 1970.

(241) Valeri, C.R. and F.B. Collins, "Physiologic Effects of 2,3-DPG-Depleted Red Cells with High Affinity for Oxygen," *Journal of Applied Physiology*, 31:823–827, 1971.

(242) McConn, R. and J.B. Derrick, "The Respiratory Function of Blood: Transfusion and Blood Storage," *Anesthesiology*, 36:119–127, 1972.

(243) Kopriva, C.J., J.L. Ratliff, J.R. Fletcher, N.L. Fortier and C.R. Valeri, "Biochemical and Hematological Changes Associated with Massive Transfusion of ACD-stored Blood in Severely Injured Combat Casualties," *Annals of Surgery*, 176:585–589, 1972.

(244) Woodson, R.D., B. Wranne and J.C. Detter, "Effect of Increased Blood Oxygen Affinity of Work Performance of Rats," *Journal of Clinical Investigation*, 52:2717–2724, 1973.

(245) Wranne, B., L. Nordgren and R.D. Woodson, "Increased Blood Oxygen Affinity and Physical Work Capacity in Man," *Scandinavian Journal of Clinical and Laboratory Investigation*, 33:347–352, 1974.

(246) Collins, J.A., "Problems Associated with the Massive Transfusion of Stored Blood," *Surgery*, 75–274–295, 1974.

(247) Dennis, R.C., L. Vito, R.D. Weisel, C.R. Valeri, R.L. Berger and H.B. Hechtman, "Improved Myocardial Performance Following High 2–3 Diphosphoglycerate Red Cell Transfusions," *Surgery*, 77:741–747, 1975.

(248) Boyan, C.P., "Cold or Warmed Blood for Massive Transfusions," *Annals of Surgery*, 160:282–288, 1964.

(249) Dydkjaer, E. and P. Elkjaer, "The Use of Heated Blood in Massive Blood Replacement," *Acta Anaisthesiologica Scandinavica*, 8:271–278, 1964.

(250) Mendlowitz, M., "The Specific Heat of Human Blood," *Science*, 107:97–98, 1948.

(251) Milner, R.D.G., M. Fekete, J.S. Hodge and R. Assan, "Influence of Donor Blood Temperature on Metabolic and Hormonal Changes During Exchange Transfusion," *Archives of Diseases in Childhood*, 47:933–937, 1972.

(252) Dalili, H. and J. Adriani, "Effects of Various Blood Warmers on the Components of Bank Blood," *Anesthesia and Analgesia: Current Researches*, 53:125–131, 1974.

(253) Arens, J.F. and G.L. Leonard, "Danger of Overwarming Blood by Microwave," *Journal of the American Medical Association*, 218:1045–1046, 1971.

(254) Collins, J.A., A. Braitberg and H.R. Butcher, "Changes in Lung and Body Weight and Lung Water Content in Rats Treated for Hemorrhage with Various Fluids," *Surgery*, 73:401–411, 1973.

(255) Rush, B.F. and R.J. Wilder, "Mortality and Renal Tubular Necrosis in Hemorrhagic Shock in Dogs: The Effect of Blood Handling," *Surgical Forum*, 14:1–2, 1963.

(256) Hardaway, R.M., D.G. Johnson, D.N. Houchin, E.B. Jenkins, J.W. Burns and D.R. Jackson, "The Influence of Extracorporeal Handling of Blood on Hemorrhagic Shock in Dogs," *Experimental Medicine and Surgery*, 23:28–37, 1965.

(257) Pareira, M.D., K.D. Serkes and S. Lang, "Enhanced Efficacy of Plasma After Aging in the Treatment of Tourniquet Shock," *Proceedings of the Society for Expermental Biology and Medicine*, 115:660–662, 1964.

(258) Serkes, K.D., S. Lang and M.D. Pareira, "Enhanced Protection with the Use of Gamma Globulin Proteins in the Treatment of Tourniquet Shock with Plasma Expanders," *Surgery*, 59:566–571, 1966.

(259) Louis, G.P., "Active Polypeptides Derived from Plasma Proteins," *Physiological Reviews*, 40:647–676, 1960.

(260) Strauss, H.W., R.B. Smith, P. Polimeni, A.C. Schenker, V.J. Schenker and J.H. Stuckey, "Plasma Serotonin Levels in Stored Human Blood," *Angiology*, 18:535–546, 1967.

(261) Ollodart, R. and A.R. Mansberger, "The Effect of Hypovolemic Shock on Bacterial Defense," *American Journal of Surgery*, 110:302–307, 1965.

(262) Subramanian, V., J.T. Lowman and H. Gans, "Effect of Extracorporeal Circulation on Reticuloendothelial Function," *Archives of Surgery*, 97:330–335, 1968.

(263) Wilson, J.D., H.F. Taswell and P. Didisheim, "Effects of Washed-Cell and Whole-Blood Transfusions on Reticuloendothelial Function in Dogs," *Transfusion*, 9:289, 1969.

(264) Allgower, M., "Ueber die Wirkung von Heparin, Polyanetholsulfosaurem Natrium (Liquoid Roche) und Tribasischem Natriumcitrat auf Menschliche Leukozyten *In Vitro*," *Schweizerische Medizinische Wochenschrift*, 77:40–43, 1947.

(265) Bunker, J.P., J.B. Stetson, R.C. Coe, H.C. Grillo and A.J. Murphy, "Citric Acid Intoxication," *Journal of the American Medical Association*, 157:1361–1367, 1955.

(266) Schweizer, O. and W.S. Howland, "Potassium Levels, Acid-base Balance and Massive Blood Replacement," *Anesthesiology*, 23:735–740, 1962.

(267) Smith, N.T. and A.N. Corbascio, "The Interaction of Potassium and Calcium on the Isolated Guinea Pig Atrium," *Federation Proceedings*, 23:326, 1964.

(268) Taylor, W.C., C.N. Gillis, C.W. Nash and G.L. Kullman, "Experimental Observations on Cardiac Arrhythmia During Exchange Transfusion in Rabbits," *Journal of Pediatrics*, 58:470–476, 1961.

(269) Veall, N. and P.L. Mollison, "The Rate of Red-Cell Exchange in Replacement Transfusions," *Lancet*, ii:792–797, 1050.

(270) Delivoria-Papadopoulos, M., L.D. Miller, R.E. Forster and F.A. Oski, "The Role of Exchange Transfusion in the Management of Low-Birth-Weight Infants With and Without Severe Respiratory Distress Syndrome. I. Initial Observations," Journal of Pediatrics, 89:273–278, 1976.

(271) Agarwal, J.B., R. Paltoo and W.H. Palmer, "Relative Viscosity of Blood at Varying Hematocrit in Pulmonary

Circulation," *Journal of Applied Physiology*, 29:866–871, 1970.

(272) Djojosugito, A.M., B. Folkow, B. Oberg and S. White, "A Comparison of Blood Viscosity Measured *In Vitro* and in a Vascular Bed," *Acta Physiologica Scandinavica*, 78:70–84, 1970.

(273) Braasch, D., "Red Cell Deformability and Capillary Blood Flow," *Physiological Reviews*, 51:679–701, 1971.

(274) Rowlands, S. and L. Skibo, "Erythrocyte Flow in Tubes of Capillary Size," *Canadian Journal of Physiology and Pharmacology*, 49:373–374, 1971.

(275) Greene, R., J.M. Hughes, L.D. Iliff and C.F. Pineo, "Red Cell Flexibility and Pressure-flow Relations in Isolated Lungs," *Journal of Applied Physiology*, 34:169–175, 1973.

(276) Meiselman, H.J., *"In Vivo* Viscometry: Effect of Hemodilution," *In* "Hemodilution, Theoretical Basis and Clinical Application," Karger, Basel, pp. 143–159, 1972.

(277) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publications, London, p. 645, 1972.

(278) Weisel, R.D., R.C. Dennis, J. Manny, J.A. Mannick, C.R. Valeri and H.B. Hechtman, "Adverse Effects of Transfusion Therapy During Abdominal Aortic Aneurysectomy," *Surgery*, 83:682–690, 1978.

(279) Schiff, D., J.V. Aranda, E. Colle and L. Stern, "Metabolic Effects of Exchange Transfusion. II. Delayed Hypoglycemia Following Exchange Transfusion With Citrated Blood," *Journal of Pediatrics*, 79:589–593, 1971.

(260) Carey, J.S., "Cardiovascular Response to Acute Hemodilution," *Journal of Thoracic and Cardiovascular Surgery*, 62:103–116, 1971.

(281) Varat, M.A., R.J. Adolph and N.O. Fowler, "Cardiovascular Effects of Anemia," *American Heart Journal*, 83:415–426, 1972.

(282) Beutler, E., S. Larsh and F. Tanzi, "Iron Enzymes in Iron Deficiency. VII. Oxygen Consumption Measurements in Iron-Deficient Subjects," *American Journal of Medical Sciences*, 239:759–765, 1960.

(283) Robbe, H., "Total Amount of Haemoglobin and Physical Working Capacity in Anaemia of Pregnancy," *Acta Obstetrica et Gynecologica*, 37:312–347, 1958.

(284) Rowell, L.B., H.L. Taylor and Y. Wang, "Limitations to Prediction of Maximal Oxygen Intake," *Journal of Applied Physiology*, 19:919–927, 1964.

(285) Cotes, J.E., J.M. Dabbs, P.C. Elwood, A.M. Hall, A. McDonald and M.J. Saunders, "The Response to Submaximal Exercise in Adult Females: Relation to Haemoglobin Concentration," *Journal of Physiology*, 203:79P–80P, 1969.

(286) Elwood, P.C. and D. Hughes, "Clinical Trial of Iron Therapy on Psychomotor Function in Anaemic Women," *British Medical Journal*, 3:254–255, 1970.

(287) Ericsson, P., "Total Haemoglobin and Physical Work Capacity in Elderly People," *Acta Medica Scandinavica*, 188:15–23, 1970.

(288) Vellar, O.D. and L. Hermansen, "Physical Performance and Hematological Parameters," *Acta Medica Scandinavica*, Supplement 522, 1971.

(289) Cotes, J.E., J.M. Dabbs, P.C. Elwood, A.M. Hall, A. McDonald and M.J. Saunders, "Iron-deficiency Anaemia: Its Effect on Transfer Factor for the Lung (Diffusing Capacity) and Ventilation and Cardiac Frequency During Sub-Maximal Exercise," *Clinical Science*, 42:325–335, 1972.

(290) Elwood, P.C., "Evaluation of the Clinical Importance of Anemia," *American Journal of Clinical Nutrition*, 26:958–964, 1973.

(291) Hermansen, L., "Oxygen Transport During Exercise in Human Subjects," *Acta Physiologica Scandinavica*, Supplement 399, 1973.

(292) Sproule, B.J., J.H. Mitchell and W.F. Miller, "Cardiopulmonary Physiological Responses to Heavy Exercise in Patients with Anemia," *Journal of Clinical Investigation*, 39:378–388, 1960.

(293) Davies, C.T.M. and J.P.M. Van Haaren, "Anemia: Affect of Therapy on Responses to Exercise," *Journal of Physiology*, 227:36P–37P, 1972.

(294) Ekblom, B., A.N. Goldbarg and B. Gullbring, "Response to Exercise After Blood Loss and Reinfusion," *Journal of Applied Physiology*, 33:175–180, 1972.

(295) Graettinger, J.S., R.L. Parsons and J.A. Campbell, "A Correlation of Clinical and Hemodynamic Studies in Patients with Mild and Severe Anemia with and Without Congestive Failure," *Annals of Internal Medicine*, 58:617–626, 1963.

(296) Andersen, H.T. and H. Barkve, "Iron Deficiency and Muscular Work Performance," *Scandinavian Journal of Clinical and Laboratory Investigation*, Supplement 114, 1970.

(297) Sharpey-Schafer, E.P., "Cardiac Output in Severe Anaemia," *Clinical Science*, 5:125–132, 1944.

(298) Shires, T., D. Coln, J. Carrico and S. Lightfoot, "Fluid Therapy in Hemorrhagic Shock," *Archives of Surgery*, 88:688–693, 1964.

(299) Pruitt, B.A., J.A. Moncrief and A.D. Mason, "Efficacy of Buffered Saline as the Sole Replacement Fluid Following Acute Measured Hemorrhage in Man," *Journal of Trauma*, 7:767–782, 1967.

(300) Moss, G.S. and J.D. Saletta, "Traumatic Shock in Man," *New England Journal of Medicine*, 290:724–726, 1974.

(301) Carey, L.C., B.D. Lowery and C.T. Cloutier, "Hemorrhagic Shock," *Current Problems in Surgery*, January, 1971.

(302) Collins, J.A., "The Causes of Progressive Pulmonary Insufficiency in Surgical Patients," *Journal of Surgical Research*, 9:685–704, 1969.

**4. Whole Blood (Human) Heparin**

*Generic Statement*

1. *Introduction.* The commonly used anticoagulant-preservative solutions for collection of blood contain citrate to provide a calcium binding effect to prevent clotting. There are clinical situations in which citrate might adversely affect the availability of ionic calcium in the blood of the recipient (see the section on anticoagulants in relation to whole blood). In addition there is an acid load of up to 30 to 40 mEq per liter in stored citrated blood. The excess acidity is due mainly to the citric acid in the anticoagulant and the lactic acid generated during storage (see section on acid-base alterations of whole blood). For these reasons, other substances have been considered for use as anticoagulants.

Heparin is a sulfated mucopolysaccharide that acts with a co-factor antithrombin III and is a potent anticoagulant (Ref. 1). The co-factor is present in adequate amounts in normal donor plasma so that the addition of heparin alone will provide the desired anticoagulant effect. Heparin appears to act at more than one point in the sequence of coagulation in that it appears to inhibit the conversion of prothrombin to thrombin and also inhibits the action of thrombin on fibrinogen (Ref. 1).

Heparin is not a suitable anticoagulant for long-term storage of blood. With time, its effects are neutralized by normal constituents of blood (Ref. 1). In addition, it is not a preservative of red blood cells (Refs. 2 through 4). The amount needed as an anticoagulant for human blood intended for transfusion is 75,000 units of Heparin Sodium (U.S.P.) with sufficient Sodium Chloride Injection (U.S.P.) to make 1,000 mL. Six mL of this solution as used for each 100 mL of whole blood (Ref. 6) will provide adequate anticoagulant effect for no more than 48 hours. Plasma separated from heparinized blood is not suitable for use as Single Donor Plasma (Human) or as a starting material for preparation of Cryoprecipitated Antihemophilic (Human) Factor or platelets.

2. *Analysis of indications and labeling*—a. *Indications.* This product is indicated when there is a need to provide both red blood cells and plasma and the administration of a citrate is contraindicated. Depending on the clinical situation, heparinized blood may be indicated in exchange transfusions of newborn infants, when large amounts of blood are required in patients with liver disease and who are unable to metabolize citrate rapidly and in cardiopulmonary surgery with extracorporeal circulation.

b. *Evidence of effectiveness.* It is not possible to find detailed controlled studies which establish the effectiveness of Whole Blood (Human) Heparin. There is anectodal information that it has been used, and no discernable adverse effects have resulted. Current regulations require that heparinized blood be used within 48 hours of collection. It appears that the red blood cell viability is not adversely affected by short-term storage, but the viability of red blood cells in vivo after storage of heparinized

blood has not been well documented. There is limited evidence to support the current dating time of 48 hours or to document other changes that occur in heparinized blood during storage (Refs. 2 through 5).

c. *Evidence of safety.* Heparinized blood has been used for a variety of reasons, and no documented evidence is available to indicate that when used appropriately it is unsafe. When large amounts of heparinized blood are administered, there may be sufficient heparin infused to result in a hemostatic defect in the recipient. Heparin in relatively large amounts is used in the treatment of thrombin-embolic diseases. Even with therapeutic dosages, reactions to heparin administered intravenously ae rare other than for its effect on blood coagulation and hemostasis.

Heparinized whole blood does not contain the added glucose that is present in ACD or CPD anticoagulants. This must be kept in mind in patients receiving heparinized blood in exchange transfusions.

d. *Benefit/risk evaluation.* As with all human blood products, there are risks associated with this product. Except for the possibility of coagulation or hemostatic problems resulting from the amount of heparin transfused, the risks are the same as those discussed in the section on whole blood. There are clinical situations when use of blood of a more neutral pH and which does not contain a calcium-binding anticoagulant is indicated. For this reason Whole Blood (Human) Heparin should continue to be available.

e. *Recommendations.* (1) Whole Blood (Human) Heparin should be placed in Category III A with a period of 3 years allowed for completion of further studies. The studies should include red cell survival data, the status of the coagulation system in the donor blood, activator levels, degree of kinin activation, the presence of clots, and residual heparin.

(2) Although no adverse effects have been reported following transfusion of heparinized blood stored up to 48 hours, it appears wise to limit storage of such blood to no more than 8 hours prior to use. If the product is to remain licensed during the period of additional studies, the expiration time should be reduced to 8 hours after the initial drawing of the blood.

(3) The general labeling requirements applicable to blood collected in ACD or CPD apply except for those data related to anticoagulation and red cell preservation. The labeling should also indicate that heparinization of recipients is a real possibility when multiple transfusions of heparinized blood are given.

(4) It has been the practice in some institutions to add ACD or CPD anticoagulant to heparinized blood and then to use the blood up to 12 days after collection (Ref. 5). This is not a procedure discussed in the Code of Federal Regulations. If there is a need for such a modification, additional studies will be needed to demonstrate the safety and effectiveness of the product.

**References**

(1) Biggs, R. and K.W.E. Denson, "Natural and Pathological Inhibitors of Blood Coagulation," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," Edited by Biggs, R., Blackwell, Oxford, pp. 152–157, 1976.

(2) Perkins, H.A., M.R. Rolfs and D.J. Acra, "Studies on Bank Blood Collected and Stored under Various Conditions with Particular Reference to its Use in Open Heart Surgery," *Transfusion*, 1:157–162, 1961.

(3) Abbott, J.P., J.B. Ragland, M.E. DeBakey and D.A. Cooley, "Observations on Blood Drawn and Stored for Open-Heart Surgery. A Study of Ten Anticoagulant Solutions," *American Journal of Clinical Pathology*, 33:124–134, 1960.

(4) Lobpreis, E.L., E. Raschke, Y. Watanabe and J.V. Maloney, Jr., "A Clinical Evaluation of Fresh and Stored Heparinized Blood for Use in Extracorporeal Circulation," *Annals of Surgery*, 152:947–953, 1960.

(5) Button, L.N., J.G. Gibson II, and S.V. Kevy, "The Salvage of Heparinized Blood with Acid-Citrate-Dextrose," *Transfusion*, 3:37–40, 1963.

(6) Code of Federal Regulations, 21 CFR 640.4(d)(2).

**5. Whole Blood (Human) Modified-Antihemophilic Factor Removed and Whole Blood (Human) Modified-Platelets Removed**

*Generic Statement*

1. *Introduction.* Blood collected into interconnected but separable plastic containers containing a suitable anticoagulant may be modified without contaminating the unit. Platelets may be separated from the whole blood by selective centrifugation and transfer of plasma along with most of the platelets to an integrally attached compartment. The platelets can then be concentrated by centrifugation and most of the platelet-poor plasma can be returned to the compartment containing the red blood cells. This modified blood has the characteristics of the starting whole blood except that the majority of the platelets and approximately 50 mL of plasma have been removed.

In a similar manner, Cryoprecipitated Antihemophilic Factor (Human) (cryoprecipitate) can be prepared while the containers are still integrally attached and the cryopreciptiate-poor plasma can be returned to the compartment containing the red blood cells. In this procedure plasma is separated from whole blood and transferred to an integrally attached compartment. The plasma is processed to yield the cryoprecipitated antihemophilic factor while the multicompartmented container remains attached. During the processing, the red blood cells are maintained at 4 to 6 °C. The cryoprecipitate is harvested, and the residual plasma can be returned to the compartment containing the red blood cells. As indicated in the section on Cryoprecipitated Antihemophilic Factor (Human), the residual plasma contains 15 to 35 percent of the original Factor VIII activity, about ⅓ of the original fibrinogen and approximately 90 percent of the original Factor V activity. The activity of other coagulation factors are unchanged from those of fresh plasma. The modified whole blood has the characteristics of whole blood except that most of the Factor VIII, ⅔ of the fibrinogen, and some of the Factor V have been removed.

The two processes can be combined so that both platelets and Factor VIII are removed. It is generally considered to be more practical to seal and detach the compartment containing the red blood cells before proceeding with separation of platelets or cryoprecipitate. In this way, Red Blood Cells (Human) are prepared in the usual way and the processing for platelets and/or cryoprecipitated antihemophilic factor is done independent of the Red Blood Cells (Human).

2. *Effectiveness.* The indications for the modified whole blood products are the same as for whole blood stored for more than 48 hours. When used in this manner, the effectiveness is equivalent to that of stored whole blood for red cell and plasma volume replacement.

3. *Safety.* The safety of the product is equivalent to that of whole blood. The manipulations done do not appear to have any adverse effects.

4. *Benefit/risk evaluation.* The same considerations apply as for whole blood. In most blood bank establishments, the red blood cells will be removed prior to processing for cryoprecipitate and/or platelets. In a few situations with unique requirements, this is a useful product. Because of the hepatitis risk, this product may be safer than providing red blood cells and plasma from two separate donors. However, there are no advantages in using this product in comparison to whole blood.

5. *Recommendation.* It is recommended that these products be placed in Category I, safe and effective.

6. *Labeling analysis.* The labeling requirements for whole blood apply to these products. In addition, the container labels must indicate clearly that platelets and/or cryoprecipitated antihemophilic factor have been removed.

**6. Red Blood Cells (Human)**

*Generic Statement*

1. *Introduction.* Red Blood Cells (Human) are also called Concentrated Red Blood Cells by the World Health Organization. The other designation of this whole blood component as "packed red blood cells" usually means red blood cells from which most of the plasma has been removed either by sedimentation or by centrifugation. The term can also include centrifuged cells with the buffy coat largely removed or washed red cells in which plasma and buffy coat have been removed by at least three washings. Thus, four products may be available to the clinician, each with somewhat different characteristics (Ref. 1).

Sedimented red blood cells are the most easily available type since no mechanical equipment is needed to prepare them. Sedimented cells contain practically all of the leukocytes, platelets, and almost the same concentration of potassium (less than 1 mEq difference) in the residual plasma as in the plasma of whole blood of equivalent age (Ref. 2).

Centrifuged red blood cells have similar characteristics, but permit the harvesting of more plasma, yielding a hematocrit of about 60 to 80 percent. They are more viscous because of the high hematocrit.

2. *Indications.* Red Blood Cells (Human) are administered to increase the oxygen-carrying capacity of the blood. This indication was discussed earlier in the statement on "Stored Red Blood Cell Products". Patients with hypoxic symptoms whose anemia is unresponsive to specific treatment; e.g., iron, $B_{12}$, folic acid, etc., who are not hypovolemic and who do not require plasma-clotting factors or plasma proteins may benefit from administration of red blood cells (Refs. 9 and 10). Red blood cells should not be used in cases in which whole blood is indicated for treatment of hypovolemia, unless accompanied by the administration of plasma volume expanders. Plasma volume may be expanded, at least in the face of moderate degrees of acute blood loss, by administration of crystalloid solutions.

3. *Effectiveness.* Extensive experience and research has proven the effectiveness of administering Red Blood Cells (Human) to increase the oxygen-carrying capacity of the blood (Ref. 8). Stored red blood cells, whether concentrated or not, have an increased affinity for oxygen. Because red blood cells are transfused to provide patients with adequate oxygen transport, it has been suggested that blood with high oxygen affinity is undesirable and that only blood with nearly normal oxygen affinity is suitable for transfusion. However, available data do not indicate the extent of the benefits that might result from blood cells with nearly normal oxygen affinity or the costs and risks that might be incurred in obtaining products to yield such possible benefits (Ref. 11). Red blood cells are the material of choice for transfusion of the anemic patient with limited cardiovascular reserves.

4. *Safety.* The hazards of red blood cell transfusions are the same as whole blood transfusions. The only hazards not associated with whole blood transfusions are possibly those of ammonia accumulation and citrate intoxication (Ref. 12). Since potassium from the red cells equilibrates with the plasma potassium as storage progresses, red blood cells are only slightly deficient in potassium (Ref. 2).

In general, it has been stated that fewer transfusion reactions occur with red blood cells compared with whole blood, but it should be emphasized that this is in reference to "buffy coat poor" red blood cells or previously frozen, washed cells. These latter two products are quite different from the red blood cells available in most blood banks. In one report, 59 percent of transfusion reactions were caused by red blood cells when 48 percent of all red blood cell products were given as red blood cells (Ref. 6). The reduction in plasma volume of sedimented red cell products which have a hematocrit of 65 to 70 percent is insufficient to prevent IgA reactions in sensitive recipients (Ref. 3) or hepatitis (Ref. 4). The deleterious effects of allergic reactions and anaphylactic reactions to IgA are obviated only by washed red cells (Ref. 5). Centrifuged red blood cells with the buffy coat largely, but not completely, removed contain about 30 percent of the leukocytes present in the original donor unit. Sufficient leukocytes and platelets are still present to cause allosensitization to their antigens in the previously unsensitized patient.

The 5 to 10 percent residual plasma in centrifuged red blood cells is too high to provide any protection against the development of hepatitis (Ref. 1). There has been no definitive prospective analysis to substantiate the claim that the incidence of hepatitis with red blood cells is less than that of whole blood.

Washed red blood cells are indicated for patients who have allergic transfusion reactions. Patients who develop anaphylactoid reactions to IgA must receive red blood cells almost completely free of plasma. Even the small amount of plasma (less than 1 percent) that remains in well washed red blood cells can cause transfusion reactions in some of these patients (Ref. 3).

5. *Benefit/risk evaluation.* This product allows the use of red blood cells as a byproduct of the preparation of other blood components, and it is completely adequate to treat the deficiency in red blood cell oxygen-carrying capacity associated with anemia. Red blood cells are difficult to administer rapidly and may be more expensive than whole blood if they must be administered with plasma substitutes to replace blood volume loss (Ref. 8). Sixty percent of the blood collected is used intraoperatively (Ref. 7).

6. *Recommendations.* a. Red Blood Cells (Human) should be placed in Category I.

b. The term "Red Blood Cells" should be substituted for "Red Blood Cells (Human)" and for "packed red blood cells".

c. Red Blood Cells should be labeled to indicate that their only use is to increase the oxygen-carrying capacity of the blood. When they must be used to substitute for Whole Blood then the labeling must indicate that a suitable plasma volume expander must be administered with them if hypovolemia is being treated (Ref. 13). In other situations where whole blood is indicated because of its red blood cells and plasma constituents, red cells can be used with simultaneous administration of the necessary plasma components in a separate form.

d. Labeling should indicate that red blood cells should not be reconstituted or infused with lactated Ringer's solution, 5 percent aqueous dextrose or 5 percent dextrose in 0.225 percent saline, as clumping, hemolysis, or clotting may occur (Ref. 14).

e. There is a need for the scientific community to develop a more extensive evaluation of the usefulness of red blood cells and an analysis of the complications that occur after their administration. This is especially relevant to the belief that the administration of Red Blood Cells will minimize circulatory overload.

References

(1) Chaplin, H., "Packed Red Blood Cells," *New England Journal of Medicine*, 281:364–367, 1969.

(2) Simon, G.E. and J.R. Bove, "The Potassium Load from Blood Transfusion," *Postgraduate Medicine*, 49:61–64, 1971.

(3) Leikola, J., J. Koistinen, M. Lehtinen and M. Virolainen, "IgA-induced Anaphylactic Transfusion Reactions: A Report of Four Cases," *Blood*, 42:111–119, 1973.

(4) Kliman, A., "No Hepatitis After Packed Red Blood Cells," *New England Journal of Medicine*, 297:1290, 1968.

(5) Storb, R., H.J. Kolb, T.C. Graham, V. Erickson and E.D. Thomas, "The Effect of Buffy Coat-Poor Blood Transfusion on Subsequent Hematopoietic Grafts," *Transplantation*, 15:129–136, 1973.

(6) Grindon, A.J., "The Use of Packed Red Blood Cells," *Journal of the American Medical Association*, 235:389, 1976.

(7) Kliman, A., Letter to the Editor, *Journal of the American Medical Association*, 235:2586, 1976.

(8) Valeri, C.R., "Oxygen Transport Function of Preserved Red Cells," *Clinics in Hematology*, 3:649–668, 1974.

(9) Schorr, J.B., and G.F. Marx, "New Trends in Intraoperative Blood Replacement," *Anesthesia and Analgesia*, 49:646–651, 1970.

(10) "General Principles of Blood Transfusion," Greenwalt, T.J., Editor, *American Medical Association*, Chicago, Illinois, pp. 3–5, 1973.

(11) Chaplin, H., E. Beutler, J.A. Collins, E. Giblett and H. Polesky, "Current Status of Red-Cell Preservation and Availability in Relation to the Developing National Blood Policy," *New England Journal of Medicine*, 291:68–74, 1974.

(12) McCullough, J., "Packed Red Blood Cells," *Minnesota Medicine*, 56:290–292, 1973.

(13) Barrett, D.L., Letter to the Editor, *Journal of the American Medical Association*, 235:2585, 1976.

(14) Ryden, S.E., and H.A. Oberman, "Compatibility of Common Intravenous Solutions with CPD Blood," *Transfusion*, 15:250–255, 1975.

**7. Frozen Red Blood Cells (Human)**

*Generic Statement*

1. *Introduction.* The development of methods for cryopreserving blood was predicated on the perceived need for long-term storage. Vagaries in blood collections, daily and seasonal, as well as uncertainties in usage contributed to episodic cycles of blood shortages followed by excesses and, thus, outdating. Prolonged extension of the blood's shelf life was seen as a possible way of circumventing these variables and making more effective use of collected blood.

Expansion of techniques for antibody identification and the description of new red cell phenotypes during the past two decades also resulted in the need for long-term storage. Patients with antibodies directed against high incidence antigens require a ready resource of homologous or autologous blood. This could be accomplished by extending the shelf life of blood indefinitely.

A number of techniques for red cell cryopreservation have been developed and are in routine use (Refs. 1 through 4), but only two have been licensed by the Food and Drug Administration (Refs. 1 and 3). Although methods vary considerably, they have one common major requirement: The necessity of adding the cryoprotective agent, glycerol, prior to freezing. Since the intravenous administration of large amounts of glycerol is undesirable, previously frozen, glycerol-protected blood must be washed prior to transfusion. This is also required to return the cells to an isosmotic state, since glycerol penetrates the red cells in exerting its cryoprotective effect.

The cost of washing, in both dollars and time, has restricted severely the routine use of previously frozen red cells of purposes of balancing inventory. Furthermore, techniques of freezing and washing red cells require multiple entries into the blood pack, thereby restricting the post-thaw shelf life to a mere 24 hours according to current practice. However, an impressive number of other possible advantages resulting from either freezing and/or thawing have come to light which appear to be separate from the long shelf life of frozen red cells but which at this time play a greater role in their clinical use. Verification of these presumed benefits of frozen red cells might well determine the extent of their use in the near future. Despite these considerations, it is estimated, based on data accumulated within The American Red Cross Blood Program, that no more than 3 to 5 percent of all blood transfusions are currently accomplished with frozen red blood cells.

2. *Effectiveness*—a. *Red cell studies.* The recovery of red cells after glycerolization, freezing, thawing and deglycerolization (washing) varies between 70 to 93 percent of the original starting material and depends largely on the method used for the freeze-thaw procedure (Refs. 3 and 27). Most studies report that at least 85 percent of the red cells are recovered when a high-glycerol technique is used and if deglycerolization is done using one of the three currently available centrifuge techniques. More controversy exists in evaluating the technique of cytoagglomeration where some investigators report recoveries as low as 70 percent, although others have found 85 percent recovery (Refs. 1 and 27).

Analysis in vitro of the final deglycerolized product comparing various washing technique has been performed by Valeri (Ref. 28). He found that the red cell products obtained by the cytoagglomeration techniques had higher levels of supernatant hemoglobin, extracellular potassium ion, supernatant osmolality, residual glycerol, and residual plasma protein than did cells washed by any of the currently available centrifuge methods, all of which seem to give comparable results for these measured characteristics.

Measurements of survival of deglycerolized red cells 24 hour after transfusion demonstrate differences depending on the method employed in freeze-thawing and the duration of storage in the frozen sate (Ref. 29). For the cytoagglomeration technique, in one study of 18 units stored frozen for a mean of 3.8 $\pm$ 1.5 years, a mean 24-hour survival of 73 percent plus or minus 17.5 [2 S.D.] was found. It has also been demonstrated that with this method there is a correlation between the duration of storage in the frozen state and the 24-hour red cell survival (Ref. 4). When using one of the centrifugal methods for deglycerolization, higher 24-hour survivals are usually obtained, especially in direct comparative studies with the cytoagglomeration method. Furthermore, the results obtained by these methods do not seem to be affected by duration of frozen storage.

When using the cytoaggolmeration technique it has been found that nearly 50 percent of all units have a positive direct antiglobulin test. This finding, however, could not be correlated with any alterations in the 24-hour red cell survival (Ref. 30).

Frozen deglycerolized red cells require a two-faceted evaluation; the recovery of cells in vitro after freeze-thaw injury and the survival of these cells after transfusion. These characteristics are of importance to the recipient as they relate directly to the expected benefit after transfusion of "one unit." As there is red cell loss during the freeze-thaw process which is related to variations in methods used for freeze-thawing, as well as variations in post-transfusion recovery related to the same methods, each technique could result in wide variations in therapeutic effectiveness of the resulting red cell product.

b. *Possible advantages of frozer blood.* Table 1 lists the possible advantages of frozen-deglycerolized red cells.

TABLE 1.—POSSIBLE ADVANTAGES OF FROZEN RED CELLS

| | Freezing | Washing |
|---|---|---|
| Leukocyte removal | ? | + |
| Removal of hepatitis B antigen | 0 | ? |
| Plasma protein removal | ? | + |
| Diphosphoglycerate maintenance | + | 0 |
| Long-term storage of rare types | + | 0 |
| Salvage of outdated blood | + | + |
| Inventory control | + | - |
| Microaggregate removal | 0 | + |

? Unknown; + Contributes an advantage; 0 Probably unrelated to an advantage; - Deleterious.

In each case in Table 1 the role of either the freezing or thawing processes is assessed as being contributory, unrelated, or deleterious to the desired result. In many cases, the washing procedure appears to be far more important than freezing. This suggests that washing alone without prior freezing may be sufficient to achieve many of the proposed advantages of frozen red cells. Thus, the efficiency of washing is critical in determining some of the possible advantages of frozen red cells. Variables in washing techniques, such as wash volume or whether batch or continuous flow washing is used, may determine how well suited a particular method is for achieving a desired property of the red cell preparation such as leukocyte or hepatitis agent removal. A corollary is that efforts to reduce the time and expense of the washing procedure might result in a loss of some of the possible advantageous aspects of frozen red cells. The limit of effective washing of red cells has not yet been determined.

(1) *Leukocyte removal.* For several transfusion situations, contamination of red cell preparations with leukocytes is undesirable. There are four problem areas in which the presence of leukocytes appears to play a major role: (1) Nonhemolytic febrile transfusion reactions are largely the result of immunization to leukocyte and/or platelet antigens. (2) Refractoriness to platelet transfusion has been correlated with previous transfusions with leukocyte and platelet-containing blood products. The use of previously frozen red blood cells may minimize this problem. (3) Immunization to leukocyte and platelet antigens of the HLA and other systems by transfusion may compromise the survival of future allografts, although this concept has recently been brought into serious doubt. (4) Leukocyte-borne viruses may cause disease in recipients. In addition to these problems, the transfusion of viable lymphocytes to immunosuppressed recipients has been suggested to be hazardous by virtue of causing graft versus host disease.

Compared with liquid-stored blood, frozen-washed red cells have few leukocytes and virtually no platelets. There is considerable disagreement over the extent of leukocyte removal achieved by this method. Table 2 indicates the extent of red cell losses and leukocyte reduction achieved with some current freeze-thawing techniques (Table 2). It appears that the freezing process may play an important role in Facilitating efficient leukocyte removal by simple destruction since current methods for cryopreserving red cells are not effective for preserving leukocytes or platelets. Some studies suggest that some lymphocytes may be resistant to the rigors of this method of cryopreservation (Ref. 13). Undoubtedly, the necessary post-thaw washing also plays a role in leukocyte removal. Despite this, more complete removal of HLA antigenicity may require micropore filtration during transfusion (Ref. 14). Leukocyte removal also can be achieved without freezing using a variety of separation techniques (Table 2).

TABLE 2.—RED CELL LOSSES AND LEUKOCYTE REDUCTION ASSOCIATED WITH VARIOUS CRYOPRESERVATION METHODS

| Method | Percent RBC loss | Percent leukocyte reduction | Reference No. |
|---|---|---|---|
| Freezing Procedures: | | | |
| Freezing (cytoagglomeration) (ACD) | 37 | 84 | 21 |
| Freezing (cytoagglomeration) (CPD) | 27 | 61 | |
| Freezing (centrifugal) (fresh cells) | 5 | 93 | 17 |
| Other Procedures: | | | |
| Inverted spin | 24 | 80 | 25 |
| Inverted spin plus continuous flow wash | 42 | 80 | |
| Dextran sed plus continuous flow wash | 35 | 92 | |
| Inverted spin | 21 | 73 | 19 |
| Upright spin | 20 | 72 | |
| Nylon filter | 12 | 65 | |
| Nylon filter then inverted spin | 32 | 97 | |
| Upright spin, then nylon filter | 40 | 97 | |
| Upright spin, then inverted spin | 22 | 87 | |
| Dextran sedimentation | 8 | 93 | 22 |
| Plasmagel sedimentation | 6.5 | 93.5 | |

Regardless of the underlying mechanism, the need for transfusions of leukocyte-poor blood is currently the major indication for using frozen-washed red cells.

Frozen-washed red cells appear to be effective for patients who have been transfused frequently and who have had repeated febrile reactions due to antibodies to transfused leukocytes. In some transfusion services frozen-washed red cells are used prophylactically for patients in whom long-term transfusion therapy is anticipated. Most users of frozen blood for this purpose have noted an almost complete absence of nonhemolytic, febrile transfusion reactions but published data on this point are lacking. These clinical observations have been supported by preliminary studies on the production of cytotoxic and agglutinating luekocyte antibodies following frozen blood transfusion.

Probably the most common use of frozen blood is in patients with chronic renal disease either on a dialysis program or as part of a renal transplant procedure. Approximately 50 percent of all frozen red blood cell transfusions in the Red Cross program are in this category. Here the use of frozen cells is predicated on their presumed lack of immunogenicity in the HLA system because few leukocytes are present in the final transfusion product. It is postulated that the rejection rate of a renal homograft could be diminished with the use of frozen red cell transfusions. Conversely, results from a retrospective, multicenter study have suggested that transfusion might actually be protective against renal allograft rejection possibly by stimulating the production of "blocking" antibodies (Ref. 5). More recent studies indicate that homograft survival is in fact better in recipients previously transfused with liquid stored blood containing leukocytes than in nontransfused recipients (Refs. 31, 32, 33, 39 and 40). These studies bring sharply into question the current general use of this blood product for this indication.

(2) *Risk of hepatitis.* The report of Tullis et al. (Ref. 6) on the absence of hepatitis in recipients of previously frozen blood was a major force in accelerating development of freeze-thaw technology and in the clinical use of this blood product. Another retrospective study confirms this observation (Ref. 34). In a limited prospective study, Valeri (Ref. 35) demonstated that washing blood prior to transfusion reduced the infectivity rate for Hepatitis B. Recent studies indicate, however, that HBsAg infectivity can be transmitted to chimpanzees transfused with frozen deglycerolized red blood cells washed by continuous flow techniques (Ref. 37). More extensive controlled studies on this question are necessary to quantify this effect.

It has been demonstrated that Hepatitis B surface antigen (HBsAg) cannot be detected even by the most sensitive techniques in blood thoroughly used by either a batch process or by continuous flow (Ref. 7). The latter technique, which can achieve a plasma protein dilution of 1:25,000, produce a 40-

fold greater protein dilution than triple washing in a batch process. Therefore, continuous flow might be the preferable method, particularly since HBsAg can be passively transferred to recipients even if it is transfused at great dilution. This question may be crucial since freeze-wash methods that utilize batch washing procedures may be at a theoretical, if not a real, disadvantage (Ref. 35). This difficult question requires very careful study.

(3) *Plasma protein removal.* Frozen-washed red cell preparations are largely devoid of plasma protein. Thus, transfusion reactions resulting from previous immunization to plasma proteins such as anaphylaxis due to sensitivity to IgA, or from passively administered antibodies such as those to penicillin may be eliminated by using frozen blood. Freezing may play some role by facilitating the removal during the washing procedure of some proteins previously bound to the red cell surface. A patient with sensitivity to IgA was transfused safely only with blood that was both frozen and washed but not with blood without prior glycerolization and freezing (Ref. 8).

The absence of anti-A and anti-B alloagglutinins in freeze-washed red cells makes this product safe when used judiciously in recipients of other ABO groups, Group O to any recipient, Group A or B to AB recipients. This is helpful from the point of view of the transfusion service because it permits greater flexibility in selecting compatible blood. Also, units of blood containing unexpected antibodies can be diverted into the frozen blood inventory. The antibodies present in these units are then removed during the deglycerolization-wash procedure.

(4) *Maintenance of red cell diphosphoglycerate (DPG).* Much recent research has been directed towards developing methods for maintaining DPG levels and oxygen-releasing capability in stored erythroocytes. Red cells stored in the frozen state show no diminution of DPG levels after thawing when compared with pre-freeze levels (Refs. 9 and 10). Since most blood is frozen soon after collection, DPG levels are maintained at levels approaching those of freshly drawn blood. Red cells with normal DPG levels may have some applications in special transfusion situations, but more carefully designed and controlled studies are necessary to establish this point (Ref. 12).

(5) *Long-term storage of rare blood types.* Freezing permits long-term storage of red cells which are negative for various high-incidence antigens or other uncommon antigen phenotypes for future transfusion into immunized recipients. This is an important but uncommon application of cryopreservation, which represents less than 5 percent of all frozen blood usage in the Red Cross Blood Service.

(6) *Salvage of outdated blood.* Valeri and Zaroulis have demonstrated recently that blood collected in ACD or CPD and stored at 4° C for up to 28 days can be "rejuvenated" by incubation at 37° C for 1 hour with pyruvate, inosine, glucose, and phosphate (Refs. 10 and 11). Subsequent freezing, thawing, and washing yielded an 86.6 percent in vitro recovery of red cells having a 24-hour post-transfusion survival in vivo of 80 percent. The oxygen transport function of these cells was the same as that of freshly collected blood. Post-thaw washing was necessary to remove the potentially toxic materials used for rejuvenation. This technique offers a possible new approach to control of red cell outdating. Rejuvenation and freezing may play some role where salvage of specially selected red cells such as those of uncommon phenotype is necessary.

(7) *Removal of microaggregates.* It is generally assumed that the majority of microaggregates in stored blood are removed during the washing procedure although data establishing this point are lacking. A recent study suggests that some microaggregates remain which can be removed by micropore filtration (Ref. 14).

3. *Safety.* In general, most of the hazards related to liquid-stored whole blood or red blood cells apply to frozen deglycerolized cells as well. Some of the areas where it has been well established that frozen deglycerolized red cells have higher levels of safety include: treatment of patients with previous nonhemolytic febrile transfusion reactions, treatment of patients with allergy to plasma proteins, in decreasing immunization to leukocyte or platelet antigens where that may be desirable, in maintenance of red cell DPG levels, and in non-ABO specific transfusions where alloantibody removal is desirable. Increased safety related to hepatitis transmission has not been proven. Use of frozen blood in hemodialysis patients for improving later allograft survival now seems questionable.

The freeze-thaw process itself adds certain potential hazards. Adequate removal of glycerol must be achieved. The ionic constitution and concentration of the final wash solutions may be of some concern if they do not approach normal plasma levels in the final preparations. The possibility of bacterial contamination of the final product because of its preparation in an open system is an additional hazard. The current 24-hour post-wash shelf life for frozen deglycerolized blood is consistent with similar guidelines for other blood preparations prepared in open systems. In one study of this issue, units of whole blood were inoculated with a variety of bacteria prior to freezing or after deglycerolization. These units were evaluated for bacterial contamination after postdeglycerolization storage for 72 hours at 4 °C (Ref. 36). It was demonstrated that, (a) the deglycerolization procedure reduces the bacterial inoculum substantially and (b) the bacteria evaluated in this study do not proliferate in the deglycerolized red cell product for up to 72 hours when properly stored. It was later noted that one cryophillic bacterial species did proliferate under these conditions.

4. *Recommendations.* a. The Panel recommends that Frozen Red Blood Cells (Human) be placed in Category I.

b. Frozen deglycerolized red blood cells must be prepared by a method that results in a minimum in vitro yield of 80 percent of the original red cell mass.

c. Frozen deglycerolized red blood cells must meet the same viability requirements as liquid stored blood, namely, the method must be designed to assure that, on the last storage day, at least 70 percent of the cells survive in the recipient 24 hours after transfusion.

d. The effective yield after deglycerolization must be 65 percent. The effective yield is determined by multiplying the mean in vitro yield after deglycerolization by the mean percentage in vivo survival 24 hours after transfusion.

e. If the above criteria are met and if it can be shown that there is no increased risk to the recipient of bacterial contamination when compared with liquid-stored blood prepared in a closed system, the post-deglycerolization shelf life should be extended beyond the presently permitted 24 hours.

f. Glycerolized blood may be stored in the frozen state for any period of time as long as it has been demonstrated that the above criteria are met.

g. After deglycerolization, the final suspending solution should be isotonic and contain between 130 and 160 mEq sodium per liter.

h. In-process controls of the freezing and deglycerolization procedure should be such as to assure that there shall be no more than 0.5 gram per dL of glycerol and 175 mg per dL of supernatant hemoglobin in the final product (Ref. 38).

**References**

(1) Huggins, C.E., "Practical Preservation of Blood by Freezing," *in* "Red Cell Freezing,

American Association of Blood Banks Workshop," pp. 31–54, 1973.

(2) Rowe, A.W., "Preservation of Blood by the Low Glycerol-Rapid Freeze Process," *in* "Red Cell Freezing, American Association of Blood Banks Workshop," pp. 55–72, 1973.

(3) Meryman, H.T., "A High Glycerol Red Cell Freezing Method," *in* "Red Cell Freezing, American Association of Blood Banks Workshop," pp. 73–86, 1973.

(4) Valeri, C.R., "Principles of Cryobiology, High Glycerol Storage at −80 °C and Low Glycerol and Storage at −150 °C," *in* "Red Cell Freezing, American Association of Blood Banks Workshop," pp. 73–86, 1973.

(5) Opelz, G. and P.A. Terasaki, "Poor Kidney-Transplant Survival in Recipients with Frozen-Blood Transfusion or No Transfusions," *Lancet* ii:696–698, 1974.

(6) Tullis, J.L., J. Hinman, M.T. Sproul and R. Nickerson, "Incidence of Posttransfusion Hepatitis in Previously Frozen Blood," *Journal of the American Medical Association*, 214:719–723, 1970.

(7) Button, L.N., S.V. Kevy, S.B. Shohet and M.N. Oxman, "The Effects of Continuous-flow Washing in Stored Red Blood Cells," *Transfusion*, 12:84–93, 1972.

(8) Miller, W.V., P.V. Holland, E. Sugarbaker, W. Strober and T. Waldmann, "Anaphylactic Reactions to IgA," *American Journal of Clinical Pathology*, 54:618–621, 1970.

(9) Valeri, C.R., "Viability and Function of Preserved Red Cells," *New England Journal of Medicine*, 284:81–88, 1971.

(10) Valeri, C.R. and C.G. Zaroulis, "Cryopreservation and Red Cell Function," *in* "Progress in Transfusion and Transplants," published by American Association of Blood Banks, pp. 343–365, 1972.

(11) Valeri, C.R. and C.G. Zaroulis, "Rejuvenation and Freezing of Outdated Stored Human Red Cells," *New England Journal of Medicine*, 287:1307–1313, 1972.

(12) Valeri, C.R., "Viability and Function of Preserved Red Cells," *Wadley Medical Bulletin*, 5:205–238, 1975.

(13) Telischi, M., E. Krmpotic and G. Moss, "Viable Lymphocytes in Frozen Washed Blood," *Transfusion*, 15:481–484, 1975.

(14) Crowley, J.P., M. O'Donnell, K.W. Sell and C.R. Valeri, "The Purification of Red Cells for Transfusion by Freeze-Preservation and Washing. IV. The Use of Micropore Filtration to Reduce the Residual HL-A Antigenicity of Previously Frozen, Washed Red Cells," *Transfusion*, 15:34–38, 1975.

(15) Crowley, J.P. and C.R. Valeri, "The Purification of Red Cells for Transfusion by Freeze-Preservation and Washing: III. Leukocyte Removal and Red Cell Recovery After Red Cell Freeze-Preservation by the High or Low Glycerol Concentration Method," *Transfusion*, 14:590–594, 1974.

(16) Fuller, T.C., C.E. Huggins and P.S. Russell, XIV Congress of the International Society of Blood Transfusion, Helsinki, Finland, Book of Abstracts, p. 63, 1975.

(17) Meryman, H.T. and M. Hornblower, "Red Cell Recovery and Leukocyte Depletion Following Washing of Frozen-thawed Red Cells," *Transfusion*, 13:388–393, 1973.

(18) Miller, W.V., R. Luke and R. Schmidt, XIV Congress of the International Society of Blood Transfusion, Helsinki, Finland, Book of Abstracts, p. 64, 1975.

(19) Miller, W.V., M.J. Wilson and H.J. Kalb, "Simple Methods for Production of HL-A Antigen Poor Red Blood Cells," *Transfusion*, 13:189–193, 1973.

(20) Perkins, H.A., "Prevention of HL-A Antibody Formation in Dialysis Patients," *Transfusion*, 14:509, 1974.

(21) Perkins, H.A., I. Senecal and E. Howell, "Leukocyte Contamination of Red Cells in Leukocyte-Poor and Frozen-Deglycerolized Units," *Transfusion*, 13:194–199, 1973.

(22) Polesky, H.F., J. McCullough, M.A. Helgerson and C. Nelson, "Evaluation of Methods for the Preparation of HL-A Antigen-Poor Blood," *Transfusion*, 13:383–387, 1973.

(23) Polesky, H.F., J. McCullough, M.A. Helgerson and M. Bolemendal, XIV Congress of the International Society of Blood Transfusion, Helsinki, Finland, Book of Abstracts, p. 63, 1975.

(24) Sumida, S. and M. Sumida, XIV Congress of the International Society of Blood Transfusion, Helsinki, Finland, Book of Abstracts, p. 65, 1975.

(25) Tenczar, F.J., "Comparison of Inverted Centrifugation, Saline Washing, and Dextran Sedimentation in the Preparation of Leukocyte-poor Red Cells," *Transfusion*, 13:183–188, 1973.

(26) Tovey, G.H., R.M. Hutchinson, S.A. Sejeny and I.D. Fraser, XIV Congress of the International Society of Blood Transfusion, Helsinki, Finland, Book of Abstracts, p. 63, 1975.

(27) Valeri, C.R., "Blood Banking and The Use of Frozen Blood Products," Canadian Red Cross Press, p. 178, 1976.

(28) Valeri, C.R., "Blood Banking and The Use of Frozen Blood Products," Canadian Red Cross Press, pp. 85 and 177, 1978.

(29) Valeri, C.R. and A.H. Runck, "Long-term Frozen Storage of Human Red Blood Cells: Studies *in vivo* and *in vitro* of Autologous Red Blood Cells Preserved up to Six Years with High Concentrations of Glycerol," *Transfusion*, 9:5–14, 1969.

(30) Valeri, C.R., "The *in vivo* Survival of Coombs Positive Autologous Erythrocytes Produced by Agglomeration," *Transfusion*, 6:247–253, 1966.

(31) Festenstein, H., J.A. Sachs, A.M. I. Paris, G.D. Pegrum and J.F. Moorhead, "Influence on HLA Matching and Blood-Transfusion on Outcome of 502 London Transplant Group Renal-Graft Recipients," *Lancet*, i:157–161, 1976.

(32) Opelz, G. and P.I. Terasaki, "Pro-Longation Effect of Blood Transfusions on Kideny Graft Survival," *Transplantation*, 22:380–383, 1976.

(33) van Es, A.A., R.L. Murquet, J.J. Van · Rood, M.W. Klaff and H. Balner, "Blood-transfusions Induce Prolonged Kidney Allograft Survival in Rhesus Monkeys," *Lancet*, i:506–509, 1977.

(34) Huggins, C.E., P.S. Russell, H.J. Winn, T.C. Fuller and C.H. Beck, "Frozen Blood in Transplant Patients: Hepatitis and HL-A Isosensitization," *Transplantation Proceedings*, 5:809–812, 1973.

(35) Valeri, C.R., "Blood Banking and The Use of Frozen Blood Products," *Canadian Red Cross Press*, pp. 342–353, 1976.

(36) Kahn, R.A., H.T. Meryman, R.L. Syring and L.J. Flinton, "The Fate of Bacteria in Frozen Red Cells," *Transfusion*, 16:215–220, 1976.

(37) Alter, H.J., E. Tabor, H.T. Meryman, J.H. Hoofnagle, R.A. Kahn, P.V. Holland, R.J. Gerety and L.F. Barker, "Transmission of Hepatitis B Virus Infection by Transfusion of Frozen-deglycerolized Red Blood Cells," *New England Journal of Medicine*, 298:637–642, 1978.

(38) Valeri, C.R., "Simplification of the Methods for Adding and Removing Glycerol During Freeze-Preservation of Human Red Blood Cells with the High or Low Glycerol Methods: Biochemical Modification Prior to Freezing," *Transfusion*, 15:195–218, 1975.

(39) Opelz, G. and P.I. Terasaki, "Improvement of Kidney-Graft Survival with Increased Numbers of Blood Transfusions," *New England Journal of Medicine*, 299:799–803, 1978.

(40) Vincenti, F., R. Duca, W. Amend, H.A. Perkins, K.C. Cochrum, N.J., Feduska and O. Salvatierra, "Immunologic Factors Determining Survival of Cadaver-Kidney Transplants," *New England Journal of Medicine*, 299:793–798, 1978.

### 8. Cryoprecipitated Antihemophilic Factor

*Generic Statement*

1. *Introduction.* In 1954 Brinkhous (Ref. 1) first made the observation that factor VIII (antihemophilic factor, AHF) was a cold insoluble protein. In 1959, Pool and Robinson (Ref. 2) made a similar observation while studying plasma preparations of factor VIII. However, it was not until 1965 that Pool and Shannon (Ref. 3) described a method for the practical utilization of factor VIII cryoprecipitability to prepare cryoprecipitated Antihemophilic Factor (Human) ["Cryoprecipitate", "Cryo"] as a part of routine blood banking. The procedure involves freezing plasma with subsequent thawing at 4° C yielding a precipitate containing about 45 percent of the original factor VIII and 30 to 40 percent of the fibrinogen. After centrifuging, the supernatant plasma is drained and the residual cryoprecipitated factor VIII is refrozen. It is a simple, inexpensive way to provide factor VIII as a byproduct of component blood banking. The major problem has been the unpredictable yield of factor VIII making dosage calculations difficult (Ref. 4). However, recent studies (Refs. 5 and 6) have analyzed the variables of production which may affect yield. This has given a standardized method which consistently provides an average of 60 percent of the available plasma factor VIII in the cryoprecipitate. In addition to Cryoprecipated Antihemophilic Factor (Human), commercial Antihemophilic Factor (Human) has subsequently been licensed and is reviewed elsewhere in this document.

2. *Factor VIII assay.* The two major techniques of assaying factor VIII are based on the partial thromboplastin time (PTT) (Ref. 7) or thromboplastin generation time (TGT) (Ref. 8). These methods originally were developed for measuring factor VIII levels in plasma. One hundred percent activity was based on an appropriate-sized normal donor pool (10 to 30 donors) or the then-available NIH reference standard. These assays were shown to predict the recovery of factor VIII when plasma was transfused into hemophilia A recipients. Although the assays correlate with each other to a high degree, both have a variability within the assay system of 7 to 10 percent. The increased concentration of factor VIII in more recent cryoprecipitate procedures has required modification of the assay systems to give reliable measurements. The major change suggested for both assays (Refs. 3 and 9) was an initial dilution of cryoprecipitate 1 to 9 in hemophiliac plasma with further dilutions in buffer to give a factor VIII concentration within the range of the standard assay curves; i.e., 0 to 100 percent activity. In spite of these modifications the assays may not predict the recovery in vivo (Refs. 3 and 5). However, studies comparing the two methods for measuring factor VIII in cryoprecipitates have shown that they are comparable (Refs. 5 and 10). Because of the often unexplained differences between in vitro factor VIII assays and in vivo factor VIII recoveries (Refs. 3, 5 and 11 through 15), facilities preparing Cryoprecipitated Antihemophilic Factor (Human) should document the reliability of the in vitro assay system used by measuring in vivo recoveries of factor VIII following the infusion of their cryoprecipitate into hemophilia A recipients (Refs. 3 and 5).

3. *Donor variables.* Several different characteristics of the donor have been claimed to be associated with higher plasma factor VIII levels and presumably a greater yield of factor VIII in cryoprecipitates prepared from this starting plasma.

a. *Factor VIII levels in the normal population.* It has consistently been shown that the normal population has a wide range of factor VIII activity from 50 to 200 percent and that this level may not even be the same for a donor on every occasion (Refs. 7 and 16 through 19). The greater the factor VIII activity of the initial plasma the greater the expected yield of factor VIII in cryoprecipitate. However, some studies have suggested that not all donors have the same degree of cryoprecipitability (Refs. 6 and 17). Nevertheless, this baseline factor VIII variability in the donor is probably the major factor in the spread of factor VIII activity in individual units of cryoprecipitate.

b. *Exercise.* Exercise has been shown to increase the factor VIII concentration in plasma 1½ to 3 times normal (Refs. 14 and 20 through 25) and in those studies where it has been evaluated an increase in factor VIII antigen has also been found. The immunologic data suggest that the increase in procoagulant activity represents a true elevation of factor VIII protein.

However, transfusions of plasma from exercised donors into hemophiliacs have shown a decreased factor VIII recovery (Ref. 20) and shortened half-life of 5 hours compared to the normal of 10 to 13 hours (Ref. 22). In vitro assay of cryoprecipitates prepared from exercised plasma donors over-estimated the in vivo yield (Ref. 14). Therefore, exercising donors does not represent a useful means of increasing the production of factor VIII.

c. *Other variables.* Age, sex, and blood group are other possible donor variables. Preston (Ref. 16) found factor VIII activity to be 6.5 percent greater in females ($p < 0.05$), 8 percent greater in A or B blood group donors than those of group O ($p < 0.01$) and unaffected by the age of the donor in an analysis of plasma from 410 individuals. In contrast, similar studies by Burka (Ref. 17) in 169 donors showed no significant differences in any of these parameters.

4. *Preparation variables*—a. *Sources.* Either single units of whole blood or plasmapheresis may be used as a source of starting plasma. Some studies have reported an averaged 15 percent reduction in factor VIII activity in the second unit of a double plasmapheresis (Refs. 17 and 26), while others have found no differences (Refs. 5 and 6). The reported differences in plasma factor VIII levels between plasmapheresis units are small enough that they do not statistically affect factor VIII yield in cryoprecipitates (Ref. 17).

b. *Collection*—(1) *Anticoagulant.* The anticoagulant used, whether ACD or CPD, does not affect the yield of factor VIII in cryo (Refs. 5, 17, 27, and 28) nor does the addition of adenine (Ref. 29). Factor VIII blood is mixed thoroughly at the end of collection. Factor VIII content is most stable at pH values greater than 6.8 (Ref. 28) and preparation of cryoprecipitate from ACD plasma with a pH of 6.5, as may occur after preparation of platelet concentrates, is associated with a 43-percent average reduction in the in vivo factor VIII yield (Ref. 11).

(2) *Container.* The collection container, plastic or glass, does not affect AHG yield (Refs. 5, 18, and 19).

(3) *Mixing during collection.* Perkins (Ref. 19) found a significant improvement in factor VIII levels in blood collected by a rocking vacuum device compared to gravity blood flow. Plasma Factor VIII levels were better in fresh plasma with approximately 93 percent of expected levels with the vacuum method versus 80 percent by gravity flow ($p < 0.05$). Similar differences were found after frozen storage of the plasma for 2 months. Subsequent studies, however, have shown that as long as the blood is mixed thoroughly at the end of collection, factor VIII content of cryoprecipitate does not differ significantly from that prepared from blood agitated throughout the collection (Refs. 5 and 6).

(4) *Delay before processing.* Whole blood stored at 4° C progressively loses factor VIII activity (Refs. 5, 6, and 30) with a loss at 24 hours approaching 50 percent of the initial factor VIII activity. However, if the plasma has been frozen solid within 6 hours of collection, the loss is only 10 percent (Ref. 5). Further fractionation of this plasma showed recovery of factor VIII in the cryoprecipitate is also 10 percent less both in vitro and in vivo. This loss appears to be acceptable to provide flexibility in processing blood from mobile blood collection facilities. Alternatively, mobile laboratories for cryoprecipitate production have been shown to be feasible (Ref. 31). As expected, outdated 21-day-old blood has been shown to be an unacceptable source of factor VIII because of the low starting levels of factor VIII (30 percent), lower cryoprecipitability of this material, and high plasma hemoglobin levels in blood more than 14 days old (Ref. 32).

c. *Plasma processing*—(1) *Centrifugation.* Centrifugation at 4,500 X g for 10 minutes leaves an average residual platelet count of 25,000/microliter (Ref. 5). Longer periods of centrifugation to reduce the level of platelets was not associated with any difference in factor VIII recovery in cryoprecipitate (Refs. 5 and 17).

(2) *Freezing rate, freezing temperature and volume of plasma.* Fifteen to thirty percent of the original factor VIII activity has been reported to be lost consistently during plasma freezing at −30 °C or −70 °C (Refs. 3, 13, 18, and 33) with subsequent storage at −30 °C. Later studies by Perkins (Ref. 19) and Rappaport (Ref. 34) have documented only a 10-percent loss in factor VIII activity after 2 months of plasma storage

and 20 percent after 1 year at −30 °C. They, as well as others (Ref. 35), have suggested that the major loss of factor VIII activity occurs with freezing and that factor VIII is stable during storage.

Factor VIII yield in frozen plasma can be improved by reducing the plasma volume (Refs. 5 and 13) or conversely, by increasing the size of the bag and thus the surface-to-volume ratio (Ref. 6). Therefore, studies of factor VIII recovery in plasma and its stability with storage must be done using the volume and bag size routinely used in blood banking. Certainly, some of the differences in factor VIII yield in the reported studies may be related to freezing rate if too many bags are put in the freezing container at one time thereby changing the time-temperature relationship and subsequently the rate of freezing. Although the freezing temperature of −30 °C vs. −70 °C has been suggested to be unimportant (Ref. 6), it is not clear that these experiments were done with the usually accepted volume of plasma, i.e., 250 mL. Other investigators have clearly shown that with full plasma volumes the freezing temperature must be −70 °C or below and that this temperature maintains 100 percent factor VIII recovery in the plasma for storage periods up to 3 months (Ref. 5).

Clearly, one significant technical problem may be the speed with which the factor VIII assay is done after sample thawing, as Hawkey (Ref. 18) has shown that after 1 hour at room temperature, the factor VIII level falls by 25 to 56 percent. In addition, Perkins (Ref. 19) has shown the instability of previously frozen factor VIII by documenting that refreezing plasma causes a further 50-percent reduction in factor VIII activity.

These data suggest that freezing at temperatures below −70 °C preserves 100 percent of factor VIII activity and subsequent storage at or below −30 °C will be associated with negligible loss of factor VIII activity. If freezing is done in a liquid medium, an overwrap should be used to prevent interaction of the freezing liquid with the plastic bag and its contents.

(3) *Thawing*—(a) *Temperature of thawing.* The most critical variables in cryoprecipitate production are probably the thawing temperature, the degree of thawing, i.e., to slush with ice crystals or completely thawed, and the solubility of cryoprecipitated factor VIII in its supernatant plasma. The usual yield of factor VIII in cryoprecipitate based on the factor VIII in fresh plasma has been in the range of 35 to 55 percent (Refs. 3, 13, 17, 35, and 36) with an average of 45 percent. These results are found when plasma is thawed at 4 °C in air, a process requiring 18 to 24 hours. Brown (Ref. 9) first demonstrated that rapid thawing of plasma at 6 to 8 °C, which takes approximately 90 minutes, yielded 87 percent of the original factor VIII content of the plasma minus the amount of factor VIII found in the cryo-poor supernatant which averaged 22 percent. However, in this study the plasma was transferred to 610 cc bags for freezing between metal plates, and therefore the results of this study are not applicable to clinical practice. Waumens (Ref. 12) reduplicated the original study, except he employed commonly used plasma volumes and bag sizes. There was a 26-percent factor VIII recovery in cryoprecipitate when plasma was thawed at 4 °C in air compared to 50 percent recovery for 6 to 8 °C water-thawed cryoprecipitate in this study. Subsequent in vivo recovery of this rapidly thawed cryoprecipitate was 90 percent of predicted. A subsequent study comparing 4 °C air to 4 °C water thawing has shown a consistent yield of 58 percent when water thawing is used compared to 45 percent when thawing was in air ($p < 0.01$) (Ref. 5). After in vivo infusion of these materials there was an even greater benefit of the water-thawed compared to the air-thawed material. However, these studies have not been confirmed by others (Refs. 6, 30, 37, and 38).

(b) *Partial thawing.* Cooke (Ref. 39) suggested that cryoprecipitates be thawed until the formation of ice crystals (slush phase) and that the crystals would act as a filter to retain the cryoprecipitate when the supernatant plasma was expressed. Both Burka (Ref. 17) and Slichter (Ref. 5) showed an increased recovery of factor VIII in cryoprecipitates brought to the slush phase compared to complete thawing at 4 °C in air—51 percent vs. 43 percent and 63 percent vs. 45 percent, respectively. However, in vivo infusions demonstrated that recovery was the same for both products (Ref. 5). It is difficult to standardize the end point at the slush phase.

(c) *Complete thawing.* The stability of cryoprecipitated factor VIII in superantant plasma after complete thawing has been studied. With 4 °C water thawing, cryoprecipitated factor VIII is stable for at least 2 hours (Refs. 5 and 6) with levels dropping to 61 percent plus or minus 12 at 33 hours ($p < 0.05$) and to 58 percent plus or minus 11 ($p < 0.01$) at 5 hours compared to a level of 69 percent plus or minus 11 for cryo in which the supernatant is immediately removed (Ref. 6). Similarly with air-thawed material at 4 °C, factor VIII activity in the cryoprecipitate decreases progressively after 12 hours of thawing with a concomitant increase in activity in the cryo supernatant plasma (Ref. 38).

After complete air-thaw factor VIII is stable for at least 6 hours in one study, 46 percent vs. 40 percent (Ref. 5), but significantly different at 4 hours in another, 53 percent vs. 47 percent ($p < 0.01$) (Ref. 6.).

(4) *Removal of supernatant plasma.* It does not seem to matter whether the cryo-poor supernatant plasma is drained off or expressed (Ref. 38).

5. *Cryoprecipitate Antihemophilic Factor storage and preparation for use*—a. *Freezing.* The available data indicate that for best results, cryoprecipitate after preparation should be refrozen at −30 °C or below (Ref. 6).

b. *Storage.* Factor VIII in frozen cryoprecipitate is stable at storage temperatures of −18 °C or below (Ref. 40).

c. *Thawing.* All studies reported in the literature have thawed the cryoprecipitate at 37 °C in a waterbath with gentle mixing. It is important that the bags are thawed for at least 15 minutes to ensure maximum factor VIII recovery (Ref. 5).

d. *Resuspension.* Cryoprecipitate has been reconstituted in either plasma, saline, or buffered saline (Ref. 28). When cryoprecipitate was prepared from small volumes of plasma (50 mL), thawed and resuspended, the dissolving solution made no difference (Ref. 28). Later studies have provided conflicting data on the best way to dissolve the cryoprecipitate. One study (Ref. 6) has shown that 20 ml. of plasma vs. 20 mL of saline gave factor VIII recoveries in the cryoprecipitate of 53 percent plus or minus 17 vs. 49 percent plus or minus 19, not statistically different. Furthermore, the duration of time that the material was within the bag before withdrawing did not affect factor VIII recovery. Another study (Ref. 5) has shown an optimum volume of 20 mL of saline left in the bag for 15 to 20 minutes before withdrawing gave factor VIII yields of 56 percent vs. 42 percent for 10 mL of plasma. These differences, confirmed in vivo by cryoprecipitate infusions into hemophiliac recipients, were significant ($p < 0.001$). In another study, draining the bag completely vs. leaving 5 mL of plasma made a significant difference in factor VIII recovery in vitro, 55 percent vs. 67 percent, respectively (Ref. 38).

Since saline resuspended cryoprecipitates can be provided on a nonblood group specific basis to most recipients, saline would seem to be the preferred diluent. If plasma is used as the diluent, the cryopercipitate has to be given as blood group ABO compatible.

How long the factor VIII activity is stable in the resuspended material has not been documented, but it has been shown that it cannot be refrozen or refrigerated without loss of 20 to 40 percent of the activity (Ref. 12).

e. *Pooling.* Pooling can be accomplished by syringe or vacuum devices, but should be done by experienced personnel either at the blood center before the material is sent out or at the hospital to ensure complete removal of all the concentrated material from each bag. When used for home care by hemophiliacs, appropriate training in its use must be provided. The pooled cryoprecipitates should be used as soon as possible, but must be used within 4 hours of entering the container. The resuspended cryoprecipitate should be left at room temperature prior to use (Ref. 12).

6. *Safety*—a. *Hepatitis.* Cryoprecipitate is expected to have the same risk of hepatitis as single donor plasma, but no data are available on this point. At least four cases of hepatitis have apparently been transmitted by cryoprecipitates (Refs. 43 through 46).

b. *Reactions.* Aberns (Ref. 47) reported 7 of 46 patients who had received cryoprecipitate from 4,363 donors had febrile reactions without other symptoms. Meyer (Ref. 43) reported no side-effects after the transfusion of 650 units of cryoprecipitate to 13 recipients.

Allergic reactions associated with cryoprecipitate are less severe and less frequent than with plasma (Ref. 40). Anaphylactic reactions have been described (Ref. 47).

c. *Factor VIII anticoagulants.* Two cases of patients with factor VIII inhibitors have specifically been reported following the administration of cryoprecipitates. One patient had received numerous plasma transfusions before being treated with cryoprecipitates for 13 days (Ref. 48) and the other had undergone three short courses of cryoprecipitate treatment in 4 weeks (Ref. 9). In 1969, 4 years after the introduction of cryoprecipitate, Strauss reported the incidence of acquired circulating anticoagulants in hemophilia A as 12 percent in the hemophilic patients studied (Ref. 49). However, the proportion was 16 of 77 (21 percent) of patients with factor VIII levels less than 1 percent of normal. Inhibitors did not occur on a familial basis, were found at a median age of 8 years (range 1 to 19 years), and developed after 20 to 90 exposure-days to factor VIII. No data were given on the relationship between a specific transfusion product and inhibitor formation.

It is apparent that cryoprecipitate transfusions are associated with the development of inhibitors but there is no evidence that their frequency is either more or less than that associated with other transfusion products containing factor VIII.

d. *Hemolysis due to blood group antibodies.* The titers of anti-A and anti-B in cryoprecipitates are the same as those of the starting plasma (Refs. 40 through 42). Severe hemolytic transfusion reactions have been reported after the transfusion of cryoprecipitates dissolved in plasma to ABO incompatible recipients (Refs. 41 and 50).

e. *Blood group isoantigen content of cryoprecipitate.* McShine (Ref. 51) has documented an increase in immune anti-A and anti-B titers following the transfusion of cryoprecipitates to patients with hemophilia and von Willebrand's disease. The exact interpretation of this observation is not clear.

f. *Hyperfibrinogenemia.* Since fibrinogen is concentrated in cryoprecipitates, repeated infusions may lead to high levels of fibrinogen. This hyperfibrinogenemia is usually innocuous (Ref. 39). However, roulex formation may be seen in blood films and samples (Refs. 35 and 52).

g. *Pulmonary reaction.* One case report has documented pulmonary infiltrates and hypoxemia resulting from cryoprecipitate administration (Ref. 53).

7. *Effectiveness*—a. *Factor VIII deficiency (Hemophilia A).* It has been well documented that Cryoprecipitated Antihemophilic Factor (Human) is effective in controlling spontaneous and operative bleeding in hemophilia (Refs. 9, 13, 39, 41, and 54 through 58). The dosage can be calculated on the basis of recovery of factor VIII in cryoprecipitate and the plasma volume of the recipient. There is an initial rapid disappearance of factor VIII activity, with a half-life of 3 to 5 hours and a subsequent slower disappearance with an apparent half-life of 8 to 12 hours. Transfusions of factor VIII are usually given on a 12-hour schedule in an attempt to maintain minimum levels of 10- to 15-percent factor VIII activity in the postoperative patient to prevent bleeding (Ref. 58).

Cryoprecipitate has also been shown to be effective in preventing spontaneous bleeding in hemophilics (Refs. 59 and 60).

b. *von Willebrand's disease.* Perkins and Bennett (Refs. 61 and 62) have reported correction of the bleeding time defect and elevation of factor VIII levels in patients with von Willebrand's disease given cryoprecipitates. In two of Perkins patients, purified preparations of factor VIII (Hyland's Hemophil™ and the American Red Cross Intermediate Potency AHG) were unable to correct the bleeding time although the factor VIII level was increased. Subsequently, Profilate (Abbott Laboratories) was shown to have similar properties. (Ref. 63). In fact, several studies have shown that failure to correct the bleeding time with commercial AHG concentrates was associated with continued bleeding even though factor VIII activity, factor VIII antigen and VW factor associated with platelet aggregation to ristocetin were appropriately increased following transfusion (Refs. 63 through 65). In the same patients in these studies cryoprecipitate improved the bleeding time and controlled the bleeding.

c. *Hypofibrinogenemia.* Since cryoprecipitates contain approximately one-third to one-fifth of the available plasma fibrinogen, it is possible to use pooled cryoprecipitates as a source of fibrinogen (Refs. 3, 9, 12, 29, and 43). Presumably a small pool of cryoprecipitates would result in a decreased incidence of hepatitis compared to transfusion of fibrinogen pooled commercial derived from plasma (Ref. 66). A fibrinogen level of 60 mg/100 mL is probably adequate to provide hemostasis; a rise in fibrinogen of this amount was obtained in two hemophilic patients with the transfusion of 10 units of cryoprecipitate once a week (Ref. 66). A normal in vivo disappearance rate of fibrinogen transfused from this material has been documented in rabbits (Ref. 67). In addition, Hattersley (Ref. 69) described the successful management of surgery in a woman with congenital fibrinogenemia with cryoprecipitates, as well as the treatment of patients with disseminated intravascular coagulation (DIC) and hypofibrinogenemia (Ref. 70).

8. *Recommendations.* It is recommended that Cryoprecipitated Antihemophilic Factor (Human) be placed in Category I. Further recommendations include:

a. Standardization of the factor VIII assay should be done by each registered establishment with the United States Standard as a reference or alternatively with a donor plasma pool of 10 to 30 normal individuals. In addition, in vitro assay results of cryoprecipitates must be correlated with the results of in vivo cryoprecipitate transfusions in which factor VIII recovery and survival in hemophilia A recipients is measured to document further the validity of the assay. Significant changes in the production process must be validated with repeat in vitro and in vivo factor VIII assays.

b. Assays of at least four units of cryoprecipitate per month should be done by each registered establishment to assure maintainance of an average potency of no less than 80 units of factor VIII per bag.

c. The following studies should be done in the future by the general medical research community of Federal agencies:

(1) To define the freezing and storage temperature of plasma to provide optimal initial and long-term stability of factor VIII,

(2) To document the best freezing temperature of the cryoprecipitate and its stability at varying storage temperatures, i.e., −20 °C, −30 °C vs. −70 °C and

(3) To evaluatte the best way to dissolve the thawed cryoprecipitate to maximize factor VIII yield and stability after resuspension. Measurements should be made at room temperature.

d. Labeling should indicate that:

(1) Cryoprecipitate contains approximately 80 units of factor VIII/bag.

(2) Cryoprecipitate usually contains at least 150 mg of fibrinogen/bag

(3) Good patient management requires monitoring treatment responses to cryoprecipitate transfusions with periodic plasma factor VIII or fibrinogen assays in hemophilia A and hypofibrinogenemic recipients respectively.

**References**


(1) Brinkhous, K.M. "Plasma Antihemophilic Factor Biological And Clinical Aspects," *Le Sang Biologie et Pathologie*, 25:738–741, 1954.

(2) Pool, J.G. and J. Robinson. "Observations on Plasma Banking and Transfusion Procedures for Haemophilic Patients Using a Quantitative Assay for Antihaemophilic Globulin (AHG)," *British Journal of Haematology*, 5:24–30, 1959.

(3) Pool, J.G. and A.E. Shannon. "Production of High-Potency Concentrates of Antihemophilic Globulin in a Closed-bag System," *New England Journal of Medicine*, 273:1443–1447, 1965.

(4) International Forum: "Can Hemophilic Patients be Adequately Maintained With Cryoprecipitates? Or is it Desirable or Even Necessary to Manufacture and Administer Highly Concentrated AHF Products?" *Vox Sanguinis*, 22:554–565, 1972.

(5) Slichter, S.J., R.B. Counts, R. Henderson and L.A. Harker, "preparation of Cryoprecipitated Factor VIII Concentrates," Transfusion, 16:616–626, 1976.

(6) Kasper, C.K., B.A. Myhre, J.D. McDonald, Y. Nakasako and D.I. Feinstein, "Determinants of Factor VIII Recovery in Cryoprecipitate," *Transfusion*, 15:312–322, 1975.

(7) Langdell, R.D., R.H. Wagner and K.M. Brinkhous, "Effect of Antihemophilic Factor on One-Stage Clotting Tests. A Presumptive Test for Hemophilia and a Simple One-stage Antihemophilic Factor Assay Procedure," *Journal of Laboratory and Clinical Medicine*, 41:637–647, 1973.

(8) Pool, J.G. and J. Robinson, "Assay of Plasma Antihaemophilic Globulin (AHG)," *British Journal of Haematology*, 5:17–23, 1959.

(9) Brown, D.L., R.M. Hardistry, M.H. Kosoy and C. Bracken, "Antihaemophilic Globulin: Preparation by an Improved Cryoprecipitation Method and Clinical Use," *British Medical Journal*, 2:79–85, 1967.

(10) Frommel, D. and M.R. de Angulo, "Is the Determination of AHF Activity Feasible for Individual Cryoprecipitates?" *Vox Sanguinis*, 29:228–230, 1975.

(11) Gilchrist, G.S. and H. Ekert, "Reduction of Factor VIII Activity in Cryoprecipitate Obtained from Acidified Plasma," *Transfusion*, 8:294–298, 1968.

(12) Waumans, P., R. Van Itterbeek and M. Verstraete, "The Preparation of a Human Plasma Fraction by Cryoprecipitation and its Use in Haemophilia," *Acta Clinica Belgica*, 23:139–152, 1968.

(13) Verstraete, M., A. Lust and J. Vermylen, "*In Vitro* and *In Vivo* Recovery of Cryoprecipitated Factor VIII," *Bibliography of Haematology*, 34:9–17, 1970.

(14) Strand, C.L., J.R. Beene, T. Geiger, M.O Eckel, K. Kunkel and G. Bull, "Production of High-potency Cryoprecipitate from Exercised Blood Donors and the Treatment of Hemophilia A With This Material," *American Journal of Clinical Pathology*, 62:498–501, 1974.

(15)Biggs, R., C.R.C. Rizza, E. Blackburn, T. Cleghorn, R. Cumming, I. Delamore, K. Dormandy, A. Douglas, J. Grant, R. Hardisty, G. Ingram, R. Kekwick, W. Maycock and J. Wallace, "Factor VIII Concentrates Made in the United Kingdom and the Treatment of Haemophilia Based on Studies Made During 1969–72," *British Journal of Haematology*, 27:391–405, 1974.

(16) Preston, A.E. and A. Barr, "The Plasma Concentration of Factor VIII in the Normal Population. II. The Effects of Age, Sex and Blood Group," *British Journal of Haematology*, 10:238–245, 1964.

(17) Burka, E.R., T. Puffer and J. Martinez, "The Influence of Donor Characteristics and Preparation Methods on the Potency of Human Cryoprecipitate," *Transfusion*, 15:323–328, 1975.

(18) Hawkey, C.M., H.B. Anstall and M. Grove-Rasmussen, "A Study of Comparative Antihaemophilic Factors Levels in Fresh Frozen Plasma *In Vitro* and *In Vivo*," *Transfusion*, 2:94–99, 1962.

(19) Perkins, H.A., M.R. Rolfs and D. Acra, "The Stability of Factor VIII (Antihemophilic Globulin) in Fresh-frozen Blood Bank Plasma," *Transfusion*, 2:313–320, 1962.

(20) Ikkala, E., G. Myllä and H. Nevanlinna, "Normal Post-exercise Plasma Transfusion in Patients with Haemophilia A and von Willebrand's Disease," *Scandinavian Journal of Haematology*, 1:300–307, 1964.

(21) Van Gastel, C., J.J. Sixma, E. Borst-Eilers, M. Leautaud, M. Moes, P. Van Der Plas, B. Bouma and J. Sybesma, "Preparation and Infusion of Cryoprecipitate from Exercised Donors," *British Journal of Haematology*, 25:461–466, 1973.

(22) Prentice, C.R.M., C.D. Forbes, et al., "Rise of Factor VIII After Exercise and Adrenaline Infusion, Measured by Immunological and Biological Techniques," *Thrombosis Research*, 1:493–506, 1972.

(23) Bennett, B. and O.D. Ratnoff, "Changes in Antihemophilic Factor (AHF, Factor VIII) Procoagulant Activity and AHF-like Antigen in Normal Pregnancy, and Following Exercise and Pneumoencephalography," *Journal of Laboratory and Clinical Medicine*, 80:256–263, 1972.

(24) Rizza, C.R. and J. Eipe, "Exercise, Factor VIII and the Spleen," *British Journal of Haematology*, 20:629–635, 1971.

(25) Egeberg, O., "The Effect of Exercise on the Blood Cloting System," *Scandinavian Journal of Clinical and Laboratory Investigation*, 15:8–13, 1963.

(26) Pool, J.G., T. Cohen and W. Creger, "Biological Half-life of Transfused Antihaemophilic Globulin (Factor VIII) in Normal Man, *British Journal of Haematology*, 13:822–828, 1967.

(27) Shanberge, J.N., M.C. Gruhl, R. Ikemori, K. Inoshita, M. Chalos and R. Aster, "A Comparison of Factor VIII Activity in Cryoprecipitates Prepared from ACD and CPD Plasma," *Transfusion*, 12:251–258, 1972.

(28) Pool, J.G., "The Effect of Several Variables on Cryoprecipitated Factor VIII (AHG) Concentrates," *Transfusion*, 7:165–167, 1967.

(29) Graybeal, F.Q., D.E. Mooreside and R.D. Langdell, "Clotting Factor Activity in Cryoprecipitates and Supernatant Plasma Prepared from Blood Collected in ACD, ACD-Adenine, CPD, and CPD-Adenine and from Plasma Collected by Plasmapheresis," *Transfusion*, 9:135–140 1969.

(30) Bloom, A.L., J.C. Giddings, B. Bevan, M. Letton and R. Drummond, "Comparison of Quick and Slow Thaw Methods of Producing Cryoprecipitate Antihaemophilic Factor from Fresh and 24-hour-old Blood," *Journal of Clinical Pathology*, 22:447–452, 1969.

(31) Keating, L.J., "The Preparation of Cryoprecipitate in a Mobile Laboratory: A Five-year Experience," *Transfusion*, 14:283–286, 1974.

(32) Burka, E.R., T.M. Puffer, R. Holburn and W.S. Sherwood, "The Unsuitability of Outdated Blood for Making Therapeutically Effective Cryoprecipitate," *Transfusion*, 13:412–417, 1973.

(33) Britten, A. and M. Grove-Rasmussen, "Stability of Factor VIII in the Frozen State," *Transfusion*, 6:230–233, 1966.

(34) Rapaport, S.I., M.J. Patch and J.E. Casey, "The Antihemophilic Globulin in Plasma," *California Medicine*, 93:203–210, 1960.

(35) Verstraete, M., P. Olislaegers, H. Van Itterbeek, P. Waumans and A. Lust, "Human Plasma and Plasma Fractions as Sources of Factor VIII (Antihaemophilic Factor)," *Vox Sanguinis*, 16:382–397, 1969.

(36) Uteg, K.H. and W. Sander, "Untersuchungen and Kryopräzipitaten," *Folia Haematology*, Leipzig, 97:322–331, 1972.

(37) Bennett, E., K.M. Dormandy, W. Churchill, A. Coward, M. Smith and T. Cleghorn, "Cryoprecipitate and the Plastic Blood-bag System: Provision of Adequate Replacement Therapy for Routine Treatment of Hemophilia," *British Medical Journal*, 2:88–91, 1967.

(38) Rock, G. and P. Tittley, "Variations in Cryoprecipitate Production," *Transfusion*, 17:50–53, 1977.

(39) Cooke, J.V., P.V. Holland and N.R. Shulman, "Cryoprecipitate Concentrates of Factor VIII for Surgery in Hemophiliacs," *Annals of Internal Medicine*, 68:39–47, 1968.

(40) Pool, J.G., "Cryoprecipitated Factor VIII Concentrate," *Bibliography of Haimatology*, 34:23–29, 1970.

(41) Masure, R., "Human Factor VIII Prepared by Cryoprecipitation," *Vox Sanguinis*, 16:1–9, 1969.

(42) Roth, G.J. and K.I. Tobias, "Clotting Factors in Supernatant Plasma Following Cryoprecipitation," *Transfusion*, 14:155–157, 1974.

(43) Meyer, K., J.G. Eernisse, J. Veltkamp, H. Hemker and E. Loeliger, "Treatment of Haemophila A with Purified Factor VIII Obtained from Human Plasma by Cryoprecipitation," *Folia Medica Meerlandica*, 10:49–60, 1967.

(44) Wickerhauser, M., "Levels of Hepatitis B Antigen and Isoagglutins in Clinical Concentrates of Factor VIII and Prothrombin Complex," *Developments in Biological Standardization*, 27:172–177, 1974.

(45) Del Duca, V., Jr. and R.B. Eppes, "Hepatitis Transmitted by Antihemophilic Globulin," *New England Journal of Medicine*, 275:965–966, 1966.

(46) Prentice, C.R.M., R.T. Breckenridge, W. B. Forman and O.D. Ratnoff, "Treatment of Hemophilia (Factor–VIII Deficiency) With Human Antihemophilic Factor Prepared by the Cryoprecipitate Process," *Lancet*, 1:457–460, 1967.

(47) Ahrons, S., S. Glavind-Kristensen, O. Drachmann and F. Kissmeyer-Nielsen, "Severe Reactions After Cryoprecipitated Human Factor VIII," *Vox Sanguinis*, 18:182–184, 1970.

(48) Hattersley, P.G., "The Treatment of Classical Hemophilia With Cryoprecipitates," *Journal of the American Medical Association*, 198:153–157, 1966.

(49) Strauss, H.S., "Acquired Circulating Anticoagulants in Hemophilia A," *New England Journal of Medicine*, 281:866–873, 1969.

(50) Brauer, P., S. Pochstein, K. Wilms, E. Wulff and J. Roewer, "Serologische Qualitätsanforderungen für Kryopräzipitate," *Folia Haemotology*, Leipzig, 101:674–678, 1974.

(51) McShine, R.L. and V.A. Kunst, "The Stimulation of Immune Antibodies Anti-A and Anti-B in Patients After Treatment With Cryoprecipitate and Factor IX Concentrate," *Vox Sanguinis*, 18:435–440, 1970.

(52) Kekwick, R.A. and P. Wolf, "A Concentrate of Human Antihemophilic Factor. Its Use in Six Cases of Hemophilia," *Lancet*, 1:647–650, 1957.

(53) Reese, E.P., J.J. McCullough and P.R. Craddock, "An Adverse Pulmonary Reaction to Cryoprecipitate in a Hemophiliac," *Transfusion*, 15:583–588, 1975.

(54) Bloom, A.L. and J.H. Emmanuel, "Use of Cryoprecipitate Antihaemophilic Factor for the Treatment of Haemophilia," *Quarterly Journal of Medicine*, 37:291–302, 1968.

(55) Schwartz, J.M., B.D. Cohn, N.D. Ritz and T. Levy, "Appendectomy in Hemophilia with the Use of Cryoprecipitated Human Factor VIII to Control Bleeding," *Journal of the American Medical Association*, 198:153–157, 1968.

(56) O'Brien, J.R., "The Use of Pool Cryoglobulin Factor VIII Concentrate in the Management of Haemophilia," *Proceedings of the Royal Society of Medicine*, 60:13–14, 1967.

(57) Peetermans, M. and J. Casman-Govaerts, "Le Traitement des Hemophilies Par le Cryoprecipite," *Acta Clinica Belgica*, 23:291–303, 1968.

(58) Shulman, N.R., D.H. Cowan, E. Plibre, S.P. Watkins and V.J. Marder, "The Physiologic Basis for Therapy of Classic Hemophilia (Factor VIII Deficiency) and Related Disorders," *Annals of Internal Medicine*, 67:856–882, 1967.

(59) Robinson, P.M., P. Tittley and R.K. Smiley, "Prophylactic Therapy in Classical Hemophilia: A Preliminary Report," *The Canadian Medical Association Journal*, 97:559–561, 1967.

(60) Lazerson, J., "Hemophilia Home Transfusion Program: Effect of Cryoprecipitate Utilization," *Journal of Pediatrics*, 82:857–859, 1973.

(61) Perkins, H.A., "Correction of the Hemostatic Defects in von Willebrand's Disease," *Blood*, 30:375–380, 1967.

(62) Bennett, E. and K. Dormandy, "Pool's Cryoprecipitate and Exhausted Plasma in the Treatment of von Willebrand's Disease and Factor XI Deficiency," *Lancet*, 2:731–732, 1966.

(63) Green, D. and E.V. Potter, "Failure of AHF Concentrate to Control Bleeding in von Willebrand's Disease," *The American Journal of Medicine*, 60:357–360, 1976.

(64) Blatt, P.M., K.M. Brinkhous, H.R. Culp, J.S. Krauss and H.R. Roberts, "Antihemophilic Factor Concentrate Therapy in von Willebrand Disease. Dissociation of Bleeding-Time Factor and Ristocetin-Cofactor Activities," *Journal of the American Medical Association*, 236:2770–2775, 1976.

(65) Chediak, J.R., M.C. Telfer and D. Green, "Platelet Function and Immunologic Parameters in von Willebrand's Disease Following Cryoprecipitate and Factor VIII Concentrate Infusion," *The American Journal of Medicine*, 62:369–376, 1977.

(66) Mainwaring, R.L., and G.G. Brueckner, "Fibrinogen-Transmitted Hepatitis. A Controlled Study," *Journal of the American Medical Association*, 195:437–441, 1966.

(67) Sherman, L.A., *"In Vivo* Stability of Cryoprecipitate Fibrinogen," *Transfusion*, 17:59–61, 1977.

(68) Soloway, H.B. and C.E. Bereznak, "Plasma Fibrinogen Levels Following Cryoprecipitate Infusion," *Transfusion*, 10:326–328, 1970.

(69) Hattersley, P.G. and M.L. Dimick, "Cryoprecipitates in Treatment of Congenital Fibrinogen Deficiency," *Transfusion*, 9:261–264, 1969.

(70) Hattersley, P.G. and M. Kunkel, "Cryoprecipitates as a Source of Fibrinogen in Treatment of Disseminated Intravascular Coagulation (DIC)," *Transfusion*, 16:641–645, 1976.

**9. Single Donor Plasma (Human)**

*Generic Statement*

1. *Introduction.* As indicated in the review of whole blood, an important consideration in the management of hemorrhage is maintenance of the circulating blood volume. During World War II, plasma was used extensively in combat settings for the treatment of acute blood loss (Ref. 1). Plasma was effective in improving the pathophysiologic defect resulting from trauma and acute blood loss, but there was a significant incidence of hepatitis in patients transfused with plasma. The product used at that time was prepared by pooling plasma from many individuals and freeze-drying large batches. It was noted that the incidence of hepatitis in patients transfused with plasma from a large pool of donors was greater than in patients transfused with plasma from a small pool of donors (Ref. 2). It has been shown that plasma retains hepatitis infectivity even when very dilute (Ref. 3).

At one time, it was believed that the risk of transmission of hepatitis by pooled donor plasma could be reduced by storing the plasma at 30 to 32 °C for 6 months or more prior to use (Ref. 4). In a well-controlled study, however, it was demonstrated that storage of plasma at 30 to 32 °C did not significantly reduce the risk of hepatitis (Ref. 5). In a summary of the clinical use of pooled plasma, the Committee on Plasma and Plasma Substitutes of the National Research Council concluded that the use of whole, pooled human plasma should be discouraged or discontinued unless a clear-cut case could be made that is met a unique requirement (Ref. 6). When plasma infusion is indicated, it is generally believed that the risk of causing post-infusion hepatitis can be greatly reduced by using Single Donor Plasma. Although a risk is still present, it is of the same order of magnitude as that associated with the transfusion of whole blood (Ref. 7).

Plasma is relatively stable during short term storage in the liquid state except for certain labile components. The factors affecting blood during short term storage in plastic bags have been considered in the review of stored Red Blood Cell Products. During prolonged storage there is apparently a loss of fluid from the contents of the plastic container and unless additional glucose is provided, fibrinogen will precipitate. In order to avoid the changes associated with storage in the liquid state, plasma should be stored in the frozen state. Once converted to the frozen state, little or no further change occurs in plasma

during long periods of storage. Individual units of plasma stored in this way, when thawed, are reasonably equivalent to the plasma at the time of freezing.

In addition to its volume and colloid osmotic effect, plasma has been used as a source of plasma coagulation factors. Two of the clotting factors (V and VIII) deteriorate rather rapidly in blood or plasma stored at 4 to 6 °C, but are relatively stable when stored in the frozen state (Refs. 8 through 10). Plasma separated from whole blood and rapidly frozen within 6 hours of collection contains almost all the original activity of factor V and factor VIII. This product is called "Single Donor Plasma-Fresh Frozen" to distinguish it from "Single Donor Plasma" that has been separated from whole blood after longer periods of storage at 4 to 6 °C. The other clotting factors are more stable in plasma, and there is little loss of activity of these clotting factors in plasma which is stored in the frozen state (Ref. 11). No doubt there are a number of plasma constituents that do deteriorate during storage, but the importance of these in transfusion therapy has not yet been demonstrated.

The blood group antigens, except those of the Lewis system, are related to the red blood cells and are not present in the plasma. Provided the blood cells are not inadvertently present in plasma, many of the risks related to transfusion of whole blood are not applicable to the use of plasma. However, there are risks related to antibodies that may be present in plasma. Plasma from individuals whose red blood cells lack A or B antigens contain antibodies active against the antigens which are lacking. Thus, anti-A and anti-B antibodies are present in the plasma of group O individuals; anti-A is present in the plasma of group B individuals, and anti-B is present in the plasma of group A individuals. Antibodies of this type have produced hemolytic transfusion reactions when transfused into individuals whose red blood cells contain the antigen for which the antibodies are specific (Refs. 12 through 14). It has been estimated that approximately 40 percent of group O individuals have sufficient antibody levels to cause hemolysis when their plasma is transfused into a group A recipient (Ref. 12). Hemolytic reactions have been reported with transfusion of plasma with anti-A and anti-B antibodies reactive in the cold (Refs. 12 and 13) as well as those reactive at 37 °C (Ref. 14). Antibodies reactive with other blood group antigens are much less likely to cause hemolysis when infused into a recipient whose red cells carry the relevant antigen (Ref. 15).

The development of vasoactive substances during plasma storage has been considered in the review of Stored Red Blood Cell Products. Mollison (Ref. 16) cites several reports indicating the occurrence of vasoactive substances apparently related to enzyme action on plasma proteins. In view of the recent observations on prekallikrein activator in plasma fractions (Ref. 17) it is clear that under certain circumstances vasoactive substances in plasma can be clinically significant.

2. *Indications for administration of Single Donor Plasma*—a. *Plasma volume expansion*—(1) *Effectiveness.* There is a considerable amount of clinical experience to indicate that infusion of plasma will effectively expand the plasma volume of the recipient, although there is a report that some hypovolemic recipients of homologous plasma may exhibit little expansion of plasma volume (Ref. 18). There are other products that do this equally well or better, but plasma is usually effective.

(2) *Safety.* (a) There is a risk of transmission of hepatitis with the infusion of plasma. This can be decreased by careful selection of donors and testing each unit for HBsAG, but a risk remains.

(b) There is a risk of hemolytic transfusion reaction associated with infusion of plasma without consideration of the ABO groups of the donor and recipient. This can be minimized by using group-specific plasma.

(3) *Benefit/risk.* There are several other products that produce the same or a similar clinical effect that are not associated with the same risks. In comparison to these products, the risks of using single donor plasma exceed the benefits for this indication.

b. *Supply of coagulation factors other than V and VIII*—(1) *Effectiveness.* Plasma clotting factors other than factors V and VIII are present in Single Donor Plasma in approximately normal amount. When administered intravenously, the activity in the circulation is proportional to the volume given. In severely deficient subjects, the circulating level can be increased to approximately 20 percent of normal without producing circulatory overload. This will often provide adequate hemostasis in uncomplicated cases. Such treatment is not adequate for severe bleeding episodes or when surgery is required.

(2) *Safety.* (a) The risk of hepatitis is present.

(b) The danger of circulatory overload must be considered when attempting to produced and maintain hemostatic clotting factor levels.

(3) *Benefit/risk.* When a relatively small increase in circulating levels of deficient coagulation factors is desired, the benefits of Single Donor Plasma are considerably greater than the associated risks for this indication.

c. *Recommendations.* (1) Single Donor Plasma (Human) should be placed in Category I.

(2) The use of this product for plasma fractionation should be encouraged.

(3) The name of the product should be "Single Donor Plasma".

(4) Indications for use in hypovolemia should be stated in labeling in relation to the hepatitis risk.

3. *Indications for the administration of Single Donor Plasma (Human)-Fresh Frozen*—a. *Source of factor V and VIII—(1) Effectiveness.* Plasma clotting factors, including factors V, are present in approximately normal amounts in this product. When administered intravenously, the circulating levels are increased proportionally to the volume infused. Levels approaching 20 percent of normal can be achieved by infusing this product into severely deficient patients.

(2) *Safety.* (a) The risk of hepatitis is present.

(b) The risk of circulatory overload is present.

(3) *Benefit/risk.* (a) This product is the only available source of factor V for human use. When used appropriately in patients with a bleeding episode associated with severe factor V deficiency, the benefits far exceed the risks.

(b) This product is a source of factor VIII in relatively small amounts. In view of the availability of other more concentrated sources of factor VIII the benefits expected are minimal.

(c) As a source of coagulation factors other than factor V and VIII, the benefits/risks are equivalent to those of Single Donor Plasma.

(4) *Recommendations.* (a) Single Donor Plasma (Human)-Fresh Frozen should be placed in Category I as a source for the administration of factor V.

(b) The name of the product should be "Single Donor Plasma (Human)-Fresh Frozen".

(c) The utilizaton of more of this product as a starting material for preparation of factor VIII concentrates should be encouraged.

(d) Studies to develop a factor V concentrate should be encouraged.

References

(1) Kendrick, D.B., "Blood Program in World War II," Department of the Army, Washington, D.C., 1964.

(2) Lehane, D., C.M.S. Kwantes, M. G. Upward and D.R. Thomson, "Homologous Serum Jaundice," *British Medical Journal*, ii:572–574, 1949.

(3) Barker, L.F. and R. Murray, "Relationship of Virus Dose to Incubation Time of Clinical Hepatitis and Time of Appearance of Hepatitis-Associated Antigen," *American Journal of the Medical Sciences*, 263:27–33, 1972

(4) Allen, J.G., C. Sykes, D.M. Enerson, P.V. Moulder, R.M. Elghammer, B.J. Grossman, C.L. McKeen and N.J. Galluzzi, "Holomogous Serum Jaundice and its Relation to Method of Plasma Storage," *Journal of the American Medical Association*, 144:1069–1074, 1950.

(5) Redeker, A.,C. Hopkins, B. Jackson and P. Peck, "A Controlled Study of the Safety of Pooled Plasma Stored in the Liquid State of 30–32° C for Six Months," *Transfusion*, 8:60–64, 1968.

(6) Committee of Plasma and Plasma Substitutes of the Division of Medical Sciences, National Research Council, "Statement on Normal (Whole, Pooled) Human Plasma," *Transfusion*, 8:57–59, 1968.

(7) Medical Research Council, "Homologous Serum Jaundice after Transfusion of Whole Blood, Dried Small-Pool Plasma, Dried Irridiated Plasma and Kaolin-Treated Filtered Liquid Plasma," *Lancet*, i:1328–1329, 1954.

(8) Perkins, H.A., M.R. Rolfs and D.J. Acra, "The Stability of Factor VIII (Antihemophilic Globulin) in Fresh-Frozen Blood Bank Plasma," *Transfusion*, 2:313–320, 1962.

(9) Bowie, E.J.W., J.H. Thompson, Jr. and C.A. Owen, Jr., "The Stability of Antihemophilic Globulin and Labile Factor in Human Blood," *Mayo Clinic Proceedings*, 39:144–151, 1964.

(10) Weaver, R.A. and R.D. Langdell, "Antihemophilic Factor (AHF) Stability in Fresh Frozen Blood Bank Plasma," *Transfusion*, 6:224–229, 1966.

(11) Mooreside, D.E., F.Q. Graybeal and R.D. Langdell, "Effects of Adenine on Clotting Factors in Fresh Blood, Stored Blood, and Stored Fresh Frozen Plasma," *Transfusion*, 9:191–197, 1969.

(12) Aubert, E.F., K.E. Boorman, B.E. Dodd and J.F. Loutit, "The Universal Donor with High Titre Iso-agglutinins; the Effect of Anti-A Iso-agglutinins on Recipients of Group A," *British Medical Journal*, i:659–664, 1942.

(13) Tisdall, L.H., D.M. Garland, P.B. Szanto, A.M. Hand and J. Bonnett, "The Effects of the Transfusion of Group O Blood of High Iso-agglutinin Titer into Recipients of Other Blood Groups," *American Journal of Clinical Pathology*, 16:193–206, 1946.

(14) Grove-Rasmussen, M., R.S. Shaw and E. Marceau, "Hemolytic Transfusion Reaction in Group-A Patient Receiving Group O Blood Containing Immune Anti-A Antibodies in High Titer," *American Journal of Clinical Pathology*, 23:828–832, 1953.

(15) Mohn, J.F., R.M. Lambert, H.S. Bowman and F.W. Brason, "Experimental Transfusion of Donor Plasma Containing Blood-Group Antibodies into Incompatible Normal Human Recipients. I. Absence of Destruction of Red-Cell Mass with Anti-Rh, Anti-Kell and Anti-M," *British Journal of Haematology*, 7:112–129, 1961.

(16) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 4th Ed., F.A. Davis Company, Philadelphia, p. 800, 1967.

(17) Alving, B.M., Y. Hojima, J.J. Pisano, B.L. Mason, R.E. Buckingham, Jr., M.M. Mozen and J.S. Finlayson, "Hypotension Associated with Prekallikrein Activator (Hageman-Factor Fragments) in Plasma Protein Fraction," *New England Journal of Medicine*, 299:66–70, 1978.

(18) Gruber, U.F. and S.E. Bergentz, "Autologous and Homologous Fresh Human Plasma as a Volume Expander in Hypovolemic Subjects," *Annals of Surgery*, 165:41–48, 1967.

**10. Normal Serum Albumin (Human)**

*Generic Statement*

1. *Introduction.* Albumin has at least two major functions, providing plasma-specific osmotic activity, and performing an important carrier function by transporting various substances in a bound state. Both of these functions relate to albumin in the plasma. Most albumin normally exists in extravascular sites. It is not known whether this albumin performs any specific functions or represents preformed, stored material available in case of sudden need.

a. *Plasma-specific osmotic activity.* Starling's law of fluid exchange across the capillary bed postulates a major role for plasma-specific osmotic activity in determining the distribution of fluid across the capillary membrane (Ref. 1). Normally, 70 percent of this activity is provided by albumin. Starling's law is not fundamentally a biological phenomenon, but is rather the application of basic and well-established physical principles to the biological situation. Some relatively recent "criticism" of this law (Ref. 2) has tended to confuse the validity of the formulation with the definition of the conditions under which it operates. Starling's original formulation was clearly a gross oversimplification, but was based on what was known at that time. Almost all relevant conditions have since been defined in much greater detail. Perhaps most importantly, it is now apparent that the conditions under which this principle operates are different in different parts of the body: Interstitial fluid pressure, interstitial albumin concentration, intravascular pressure, and even vascular permeability all vary in different organs and regions. Failure to take these differences into account explains most if not all of the discrepancies that have been claimed to exist relative to Starling's law (Ref. 3).

Understanding of the situtation is further complicated by some of the self-correcting features of lowering the concentration of albumin in the plasma. There is a concurrent lowering of the interstitial concentration of albumin, minimizing the change in the transcapillary gradient, a rise in interstitial fluid pressure as fluid accumulates which also resists egress of fluid from the capillaries, and, in many organs, an increase in lymphatic return to minimize the extravascular accumulation of edema. In addition, the normal level of albumin in plasma is well above that necessary to prevent gross extravascular shifts of fluid. Nevertheless, numerous studies have shown that when albumin concentration is lowered, it is easier to induce the formation of interstitial edema, and this is the essence of Starling's formulation. Clinical experience is also concordant with the above relationship, but the quantitative details are far from clear. Certain populations of patients can tolerate hemodilution quite well; the level of hypo-albuminemia at which clinically worrisome changes appear in other patients is very variable. Thus, empiricism and experience still dominate clinical practice, and much more detailed knowledge of transcapillary fluid dynamic will be needed before clinical use of albumin for its osmotic effects can be placed on a firm rational basis. Some of what is known about various disease states will be reviewed later.

b. *Carrier protein.* Albumin is second only to hemoglobin as the major "carrier" material in the blood. A large number of naturally occurring and therapeutically administered substances are transported in the blood partially bound to albumin (Ref. 4). Albumin can bind substances with positive or negative charges, as well as a wide variety of uncharged substances. Among the natural substances carried by albumin, the most important may be the long-chain fatty acids. These are the major fuel substrates for the body, but are toxic in even small concentrations if unbound or nonesterified. They are carried almost totally bound to albumin, with varying degrees of affinity (Ref. 5). In the bound form they do not damage cell membranes or capillary walls. A variety of other lipids are also carried largely bound to albumin, as are certain divalent metals (calcium, copper and possibly zinc), bilirubin, tryptophan which is the only amino acid present in bound form in the circulation, and many more substances. The binding of bilirubin as in hemolytic disease of the newborn and of tryptophan as in cases of hepatic encephalopathy may be closely related to these and other

disease states. Similar clinical disorders have not been identified for the bound lipids, although marked hyperlipemia is characteristic of severe hypo-albuminemia and reverses when albumin is administered. Binding of certain hormones may also have physiologic significance, as may the binding and transport of many other substances normally carried in the blood.

A very large variety of drugs are carried in the blood partially bound to albumin (Ref. 6). The important pharmacodynamic features of these drugs such as levels in the interstitial fluid and urinary excretion are usually determined by the proportion of the drug that is unbound.

In spite of these considerations, it has been difficult to attribute specific harmful effects to loss of the carrier function of albumin in severe hypoalbuminemia except in hemolytic disease of the newborn. There are many interrelationships between and among substances bound to albumin with some, especially the fatty acids and certain drugs, interfering with the binding of many others. Competitive binding must certainly accentuate effects at lower-than-normal concentrations of albumin. As knowledge of pharmacodynamics increases, the binding function of albumin is likely to be increasingly recognized as important.

c. *Normal albumin dynamics.* Albumin has been difficult to study because of its long persistence, 15 to 20 days, and multicompartmental distribution with varying equilibration times. This requires a long period of steady state conditions for the establishment of equilibration curves and precludes the study of many important but unstable clinical states. The normal total mass of albumin in a 70 kg adult probably exceeds 300 grams with a turnover of 15 grams per day (Refs. 4 and 7).

(1) *Albumin production.* Albumin is synthesized in the liver and seems to be released directly into hepatic sinusoidal blood rather than by way of the thoracic duct. The rate of synthesis is very sensitive to the supply of amino acids presented to the liver. Complete fasting can reduce the rate of synthesis by 50 percent within a few hours, with recovery beginning within minutes of refeeding. A number of amino acids are specifically effective in stimulating synthesis of albumin. All of these also stimulate synthesis of urea. Some of these, tryptophan and ornithine specifically, are incorporated sparingly or not all all into the protein synthesized.

Hormonal balance probably influences the rates of synthesis for albumin. Cortisol, thyroxine, and growth hormone appear to stimulate synthesis. Although not specifically studied, glucagon is likely to have the opposite effect. A certain amount of insulin may be necessary to achieve maximum rates of albumin synthesis.

One of the main mechanisms controlling albumin metoliusm is the concentration of colloid in the interstitial spaces of the liver (Ref. 8). As this concentration increases, the rate of synthesis of albumin decreases. Almost any osmotically active material seems to be effective in decreasing the rate of synthesis: dextran, gamma globulin, or albumin itself. Some authors seem to believe that hyperosmolality due even to small molecular species will inhibit synthesis. The rate of degradation does not decrease proportionately, and the level of albumin in the blood falls until the concentration of large molecular colloid in the hepatic interstitial space returns to normal.

(2) *Degradation of albumin.* Remarkably little is known about the site or control of degradation of albumin, when one considers its physiological importance and the large amount, about 15 grams, normally catabolized daily. Several experiments suggest that synthesis and degradation are not interdependent. In the absence of better data, the liver seems to be a likely site for degradation of albumin, but in vitro studies on liver slices do not confirm this.

Rates of degradation increase markedly with induced hyperalbuminemia and decrease during starvation. The great void in our knowledge regarding albumin degradation and its control seriously impair understanding of the overall control of albumin metabolism.

(3) *Body distribution of albumin.* Although there is some disagreement about details, two different methods of analysis indicate that most of the albumin is normally outside the plasma, probably 60 to 67 percent (Ref. 9). Most of the extravascular albumin is present in the skin, less in muscle which has a low concentration of albumin in a large total volume of interstitial fluid, less in the gut, and very little in the liver or other viscera. Extravascular albumin equilibrates at different rates with the plasma pool; it is most rapid for muscle, slower for the skin, and very slow for the gut. The extravascular albumin returns to the plasma mainly by the thoracic duct. The rate of return of albumin from all extravascular sites is very much slower than the rate of return of interstitial water. This suggests that there is a distinct holding mechanism for albumin in the interstitial matrix similar to molecular sieving, with different features of the general process in different tissues.

2. *Indications for the clinical use of albumin.* Albumin is used clinically for many different reasons. The survey recently reported by Sgouris and Dorsey generally confirms the usually stated categories of reasons given for usage; these are the only such data available in the U. S. (Ref. 10). Some of the present albumin usage is plainly mistaken because of oversights in ordering its administration (Ref. 11), but much of its use follows a certain logic. Before considering some of these specific categories, some general comments may be useful.

Personal experience of members of the Panel indicates that very few physicians, including well-trained house staff, understand the arithmetic of the distribution of administered albumin. Many physicians are completely unaware of the existence of extravascular stores of this protein in equilibrium with the plasma; very few know the approximate size of these stores or are aware of the complex, changing relationships between blood levels and interstitial levels that occur as hypoalbuminemia develops. All of these voids in knowledge lead to very gross underestimations of the amount of albumin needed to achieve a desired effect. Most clinicians also seriously underestimate the half-life of human albumin, but this error is not enough to offset their gross underestimation of requirements. Just as importantly, few clinicians can really explain why the blood level of albumin they have chosen is desirable. Perhaps the most rational practitioners are the complete empiricists who administer albumin until the blood levels increase or, if appropriate, blood pressure, urinary output or arterial oxygen pressure increase, or until edema subsides. Sometimes the end point of this pattern of administration is very vague, but usually it is a rational goal. Given the regrettable ignorance of most clinicians about the physiology of the product they are prescribing and its quantitative aspects, the empirical approach is perhaps the safest for the individual patient. It is not the best for the blood, plasma, and albumin supply system, however. As Lundsgaard-Hansen has implied for Switzerland (Ref. 12), and also in the United States, albumin is used in too many patients in quantities too small to do many of them much good even if they did need it.

a. *Hypovolemia*—(1) *Rationale and effectiveness for use in hypovolemia.* Probably the commonest reason for using albumin is to expand blood volume. Occasionally it is used as the primary agent for this purpose; more commonly it is used to supplement simple salt solutions, and occasionally it is used to supplement administration of sedimented or frozen, washed red cells. Some of this use is for a combined indication of hypovolemia with hypoalbuminemia when an increase in cardiac output is sought in such a patient who may also already have peripheral edema.

The normal response to hemorrhage consists of an initial intravascular shift of protein-poor interstitial fluid. There is a gradual shift of albumin back into the vascular space, largely via the thoracic duct, with an overall "buffering" of the intravascular mass of albumin by a greater decrement in the extravascular mass once equilibrium is reached (Refs. 7 and 13). This is characteristic of the response to sudden loss of albumin regardless of the cause. The sites of extravascular albumin storage are primarily the very organs in which capillary pressure is reduced in response to hypovolemia, especially the skin. This suggests that physical forces have much to do with this buffering mechanism. No other control mechanism has been identified or suggested.

The rate of synthesis of albumin varies inversely, and the rate of degradation varies directly with its concentration in the interstitial space of the liver. The mechanisms of this regulation are unknown. The intravascular concentration of albumin is thus restored back nearly to normal within a few days even without supplementation by administered albumin.

One disadvantage to the use of albumin to restore blood volume is its long persistence. If the need for red cells becomes apparent after administration of a large volume of albumin, one must either wait for its equilibration throughout the system, or perform phlebotomy or plasmapheresis, or run the risk of overloading the circulation with the administered cells. The practical disadvantages of albumin therapy are those of cost and availability.

(2) *Burns.* Burn treatment represents a special situation. Pruitt and associates (Ref. 14) and Baxter (Ref. 59) have presented evidence in patients that supplemental albumin with isotonic or slightly hypotonic salt solutions contributes nothing to the expansion of the plasma volume in the first 24 hours after a major burn. Its use in these circumstances does not seem rational. A recent study, however, indicates that supplemental albumin may be useful in the early post-burn period if used with hypertonic saline solutions (Ref. 60). Interestingly, these patients had normal rates of disappearance of albumin from the circulation, in marked contrast to patients treated with other regimens and studied in this and other series. A number of unanswered questions remain, and more study is clearly needed.

Large amounts of protein are lost into the burn wound for significant periods of time. One of the major sites of albumin storage, i.e., the skin, is partially destroyed and the albumin that has been thermally altered by the burn is almost certainly removed at an accelerated rate. Paralytic ileus usually occurs in burned patients and interferes with nutrition. Some degree of infection is always present, and a prolonged maximum stress response with a prolonged catabolic state is also produced. Massive edema usually develops. Repeated skin grafting operations are necessary. All of this can create the need for administering very large amounts of albumin therapeutically. There is still disagreement about administering albumin early after burn injury, but even extensive nutritional support may have to be supplemented with the administration of albumin later in the care of such patients until the burn wounds are healed.

(3) *Miscellaneous uses of albumin in hypovolemia.* Albumin is used to replace blood volume in a variety of special situations, such as exchange plasmapheresis, "total body washout," and to supplement extensive use of red blood cell concentrates or frozen, washed red blood cells. In these circumstances, clotting factors are not replaced exogenously, and there is often a lack of awareness of the significant amount of citrate in these preparations. Other indications for the use of albumin are quite nonspecific and represent combinations of hypovolemia and hypoalbuminemia as in pancreatitis, trauma, hemorrhage, "shock," cardiopulmonary bypass, and hemodialysis.

(4) *Effectiveness of the use of albumin for hypovolemia.* The older literature confirms the effectiveness of albumin prepared by the Cohn fractionation method in supplementing circulating levels of albumin in the recipient with a variety of illnesses, including hypovolemia, and in restoring blood volume toward normal (Ref. 15). The specific treatment of blood loss with plasma proteins, however, has been an uncertain area. There is much experimental and some clinical evidence of less-than-expected effectiveness of albumin administration in promoting survival (Ref. 16). Most of these studies used raw plasma rather than albumin, and it is likely that there were differences in the degree of protein denaturation. The role of albumin prepared by Cohn fractionation in resuscitating patients from hemorrhage remains to be defined, especially as it can be compared with other currently used treatments for this condition. Recent evidence indicates that simple electrolyte solutions may be equally effective in many patients at far less cost (see section on acute pulmonary insufficiency).

(5) *Safety albumin for use in hypovolemia.* Albumin appears to be inherently safe. The main potential problems of its use relate to its physiologic effects. The restoration of blood volume in a hypovolemic patient may result in renewed bleeding from transected blood vessels. The expansion of blood volume by administering albumin without red blood cells was discussed above. Concentrated albumin, above 5 grams/dL, requires the administration of additional noncolloid containing fluids unless the patient is already overload with interstitial fluid. Administering to much albumin can overload the circulation and precipitate pulmonary edema.

(6) *Benefit/risk evaluation of albumin for use in hypovolemia.* When properly used for hemorrhage, albumin appears to be significantly beneficial at very little risk.

(7) *Recommendations for albumin administration in hypovolemia.* Hypovolemia is a valid indication for administering albumin. It is not however clear that albumin adds any therapeutic effect to the use of simpler electrolyte solutions when treating limited hemorrhages. (See the section on pulmonary insufficiency).

(8) *Labeling changes for use in hypovolemia.* The appropriate precautions discussed here should be included in all labeling. Use of 25-percent albumin as the primary treatment for hypovolemia is questionable, and it should not be used as such unless the patient is already edematous. If the 5-percent preparation of albumin is not available, 25 percent albumin may be used with concurrent administration of an appropriate volume and kind of fluid

b. *Hypoproteinemia*—(1) *Rationale and effectiveness for use in hypoproteinemia.* Albumin is ofter used to mobilize or prevent the formation of

periheral edema in patients with significant hypoalbuminemia. As previously discussed, the deficit in albumin is usually grossly underestimated, and in situations with large continuing losses of albumin this treatment will have very temporary effects. Aside from the specific effects on pulmonary function, it is not clear what is gained therapeutically by increasing the plasma concentration of albumin, and what, it any, is the minimum desirable level. Hypoproteinemia is one of the conditions that is associated with impaired healing of wounds (Red. 17). It is not known to what extent hypoalbuminemia contributes to this, and how effective the infusion of albumin might be in restoring the capacity for healing wounds. Congenital analbuminemia is rare but seemingly well tolerated. There are undoubtedly several compensatory mechanisms in this condition which may not operate in acquired hypoalbuminemia. To the extent that the cause of the hypoalbuminemia can be identified and corrected, it should be, as this will be much more effective from every viewpoint.

There are a number of clinical situations in which chronic hypoproteinemia is common. Each has special considerations. There are at least two separate problems in patients with cirrhosis. The rate of sythesis of albumin may be decreased because of functional impairment of the liver, but ofter this can be returned to normal by stopping the ingestion of alcohol and providing adequate nutrition (Ref. 18). The rate of degradation of albumin is also decreased, but not sufficiently to preserve normal blood levels. Administered albumin effectively, but temporarily, restores blood levels toward normal in the absence of ascites. If ascites is present, the sequestration of albumin in ascitic fluid can constitute a marked distributional abnormality. Albumin appears to enter the ascites directly from the liver. The total mass of body albumin may be greater than normal, but severe hypoalbuminemia is usually present. Administered albumin ofter has little effect in reducing the ascites if the ascites has proven resistant to currently available diuretics and/or aldosterone antagonists.

The nephortic syndrome epitomizes the pathological losses of albumin that can occur with renal disease. With marked albuminuria, synthetic rates are markedly increased provided nutrition is maintained. Rates of albumin degradation are decreased. The compensatory shift of extravascular albumin to the plasma can be altered by extensive peripheral edema with expansion of the interstitial space. Infusions of albumin can help mobilize edema, but he effects will be very brief as long as rapid loss of albumin continues.

Interpretation of albumin dynamics in the patient with gastrointestinal disease can be very difficult. The gut can certainly shed large quantities of albumin and, like the kidney, constitutes a site of major loss. Many gastrointestinal diseases will also produce impaired absorption of nutrients (Ref. 19). The responses in albumin production of these patients to total parenteral nutrition indicates that malabsorption dominates in many patients with inflammatory bowel disease.

Pemphigus is another condition in which very large amounts of albumin can be lost continously. If the oral cavity is involved, nutrition may also be impaired. Any extensive exfoliative condition of the skin can do the same.

(2) *Safety of the administration of albumin in hypoproteinemia.* Again, caution is required when using albumin in an anemic patient, because the expansion of plasma volume will decrease the concentration of hemoglobin in the blood.

(3) *Benefit/risk of the administration of albumin for hypoproteinemia.* Older literature and current clinical experience supports the effectiveness of currently available preparations of albumin in restoring the plasma levels of albumin back toward normal in these conditions, if the distributional aberrations are taken into consideration (Ref. 15). With rapid continued loss of albumin, the effects of its administration will be very transient.

The risk of administrating albumin is low except when concentrated albumin is given rapidly to an edematous, hypoalbuminemic patient. It is estimated that 1 gram of albumin holds 17 to 18 mL water in the plasma volume. Rapid administration of the 25-percent concentration material to an edematous patient can easily precipitate pulmonary edema. The concurrent administration of a non plasma expanding diuretic to reduce plasma volume may be useful in this situation, but careful monitoring and slower rates of administration are even more desirable.

(4) *Recommendations for the administration of albumin in hypoproteinemia.* More basic research is needed to define the levels at which hypoalbuminemia becomes harmful, and when correction by supplementation is worthwhile.

(5) *Recommendations for labeling of albumin for administration for hypoproteinemia.* Labeling should emphasize the danger of inducing pulmonary edema when giving concentrated (25 percent) albumin to an edematous, hypoalbuminemic patient. Correction of the underlying defect should also be emphasized as the preferable approach to treating hypoalbuminemia.

c. *Acute pulmonary insufficiency*—(1) *Rationale for use of albumin in acute pulmonary insufficiency.* There is considerable disagreement concerning the role of plasma concentrations in the development and treatment of acute pulmonary insufficiency. On one side, it is clear that decreasing the albumin concentration in the prefusate of the isolated lung increases the ease with which pulmonary edema forms (Refs. 20 and 21). Arterial oxygenation in patients with acute pulmonary insufficiency may improve with the concurrent administration of albumin and diuretics (Refs. 22 and 23). Some studies show a significant degree of hypoalbuminemia in most patients with acute respiratory failure not due to left ventricular failure (Refs. 23 through 25, 61 and 62), but this does not prove a cause-and-effect relationship. Skillman et al. have shown in a prospective, semi-controlled study on surgical patients that adding albumin to the therapeutic fluid regimen is associated with less subsequent impairment of oxygenation (Ref. 26), but the patients were treated with predetermined volumes of fluid. Elective hemodilution with solutions containing albumin appeared to cause less impairment of pulmonary function than hemodilution with simple salt solutions, but the studies were not concurrent or randomized (Ref. 63).

On the other side of the question, there are now several prospective, well-controlled studies in patients resuscitated from serious injury or studied through major intraabdominal operations, in which treatment with isosmotic albumin was compared with treatment with simple electolyte solutions. No differences were observed, either in gross clinical results or on sophisticated testing of pulmonary function (Refs. 64 and 65). Several studies are noteworthy because of the surprisingly small decreases in albumin concentration that were produced by the use of simple salt solutions as treatment for major hemorrhages (Refs. 64 and 66). In one study, serum colloid osmotic pressure was reduced to about 60 percent of normal, perhaps because the study group was comprised of older patients undergoing extensive

retroperitoneal dissection (Ref. 65). These patients were carried through the operative period with acceptable pulmonary function, at least equal to that of the control group treated with supplemental albumin. These patients were very carefully monitored for changes in pulmonary capillary wedge pressure, however, and this may be a requirement for such methods in patients of this type. More clinical studies of a similar type are currently underway, involving various specific groups of patients. Such studies will greatly clarify the extent to which supplemental albumin is needed (or not needed) in the treatment of acutely ill patients. The best current data relate to patients treated for acute hemorrhage and indicate that extensive blood loss can be treated with simple electrolyte solutions without use of supplemental albumin, even when red cell preparations must also be used.

The physiological basis for this surprising result is now being investigated in controlled laboratory experiments. Much of this work is also still in progress, but studies of the lymphatic drainage of the lungs indicates that the consentration of albumin in the interstitial fluid of the lungs falls rapidly with an acute decrease in the concentration in the plasma, thereby tending to minimize a change in the transcapillary gradient. In addition, the rate of pulmonary lymphatic drainage can increase markedly, protecting the lungs from flooding. One result of this relative resistance of the lungs to flooding is that excessive amounts of salt and water tend to be sequestered in other sites in the body, especially skin, fat, and muscle (Ref. 67).

Most of these studies only cover the acute phase and deal with otherwise normal individuals. These results might not occur in other clinical circumstances. It is worth noting that the incidence of pulmonary dysfunction after use of large amounts of salt and water may also be effected by post-resuscitative renal function, indicating that the compensatory mechanisms are limited (Refs. 68 and 69). Even with gross overloading with salt and water, hydrostatic pressure may be a more important determinant of the formation of pulmonary edema than plasma osmotic pressure (Refs. 65 and 70).

The proper use of supplemental albumin in patients with already established acute pulmonary insufficiency without chronic lung disease is even less clear. Several published studies indicate a rough correlation between the degree of hypoproteinemia and various measures of pulmonary insufficiency in such patients, but there is no study showing clear improvement following administration of albumin only (Refs. 23 through 25, 61 and 62). It is possible, especially in infected patients, that this concurrence of hypoproteinemia and pulmonary insufficiency represents the effects of another common cause rather than direct cause and effect. At least one study now in progress on such patients who are also hypovolemic compares resuscitation with simple salt solutions versus isomotic albumin (Ref. 71). No functional differences were found. It is unfortunate that concentrated albumin was not used as a test solution. As with resuscitation from simple blood loss, however, the expected benefits of supplemental albumin in hypoproteinemic patients in ventilatory failure are proving unexpectedly difficult to document.

Established pulmonary failure is often associated with markedly increased amounts of albumin in the lungs, reflecting a probable increase in pulmonary capillary premeability (Ref. 27). If such indeed, occurs, administering albumin would be of little help. Such lesions may be irregular in distribution, however, (Ref. 72), and the relatively normal areas of lung might be protected by maintaining albumin concentrations in the plasma near normal. Recent studies in large primates (Refs. 28 and 29) and in rodents (Ref. 30) indicate that use of albumin or plasma during resusitation from severe hemorrhage may in fact increase the sequestration of fluid in the lungs and the pulmonary ultrastructural changes demonstrable after resuscitation. Some studies in primates come to the opposite conclusion (Ref. 31). Such studies in animals must be balanced against the reported similar studies in patients, with one exception discussed below, in which use of albumin was not demonstrably harmful.

There is a single published study in which use of supplemental albumin in acutely injured patients was associated with higher morbidity, especially pulmonary insufficiency, than use of simple electrolyte solutions (Ref. 73). The patients treated with albumin in this study received the albumin on a predetermined schedule, and had demonstrably higher blood volumes and very much higher cardiac-filling pressures. It seems from the data that too much albumin was given to these patients, with overexpansion of blood volumes to the point of pulmonary edema.

(2) *Safety of albumin administration for acute pulmonary insufficiency.* As noted, the possibility exists that in certain situations, albumin might worsen problems of ventilation and gas exchange. Aside from overexpansion of blood volume, however, this is conjectural, and current evidence favors avoiding hypoalbuminemia if possible in patients in acute respiratory failure. The expected beneficial effects, however, still lack clear documentation in properly controlled studies.

(3) *Benefit/risk of administration of albumin for acute pulmonary insufficiency.* The benefits probably significantly outweigh the risks for this indication, but more study is clearly needed.

(4) *Recommendations for the administration of albumin in acute pulmonary insufficiency.* Considerably more investigation is urgently needed on this important problem. Some of this research is now underway.

(5) *Labeling recommendations for the administration in acute pulmonary insufficiency.* In the absence of better and more complete data, no firm recommendations can be made. Any labeling dealing with this indication should indicate that some controversy exists.

d. *Malnutrition*—(1) *Rationale and effectiveness of the administration of albumin in malnutrition.* Hypoalbuminemia develops during protein or protein-calorie deprivation. Inadequate nutritional intake leads to rapid diminution in rates of albumin synthesis and degradation with some decrease in the total mass of albumin and the expected shift of extra-vascular albumin into the vascular space. This compensatory shift which masks much of the true decrease in total body albumin mass had led to numerous statements about the poor correlation between serum levels of albumin and nutritional status. Better understanding of the dynamic processes involved and more precise methods of measurement have shown that the serum level of albumin does indeed vary in the expected manner with alterations in nutritional status. While administration of albumin is effective in temporarily correcting nutritional hypoalbuminemia (Ref. 15), the clearly preferred treatment is the correction of the malnutrition. Sometimes this requires the use of total parenteral nutrition, which carries with it some danger, so that costs and benefits must be carefully evaluated.

Albumin given intravenously is not a good sole source of high quality protein because of its relative deficiency in two essential amino acids, leucine and

tryptophan, and because of its slow rate of degradation after infusion. It can, however, support growth for short periods. Better products are now available consisting of mixtures of amino acids for parenteral use. These do not require human sources for production and are superior products for parenteral nutritional use.

(2) *Safety of the administration of albumin for malnutrition.* Albumin is safe, if less than optimally effective when used for this indication.

(3) *Benefit/risk of the administration of albumin for malnutrition.* While the benefit/risk ratio is acceptable because of the low risk, there are clearly more effective and efficient methods of treatment of malnutrition available.

(4) *Recommendation for the administration of albumin for malnutrition.* It is recommended that this indication for use be eliminated.

(5) *Labeling recommendations for the administration of albumin for malnutrition.* Labeling should not promote or suggest the use of albumin as either the primary or a supplemental treatment for nutritional deficiencies when preferable forms of treatment are available. Use of these other methods should be strongly suggested, if malnutrition is discussed at all in the labeling.

e. *Trauma and infection*—(1) *Rational for the effectiveness of the administration of albumin for trauma and infection.* Synthesis of albumin decreases markedly after injury in animals; only about half of this is due to inanition (Ref. 32). It is likely that the same occurs in man, as the degree of hypo-albuminemia that develops is greater than would be expected from sequestration in wounds. In some states of infection, hypergammaglobulinemia may be associated with a decrease in the synthesis of albumin, but the quantitative aspects of this relationship are unclear. In addition there can be sequestration of large amounts of albumin in areas of injury, operation, or infection.

Severe trauma and infection are both characterized by prolonged negative nitrogen balance (catabolism) far exceeding that due to starvation, a state that is resistant to supplemental nutrition. An expansion of the interstitial fluid space also occurs. It is likely that much of this is hormonally mediated, but the details of the involved mechanisms are not at all clear (Ref. 33). It seems likely that albumin shares in the generalized protein catabolism. However, the rapid changes in metabolism, pool sizes, and clinical condition have made detailed studies of the metabolism and distribution of albumin in such patients impossible. This is very unfortunate, as these patients represent perhaps the single largest group of potential recipients of albumin in current medical practice. The fate of albumin administered to these patient, for example, is largely unknown.

Supplemental albumin is effective in restoring blood levels after extensive operations or major injury; the effectiveness of albumin administration seems to be somewhat less with major infection. Whether this difference is due to greater sequestration or to increased catabolism is uncertain.

(2) *Safety of the administration of albumin for trauma and infection.* If overloading of the circulation can be avoided, the use of albumin seems safe for these indications.

(3) *Benefit/risk of the administration of albumin for trauma and infection.* With a very low risk, almost any benefit establishes an acceptable ratio. There probably is some benefit in these circumstances, although its exact nature and value is not clear.

(4) *Recommendations for the administration of albumin for trauma and infection.* Methods for evaluating rates of synthesis, rate of degradation, and pool sizes which measure the effects of albumin administered for these conditions are needed.

(5) *Labeling recommendations for the administration of albumin for trauma and infection.* There are no specific recommendations for labeling changes.

f. *Post-operative hypoproteinemia.* Operations involving large wounds are accompanied and followed by sequestration and loss of albumin (Ref. 34). The quantities involved can be very large, especially with extensive procedures in the pelvis or retroperitoneum, where effective immediate sealing of the wound is difficult. If drainage to the outside is present, significant losses may continue for days. These sudden losses occur in a setting of protein starvation, so that the anticipated increase in rates of synthesis is almost certainly delayed. Recent studies indicate that parenteral supplementation of nutrition with amino acids is sufficient to increase rates of synthesis of albumin significantly in post-operative patients (Ref. 35). With extensive surgical procedures, however, infusion of albumin itself during and after the operation may be necessary.

g. *Hemolytic disease of the newborn.* It is the unbound unconjugated fraction of plasma bilirubin that causes neurological damage in icteric newborns. Albumin is the major plasma binding substance and thus offers some protection against brain injury by bilirubin. Synthesis of albumin may be impaired in some sick newborns, and the concentration of the patient's albumin must be measured and maintained near normal. If exchange transfusion becomes necessary, supplemental albumin before and during the exchange may increase the efficiency of removal of bilirubin from infants, even those with relatively normal concentrations of albumin (Refs. 36 through 38). If care is taken to avoid circulatory overloading from induced hypervolemia, little harm and some benefit probably result. Drugs that compete with bilirubin for binding to albumin must be avoided in these infants. Pertinent specific references should be cited in the labeling if this indication is listed.

h. *Cardiopulmonary bypass*—(1) *Rational for the administration of albumin in cardiopulmonary bypass.* Albumin is often used to avoid induction of excessive edema during cardiopulmonary bypass with priming solutions which do not contain blood, and with massive single-pass exchange transfusions ("total body washout"). The amount of albumin that is used varies considerably, and it is clear that normal levels are not necessary during bypass to achieve good results. The minimum acceptable levels are also not known, but restoration of albumin concentration after bypass is clearly more important than maintenance during bypass.

(2) *Safety of the administration of albumin for cardiopulmonary bypass.* Under the circumstances of close monitoring during treatment that prevails in these patients, use of albumin to mobilize excess salt and water from the interstitial space seems safe.

(3) *Benefit/risk of the administration of albumin for cardiopulmonary bypass.* With proper monitoring to detect left ventricular failure, the benefit/risk ratio is acceptible.

(4) *Recommendations for the administration of albumin for cardiopulmonary bypass.* Clinical data indicating the most efficient time for administration and the lowest doses needed for acceptable effects would help reduce wastage of albumin.

(5) *Labeling recommendations for albumin administration for cardiopulmonary bypass.* Labeling should emphasize the need for careful monitoring of patients and the lack of data needed to define the most efficient patterns of administration of albumin if this indication is listed.

i. *Cerebral edema.* Cerebral edema has appeared briefly in the literature as an indication for the parenteral administration of human albumin (Refs.

39 through 41). The clinical experience cited is very brief, completely uncontrolled, and unsubstantiated by documentation of preexisting hypoalbuminemia that was corrected. Current concepts of cerebral edema focus on the mobilization of intracellular fluid as well, by use of small molecular, osmotically active substances such as mannitol. There is little theoretical, experimental, or clinical data to support the use of albumin for the treatment of cerebral edema in a nonhypoalbuminemic patient. This indication should not be approved for labeling.

j. *Miscellaneous.* Most other listed indications for use, such as pancreatitis and toxemia, are not specific but are rather diseases in which hypovolemia and/or hypoalbuminemia may occur in varying combinations of severity.

3. *Safety issues related to the manufacture of albumin*—a. *Polymers.* There is significant variation in the proportion of albumin which exists in polymeric form in various preparations. Factors which bear on this include the quality of the starting material, the amount and duration of heating, the temperature during storage, the method of fractionation, and the concentration of the albumin in solution (Refs. 42 through 47). It is noteworthy that the percentage of monomer declines with reheating during the manufacturing process, increasing age of the starting material, and prolongation of storage. Some manufacturers achieve a product with over 90 percent of the albumin in monomeric form; for others, some lots may be as low as 70 percent and perhaps even lower (Refs. 44 through 47). For all manufacturers, the monomeric fraction apparently decreases with storage, but apparently at different rates.

There is very little evidence on the effectiveness of polymeric albumin. What data there are suggest that it is removed rapidly from the circulation after it is infused. There seems to be only one study on the fate of infused human albumin dimers in man (Ref. 48). That study revealed only a modest shortening of the biological half-life of the albumin in the few subjects studied. There seems to be no evidence of albumin dimers dissociating back to monomers after infusion. If this is the case, the dimeric form would then have half the osmotic effect of the monomeric form on a weight basis. It is likely, but not proven, that higher polymers contribute little or nothing to the desired therapeutic effects of infused albumin. There is, therefore, concern about the variation in composition of albumin monomers and oligomers which may in fact result in surprisingly wide variations in effect in vivo. Clearly, much more data are necessary to evaluate the significance of oligomers in these products, but it seems prudent and reasonable to require better control of the amount of polymers in the products pending the availability of such data.

b. *Placental source materials.* A portion of the source albumin currently used in manufacturing by one producer is derived from human placentas. There are some differences in the processing and properties of this source material compared to venous plasma from blood or plasma donors.

Placental material from each donor is not individually tested for hepatitis B surface antigen (HBsAg). Data from the single current manufacturer indicates that at least 0.2 percent (and probably more) of their donor population carry detectable HBsAg. Numerous previous studies have shown that HBsAg can be carried through the usual cold ethanol fractionation process and be detectable in albumin (Refs. 49 through 53). Similar studies with the exact method used to process placental material have not been done. It is unlikely that albumin produced from placental sources is infectious for hepatitis B virus (HBV), but it is likely that some HBsAg is carried through processing into the final product. The concentration is likely to be too low to be detected by currently available methods, but it is not known if such low concentrations can produce a detectable antibody response in recipients of this product. If such occurs, it could certainly result in diagnostic confusion and uncertainty when later detected in former recipients. If such is to be expected with significant frequency, then at least the labeling should warn of this unexpected and undesired possibility. A rather simply designed study could answer this question and should include as controls, recipients of albumin prepared from venous sources individually tested for HBsAg by radioimmunoassay (RIA).

Albumin can tightly bind a wide variety of biological materials found circulating in blood or produced by placentas. Such physiochemical binding is one of its important biological properties. Placental starting material has more hemoglobin, blood group substances A and B, HL-A antigen and a wide variety of hormonal agents than venous plasma (Refs. 54 and 55). Women in labor in the United States are quite likely to have received a variety of drugs immediately before or during delivery. Some of these drugs would be expected to be bound to albumin in the placental source material. The fact that alkaline phosphatase of placental origin is found in albumin produced from placentas demonstrates that at least some of this material can be expected to remain attached to albumin or be carried through the fractionation process used in the United States and thus be present in the final product (Refs. 56 and 57). Small amounts of placental lactogen are also found in the final product, another demonstration of the same principle. Comparative studies suggest that the method used in the United States to remove excess hemoglobin from the placental source material is less effective than some alternatives in removing hemoglobin, blood group substances A and B, alkaline phosphatase, and transaminase (Ref. 58). The United States manufacturer reports undetectable levels of blood group substances A and B, and the level of hemoglobin meets current standards, but the marketed material is largely diluted with albumin derived from venous plasma, and placental alkaline phosphatase is still present in significant amounts. There are very few data available on the probability of various drugs being carried through the processing into the final product. Of these, penicillin might be the most likely one, but by no means the only one, with significant dangerous potential.

On the other hand, there is a long history of the use of placental albumin in the United States and other countries without recognition of significant clinical problems of the type discussed.

4. *Recommendations for Normal Serum Albumin*—a. Normal Serum Albumin (Human) should be placed in Category I.

b. The sodium content of all products should be limited to 130 to 160 mEq/L.

c. The Bureau of Biologics should be informed by the manufacturer of the amount of "reworking" on the production of each lot released.

d. Manufacturers using placental source material should demonstrate that penicillin is not carried over into the final product by performing a sensitive assay for penicillin allergen on a significant number of lots.

e. The manufacturer's production process should be designed to assure that the final product contains a maximal amount of albumin in the monomeric form. Current data suggest that this should be no less than 85 percent of the albumin in monomeric form at the time of release and no less than 75 percent of the albumin in monomeric form at the time of outdating.

f. *Labeling recommendations.* (1) The name of the product should be "Human Albumin." The terms "Normal" and "Salt Poor" should be discontinued in labeling. "Albumin" alone will suffice if albumin from other species is not

marketed in a form likely to be confused with this.

(2) Much current labeling and advertising do not reflect the best current information as discussed earlier. Albumin should not be promoted as a nutritional agent. When recommended to treat hypoalbuminemia, the labeling should also point out that improvement of the patient's nutritional status is a necessary and preferable approach, where possible. Administration of albumin in the shock phase within 24 hours after major burns is of questionable value as is its administration for cerebral edema. Specific diseases should be listed only as examples of broader, stated indications. Where specific circumstances apply, e.g., hemolytic disease of the newborn, this should be pointed out and appropriate references cited.

(3) More emphasis is needed in most labeling on:

(a) The potential for pulmonary edema with rapid administration of the 25 percent albumin product.

(b) Individualization of doses and rates of administration.

(c) Correcting the underlying cause of the condition requiring use of albumin.

(d) The hazards of use in patients with severe anemia.

(e) The potential for microbial contamination once the package is entered.

(4) Material prepared from placental sources should indicate in the labeling that a variety of biological materials may be present in small amounts which are not found in material from venous plasma.

(5) The approximate concentrations of chloride and potassium ions should be given in the package insert.

d. *Stability*: The current shelf-life expiration times may need to be revised as more studies are performed, and particularly if the requirement for minimum monomer content is adopted.

e. *Research*—(1) There is a great need for methods of measuring the dynamics and in vivo distribution of albumin; these methods must be more rapid and less cumbersome than those now available. This will allow needed studies to be carried out in acutely ill, unstable patients.

(2) It is still not clear at what levels and in what circumstances low concentrations of albumin in patients should be supplemented with albumin administered intravenously, and which are the best methods for doing so.

(3) The fate of albumin administered to acutely ill patients needs to be determined, especially for those patients with large losses of relatively sudden onset and those who are in markedly catabolic states.

(4) The precise relationship between concentration of albumin in the plasma and its effects on pulmonary function is still debated, especially when the lungs are damaged. This is an important clinical question that needs to be answered soon.

(5) The entire area of the clinical importance of the binding and carrier functions of albumin and the same functions of albumin products deserves considerably more investigative support and attention. Modification of regulations may be necessary as a result of such investigations if there are differences in clinically important binding and carrier functions that relate to methods of manufacture.

(6) The fate and function of albumin in monomeric, dimeric, and polymeric forms needs to be established so that proper criteria can be established for the manufactured product. The current Panel recommendation on monomeric limits are based on very incomplete data, but are regarded as reasonable interim standards based upon the results that current manufacturing practices can already achieve.

(7) The use of placental source material raises many potential problems because of the likelihood that a variety of substances are carried over into the final product. Albumin derived from placental source material needs to be tested for immunizing potential against HBsAg, placental lactogen, and perhaps other placental hormones. Drugs commonly administered to women in labor may be present in the final product, and their potential for harm needs to be evaluated. The immunizing potential of the small amounts of HL-A antigenic material in this product needs to be defined. Changes in regulations and labeling of placental albumin may be necessary, depending on the results of such studies.

**References**

(1) Landis, E.M., and J.R. Pappenheimer, "Exchange of Substances Through the Capillary Walls," Handbook of Physiology, Hamilton, W.F. and P. Dow, Section 2, Circulation, Volume II, Washington, D.C., American Physiology Society, p. 961, 1963.

(2) Marty, A.T., "Hyperoncotic Albumin Therapy," *Surgery, Gynecology and Obstetrics*, 139:105–109, 1974.

(3) Taylor, A.E. and R.E Drake, "Fluid and Protein Exchanges," *Lung Biology in Health and Disease*, Vol. 10 Lung and Solute Exchange, Staub, N.C., editor, in press.

(4) Peters, T., "Serum Albumin," *Advances in Clinical Chemistry*, 13:37–110, 1970.

(5) Ashbrook, J.D., A.A. Spector, E.C. Santos and J.E. Fletcher, "Long Chain Fatty Acid Binding to Human Plasma Albumin," *Journal of Biological Chemistry*, 250:2333–2338, 1975.

(6) Kock-Weser, J., and E.M. Sellers, "Drug Therapy: Binding of Drugs to Serum Albumin," *New England Journal of Medicine*, 294:311–316 and 526–531, 1976.

(7) Rothschild, M.A., M. Oratz and S.S. Schreiber, "Albumin Metabolism," *Gastroenterology*, 64:324–337, 1973.

(8) Oratz, M., "Oncotic Pressure and Albumin Synthesis," *in* "Plasma Protein Metabolism," edited by Rothschild, M.A. and T. Waldmann, Academic Press, New York, pp. 223–238, 1970.

(9) Rosenoer, V.M. and M.A. Rothschild, "Albumin: Structure, Function, and Uses in Man," Pergamon Press, New York, 1976.

(10) Sgouris, J.T. and H.W. Dorsey, "Survey of the Use of Plasma Expanders in the United States," *Proceedings of the Workshop on Albumin*, February 12–13, 1975. Sgouris, J.T. and A. Rene, editors, DHEW Publication No. (NIH) 76–925, p. 137, 1976.

(11) Sherman, L.S. "Survey of the Use of Plasma Expanders in the United States," *Proceedings of the Workshop on Albumin*, February 12–13, 1975. Sgouris, J.T. and A. Rene, editors, DHEW Publication No. (NIH) 76–925, p. 235, 1976.

(12) Lundsgaard-Hanson, P., "Oncotic Deficit and Albumin Treatment," *Proceedings of the Workshop on Albumin*, February 12–13, 1975. Sgouris, J.T., and A. Rene, editors, DHEW Publication No. (NIH) 76–925, p. 242, 1976.

(13) Skillman, J.J., H.K. Awwad, and F.D. Moore, "Plasma Protein Kinetics of the Early Transcapillary Refill After Hemorrhage in Man," *Surgery, Gynecology and Obstetrics*, 125:983–996, 1967.

(14) Pruitt, B.A., "The Burn Patient: I. Initial Care," *Current Problems in Surgery*, 16, No. 4, 1979.

(15) Janeway, C.A., "Human Serum Albumin: Historical Review," *Proceedings on Workshop on Albumin*, February 12–13, 1975, Sgouris, J. T., and A. Rene, editors, DHEW Publication No. (NIH) 76–925, p. 3, 1976.

(16) Collins, J. A., "Massive Blood Transfusion" (cf. section on denatured proteins), *Clinics in Hematology*, 5:201–222, 1976.

(17) Madden, J.W., "Wound Healing: Biologic and Clinical Features," *in* "Textbook of Surgery," 10th Ed., Edited by Sabiston, D.C., Jr., Davis-Christoper, Saunders, Philadelphia, p. 249, 1972.

(18) Rothschild, M.A., M. Oratz, D. Zimmon, S. Scheriber, I. Weiner and A. Van Caneghem, "Albumin Synthesis in Cirrhotic Subjects with Ascites, Studied with Carbonate-$^{14}$C," *Journal of Clincial Investigation*, 48:344–350, 1969.

(19) Jensen, B.K., and S. Jarnum, "Albumin and IgG Turnover in Ulcerative Colitis and Crohn's Disease," *in* "Plasma Protein Turnover," Edited by Bianchi, R., G. Mariani and A.S. McFarlane, University Park Press, Baltimore, p. 45, 1976.

(20) Gaar, K.A., A.E. Taylor, L.J. Ownes and A.C. Guyton, "Effect of Capillary Pressure and Plasma Protein on Development of Pulmonary Edema," *American Journal of Physiology*, 213:79–82, 1967.

(21) Levine, O.R., R.B. Mellins, R.M. Senior and A.P. Fishman, "The Application of Starling's Law of Capillary Exchange to the Lungs," *Journal of Clinical Investigation*, 46:934–944, 1967.

(22) Skillman, J.J., B.M. Parikh and B.J. Tanenbaum, "Pulmonary Arteriovenous Admixture: Improvement with Albumin and Diuresis," *American Journal of Surgery*, 119:440–447, 1970.

(23) Giordano, J.M., W.L. Joseph, C.H. Klingenmaier and P.C. Adkins, "The Management of Interstitial Pulmonary Edema: Significance of Hypoproteinemia," *Journal of Thoracic and Cardiovascular Surgery*, 64:739–746, 1972.

(24) Gump, F.E., J.M. Kinney, M. Iles and C.C. Long, "Duration and Significance of Large Fluid Loads Administered for Circulatory Support," *Journal of Trauma*, 10:431–439, 1970.

(25) Gutierrez, V.S., I.R. Berman, H.B. Soloway and H.F. Hamit, "Relationship of Hypoproteinemia and Prolonged Mechanical Ventilation to the Development of Pulmonary Insufficiency in Shock," *Annals of Surgery*, 171:385–393, 1970.

(26) Skillman, J.J., D.S. Restall and E.W. Salzman, "Randomized Trial of Albumin vs. Electrolyte Solutions During Abdominal Aortic Operations," *Surgery*, 78:291–303, 1975.

(27) Gump F.E., Y. Mashima, A. Ferenczy and J.M. Kinney, "Pre and Postmortem Studies of Lung Fluids and Electrolytes," *Journal of Trauma*, 11:474–482, 1971.

(28) Moss, G.S., D.C. Siegel, A. Cochin and V. Fresquez, "Effects of Saline and Colloid Solutions on Pulmonary Function in Hemorrhagic Shock," *Surgery, Gynecology and Obstetrics*, 133:53–58, 1971.

(29) Holcroft, J.W. and D.D. Trunkey, "Extravascular Lung Water Following Hemorrhagic Shock in the Baboon," *Annals of Surgery*, 180:408–417, 1974.

(30) Collins, J.A., A. Braitberg and H.R. Butcher, "Changes in Lung and Body Weight and Lung Water Content in Rats Treated for Hemorrhage with Various Fluids," *Surgery*, 73:401–411, 1973.

(31) Gaisford, W.D., N. Pandey and C.G. Jensen, "Pulmonary Changes in Treated Hemorrhagic Shock. II. Ringer's Lactate Solution Versus Colloid Infusion," *American Journal of Surgery*, 124:738–743, 1972.

(32) Mouridsen, H.T., "The Extravascular Retention of Albumin in Wound Tissue and its Contribution to the Postoperative Hypoalbuminemia in Rabbits," *Clinical Science*, 37:431–441, 1969.

(33) Moore, F.D. and M.F. Brennan, "Surgical Injury: Body Composition, Protein Metabolism and Neuroendocrinology, in Man," *in* "Manual of Surgical Nutrition," Edited by Ballinger, W.F., J.A. Collins, W.R. Drucker, S.J. Dudrick and R. Zeppa, Saunders, Philadephia, p. 169, 1975.

(34) Hoye, R.C., D.F. Paulson and A.S. Ketcham, "Total Circulating Albumin Deficits Occurring with Extensive Surgical Procedures," *Surgery, Gynecology and Obstetrics*, 131:943–952, 1970.

(35) Skillman, J. J., V. M. Rosenoer, P. C. Smith and M. S. Fang, "Improved Albumin Synthesis in Postoperative Patients By Amino Acid Infusion," *New England Journal of Medicine*, 295:1037–1040, 1976.

(36) Kitchen, W. H., V. I. Krieger and M. A. Smith, "Human Albumin in Exchange Transfusion. A Quantitative Study of the Influence of Added Human Albumin on Bilirubin Removal," *Journal of Pediatrics*, 57:876–883, 1960.

(37) Odell, G.B., S.N. Cohen and E.H. Gordes, "Administration of Albumin in the Management of Hyperbilirubinemia by Exchange Transfusions," *Pediatrics*, 30:613–621, 1962.

(38) Comley, A. and B. Wood, "Albumin Administration in Exchange Transfusion for Hyperbilirubinaemia," *Archives of Diseases in Childhood*, 43:151–154, 1968.

(39) Gates, E. M. and W. M. Craig, "The Use of Serum Albumin in Cases of Cerebral Edema: Preliminary Report," *Staff Meetings of the Mayo Clinic*, 23:89–93, 1948.

(40) Seldon, T. H., A. Faulconer, R. F. Courtin and D. M. Pino, "Postanesthetic Encephalopathy: The postulation of Cerebral Edema as a Basis for Rational Treatment," *Staff Meetings of the Mayo Clinic*, 24:370–374, 1949.

(41) Cole F., "Use of Human Serum Albumin in Cerebral Edema Following Cardiac Arrest," Report of a Case, *Journal of the American Medicol Association*, 147:1563–1564, 1951.

(42) Finlayson, J. S., R. T. Suchinsky and A. L. Dayton, "Effects of Long-Term Storage on Human Serum Albumin: I. Chromatographic and Ultracentrifugal Aspects," *Journal of Clinical Investigation*, 39:1837–1840, 1960.

(43) Finlayson, J. S., "Effect on Long-Term Storage on Human Serum Albumin: II. Follow-up of Chromatographically and Ultracentrifugally Detectable Changes," *Journal of Clinical Investigation*, 44:1561–1565, 1965.

(44) Friedli, H. and P. Kistler, "Polymers in Preparations of Human Serum Ablumin," *Vox Sanguinis*, 18:542–546, 1970.

(45) Wickerhauser, M., C. Glaser and W. Westcott, "Large-scale Procedure for Reprocessing Outdated Clinical Albumin," *Transfusion*, 10:264–271, 1970.

(46) Roelands, J. F., M. F. Moody and P. Cohen, "Effects of Repeated Hearing on Human Albumin," *Vox Sanguinis*, 26:415–424, 1974.

(47) Skoog, B. and B. Granstrand, "Quantitative Determination of Albumin Dimer in Albumin Preparations by Combined Starch-gel Electrophoresis and Immunoprecipitation," *Vox Sanguinis*, 32:242–246, 1977.

(48) Woolf, I. L., P. Pappas, R. B. Pennell and B. M. Babior, "Rate of Disappearance of Infused Aged Albumin Subjects," *Transfusion*, 12:123–125, 1972.

(49) Schroeder, D. D. and M. M. Mozen, "Australia Antigen: Distribution During Cohn Ethanol Fractionation of Human Plasma," *Science*, 168:1462–1464, 1970.

(50) Andrassy, K., E. Ritz and R. Sanwald, "Australia-Antigen/Nachweis in Fibrinogenkonzentraten und Andersen Gerinnungsaktiven Proteinen," *Deutsche Medizinische Wochenschrift*, 95:2467–2469, 1970.

(51) Berg, R., H. Bjorling, K. Berntsen and A. Espmark, "Recovery of Australia Antigen from Human Plasma Products Separated by a Modified Cohn Fractionation," *Vox Sanguinis*, 22:1–13, 1972.

(52) Holland, P. V., H. J. Alter, R.H. Purcell, J. J. Lander, J. T. Sgouris and P. J. Schmidt, "Hepatitis B Antigen (HBAg) and Antibody (Anti-HBAg) in Cold Ethanol Fractions of Human Plasma," *Transfusion*, 12:363–370, 1972.

(53) Zuckerman, A. J., P. E. Taylor, R. G. Bird and S. M. Russell, "Thus Australia (Hepatitis-Associated) Antigen in Fibrinogen and Other Fractions of Human Plasma," *Journal of Clinical Pathology*, 24:2–7, 1971.

(54) Pla, J., J. Liautaud, A. Debrus, P. Gattel, R. Plan and L. Peyron, "Preparation de L'albumine Humanine a Partir de Sang Hemolyse Extrait de Placentas Congeles. II. Elimination de Certaines Impuretes au Cours de la Purification," 13th International Congress of International Association of Biological Standardization, Budapest, 1973, *Developments in Biological Standardization*, 27:115–122, 1974.

(55) Knoop, J. and R. Johannsen, "Blood Group and HL–A Specific Substances in Immune Globulin and Albumin Preparations of Human Placental Origin," 13th International Congress of International Association of Biological Standardization, Budapest, 1973, *Developments in Biological Standardization*, 27:129–136, 1974.

(56) Bark, C.J., "Artifactual Serum Alkaline Phosphatase from Placental Albumin," *Journal of the American Medical Association*, 207:953, 1969.

(57) Schiffner, J.H., "Artificially Elevated Serum Alkaline Phosphatase," *New England Journal of Medicine*, 282:631–632, 1970.

(58) Liautaud, J., J. Pla, A. Debrus, P. Gattel, R. Plan and L. Peyron, "Preparation de L'albumine Humaine a Partir de Sang Hemolyse Extrait de Placentas Congeles. I. Technique de Preparation et Qualite du Produit," 13th International Congress of International Association of Biological Standardization, Budapest, 1973, *Developments in Biological Standardization*, 27:107–114, 1974.

(59) Baxter, C.R., "Fluid Volume and Electrolyte Changes of the Early Postburn Period," *Clinics in Plastic Surgery*, 1:693–709, 1974.

(60) Jelenko, C. III, J.B. Williams, M.L. Wheeler, B.D. Callaway, V.K. Fackler, C.A. Albers and A.A. Barger, "Studies in Shock and Resuscitation. I: Use of a Hypertonic, Albumin-containing, Fluid Demand Regimen (HALFD) in Resuscitation," *Critical Care Medicine*, 7:157–167, 1979.

(61) Weil, M.H., R.J. Henning, M. Morissette and S. Michaels, "Relationship Between Colloid Osmotic Pressure and Pulmonary Artery Wedge Pressure in Patients with Acute Cardiorespiratory Failure," *American Journal of Medicine*, 64:643–650, 1978.

(62) Rackow, E., A. Fein and J. Leppo, "Colloid Osmotic Pressure as a Prognostic Indicator in Critically Ill Patients," *Chest*, 70:439, 1976.

(63) Laks, H., N.E. O'Connor, W. Anderson and R.N. Pilon, "Crystalloid Versus Colloid Hemodilution in Man," *Surgery, Gynecology and Obstetrics*, 142:506–512, 1976.

(64) Lowe, R.J., G.S. Moss, J. Jilek and H.D. Levine, "Crystalloid vs. Colloid in the Etiology of Pulmonary Failure After Trauma: A Randomized Trial in Man," *Surgery*, 81:676–683, 1977.

(65) Virgilio, R.W., C.L. Rice, D.E. Smith, D.R. James, C.K. Zarins, C.F. Hobelmann and R.M. Peters, "Crystalloid vs. Colloid Resuscitation: Is One Better? A Randomized Clinical Study," *Surgery*, 85:129–139, 1979.

(66) Cloutier, C.T., B.D. Lowery and L.C. Carey, "The Effect of Hemodilutional Resuscitation on Serum Protein Levels in

Humans in Hemorrhagic Shock," *Journal of Trauma*, 9:514–521, 1969.

(67) Pappova, E., W. Bachmeier, J. L. Crevoisier, J. Kollar, M. Kollar, P. Tobler, H.W. Zohler, D. Zaugg and P. Lundsgaard-Hansen, "Acute Hypoproteinemic Fluid Overload: Its Determinants, Distribution and Treatment with Concentrated Albumin and Diuretics," *Vox Sanguinis*, 33:307–317, 1977.

(68) Abrams, J.S., R.S. Deane and J.H. Davis, "Adverse Effects of Salt and Water Retention on Pulmonary Function in Patients With Multiple Trauma," *Journal of Trauma*, 13:788–798, 1973.

(69) Lucas, C.E., A.M. Ledgerwood, M.R. Shier and V.E. Bradley, "The Renal Factor in the Posttraumatic 'Fluid Overload' Syndrome," *Journal of Trauma*, 17:667–675, 1977.

(70) Demling, R.H., "Correlation of Changes in Body Weight and Pulmonary Vascular Pressures With Lung Water Accumulation During Fluid Overload," *Critical Care Medicine*, 7:153–156, 1979.

(71) Virgilio, R.W., D.E. Smith and C.K. Zarins, "Balanced Electrolyte Solutions/ Experimental and Clinical Studies," *Critical Care Medicine*, 7(3):98–106, 1979.

(72) Teplitz, C., "The Core Pathobiology and Integrated Medical Science of Adult Acute Respiratory Insufficiency," *Surgical Clinics of North America*, 56:1091–1133, 1976.

(73) Lucas, C.E., D. Weaver, R.F. Higgins, A.M. Ledgerwood, S.D. Johnson and D.L. Bouwman, "Effects of Albumin Versus Non-albumin Resuscitation on Plasma Volume and Renal Excretory Function," *Journal of Trauma*, 18:564–570, 1978.

*Product Reviews*

There were 15 different suppliers of Normal Serum Albumin (Human) subject to this review, all with great similarity in the basic plasma processing procedures, but with many differences in details which conceivably could be significant. The products of each individual manufacturer are therefore described only with respect to obvious departures from common practices, along with comments on the labeling and advertising.

1. *Source.* Most manufacturers use Source Plasma (Human) and plasma from outdated whole blood. Both contain citrate anticoagulants and may have been frozen at least for transportation. Some manufacturers specifically state in their data submissions (Refs. 1 through 15) that each source unit was tested for hepatitis-B sulface antigen by radioimmunoassay and was free of such antigen. A few manufacturers are licensed to use placental material.

2. *Processing.* All manufacturers use the cold alcohol plasma fractionation process, described as the Cohn method 6, with many small variations. Placental material is handled by a somewhat different process.

3. *Composition.* The 5-percent (plus or minus 0.3 percent) solution of albumin is brought to volume with 0.15 M sodium chloride, with 0.004 M sodium acetyltryptophanate and 0.004 M sodium caprylate added as stabilizers. The 25-percent (plus or minus 1.5 percent) solution of albumin contains 0.02 M sodium acetyltryptophanate and 0.02 M sodium caprylate. None contain preservatives. All are at least 96-percent albumin, expressed as the percent of total protein present, with less than 3-percent globulins. Heme concentrations are less than 1 mg/5 grams albumin; pH is 6.9 plus or minus 0.5. All are sterilized by filtration, and heated to 60 °C plus or minus 0.5° for at least 10 hours. Final sodium content ranges from 100 to 160 mEq/L.

4. *Safety.* Lots and batches are visually checked during 7 days storage at 18 to 35 °C. Specified samples are randomly selected for culture for bacterial growth. All manufacturers check each lot in animals for febrile response and gross vasomoter reactions. Most manufacturers also check each lot in human volunteers for febrile response, effect on pulse rate and blood pressure, and symptomatic effects. All manufacturers keep records of reported reactions. Some manufacturers have voluntarily recalled lots associated with reported febrile responses. The commonest reported adverse reactions are chills and fever; much less commonly reported are tachycardia, hypotension which is rarely severe, urticaria, nausea, vomiting, increased salivation, and a skin rash. Transmitted diseases have not been documented to occur from properly processed material.

5. *Effectiveness.* No manufacturer has submitted effectiveness data for its specific product. All rely on the assumed similarity and homogeneity of this material in relation to that used in earlier studies. It is likely that some of the early published studies on effectiveness of albumin used material produced by methods similar to present methods in the Massachusetts Public Health Biological Laboratories.

6. *Labeling.* The bottle and package labels are all similar, including the product name, concentration of albumin, total volume, manufacturer's name and location, lot number, various other identifying numbers, United States License Number, osmotic equivalent as citrated plasma, date of expiration and added stabilizers. Instructions and warnings include: Temperature of storage, "contains no preservative", "do not use if turbid", caution against patient dehydration, "single dose container", "for intravenous use", the prescription legend and "see enclosed circular". All 25 percent albumin preparations were labeled "salt poor" at the time of the data submission, but recently published regulations require this designation to be removed.

The package inserts share several features in common. Indications for use include: Hypovolemia, hypoalbuminemia, and hemolytic disease of the newborn. Some inappropriate indications are mentioned below for individual manufacturers. Warnings, precautions and contraindications include cardiac failure due to hypervolemia, renewed bleeding as blood volume expands and perfusion improves, "dehydration" of the patient when 25 percent albumin is used as treatment for hypovolemia without supplemental fluids and electrolytes, severe anemia, and the fact that the material contains no preservatives and thus should not be used if turbid and should not be stored once opened. A statement is made that heat treatment at 60 °C for 10 hours probably eliminates the risk of hepatitis. Possible adverse reactions are described. Suggested doses for various clinical conditions are given. Essentially all of the information from the container and the package labels are usually repeated.

Advertising occasionally makes claims beyond those contained in the labeling. This is discussed where applicable in the review for each of the following products, realizing that manufacturers may have revised their labeling and advertising since the date of the submissions which were reviewed:

(1) *Abbott Laboratories (Albutein™)* (Ref. 1). A reasonable discussion in labeling of individual-specific dosing is present. The labeling also lists "adjunct in hemodialysis and cardiopulmonary bypass" as an indication for use. Advertising separates traumatic from hemorrhagic shock, mentions "ischemic (reversible)" and "stagnant (irreversible)" forms claims that early loss in "endotoxic" shock is plasma loss, and mentions cardiogenic shock as a distinct indication for administration of albumin. All of these statements are questionable if not objectionable. The indication for use of albumin in shock is hypovolemia; various theories of pathophysiology and categorization of shock are better avoided in labeling until more firmly established scientifically. This section of the labeling would be much better if so simplified and clarified. With respect to labeling for administration in burns, see the earlier Generic Statement on Normal Serum Albumin (Human). In discussing hypoproteinemia, correction of the underlying cause is correctly emphasized. Acute pancreatitis,

cerebral edema, and nutritional hypoproteinemia are mentioned as specific indications. It is concluded that the reviewed advertising for this product falls well below the quality of the package insert labeling and borders on being misleading.

(2) *Armour Pharmaceutical Company (Albuminar™)* (Ref. 2). The labeling does not list hemolytic disease of the newborn as an indication for use. It does list use in the shock phase which occurs immediately after major burns (see above). The labeling properly includes severe anemia as a contraindication.

(3) *Connaught Laboratories, Limited* (Ref. 3). The labeling specifies storage at 2 to 10 °C; therefore, it has a 5-year dating period. Apparently there is no testing in humans before lots are released. Connaught was no longer a licensed U.S. producer at the completion of this review.

Labeling is rather minimal. Hemolytic disease of the newborn is not mentioned as an indication for use, but burns are. Severe anemia is not specifically mentioned as a possible contraindication, and the lack of clotting components in this preparation is not pointed out. There has been no advertising in 5 years.

(4) *Cutter Laboratories, Incorporated* (Ref. 4). Burns and cerebral edema are mentioned as indications for use in labeling. Hemolytic disease of the newborn is not listed. Directions for use were not included in the package insert. There is separate packaging for material derived from blood collected from the American National Red Cross and paid for by the Red Cross. Advertising is minimal, but contains the potentially misleading statement that "cardiac output is greater than that produced by whole blood." Testing of lots in human volunteers is not described.

(5) *Dow Chemical (Proserum™)* (Ref. 5). Placental origin material was used until mid-1971. Menthanol is occasionally used as the precipitating alcohol. The process permits the product to be reheated up to five times to eliminate pyrogenic reactions.

The package insert for 25-percent albumin incorrectly suggests use in cerebral edema and use as a vehicle for delivering red cell concentrates as indications. Labeling for other indications has a more balanced presentation. The rise in alkaline phosphatase in recipients of the placental material is mentioned. The package insert for 5 percent albumin lists only hypovolemia as an indication.

Five and three lots of 25 percent and 5 percent albumin respectively have been tested in humans for adverse reactions. Two lots of 25 percent material were recalled in 1974 because of a reported incidence of adverse reactions in 17 patients. Dow Chemical was no longer a licensed producer at the completion of this review.

(6) *Hyland Division, Travenol Laboratories (Buminate™)* (Ref. 6). Production methods are very sketchily outlined in the submission to the Panel.

There are separate packages and labels for material produced for the New York Blood Center, and material for bulk use which is exported. The standard package insert points out lack of clotting factors in albumin and the inability to make absolute statements about the risk of transmission of viral diseases by the material. Hemolytic disease of the newborn is not mentioned as an indication for use. In general, the discussion is reasonably balanced. The precautions do not fully emphasize the necessary safeguards against bacterial contamination, and severe anemia is not mentioned as a contraindication. Instructions for use are detailed. Cerebral edema is incorrectly suggested as an indication for use with the 25-percent preparation. Hemolytic disease of the newborn is not mentioned.

(7) *Lederle Laboratories Division American Cyanamid (Pro-Bumin™)* (Ref. 7). Lederle has used placental starting material in the past, although reportedly this is no longer the case. The package inserts are adequate in their precautionary statements. Cirrhosis, nephrosis, and pancreatitis are listed as specific indications for use of the 25 percent preparation; the potential value of 25-percent albumin for cirrhotic ascites is overstated. In advertising, "prothrombin levels" are mentioned were "clotting factors" are meant; this may be confusing. The Panel disagrees with the statement that 25-percent albumin "has its greatest application in the treatment of shock." There has been some testing for safety in humans in the past.

(8) *Massachusetts Public Health Biologic Laboratories* (Ref. 8). Hemolytic disease of the newborn is not mentioned as an indication in the labeling. Starvation is mentioned twice; this should be updated to indicate currently preferred approaches to treatment of malnutrition. There has been no advertising.

(9) *Merck Sharp and Dohme, Division of Merck and Company, Inc. (Albumisol ™)* (Ref. 9). Nutritive value is inappropriately mentioned in the package insert. Many specific diseases are mentioned under the usual broad categories of indications for use. Severe anemia is not mentioned as a contraindication. Detailed electrolyte content is given on some packages. Hemolytic disease of the newborn is not mentioned as an indication in most package inserts.

There were unusually large numbers of reactions reported in 1972 for the 5 percent product. Two of three lots were withdrawn and distribution of the third was discontinued. Retesting (not described) failed to reveal the cause.

(10) *Michigan Department of Public Health* (Ref. 10). Placental material has been used in the past. A questionable statement "at least 95 percent albumin" is used in the labeling. The package insert is very brief. Nutritional hypoproteinemia is inappropriately mentioned as an indication; hemolytic disease of the newborn is not mentioned. Precautions do not mention the possibility of inducing severe anemia. Each lot is reported to be tested in normal humans for adverse reactions. No adverse reactions were reported from clinical use.

(11) *North American Biologicals* (Ref. 11). The package insert inappropriately mentions effects on the pH buffer capacity of blood, which is minimal when compared with hemoglobin. Suggested use to provide a large mobile reserve of amino acids clearly has inappropriate nutritional implications. Hypoproteinemia of starvation and burns are also listed as indications

Various lots have been tested for adverse effects on over 100 patients and volunteers. No mention is made of adverse reactions in clinical recipients. No data were given on actual composition of the product. This firm was no longer a licensed producer at the completion of this review.

(12) *Ortho Diagnostics, Incorporated (Orthobumin™)* (Ref. 12). Acute pancreatitis and cerebral edema are inappropriately mentioned as indications for use. Four lots were reported to have been tested for safety in normal humans.

(13) *Osterreichisches Institut Fur Haemoderivate* (Ref. 13). All lots are reported to be tested in humans before release. There was no mention of reports of adverse reactions in patients. Cerebral edema and eclampsia which are included as indications in the labeling should be eliminated.

(14) *Parke, Davis and Company* (Ref. 14). Placental source material is used in combination with venous source material. Venous sources are tested for HBsAg, but individual placentas are not tested for HBsAg. Each lot is tested in patients before release. A rather large number of reactions were reported for 1970 without explanatory comment. Nutritional use as mentioned in advertising material should be

eliminated. Safety should be evaluated as recommended for placental source material in the earlier Generic Statement on Normal Serum Albumin (Human).

(15) *E.R. Squibb and Sons* (Ref. 15). The labeling precautions include possible elevation of alkaline phosphatase in recipients, even though the material is not of placental origin. The package insert is well balanced, although hints at nutritional advantages in anuric patients should be eliminated. No information was available regarding further testing, safety, and reported reactions in recipients.

**References**


(1) BER Volume 6024
(2) BER Volume 6075.
(3) BER Volume 6036.
(4) BER Volume 6016.
(5) BER Volume 6043, 6044 and 6045.
(6) BER Volume 6069 and 6069A.
(7) BER Volume 6019.
(8) BER Volume 6035A.
(9) BER Volume 6009.
(10) BER Volume 6042.
(11) BER Volume 6125.
(12) BER Volume 6085, 6086, and 6087.
(13) BER Volume 6101.
(14) BER Volume 6004 and 6004A.
(15) BER Volume 6031.


**11. Plasma Protein Fraction (Human)**

*Generic Statement*

Plasma Protein Fraction (PPF) was developed in 1957 (Ref. 1). The composition of the product is essentially that of Fraction IV–4 plus Fraction V which are obtained by method 6 developed by Cohn et al. (Ref. 2) to fractionate the proteins of human plasma. At the time of the development of plasma proteins during World War II only human serum albumin was available as a 25-percent concentration in 100 mL volume (Ref. 3). This solution often proved to be ineffective in restoring blood pressure without the addition of intravenous saline, especially in dehydrated patients. Thus, a 5-percent solution of plasma protein was readily received because of its ease of administration (Ref. 4). Also PPF preserves the national blood resources: there is 25 to 30 percent more yield of usable plasma proteinf solution from a unit of blood than when albumin is produced (Ref. 5).

Nearly all commercial fractionation methods are based upon the exploitation of solubility differences. Thus, the chemistry of protein ractionation is the chemistry of protein solubility. Protein solubility is affected by a number of variables, and if these variables are controlled, they can form the basis of systematic protein fractionation. In the fracttionatio of most natural protein systems, the presence of a large number of components and the similarity of many of them makes it necessary to control a number of variables if sufficiently large differences in solubility are to be obtained to give usefully precise separation.

One of the most difficult problems in protein fractionation is to avoid alterations of the proteins during their separation. Proteins are subject to irreversible alterations from many causes. The extent and nature of these alterations are often difficult to evaluate. In the fractionation of the proteins of human plasma, it is particularly important that unaltered proteins be made available for subsequent use in humans, since irreversible alteration might well lead to substances of new antigenic specificity if not more general changes in biological activity.

Production of PPF requires manufacturing methods that include low temperatures (−3 to −5° C) various concentrations of ethyl alcohol (8 to 30 percent), varying hydrogen ion levels (pH 4.6 to 7.2), and separation of precipitates. Virtually every step in the manufacturing process has the potential for causing protein denaturation, i.e., an alteration in the protein's molecular structure (Ref. 6).

*PPF and hypotension.* Other labile proteins may be altered by the fractionation process. For example, recent lots of PPF that produced hypotension were found to have high levels of prekallikrein activator (PKA), although most lots of PPF have low levels of this activator. PKA is perhaps better known as Hageman Factor Fragment (Table 1). Activated Hageman Factor can act to trigger blood coagulation and fibrinolysis, and also can activate prekallikrein to kallikrein which in turn acts upon high molecular weight kininogen to produce bradykinin (Table 2).

*Table 1.—Some Components of the Kallikrein-Kinin System*

| | |
|---|---|
| 1. Hageman Factor.... | Factor XII–MW about 80,000. |
| 2. Prekallikrein Activator(s) or Hageman Factor Fragment(s). | "PKA"—MW about 28,000.<br>Generated from Factor XII.<br>Catalyze(s) Prekallikrein Kallikrein. |
| 3. Plasma Prekallikrein. | "PK"—MW about 100,000. |
| 4. Plasma Kallikrein.. | MW about 100,000.<br>Catalyzes release of BK from HMWK.<br>Has esterolytic activity |
| 5. High Molecular Weight Kininogen(s). | "HMWK"—MW about 200,000.<br>Preferred substrate for plasma kallikrein. |
| 6. Bradykinin..... | "BK"—a nonapeptide. MW about 1,000.<br>Has vasodilatory activity.<br>Causes smooth muscle contraction |

TABLE 2

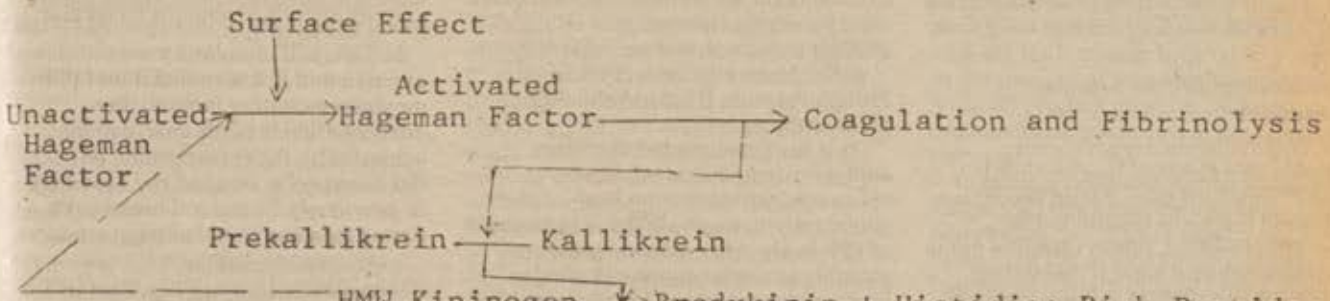



Diagram of the relationship of proteins of the kinin-generating pathway to the mechanism of Hageman factor.

Bradykinin is nonapeptide with a molecular weight of about 1,000 which has vasodilator activity and causes smooth muscle contraction. In the normal circulation, bradykinin is rapidly inactivated largely by kininases, proteolytic enzymes that degrade kinins to inactive forms. The half-life of bradykinin in blood is about 20 seconds; it is almost totally destroyed in one passage through the pulmonary circulation (Ref. 8).

It has previously been reported that during surgical procedures bradykinin levels increase from low (nanogram) levels to considerably higher levels (Ref. 9). If this occurs and another generator of bradykinin is added to the system (PPF) or if a kininase is removed from the system or the level of an inhibitor in this system is suppressed, there can be a resultant increase in bradykinin that can cause hypotension.

In the original work of Bland and his associates (Ref. 10) it was postulated that it was bradykinin that caused the hypotension produced by PPF. Recent studies at the Bureau of Biologics with samples of PPF retained from Bland's original studies were found to be high in PKA activity (Ref. 11). It has been shown that there is direct correlation between high levels of PKA and the amount of hypotension produced in animal models (Ref. 12).

In the "blocked rat" model, treated to inhibit kininases so that any bradykinin generated stays in the circulation, there is a linear correlation between the drop in mean arterial pressure and the concentration of PKA in the product administered. However, in unblocked rats it takes much more bradykinin, either generated or administered to produce a given fall in blood pressure, and the relationship tends to be much less linear (Ref. 13).

There is some evidence that there are higher PKA levels in salvaged plasma than in fresh frozen plasma, although there is not general agreement with this observation (Ref. 14).

PKA activity has been found in only a few lots of albumin. Indeed this is reasonably consistent because a further fractionation process is necessary to produce albumin, Fraction V; most of the PKA is removed by these additional steps. These protein fractions, however, are never so "clean" that the presence or absence of PKA can be absolutely predicted. PKA tends to concentrate in Fraction IV, but on rare occasions may be found in albumin which is made from Fraction V. After heating to 60 degrees for pasteurization bradykinin may still be present, kallikrein has been destroyed, kininogen is still present but at very low levels, and prekallikrein activator in present in various amounts and maintains its activities.

It is well known that the administration of PPF fractions do not cause adverse responses in all people. People have different prekallikrein, kininogen, and enzyme inhibitors in the circulation. Individuals vary in their ability to destroy bradykinin. They may also have differing levels of PKA because the trauma of surgery activates Hageman Factor.

There is evidence that ammonium sulfate as sometimes used in fractionation (Ref. 15) and cooling to a temperature of 4° C both activate Hageman Factor. These steps were used in the manufacturing process for PPF by one supplier until 1976. There is also the possibility that PKA could be generated in plasma which has been thawed to obtain cryoprecipitate (Ref. 16). Kallikrein can be rapidly inhibited by C 1 esterase inhibitor and by alpha 2-macroglobulin and more slowly by antithrombin III. Heating probably inactivates all these inhibitors.

Potentially, chemical reactions producing PKA can occur at almost any stage in plasma derivative manufacture, in the source plasma, during the fractionation, in partially fractionated products, in the paste, in the powder, in the bulk, and finally perhaps even on the shelf.

*Composition of PPF.* The protein composition of PPF is determined by methods that have been approved for each manufacturer. The protein content is set at 5.0 plus or minus 0.3 percent. In addition to the alpha and beta globulins present in the PPF (usually about 12 percent) the albumin exists at both a monomer and a dimer. The effect of albumin dimer on the oncotic characteristics and drug-binding properties of the albumin has not been determined. PPF Is composed of at least 83 percent (usually about 88 percent) albumin, no more than 1 percent gamma globulin, 130–160 mEq/L of sodium, less than 2 mEq/L of potassium, and has a pH of 7.0 plus or minus 0.3. This solution is stabilized with 0.004 molor sodium acetyltryptophanate and 0.004 molar sodium caprylate. After being

introduced into the final container the PPF solution is heated at an attained temperature of 60°C plus or minus 0.5°C for 10 hours. The dating period is 5 years when stored at 5°C or 3 years at 30°C or less.

*Evaluation of PPF for Labeled Indications*

1. *Hypovolemia.* Hypovolemia, whether due to blood loss or "third space" sequestration of fluid (exclusive of burns) responds readily to PPF.

a. *Effectiveness.* PPF is effective in the maintenance of a normal circulating blood volume (Ref. 4), but has not been proved to be effective in the maintenance of oncotic pressure. The same labeling claims are made by all the manufacturers of PPF, although there may be possible differences in effectiveness among products relating to the methods of preparation. At the present time there is no information available about the effect of various methods of preparation of PPF upon the metabolism and oncotic effect of its albumin.

Precautions about PPF administration at a rate greater than 10 mL/minute may limit its usefulness as a rapid plasma volume expander when blood is not available unless efforts to reduce the hypotensive reactions are successful.

Much of PPF administration today is arbitrary or pragmatic. The advent of a clinical oncometer so that oncotic pressure could be measured before and after PPF administration should result in a better quantification of the effects of PPF and clarification of the need for its administration. These studies have not been done.

b. *Safety.* The safety of PPF has been assumed in the past to be so high that complications have already been reported even though some may have occurred. The reaction rate for various adverse side effects such as urticaria, chills, fever or vasodepressor effects are few and involve between 0.5 and 1.5 percent of the production lots. These reactions are for the most part mild and short-lived. The vasodepressor effects have been increasingly reported and may be significant in some patients.

As a result of the unusual stability of albumin, it is possible to heat the product routinely during processing to 60°C for 10 hours, thus achieving inactivation of hepatitis viruses. The only established cases of hepatitis after PPF infusion have apparently come from a failure in processing so that 60°C treatment for 10 hours was not achieved (Ref. 17).

c. *Benefit/risk evaluation.* Properly administered, PPF has an acceptable benefit-to-risk ratio. Until clarification of the frequency of occurrence and clinical significance of hypotensive episodes has been determined, an evaluation of the ultimate benefit-to-risk ratio for rapid, emergency administration cannot be achieved.

d. *Recommendations.* (1) Plasma Protein Fraction (Human) should be place in Category I.

(2) It is recommended that more sophisticated clinical studies be sponsored within the medical community to evaluate the effectiveness of PPF in elevating oncotic pressure possibly in conjunction with similar studies recommended for albumin. This information would clarify the many clinical disorders that exist in which there is incomplete or conflicting data on the effectiveness of PPF therapy and should define further the situations in which no benefit from PPF administration occurs, despite the presence of hypoalbuminemia.

(3) Manufacturers of PPF should have a control testing program for measuring PKA consistent with available technology.

(4) Acceptable levels of PKA should be no more than 25 percent of the present Bureau of Biologics reference standard.

(5) Limits for bradykinin content should be established when data are developed to substantiate measurable safe levels.

(6) The product name should be "Plasma Protein Fraction".

e. *Labeling recommendations for hypovolemia.* The package inserts should be revised to inform physicians of the possibilities of hypotension occurring after PPF administration and that this hypotensive effect can be reversed with the use of vasopressors. Also, the package insert should note that no evidence exists that PPF appreciably increases the colloid oncotic pressure of the plasma.

2. *Burns.* Acute therapy in burns is directed during the first 24-hours to the administration of large volumes of crystalloid solution to expand the constructed extracellular fluid volume. For continuation of therapy beyond 24-hours, albumin, often as PPF, and lesser amounts of crystalloids are generally used. Recommendations are the same as for hypovolemia.

3. *Red cell resuspension medium*—a. *Effectiveness.* During certain types of exchange transfusion or when very large volumes of packed red blood cells have been administered to correct blood loss, PPF may be used as a resuspension menstruum in order to avoid excessive hypoalbuminemia during such transfusion therapy. Although such blood is deficient in coagulation factors and platelets, sufficient equilibrium exists between intravascular and extravascular clotting factors to maintain adequate hemostasis during blood exchanges of less than 90 percent.

b. *Safety.* If circulatory overload is avoided and if it is realized that PPF has no plasma-clotting factors, then adequate levels of albumin can be achieved by the resuspension of packed red blood cells, washed red blood cells or previously frozen red blood cells during massive transfusion procedures.

c. *Recommendations.* Recommendations are the same as for hypovolemia.

**References**

(1) Hink, J.H., J. Hidalgo, V.P. Seeberg and F.F. Johnson, "Preparation and Properties of a Heat-Treated Human Plasma Protein Fraction," *Vox Sanguinis*, 2:174–188, 1957.

(2) Cohn, E.J., L.E. Strong, W.L. Hughes, D.J. Mulford, J.N. Ashworth, M. Melin and H.L. Taylor, "Preparation and Properties of Serum and Plasma Proteins. IV. A System for the Separation into Fractions of the Protein and Lipoprotein Components of Biological Tissues and Fluids," *Journal of the American Chemical Society*, 68:459–475, 1946.

(3) Janeway, C.A., S.T. Gibson, L.M. Woodruff, J.T. Heyl, O.T. Bailey and L.R. Newhouser, "Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation. VII. Concentrated Human Serum Albumin," *Journal of Clinical Investigation*, 23:465–490, 1944.

(4) Bertrand, J.J., T.V. Feichtmeir, N. Kolomeyer, J.O. Beatty, P.L. Murphy, W.D. Waldschmidt and E.B. McLean, "Clinical Investigations with a Heat-Treated Plasma Protein Fraction-Plasmanate," *Vox Sanguinis*, 4:385–402, 1959.

(5) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents, Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 220, September 15–16, 1977.

(6) Watt, J.G., "Plasma Fractionation," *Clinics in Hematology*, 5:95–111, 1976.

(7) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents, Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 16, September 15–16, 1977.

(8) Ryan, J.W., J. Roblero and J.M. Stewart, "Inactivation of Bradykinin in Rat Lung," *Advances in Experimental Medicine and Biology*, 8:263–267, 1970.

(9) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents, Bureau of Biologics, Food and Drug Administration, Bethesda, MD, pp. 23 and 172, September 15–16, 1977.

(10) Bland, J.H.L., M.B. Laver and E. Lowenstein, "Vasodilator Effect of Commercial 5 Percent Plasma Protein Fraction Solutions," *Journal of the American Medical Association*, 224:1721–1724, 1973.

(11) Alving, B.M., Y. Hojima, J.J. Pisano, B.L. Mason, R.E. Buckingham, M.M. Mozen and J.S. Finlayson, "Hypotension Associated

With Prekallikrein Activator (Hageman-Factor Fragments) in Plasma Protein Fraction," New England Journal of Medicine, 299:66–70, 1978.

(12) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents. Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 65, September 15–16, 1977.

(13) Roundtable Discussion of PKA and Bradykinin Measurements in PPF and Albumin. Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 173d, March 16, 1978.

(14) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents. Bureau of Biologics, Food and Drug Administration, Bethesda, MD, pp. 42 and 180, September 15–16, 1977.

(15) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents. Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 181, September 15–16, 1977.

(16) Proceedings of the Workshop on Measurement of Potentially Hypotensive Agents. Bureau of Biologics, Food and Drug Administration, Bethesda, MD, p. 186, September 15–16, 1977.

(17) Gellis, S.S., J.R. Neefe, J. Stokes, L.E. Strong, C.A. Janeway and G. Scatchard, "Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation. XXXVI. Inactivation of Virus of Homologous Serum Hepatitis in Solution of Normal Human Serum Albumin by Means of Heat," *Journal of the Clinical Investigation*, 27:239–244, 1948.

### 12. Antihemophilic Factor (Human)

*Generic Statement*

1. *Introduction.* Antihemophilic Factor (AHF, factor VIII, antihemophilic globulin, AHG) is generally considered to be a trace protein in normal plasma which has the property of correcting the clotting defect characteristic of hemophilia A (Ref. 1). Recent work indicates that hemophilia A is not a single disease entity in which there is a deficiency of a protein which has coagulant activity. Factor VIII-like antigenic activity can be identified independent of factor VIII coagulant activity (Ref. 2). In addition, von Willebrand's disease is characterized by several plasma defects in addition to a deficiency of factor VIII coagulant activity (Ref. 3). Studies on genetic control mechanisms, synthesis and physical-chemical composition of factor VIII have a relationship to the effectiveness of therapy with factor VIII concentrates in specific disease entities (Ref. 4 through 6). However, potency of the licensed Antihemophilic Factor (Human) products is characterized on the basis of factor VIII coagulant activity. Unless otherwise specified in this review, the term factor VIII relates to only the clot-promoting properties of this protein.

Early attempts to isolate the antihemophilic activity from plasma were limited by the techniques for its assay and failure to recognize that hemophilia was not a single disease entity. It was found that plasma globulin fractions had the ability to correct the prolonged whole blood clotting time characteristic of severe hemophilia (Refs. 6 and 7). The antihemophilic activity was found to separate along with fibrinogen in fraction I of the ethanol precipitation method of Cohn, et al. (Ref. 8). The factor VIII activity of fraction I preparations was variable but it was used in the clinical management of hemophilia (Ref. 9). At the present time, no fraction I preparations are licensed for use in the treatment of hemophilia. A number of other procedures have been used for separation of factor VIII activity from plasma of humans as well as from the plasma of other species (Ref. 1). Work has been done in England on factor VIII from porcine and bovine plasmas (Ref. 10). Although high potency preparations have been obtained, the porcine and bovine materials have been found to be antigenic when used in man (Ref. 11).

Pool and associates (Ref. 12) recognized the potential of what was first regarded as a laboratory curiosity and their observations provided the basis for the materials that are currently licensed. When plasma is frozen and thawed, much of the factor VIII activity is concentrated in a small amount of poorly soluble material. This cryoprecipitate can be separated from the supernatant plasma and is the starting material for currently licensed factor VIII concentrates (Ref. 13). As with other fractionation procedures, there is also a considerable amount of fibrinogen in the cryoprecipitate.

Factor VIII is relatively stable when separated from other procoagulants but small amounts of thrombin will destroy it (Ref. 1). In order to remove procoagulants which might provide a source of thrombin, aluminum hydroxide has been found to be effective (Ref. 1). Aluminum hydroxide absorbs fibrinogen from plasma to a greater extent than factor VIII (Ref. 4). Thus much of the fibrinogen present in cryoprecipitate can be removed by this method. Since the aluminum hydroxide is insoluble it can be removed by centrifugation. Aluminum hydroxide, like other absorbants, will remove a number of other clotting accelerators that influence in vitro test results but have no in vivo antihemophilic activity. It is probably for this reason that there is good correlation between in vitro test results of factor VIII potency and the clinical effectiveness of the products prepared by this procedure.

Studies done on patients undergoing hemodialysis have indicated that aluminum is potentially toxic (Refs. 15 and 16). If aluminum hydroxide is used in the process of manufacturing factor VIII, the product must be tested to demonstrate that the aluminum has been removed.

In some procedures for the isolation of factor VIII small amounts of heparin are added (Ref. 17). This is apparently used to prevent the activation of clotting factors which would lead to thrombin formation. When heparin is added during the manufacturing process, the product must be tested to demonstrate that heparin has been effectively removed, or the residual heparin activity should be measured and indicated in the labeling.

Intermediate purity AHF (Ref. 18) is a term applied to a product in which the cryoprecipitate obtained from plasma is treated with ethanol. The cryoethanol precipitate is extracted with low ionic Tris buffer and then treated with aluminum hydroxide.

Glycine will precipitate factor VIII. Low concentrations of glycine, 3.5 percent, will precipitate nonfactor VIII proteins, mainly fibrinogen, while most of the factor VIII activity remains in the supernatant fluid. When the concentration of glycine is increased to approximately 12 percent, most of the factor VIII will precipitate. The factor VIII activity can then be extracted with a citrate solution (Ref. 19). In a similar manner polyethylene glycol (PEG) can be used as a precipitating agent (Ref. 18). At low concentrations of PEG, 2.5—5.0 percent, nonfactor VIII proteins will precipitate, while at the higher concentration of 2 percent, factor VIII will precipitate. The factor VIII can be recovered by extraction with Tris buffer. These preparations have been termed high purity AHF (Ref. 18).

2. *Indications for use.* Factor VIII concentrates are indicated when there is a hemostatic defect resulting from a deficiency of factor VIII, and it is necessary to increase and maintain factor VIII concentrations to control bleeding.

a. *Evidence of effectiveness.* (1) There is a considerable amount of available information to indicate that factor VIII when given in adequate amounts will correct both the clotting and hemostatic defects associated with factor VIII deficiency. The active material has a relatively short effect in vivo (Ref. 20) and approximately half of the coagulant activity is lost from the circulating plasma in 10 to 12 hours. In order to

maintain circulating factor VIII at therapeutic levels, additional material must be injected at approximately 12-hour intervals (Ref. 12). The currently available materials are effective only when administered intravenously.

(2) In disseminated intravascular coagulation (DIC) there is no evidence that factor VIII concentrates are therapeutically useful.

(3) A small percentage of patients with hemophilia A develop antifactor VIII anticoagulants (Ref. 22). This type of anti-factor VIII activity appears to be an antibody response to factor VIII-like antigenic material that has been administered. When this complication occurs, massive amounts of factor VIII must be supplied and even this may not be sufficient to achieve hemostatic effectiveness (Ref. 19). It is important that the in vivo effectiveness of the factor VIII material be determined by a reliable assay procedure since it is not always possible to predict in vivo effectiveness from the vitro test results.

(4) Acquired factor VIII deficiency has been reported in otherwise normal individuals following reactions to penicillin, during pregnancy, in patients with lupus erythematosus and in patients with rheumatic heart disease (Ref. 22). In such cases an anti-factor VIII anti-coagulant is apparently the basis for the coagulation defect. There may be little or no in vivo response to administered factor VIII in these patients. It is necessary to have a reliable method to evaluate the in vivo effectiveness of the infused material before Anithemophilic Factor (Human) can be evaluated for this indication.

(5) Von Willebrand's disease is a disorder in which the affected individuals have decreased levels of factor VIII, a prolonged bleeding time and other recently recognized plasma activity deficiencies (Ref. 3). The relationships among the plasma abnormalities, the hemorrhagic tendency and the genetic defect are not clear. The adminstration of normal plasma or cryoprecipitated antihemophilic factor appears to control hemorrhage, normalize the bleeding time, and increaase the circulating level of factor VIII. The response of these patients to adminstration of normal plasma is unusual in that a secondary increase in circulating factor VIII occurs over and beyond the amount of factor VIII infused. In two recent studies (Refs. 4 and 5) the response of patients with von Willebrand's disease to administration of cryoprecipitated antihemophilic factor and two of the Antihemophilic Factor (Human) concentrate products was determined. Cryhoprecipitated antihemophilic factor increased the factor VIII coagulant activity, the factor VIII antigen-like activity, the platelet aggregating factor, the ristocetin related activity of platelets, corrected the bleeding time and controlled bleeding. In equilvalent doses of factor VIII, based on coagulant activity, the concentrates failed to correct the bleeding time, and clinical evidence of hemorrhage persisted even though high levels of factor VIII coagulant activity were achieved. In view of these findings, until additional data to the contrary are available, none of the Antihemophilic Factor (Human) concentrates can be considered to be effective in controlling bleeding in von Willebrand's disease.

(6) Most commonly Antihemophilic Factor (Human) is used when a patient with a known factor VIII deficiency has an episode of bleeding or when a surgical procedure is to be done. In some patients it has been found to be advantageous to administer factor VIII prophylactically. The rationale for such therapy is that certain individuals are particularly prone to develop bleeding episodes which can be minimized by maintaining factor VIII at relatively low levels. Such therapy is indicated in a few individuals that are carefully selected on the basis of clinical history.

b. *Evidence of safety.* (1) Since pooled human plasma is the source material for Anti-hemophilic Factor (Human), the risk of hepatitis is present. Current regulations required that each donor must be tested and found nonreactive for hepatitis B surface antigen (HDsAg) by "third generation" methods. This is a relatively new requirement, and its effect on the incidence, of associated hepatitis associated with the use of factor VIII is not yet clear. However, at the present time it must be considered that these materials carry a definite hepatitis risk.

(2) Anti-A and anti-B group antibodies are present in Anti-hemophilic Factor (Human) prepared from plasma containing these antibodies. These antibodies do not appear to be concentrated along with factor VIII. When large amounts of factor VIII concentrate are given, these antibodies can cause a mild hemolytic response in the recipient whose red blood cells have the appropriate antigens (Ref. 23). The reactions reported to date have not been serious, but if this possibility is not recognized, the resulting decrease in red cell volume may be misinterpreted as evidence of bleeding.

(3) Mild allergic-type reactions have been observed following the adminstration of Antihemophilic Factor (Human), but these reactions are uncommon.

c. *Benefit-risk evaluation.* When used appropriately to increase the circulating factor VIII coagulant level, the risk is small compared to the benefits to be expected.

3. *Recommendations.* a. The licensed Antihemophilic Factor (Human) products should be placed in Category I since when used appropriately they are relatively safe and effective.

b. Studies should be encouraged within the medical community to provide a source of AHF which is free of the hepatitis agent(s).

c. Further research is needed to determine how to provide information about the content of anti-A and anti-B antibodies in the final product. Although these antibodies are present in trace amounts, they may be clinically significant when massive doses of the product are given to patients. On the basis of current information, the labeling should indicate this possibility. The manufacturers should test each final lot of the product to determine the amount of anti-A and anti-B antibodies in order to detect unexpectedly high levels in relation to those established in the product license. Upper limits should be established if adverse reactions are discovered to relate to specific antibody levels.

d. If aluminum hydroxide is used in the process, the final product must be demonstrated to contain no more than 0.1 microgram of aluminum per unit of antihemophilic factor.

e. If heparin is used in the process, the final product must be demonstrated to be free of heparin activity, or the amount of heparin activity remaining should appear in the labeling.

f. The labeling should contain information about the fibrinogen content of the final product, cautions about the risks of hepatitis and anti-A and anti-B antibody content, and a statement that the product is not indicated for the treatment of von Willebrand's disease.

g. The product name should be "Antihemophilic Factor".

**References**

(1) Brinkhous, K.M., R.D. Langdell and R.H. Wagner, "Hemostatic Disorders: Hemophilia and the Hemophiloid Diseases," *Annual Review of Medicine*, 9:159–189, 1958.

(2) Zimmerman, T.S., O.D. Ratnoff and A.E. Powell, "Immunologic Differentiation of Classic Hemophilia (Factor VIII Deficiency) and von Willebrand's Disease," *Journal of Clinical Investigation*, 50:244–254, 1971.

(3) Barrow, E.M. and J.B. Graham, "von Willebrand's Disease," *in* "Progress in Hematology IV," Edited by Moore, C.V. and E.B. Brown, Grune and Stratton, New York, p. 203, 1964.

(4) Green, D. and E.V. Potter, "Failure of AHF Concentrate to Control Bleeding in von

Willebrand's Disease," *American Journal of Medicine*, 60:357–360, 1976.

(5) Blatt, P.M., K.M. Brinkhous, H.R. Culp, J.S. Krauss and H.R. Roberts, "Antihemophilic Factor Concentrate Therapy in von Willebrand's Disease. Dissociation of Bleeding-Time Factor and Ristocetin-Cofactor Activities," *Journal of the American Medical Association*, 236:2770–2775, 1976.

(6) Pohle, F.J. and F.H.L. Taylor, "The Use of a Globulin Substance Derived from Beef Plasma as a Local Hemostatic in Hemophilia," *Journal of Clinical Investigation*, 17:677–682, 1938.

(7) Lewis, J.H., J.P. Soulier and F.H.L. Taylor, "Chemical, Clinical and Immunological Studies on the Products of Human Plasma Fractionation, XXXIII. The Coagulation Defect in Hemophilia: The Effect *In Vitro* and *In Vivo* on the Coagulation Time in Hemophilia of a Prothrombin and Febrinogen-Free Normal Plasma and its Derived Protein Fractions," *Journal of Clinical Investigation*, 25:876–1946.

(8) Cohn E.J., L.E. Strong, W.L. Hughes, D.J. Mulford, J.N. Ashworth, M. Melin and H.L. Taylor, "Preparation and Properties of Serum and Plasma Proteins. IV. A System for the Separation into Fractions of the Protein and Lipoprotein Components of Biological Tissues and Fluids," *Journal of American Chemical Society*, 68:459–475, 1946.

(9) McMillan C.W., L.K. Diamond and D.M. Surgenor, "Treatment of Classic Hemophilia: The Use of Fibrinogen Rich in Factor VIII for Hemorrhage and for Surgery," *New England Journal of Medicine*, 265:224–230, 1961.

(10) Bidwell, E., "The Purification of Antihemophilic Globulin from Animal Plasma," *British Journal of Haematology*, 1:386–389, 1955.

(11) Ingram, G.I.C., "Major Surgery in Hemophilia. Use of Animal Antihemophilic Factor in Britain," *Transfusion*, 2:88–93, 1962.

(12) Pool, J.G., and A.E. Shannon, "Production of High-Potency Concentrates of Antihemophilic Globulin in a Closed-Bag System," *New England Journal of Medicine*, 273:1443–1447, 1965.

(13) Bidwell, E., G.W.R. Dike and T.J. Sharpe, "Therapeutic Materials," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," 2nd Edition, edited by Biggs, R., Blackwell Scientific, Oxford, p. 249, 1976.

(14) Wagner, R.H., B.A. Richardson and K.M. Brinkhous, "A Study of the Separation of Fibrinogen and Antihemophilic Factor (AHF) in Canine, Porcine and Human Plasmas," *Thrombosis et Diathesis Haemorrhagica*, 1:3–8, 1957.

(15) Elliott, H.L., F. Dryburgh, G.S. Fell, S. Sabet and A.I. MacDougall, "Aluminum Toxicity During Regular Haemodialysis," *British Medical Journal*, 1:1101–1103, 1978.

(16) Dunea, G., S.D. Mahurkar, B. Mamdani and E.C. Smith, "Role of Aluminum in Dialysis Dementia," *Annals of Internal Medicine*, 88:502–504, 1978.

(17) BER Volumes 6064 and 6073.

(18) Newman, J., A.J. Johnson, M.H. Karpatkin and S. Puszkin, "Methods for the Production of Clinically Effective Intermediate-and-High-Purity Factor VIII Concentrates," *British Journal of Haematology*, 21:1–20, 1971.

(19) Webster, W.P., H.R. Roberts, G.M. Thelin, R.H. Wagner and K.M. Brinkhous, "Clinical Use of a New Glycine-Precipitated Antihemophilic Fraction," *American Journal of Medical Sciences*, 250:643–651, 1965.

(20) Brinkhous, K.M., G.D. Penick, R.D. Langdell, R.H. Wagner and J.B. Graham, "Physiologic Basis of Transfusion Therapy in Hemophilia," *Archives of Pathology*, 61:6–10, 1956.

(21) Rizza, C.R., "The Management of Patients with Coagulation Factor Deficiencies," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," 2nd Edition, Edited by Biggs, R., Blackwell Scientific, Oxford, p. 365, 1976.

(22) Biggs, R. and K.W.E. Denson, "Natural and Pathological Inhibitors of Blood Coagulation," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," 2nd Edition, Edited by Biggs, R., Blackwell Scientific, Oxford, p. 143, 1976.

(23) Rosati, L.A., B. Barnes, H.A. Oberman and J.A. Penner, "Hemolytic Anemia Due to Anti-A in Concentrated Antihemophilic Factor Preparations," *Transfusion*, 10:139–141, 1970.

**13. Factor IX Complex (Human)**

*Generic Statement*

1. *Introduction.* Factor IX deficiency (Hemophilia B) is a sex-linked hereditary coagulation disorder. It is approximately ¼ as common as factor VIII deficiency (Hemophilia A) (Ref. 25). Like factor VIII deficiency, it is a heterogenous disorder with several variants. In some patients factor IX antigen is detected by showing an immunological reaction between the patients' plasma and either a spontaneously occurring factor IX antibody or one prepared in rabbits by injecting partially purified factor IX concentrates; this is called Hemphilia B+. Those disorders in which a true deficiency exists, i.e., a factor IX protein (active or inactive) cannot be detected, are called Hemophilia B−. In a total of 179 patients studied by six different investigators, the incidence of Hemophilia B+ has been reported as between 8 and 46 percent. Much of this wide range of incidence may be due to differences in techniques. In addition, there are a small numberof patients with a variant called Hemophilia Bm. These individuals have an abnormal prothrombin time (PT) when tested with ox brain thromboplastin, suggesting that an abnormal protein is formed in these patients which interferes with the PT determination. Every combination of Hemophilia B+ or B− with Bm+ or Bm− has been reported.

Patients with factor IX deficiency can be treated with plasma infusions to control or prevent their bleeding problems. Because of difficulty in achieving levels of factor IX greater than 20 percent by plasma infusions without overloading the circulation, techniques for concentrating factor IX have been developed. Most of the techniques have taken advantage of the absorbant qualities of factor IX, as well as the other prothrombin complex factors (II, VII, X), to materials such as: tricalcium phosphate (Ref. 3), barium sulphate (Ref. 4) DEAE cellulose (Ref. 5), DEAE sephadex (Ref. 6) or aluminum hydroxide (Ref. 7). Recent modifications of the procedures have allowed preparation of factor IX concentrates from residual citrated plasma obtained as a byproduct of routine blood banking.

There are currently two United States licensed producers of factor IX concentrates. These preparations also contain factors II, VII and X. Some of the currently used European products do not contain factor VII. Of the American Factor IX Complex (Human) products, one is marketed under the trade name of Proplex™ (Hyland Laboratories) and the other as Konyne™ (Cutter Laboratories).

2. *Effectiveness*—a. *Congenital deficiencies of factors II, VII, IX or X*—(1) *Prophylaxis and treatment of bleeding disorders.* A general review of the clinical uses of factor IX concentrates by Menache (Refs. 8 and 9) provides data on products similarly prepared to those commercially available in the United States. These studies showed that factor IX concentrates were successfully used to treat hemorrhagic episodes or to prevent bleeding with major surgery in patients with deficiencies of factors II, VII, IX and X.

b. *Patients with inhibitors*—(1) *Factor IX inhibitors.* The reported incidence of these inhibitors varies widely, from 9 to 50 percent (Ref. 10). They have been found to be IgG antibodies and usually do not significantly increase the bleeding tendency of the patient. When tested in vitro they are found to be much more rapidly acting than factor VIII inhibitors. If patients with factor IX inhibitors are treated with factor IX-containing material, the antibody is eventally recalled in high titer.

(2) *Factor VIII inhibitors.* Breen and Tullis (Ref. 11) noticed shortening of the clotting time out of proportion to the elevation of clotting factors in patients with vitamin K deficiency who were infused with a clotting factor concentrate prepared by absorption on DEAE cellulose. In order to evaluate this post-transfusion hypercoagulability, a patient with factor VIII deficiency with bleeding was infused with the factor IX concentrate. Prompt cessation of the bleeding occurred with no change in the factor VIII levels. Subsequent reports (Refs. 12 through 14) have indicated that some factor IX concentrates may be able to bypass the inhibitor and provide

hemostasis. Tishkoff (Ref. 15) has confirmed the presence of variable quantities of IXa, Xa and thrombin in these products and demonstrated that they all shorten the activated partial thromboplastin time (PTT) of normal plasma. Whether this provides an explanation for their beneficial effect remains to be determined.

A recent report by a task force on the clinical use of factor IX concentrates (Ref. 16) generally agreed that the IX concentrates available at that time may have been useful in the treatment of factor VIII inhibitors but indicated that a multi-institutional study was needed to establish their exact role in treatment of this problem.

c. *Multiple coagulation factor deficiencies*—(1) *Coumarin overdosage.* Factor IX concentrates have been used successfully in the treatment of coumarin overdosage of for reversal of anticoagulant therapy in patients prior to surgery (Ref. 17).

(2) *Liver disease.* Factor IX concentrates have been given to large numbers of patients to treat the hemorrhagic diathesis associated with liver disease. The results have not always been successful. In some patients this may be because of other factor deficiencies not corrected with factor IX concentrates such as factor V (Ref. 17) or because of the high incidence of bleeding due to local lesions such as varices or ulcers.

In addition, two other major concerns have arisen about treating patients with liver disease with factor IX concentrates. These are the high risk of post-transfusion hepatitis found after giving factor IX concentrates superimposed on an already damaged liver and a hypercoagulable syndrome with thromboembolism first reported in 1959 (Ref. 18). Because of this latter observation one of the two factor IX products available in the United States also contains added heparin. Some authors originally reported no evidence of an increased incidence of thromboembolism after administration of these materials to patients with chronic liver disease (Ref. 19 through 22). However, other studies have shown a risk of thrombosis or induction of disseminated intravascular coagulation (DIC) in patients with liver disease when these materials were used (Refs. 8, 23, 24, 26 through 28 and 43). Blatt described a patient with congenital factor X deficiency who developed hepatitis following adminstration of Konyne™ (Ref. 23). A subsequent surgical procedure was required while the patient still had abnormal latex fixation tests (LFT's), and within 2 hours of her second dose of this product she died with diffuse thromboembolism. Cederbaum reported three patients with liver disease who developed DIC after infusions of Proplex™ (two patients) and Konyne™ (one patient) (Ref. 24). Hoag described two patients who developed evidence of fibrinolysis following administration of Konyne™ (Ref. 6). Kasper reported an additional four patients with chronic liver disease who developed DIC following factor IX concentrates (Ref. 26). Similar reports have come from Europe after the use of PPSB (Ref. 8). A factor IX concentrate prepared in Great Britain was associated with acute liver disease (Ref. 27). The high risk of DIC and thrombosis in these patients may be related either to failure of the role that the liver normally plays in clearing activated products of blood coagulation (Ref. 28) or, alternatively, some of these patients may already have had underlying DIC which is exacerbated by this therapy.

(3) *Newborns.* Low birth weight infants have been shown to have a high incidence of intracranial hemorrhage. If the thromboplastin generation test on the first day of life is less than 10 percent, the incidence of hemorrhage is three times greater than in those infants with activities greater than 10 percent (Ref. 29). However, in a controlled trial where factor IX concentrates were administered intraventricular hemorrhage was three times greater in the treated group (Ref. 30). One study has indicated a reduction in intercerebral hemorrhage in infants with respiratory distress syndome (RDS) who required assisted ventilation from 33 percent to 13 percent when the infants were treated with factor IX concentrates (Ref. 31). Other studies have shown that in newborns with infection, RDS, hyaline membrane disease or vitamin K deficiency, use of factor IX concentrates has produced DIC (Ref. 8).

(4) *Open heart surgery.* There are no studies which have evaluated the efficacy of factor IX concentrates in the control of bleeding in open heart surgery patients. However, these concentrates are being used in this situation as documented by a report of a very high incidence of hepatitis following open heart surgery in a group of patients who received Konyne™ (Ref. 32).

3. *Side effects*—a. *Hepatitis.* A high incidence of hepatitis has been reported following the use of factor IX concentrates with reports ranging from 28 to 70 percent (Ref. 33). Most of the patients tested were hepatitis B positive. In a report by Sandler in 1973, a lot of Konyne™ implicated in three cases of hepatitis could not be shown to be HBsAg positive by immunodifussion, immunoelectrophoresis and immunoelectrosmophoresis (Ref. 34). Iwanson's study (Ref. 33) reported two eras of this treatment: (1) 1969–1970 when patients were treated with Konyne™ or a Swedish concentrate and the hepatitis incidence was 9/26 or 35 percent, and (2) since 1971 when an additional 26 patients were treated with the Swedish concentrate with a hepatitis incidence of 2/26, or 8 percent. The reported difference may have been related to hepatitis testing by radioimmunoassay (RIA) of the source plasma since 1971. However, a more recent study reported in 1977 examined samples of Konyne™ and Proplex™ and showed that Proplex™ was positive for HBsAG by radioimmunoassay (RIA) and immune-electron microscopy (IEM), and Konyne™ was found to be positive by IEM. These data suggest that even though routine screening of each unit of plasma by RIA is performed before fractionation, this procedure may not be sufficient to protect recipients against hepatitis transmission by these products (Ref. 35).

b. *Thromboembolic events.* Thromboembolic complications of factor IX concentrates have already been discussed. In addition, there is considerable evidence to show that patients who have congenital deficiencies of factor IX without liver disease when treated with factor IX concentrates have an increased incidence of post-operative thromboembolic phenomenon. There are also scattered reports of thromboembolic problems following administration of factor IX concentrate without apparent precipitating events.

In a review article on this subject, Kasper (Ref. 26) reported only two factor IX deficient patients without liver disease or surgery who developed any such problems. One had a syncopal episode while being treated for a factor IX inhibitor, and the other had pulmonary emboli on three different occasions while being treated for muscle-skeletal bleeding. In a recent conference on thrombogenicity of factor IX concentrates the following data were provided, as shown in Table 1 (Ref. 36):

TABLE 1.—THROMBOGENICITY OF FACTOR IX CONCENTRATES

| | Post-surgery | Nonsurgical | Total |
|---|---|---|---|
| Christmas disease | [1]4/21 | 2/85 | 6/106 |
| Christmas disease and liver disease | 0/6 | 4/18 | 4/24 |
| Liver disease | 1/3 | 9/55 | 10/58 |
| Total | 5/30 | 15/158 | 20/188 (11%) |

[1]Number of patients with thrombosis/number treated.

The factor IX concentrates prepared in Europe have been reported to cause fewer complications. However, Preston (Ref. 37) infused the concentrate prepared in England into stable factor IX deficient patients and showed significant decreases in factor VIII and serum antithrombin III in all five patients studies; fibrinogen fell in four, and platelet counts decreased in two. These changes were transient, and there were no detectable clinical sequela. The study does suggest that more careful monitoring of hemostatic parameters in patients receiving these materials might show further evidence of thrombogenicity. There is one report of DIC occurring in a post-operative factor IX deficient hemophiliac which was successsfully treated with heparin; subsequently, DIC did not recur when the lot of concentrate was changed (Ref. 38) Sas (Ref. 39) described studies of the concentrate prepared in Scotland and showed that all lots of diluted concentrates on recalcification generated thrombin. Similarly, studies by Kingdon (Ref. 40) showed that materials prepared by eleven different manufacturers varied considerably regarding their thrombogenic potential as measured in vitro by a PTT assay and in vivo in a rabbit venous stasis model. The in vitro assay was more sensitive, but the in vivo assay may correlate more closely with the in vivo experience in man. Addition of 5 to 10 units of heparin/mL of reconstituted concentrate eliminated thrombus formation in the experimental animal model. However, a soybean trypsin inhibitor which inhibits factor Xa and diisopropyl fluorophosphate, an inhibitor of thrombin, VII or XIa has no effect.

Another approach to prevention of thrombogenicity by factor IX concentrates has been to add heparin in the manufacturing process to prevent factor activation and then provide for heparin removal in latter manufacturing steps (Ref. 41). This material was shown not to shorten in vitro clotting times.

4. *Benefit/risk evaluation.* Because of the high risk of hepatitis and thromboembolic complications, the use of these materials should be restricted to situations where the patient cannot be appropriately managed with single donor plasma. These would include: (1) Major surgery in patients with severe congenital deficiencies of the clotting factors contained in these concentrates, (2) life-threatening bleeding in patients with factor IX inhibitors, and (3) prophylaxis for patients with congenital clotting factor deficiencies where the value of this treatment must be weighed against the risk of hepatitis which is especially great in patients who have had few prior transfusions (Ref. 42). Factor IX concentrates should ordinarily not be used to treat bleeding during open heart surgery or for prophylactic treatment of patients with congenital deficiencies of prothrombin complex factors who also have liver disease.

5. *Recommendations.* Generically, Factor IX Complex (Human) should be placed in Category I. Specific recommendations for each producer follow in separate product reviews. Other recommendations for further research are:

a. Changes in manufacturing which can eliminate production of activated coagulation factors and contamination with hepatitis virus should be investigated.

b. Quality control technique improvements and better in vitro tests are needed for use by the manufacturers to lead to a material that is as nonthrombogenic and free of hepatitis as is possible.

c. Studies are needed to investigate the incidence of hepatitis in recipients who have received concentrates prepared from plasma pools composed of individual units which were HBsAg negative by third generation testing.

d. Studies should be encouraged to provide a source of factor IX which is free of hepatitis agents.

e. Further evaluation of the usefulness of factor IX concentrates in the treatment of patients with factor VIII inhibitors is recommended.

6. *Labeling recommendations.* a. The activity in the final product of any of the prothrombin complex factors (II, VII, IX, X) for which administration of the product is recommended as therapy must be included in the labeling.

b. The quantity of sodium, potassium, and anticoagulants in the final product must be included in the labeling.

c. The labeling should include prominent warnings about risks of hepatitis and thrombosis.

d. Indications for use should be restricted as discussed in this report.

**References**

(1) Elodi, S. and E. Puskas, "Variants of Haemophilia B," *Thrombosis et Diathesis Haemorrhagica*, 28:489–495, 1972.

(2) Brown, P., C. Hougie and H. Roberts, "The Genetic Heterogeneity of Hemophilia B," *New England Journal of Medicine*, 283:61–64, 1970.

(3) Didisheim, P., J. Loeb, C. Blatrix and J. Soulier, "Preparation of a Human Plasma Fraction Rich in Prothrombin, Proconvertin, Stuart Factor, and PTC and a Study of its Activity and Toxicity in Rabbits and Man," *Journal of Laboratory and Clinical Medicine*, 53:322–330, 1959.

(4) Surgenor, D., M. Melin, B. Steele, L. Wheaton and R. Pennell "Preparation of Barium Sulfate Eluate of Plasma for Physiological Studies in Humans," *Vox Sanguinis*, 4:71–72, 1959.

(5) Melin, M., J. Jansky, G. Leonardos, A. DiFrancesco, R. Pennell and J. Tullis, "The Preparation of a Prothrombin Containing Fraction from Human Plasma by Chromatography," *Vox Sanguinis*, 9:227, 1964.

(6) Hoag, M.S., F.F. Johnson, J. Robinson and P. Aggeler, "Treatment of Hemophilia B with a New Clotting-Factor Concentrate," *New England Journal of Medicine*, 280:581–586, 1969.

(7) Hoag, M., P. Aggeler and A. Fowell, "Disappearance Rate of Concentrated Proconvertin Extracts in Congenital and Acquired Hypoconvertinemias," *Journal of Clinical Investigation*, 39:554–563, 1960.

(8) Menache, D. and M. Guillin, "The Use of Factor IX Concentrates for Patients with Conditions other than Factor IX Deficiency," *British Journal of Haematology*, 31 (Suppl.): 247–257, 1975.

(9) Menache D., "Factor IX Concentrates," *Thrombosis et Diathesis Haemorrhagica*, 33:600–605, 1975.

(10) Lechner, K., "Factor IX-Inhibitors. Report of Two Cases and a Study of the Biological, Chemical and Immunological Properties of the Inhibitors," *Thrombosis et Diathesis Haemorrhagica*, 25:447–459, 1970.

(11) Breen, F.A. and J.L. Tullis, "Prothrombin Concentrates in Treatment of Christmas Disease and Allied Disorders," *Journal of the American Medical Association*, 208:1848–1852, 1969.

(12) Kurczynski, E. and J. Penner, "Activated Prothrombin Concentrate for Patients with Factor VIII Inhibitors," *New England Journal of Medicine*, 291:164–167, 1974.

(13) Sultan, Y., J. Brouet and P. Debre, "Treatment of Inhibitors to Factors VIII with Activated Prothrombin Concentrate," *New England Journal of Medicine* 291:1087, 1974.

(14) Abildgaard, C., M. Britton and J. Harrison "Prothrombin Complex Concentrate (Konyne) in the Treatment of Haemophilic Patients with Factor VIII Inhibitors," *The Journal of Pediactics*, 88:200–205, 1976.

(15) Tishkoff, G., "Prothrombin Complex to Treat Factor VIII Inhibition," *New England Journal of Medicine*, 292:754–755, 1975.

(16) Menache, D., "Report of the Task Force on the Clinical Use of Factor IX Concentrates," *Thrombosis et Diathesis Haemorrhagica*, 35:748–750, 1976.

(17) Sandler, S., C. Rath and A. Ruder, "Prothrombin Complex Concentrates in Acquired Hypoprothrombinemia," *Annals of Internal Medicine*, 79:485–491, 1973.

(18) Menache, D., "The Turnover Rate of the Coagulation Factors II, VII and IX Under Normal Metabolic Conditions," *Thrombosis et Diathesis Haemorrhagica*, 13 (Suppl.):187–194, 1964.

(19) Dioguardi, N. and P. Mannucci, "Prothrombin-Complex Concentrates in Liver Disease, "*Lancet*, 2:186–189, 1975.

(20) Gazzard B., J. Henderson and R. Williams, "The Use of Fresh Frozen Plasma or a Concentrate of Factor IX as Replacement

Therapy before Liver Biopsy," *Gut*, 16:621–625, 1975.

(21) Green, G., L. Poller, I. Dymock and J. Thomson, "Use of Factor-VII-Rich Prothrombin Complex Concentrate in Liver Disease," *Lancet*, 1:1311–1314, 1975.

(22) Bick, R., W. Schmalhorst and E. Shanbrom, "Prothrombin Complex Concentrate: Use in Controlling the Hemorrhagic Diathesis of Chronic Liver Disease," *Digestive Disease*, 20:741–749, 1975.

(23) Blatt, P.M., R.L. Lundblad, H.S. Kingdon, G. McLean and H.R. Roberts, "Thrombogenic Materials in Prothrombin Complex Concentrates," *Annals of Internal Medicine*, 81:766–770, 1974.

(24) Cederbaum, A., P. Blatt and H. Roberts, "Intravascular Coagulation with Use of Human Prothrombin Complex Concentrates," *Annals of Internal Medicine*, 84:683–687, 1976.

(25) "Study to Evaluate the Supply-Demand Relationship for AHF and PTC Through 1980," U.S. Department of Heath, Education and Welfare, U.S. Public Health Service, National Institutes of Health, DHEW Publication No. (77)1274, 1977.

(26) Kasper, C., "Thromboembolic Complications," *Thrombosis et Diathesis Haemorrhagica*, 33:640–644, 1975.

(27) Gazzard, B., M. Lewis, G. Ash, C. Rizza, E. Bidwell and R. Williams, "Coagulation Factor Concentrates in the Treatment of the Haemorrhagic Diathesis of Fulminant Hepatic Failure," *Gut*, 15:993–998, 1974.

(28) Deykin, D., R. Chun, A. Lopez and P. Silversmith, "The Role of the Liver in Serum-induced Hypercoagulability," *Journal of Clinical Investigation*, 45:256–263, 1966.

(29) Gray, O., A. Ackerman and A. Fraser, "Intracranial Haemorrhage and Clotting Defects in Low-Birth-Weight Infants," *Lancet*, 1:545–548, 1968.

(30) Waltl, H., R. Kurz, G. Mitterstieler, H. Fodisch, L. Hohenauer and H. Rossler, "Intracranial Haemorrhage in Low-Birth-Weight Infants and Prophylactic Administration of Coagulation-Factor Concentrate," *Lancet, 1:1284–1286, 1973.*

(31) Thomas, D. and E. Burnard, "Prevention of Intraventricular Haemorrhage in Babies Receiving Artificial Ventilation," *Medical Journal of Australia*, 1:933–936, 1973.

(32) Faria, R. and N. Fiumara, "Hepatitis B Associated with Konyne, "*New England Journal of Medicine*, 287:358–359, 1972.

(33) Iwarson, S., H. Kjellman and A. Teger-Nilsson, "Incidence of Viral Hepatitis after Administration of Factor IX Concentrates," *Vox Sanguinis*, 31:136–140, 1976.

(34) Sandler, S., C. Rath, M. Wickerhauser, R. Dodd and T. Greenwalt, "Post-Konyne Hepatitis: The Ineffectiveness of Screening for the Hepatitis B Antigen (HBAg)," *Transfusion*, 13:221–224, 1973.

(35) O'Conner, M.L., E.S. Meek and A. Simmons, "Detection of $HB_sAG$ in Coagulation Factor IX Concentrates," *Transfusion*, 17:44–46, 1977.

(36) Minutes of Workshop on Thrombogenicity of Factor IX Concentrates, held at Bureau of Biologics, October 29, 1974, Cosponsored by National Heart and Lung Institute and Bureau of Biologics.

(37) Preston, F., D. Winfield, R. Malia and E. Blackburn, "Serial Changes in the Coagulation System Following Clotting Factor Concentrate Infusion," *Thrombosis et Diathesis Haemorrhagica*, 34:475–482, 1975.

(38) Schimpf, K., K. Zimmerman and B. Kompf, "DIC and Postoperative Wound Bleeding Under Factor IX Substitution Therapy in a Case of Hempophilia B; Successful Treatment with Heparin," *Thrombosis Research*, 8:65–70, 1976.

(39) Sas, G., R. Owens, J. Smith, S. Middleton and J. Cash, "In Vitro Spontaneous Thrombin Generation in Human Factor-IX Concentrates," *British Journal of Haematology*, 31:25–35, 1975.

(40) Kingdon, H., R. Lundblad, J. Veltkamp and D. Aronson, "Potentially Thrombogenic Materials in Factor IX Concentrates," *Thrombosis et Diathesis Haemorrhagica*, 33:617–631, 1975.

(41) Johnson, A., V. Macdonald, D. Brandt S. Middleton and J. Smith, "Inhibition of Thrombotic Side Effects of II, VII, IX and X Concentrates," *Thrombosis at Diathesis Haemorrhagica*, 34:589, 1975.

(42) Kasper, C. and Kipnis, "Hepatitis and Clotting Factor Concentrates," *Journal of the American Medical Association*, 221:510, 1972.

(43) Marassi, A., V. Manzullo, V. Dicarlo and P.M. Manucci, "Thromboembolism Following Prothrombin Complex Concentrates and Major Surgery in Severe Liver Disease," Letter, *Thrombosis and Haemostasis*, 39(1):248–249, 1978.

*Product Reviews*

1. *Product.* Factor IX Complex (Human) manufactured by Cutter Laboratories, Inc., as "Konyne™" is supplied as a lypholized powder containing 500 units of factor IX per bottle. An isotonic solution for administration is made by reconstituting the powder with 20 mL sterile water (USP) supplied by the manufacturer. The product is given by intravenous administration through a filter. No preservatives are used. Other ingredients are Factors II, VII, and X in amounts roughly proportionate to their respective levels in fresh plasma. The product should be stored at 2 to 8 1°C. For travel purposes, it may be stored for up to 1 month at temperatures not to exceed 37 °C.

In an analysis of the product, Tullis (Ref. 1) reports that Konyne™ contains:

TABLE I.—KONYNE™ Components

| Substance | Amount | Concentration times plasma protein |
|---|---|---|
| Factor IX units [1] | 460–550 | 70X |
| Factor IX Specific Activity (units/mg protein). | 1.1 | |
| Factor II units [2] | 140 | 7X |
| Factor II Specific Activity | 0.28 | |
| Factor VII | | 36X |
| Factor X | | 30X |

[1] One unit = factor IX activity of 1 mL of pooled plasma.
[2] One unit = prothrombin activity of 1 mL fresh plasma (not NIH prothrombin units).

2. *Effectiveness*—a. *Treatment of deficiencies of factors II, VII, IX and X (congenital and acquired).* In studies of factor IX deficiency, six patients received 62 transfusions with Konyne™ with a post-transfusion recovery of 58 percent of the factor IX infused. Half-life of the first component was 4.6 hours and of the second 31.5 hours. Equilibration between the first and second component was 22.1 hours, and the volume of distribution was 2.7 times the plasma volume (Ref. 2). These distribution and turnover rates were the same as those found for fresh frozen plasma in three of the patients. Increases of factor II in these patients ranged from 62 to 299 percent, factor VII from 53 to 180 percent, and factor X from 72 to 232 percent. Factor II returned to control levels in 2 to 4 days, factor VII in 12 to 30 hours, and factor X at 5 days.

Tullis describes treating 14 patients with Konyne™ on 89 occasions and with Proplex™ on four occasions with clinical benefit in all instances. Diagnoses of the treated patients were: factor IX deficiency (6 patients), liver disease (6 patients), Dicumerol induced hypoprothrombinemia (2 patients), and factor VIII deficiency (1 patient) (Ref. 1).

Cutter Laboratories reported results of studies of the deficiency states and treatments shown in Table II (Ref. 20).

TABLE II.—REASONS FOR TREATMENT OF PATIENTS WITH DEFICIENCIES OF FACTORS II, VII, IX AND X

| Factor deficiency | Surgery, post-surgery | Bleeding episodes | Hemarthrosis | Dental work | Prophylaxis | Assay | Total number treatments |
|---|---|---|---|---|---|---|---|
| II | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| VII | 2 | 3 | 0 | 1 | 2 | 5 | 13 |
| IX | 22 | 59 | 13 | 6 | 5 | 21 | 126 |
| X | 1 | 3 | 2 | 0 | 0 | 0 | 6 |
| Totals | 25 | 65 | 15 | 8 | 7 | 26 | 146 |

In vivo recovery of factors II, VII, and X in factor IX deficient patients reported by Cutter Laboratories are shown in Table III (Ref. 20).

TABLE III.—IN VIVO RECOVERY OF FACTORS II, VII, AND X IN FACTOR IX DEFICIENT PATIENTS

| Deficient Factor | II | VII | X |
|---|---|---|---|
| Number of cases | 24 | 21 | 23 |
| Increase as %/unit of factor IX infused/lb | 15.5 | 5.1 | 7.3 |

For factor IX deficient patients, administration of 2 units of factor IX activity/kg body weight resulted in an immediate increase of 3 percent (range 1.7 to 5.0 percent) in factor IX levels. The same dosage resulted in an increase in factor VII of 4 percent (range 2.5 to 5.4 percent).

In the one factor II deficient patient studied, 73 units of factor IX infused/kg resulted in an increase from 1.5 percent to 185 percent of normal factor II.

In vivo results of therapy in factor X deficiency were found to be somewhat variable. To raise the circulating level by 1 percent, 0.35 to 3.9 units/kg were required (3 studies).

Other studies summarized in Table IV showed increases in in vivo response in severely deficient patients (Ref. 20).

TABLE IV.—IN VIVO RESPONSE IN SEVERELY DEFICIENT PATIENTS

[Congenital and acquired deficiencies]

| Deficient factor | Condition | No. cases | Average % increase/unit of factor IX infused/lb | Range |
|---|---|---|---|---|
| IX | Stable | 17 | 3.2 | 1.7–5.1 |
| IX | Bleeding | 24 | 4.6 | 1.7–9.6 |
| VII | Stable | 3 | 5.2 | 5.0–5.4 |
| VII | Bleeding | 8 | 5.7 | 2.5–8.4 |
| II | do | 6 | 5.0 | 2.7–7.4 |
| X | do | 7 | 4.7 | 2.1–8.8 |

b. *Treatment of patients with inhibitors*—(1) *Factor IX.* One report has described successful dental extractions in patients from one family with inhibitors of factor IX by using Konyne™ to neutralize the inhibitor and levate the factor IX level (Ref. 3).

(2) *Factor VIII.* Abildgaard (Ref. 4) has reported the use of Konyne™ in 5 hemophilia A patients with inhibitors to treat 64 bleeding episodes with 130 infusions. Prompt control of bleeding was observed in each instance with doses of 15 to 10 units of factor IX/kg. No complications were encountered.

c. *Multiple factor deficiency*—(1) *Coumarin overdosage.* Konyne™ has been used successfully to reverse bleeding secondary to coumarin overdosage in 13 patients; in 5 patients reversal of coumarine effect was required before surgery; and 1 patient was treated for vitamin K deficiency before a biopsy procedure (Refs. 1, 5, 6, and 7).

(2) *Liver disease.* Liver disease has been discussed earlier in the Generic Statement on Factor IX Complex (Human).

3. *Safety analysis.* a. In 163 courses of treatment in 113 patients, Cutter (Ref. 20) reports that 22 patients had a temperature rise above 99.6° F, 4 patients had chills, 3 patients had allergic reactions (hives and itchy eyes), 1 patient had nausea, 3 patients with liver disease had fibrinolytic reactions, and there were 15 deaths (1 patient with thrombosis, 13 in patients with multiple coagulation factor deficiencies and 1 patient with sepsis).

b. *Hepatitis.* Kasper reported that 3 of 10 B hemophiliacs over 4 years old who had received fewer than 10 prior transfusions of blood products developed hepatitis within 6 months of the first infusion of Konyne™ (Ref. 10). Other hepatitis reaction reports in patients treated with Konyne™ are summarized in Table V.

TABLE V.—HEPATITIS IN KONYNE™ Treated Patients

| Author | No. hepatitis/No. treated | Disease |
|---|---|---|
| Hellerstein (6) | 1/2 | Factor IX deficiency. |
| | 2/4 | Warfarin overdosage. |
| Faria (11) | 6/9 | Cardiac surgery (No Konyne™ with cardiac surgery hepatitis incidence was 1/23). |
| Oken (12) | 2/4 | Factor IX deficiency. |
| | 1/2 | Coumarin overdosage. |
| | 2/2 | Cirrhosis. |
| Sandler (7) | 1/8 | Coumarin overdosage. |
| | 3/4 | Coumarin overdosage with other blood products. |
| Grammens (5) | 3/15 | Factor IX deficiency. |
| | 1/12 | Coumarin overdosage or hepatic failure. |
| Boldan (13) | 4/10 | Factor IX deficiency. |
| Iwarson (14) | 2/26 | Do. |

Ten patients were studied by bilirubin, SGOT, and SGPT liver function tests following Konyne™ administration, Table VI (Ref. 20). In three, there were abnormalities noted in the liver function tests, two associated with clinical hepatitis and one with transient enzyme changes without overt disease which was considered to be subclinical hepatitis. One additional patient had clinical hepatitis at the time of starting therapy, and this subsided during treatment.

c. *Thrombosis.* Triantaphyllopoulos (Ref. 15) initially described intravascular generation of thrombin in rabbits given Konyne.™ Death occurred in 34 percent of the treated animals. Catheter injection of the material was lethal in 82 percent of the animals, while direct intravenous injection was associated with a 13-percent mortality. These differences may be related to further contact activation of the Konyne™ by the catheter during infusion. Kasper has reported that 6 of the 13 factor IX deficient patients in the post-operative period who were treated with Konyne™ developed thromboembolic problems (5 thrombophebitis and 1 pulmonary embolism) (Ref. 16). Steinbert (Ref. 17), Edson (Ref. 18), and Marchesi (Ref. 19) subsequently reported on three individual factor IX deficient patients in the post-operative period who developed a myocardial infarction associated with Konyne™ administration, elevation of serum fibrin split products after administration of Proplex™ but not after Konyne™, and pulmonary embolism with Konyne™ administration, respectively. Cutter Laboratories' experience is reported in Table VII (Ref. 20).

TABLE VI.—HEPATITIS B IN RECIPIENTS OF KONYNE™ COMPLEX

| Patient | Factor deficiency (n=total number of infusions in all patients) | No. of infusions in patients with hepatitis B | Received other blood products | Severity of disease | Incubation period |
|---|---|---|---|---|---|
| 1 | II (2) | | | | |
| 2 | VII (99) | 1 | No | NR | 2.5 mo |
| 3 | IX (844) | 3 | No | NR | 3 mo. |
| 4 | | 4 | Previously. | Jaundice. | 14 d. |
| 5 | | 7 | Yes | SGOT, SPGT elevations. | 3 mo. |
| 6 | | 13 | Yes | Jaundice. | 2 mo. |
| 7 | | 4 | Yes | NR | 3 mo. |
| 8 | | 17 | Yes | Jaundice. | 2 weeks. |
| 9 | | 10 | Yes | Elevated SGOT, SGPT, no jaundice, possible subclinical case. | 5 weeks. |
| 10 | X (9) | 3 | Yes | SPGT 1,200, SGOT 1,800, No jaundice | 2 mo |

NR=Not reported.

TABLE VII.—PATIENTS WITH DEFICENCIES OF FACTORS II, VII, IX AND X

[Development of thrombosis or hepatitis]

| Factor deficiency | Total No. patients | Total No. treatments | Total No. infusions | Number developing thrombosis | Number developing hepatitis B | Number receiving other blood products |
|---|---|---|---|---|---|---|
| II | 1 | 1 | 2 | 0 | 0 | 0 |
| VII | 7 | 13 | 99 | 0 | 1 | 2 |
| IX | 78 | 126 | 644 | 1 | [1]8 | 31 |
| X | 3 | 6 | 9 | 0 | 1 | 1 |

[1] Includes one possible subclinical case with elevated SGOT, SGPT, and no jaundice.

d. In addition to the above reactions, anaphylaxis has been reported (Refs. 8 and 9).

4. *Manufacturing analysis.* Manufacturing data are confidential, but a review indicated no reason to question the preparation of the product.

5. *Labeling recommendations.* a. It is recommended that the label should also contain:

(1) The amount of factors, II, VII, and X present by analysis if this material is recommended for treating these deficiencies.

(2) Thrombosis and hepatitis warnings.

(3) The amounts of sodium and potassium in the product in the final container.

b. The package circular should also:

(1) Give details of dosage and frequency of administration for each clotting factor deficiency to be treated.

(2) Include information about how to monitor effectiveness of treatment by employing clotting factor assays on the recipient's blood.

(3) Contain indications for use only in congenital deficiencies or urgent need for the rapid reversal of the effects of vitamin K antagonists.

(4) Include contraindications for use in newborns, liver disease, and surgical procedures in nondeficient patients, e.g., open heart surgery.

(5) State that after reconstitution, the material should be used within at least 4 hours.

6. *Recommendation.* It is recommended that the product be placed in Category I with the labeling recommendations as stated.

**References**

(1) Tullis, J. and F. Breen, "Christmas Factor Concentrates," *Bibliography of Haematology*, 34:40–51, 1970.

(2) Hoag, M., F. Johnson, J. Robinson and P. Aggeler, "Treatment of Hemophilia B With a New Clotting Factor Concentrate," *New England Journal of Medicine*, 280:581–586, 1969.

(3) George, J., G. Miller and R. Breckenridge, "Studies on Christmas Disease. Investigation and Treatment of a Familial Acquired Inhibitor of Factor IX," *British Journal of Haematology*, 21:333–342, 1971.

(4) Abildgaard, C., M. Britton and J. Harrison, "Prothrombin Complex Concentrate (Konyne) in the Treatment of Hemophilic Patients with Factor VIII Inhibitors," *Journal of Pediatrics*, 88:200–205, 1976.

(5) Grammens, G. and R. Breckenridge, "Complications with Christmas Factor (Factor IX) Concentrates," *Annals of Internal Medicine*, 80:666–667, 1974.

(6) Hellerstein, L. and D. Deykin, "Hepatitis After Konyne Administration, *New England Journal of Medicine*, 284:1039–1040, 1971.

(7) Sandler, S., C. Rath and A. Ruder, "Prothrombin Complex Concentrates in Acquired Hypoprothrombinemia," *Annals of Internal Medicine*, 79:485–491, 1978.

(8) Edell, S., "Anaphylaxis After Konyne," *New England Journal of Medicine*, 285:580, 1971.

(9) Weinreb, N. and N. Minsky, "Serious Reaction After Konyne," *New England Journal of Medicine*, 285:1151–1152, 1971.

(10) Kasper, C. and S. Kipnis, "Hepatitis and Clotting Factor Concentrates," *Journal of the American Medical Association*, 221:510, 1972.

(11) Faria, R. and N. Fiumara, "Hepatitis B Associated with Konyne," *New England Journal of Medicine*, 287:358–359, 1972.

(12) Oken, M., L. Hootkin and R. DeJager, "Hepatitis After Konyne Administration," *Digestive Diseases*, 17:271–274, 1972.

(13) Boklan, B., "Factor IX Concentrate and Viral Hepatitis," *Annals of Internal Medicine*, 74:298, 1971.

(14) Iwarson, S., H. Kjellman and A. Tegerr-Nilsson, "Incidence of Viral Hepatitis After Administration of Factor IX Concentrates," *"Vox Sanguinis*, 31:136–140, 1976.

(15) Triantaphyllopoulos, D., "Intravascular Coagulation Following Injection of Prothrombin Complex," *American Journal of Clinical Pathology*, 57:603–723, 1972.

(16) Kasper, C., "Postoperative Thromboses in Hemophilia B," *New England Journal of Medicine*, 289:160, 1973.

(17) Steinberg, M. and B. Dreiling, "Vascular Lesions in Hemophilia B," *New England Journal of Medicine*, 289:592, 1973.

(18) Edson, J., "Prothrombin-Complex Concentrates and Thromboses," *New England Journal of Medicine*, 290:403, 1974.

(19) Marchesi, S. and R. Burney, "Prothrombin-Complex Concentrates and Thromboses," *New England Journal of Medicine*, 290:403–404, 1974.

(20) BER Volumes 6013 and 6013A.

*Product Review*

1. *Product.* Factor IX Complex (Human), (Factors II, VII, IX, and X) or Proplex ™ manufactured by Hyland Division of Travenol Laboratories is supplied as a 30-mL vial containing the lyophilized material. It is intended for intravenous administration through a filter after being reconstituted with 30 mL of sterile water for injection. Each bottle is assayed for factor II and factor IX activity or in vivo recoverable units. Other ingredients include heparin not to exceed one unit per Ml of reconsitituted product. No preservatives are used. The product should be stored between 2 and 3 °C.

2. *Effectiveness*—a. *Treatment of factor IX deficiency.* Eleven patients with factor IX deficiency were treated in one study with good hemostatic results in all (Ref. 1). The concentrates used had assay values of 5 units of factor II/mL, 17 units of factor IX/mL, and 20 units of factors VII and X/mL. This represented a purification of 30 times, 272 times, and 320 times, respectively. Protein concentration was 4.4 mg/mL.

Gilchrist (Ref. 2), on the basis of six infusions in four patients with factor IX deficiency, calculated that a dose of two units of factor IX/kg produced approximately one percent rise in factor IX plasma levels. The recovery values ranged from 17.3 to 33.6 percent with a residual factor IX activity of 40 to 59 percent at 24 hours posttransfusion. There were no changes in fibrinogen concentration of fibrinolytic parameters. In these early studies, protamine sulphate, 3 mg/vial of administered material was usually given to counteract the heparin in the concentrate.

Hyland (Ref. 8) provided data from 5 investigators on 42 infusions in 14 patients with factor IX deficiency. All patients treated had evidence of improvement, and there were no untoward reactions.

Levine (Ref. 3) reported 10 patients who used Proplex ™ in a self-therapy program. This material was reported to be effective in controlling hemorrhagic manifestations of spontaneous bleeding.

b. *Treatment of patients with liver disease.* Four patients with chronic liver disease with profuse bleeding from varices and/or hemorrhagic gastritis were given Proplex ™ infusions. Factor II levels were raised to normal with control of bleeding within 1 to 2 hours of the infusion (Ref. 4). One patient rebled and died several hours after completion of the infusion with evidence of accelerated disseminated intravascular coagulation (DIC). Half-life of factor II was 18 hours (recovery 80 percent), of

factor IX, 14 hours (recovery 42 percent), of factor VII and X, 7 hours (recovery 23 percent).

Cederbaum (Ref. 5) reported three patients with liver disease who developed DIC after infusion of Proplex ™ (two patients) and Konyne ™ (one patient).

c. *Other indications.* No data were found regarding effectiveness for treatment of factor II, VII, or X deficiencies, for treatment of patients with factor IX or factor VIII inhibitors, or for treatment of Coumarin overdosage.

3. *Safety*—a. *Hepatitis.* A single reference (Ref. 6) has reported hepatitis following Proplex ™ administration in a patient with factor X deficiency. (Also see the Factor IX (Human) Generic Statement.)

b. *Thrombosis.* A recent publication reported a lot of Proplex ™ documented to have resulted in thrombosis following infusion. On analysis, this material was found to contain activated factors IXa and Xa (Ref. 7). (Also see the factor IX (Human) Generic Statement regarding the thromboembotic potential of this product.)

4. *Recommendations.* a. Proplex ™ should be placed in category I, safe and effective, for the treatment of congenital factor IX deficiency.

b. Proplex ™ should be placed in Category IIIA for use in congenital and acquired deficiencies of factors II, VII, and X. A period of 3 years is recommended for the completion of the necessary studies to demonstrate effectiveness for these indications.

5. *Labeling recommendations.* a. It is recommended that the label should also contain:

(1) The amount of factors, II, VII, and X present by analysis if this material is recommended for treating these deficiencies.

(2) Thrombosis and hepatitis warnings.

(3) The amounts of sodium and potassium in the product in the final container.

b. The package circular should also:

(1) Give details of dosage and frequency of administration for each clotting factor deficiency to be treated.

(2) Include information about how to monitor effectiveness of treatment by employing clotting factor assays on the recipient's blood.

(3) Contain indications for use only in congenital deficiencies or urgent need for rapid reversal of effects of vitamin K antagonists.

(4) Include contraindications for use in newborns, liver disease, and surgical procedures in nondeficient patients, e.g., open heart surgery.

(5) State that after reconstitution, the material should be used within at least 4 hours.

**References**

(1) Shanbron, E., "Clinical Experience with Factor IX Concentrates (Prothrombin Complex)." *Hemophilia and New Hemorrhagic States*, pp. 27–30, 1970, BER Volume 6066A.

(2) Gilchrist, G.S., H. Ekert, E. Shanbron and D. Hammond, "Evaluation of a New Concentrate for the Treatment of Factor IX Deficiency," *The New England Journal of Medicine*, 280:291–295, 1969.

(3) Levine, P., "Efficacy of Self-Therapy in Hemophilia. A Study of 72 Patients with Hemophilia A and B," *New England Journal of Medicine*, 291:1381–1384, 1974.

(4) Bick, R., W. Schmalhorst and E. Shanbrom, "Prothrombin Complex Concentrate: Use in Controlling the Hemorrhagic Diathesis of Chronic Liver Disease," *Digestive Diseases*, 20:741–749, 1975.

(5) Cederbaun, A., P. Blatt and H. Roberts, "Intravascular Coagulation with Use of Human Prothrombin Complex Concentrates," *Annals of Internal Medicine*, 84:683–687, 1976.

(6) Blatt, P.M., R.L. Lundblad, H.S. Kingdon, G. McLean and H.R. Roberts, "Thrombogenic Materials in Prothrombin Complex Concentrates," *Annals of Internal Medicine*, 81:766–770, 1974.

(7) White, G.C., H.R. Roberts, H.S. Kingdon and R.L. Lundblad, "Prothrombin Complex Concentrates: Potentially Thrombogenic Materials and Clues to the Mechanism of Thrombosis *In Vivo*," *Blood*, 49:159–170, 1977.

(8) BER Volume 6066A.

**14. Fibrinogen (Human)**

*Generic Statement*

1. *Introduction.* The end stage of coagulation is the conversion of the plasma protein fibrinogen to an insoluble polymeric gel called fibrin. The fibrinogen to fibrin conversion is a complex biochemical event catalyzed by thrombin, an enzyme generated in later stages of blood coagulation. Thrombin releases small polypeptides from fibrinogen leaving altered fibrinogen molecules, known as fibrin monomers, free to polymerize into the large fibrin units we recognize as blood clots. Deficiences or abnormalities of fibrinogen, whether hereditary or acquired, may lead to inadequate fibrin formation, a poor or absent blood clot, and abnormal bleeding.

Fibrinogen is synthesized in the liver, has a molecular weight of 340,000 plus or minus 20,000, and is normally present in plasma at a concentration of about 140–410 mg per dL of plasma (Ref. 1). Levels of fibrinogen increase in pregnancy, infection, cancer, granulomatous disease and many other pathological conditions (Ref. 1).

2. *Measurement of fibrinogen.* Fibrinogen can be measured gravimetrically, chemically, immunologically, or by approaches that utilize turbidity or light scattering (Ref. 2).

In some methods thrombin with or without calcium is added to plasma to generate clottable protein which is then measured and reported as fibrinogen (Ref. 3). Methods that utilize clot formation followed by washing, digestion, and chemical analysis of the clot are highly specific and accurate. Degradation products of fibrinogen and fibrin which are not active in the clot-forming process are not measured. These methods require meticulous attention to detail, accurate equipment, and take several hours before the answer is available, but give a reliable result. Digestion and chemical analysis of the clot can be replaced by carefully weighing the air-dried clot, but this is less accurate (Ref. 4).

The plasma clotting time after the addition of thrombin has been used as a repid screening method for afibrinogenimia (Ref. 5). More sensitive clotting time methods are also available and can be used to quantify fibrinogen in clinical settings. These have the advantage of simplicity and speed, but may not be sensitive to small changes in fibrinogen (Ref. 6).

Several turbidimetric methods are available for estimation of fibrinogen. These include salting out with ammonium sulfate (Ref. 7), sodium sulfite (Ref. 8), sodium sulfate (Ref. 9), or other chemicals. The methods are rapid and simple and in normal persons correlated well with more difficult methods. They are less reliable when the fibrinogen concentration is low or in sick persons where interfering substances may be present. In such cases a "grossly erroneous result" may be seen (Ref. 1). The turbidity that results when a dilute solution of fibrinogen reacts with thrombin can be measures easily and accurately to give a relatively sensitive, but specific, method for fibrinogen (Ref. 10).

Immunologic methods, usually based on the principle of radial immunodiffusion, are less accurate, detect fibrinogen or fibrin degradation products that have no clot-promoting activity, and usually require several days before an answer is available (Ref. 11).

Fibrinogen can be measured accurately, but many methods in common use are not completely reliable, and justification for therapeutic use of fibrinogen based on these techniques must be critically reviewed.

3. *Method of preparation.* Because fibrinogen is the least soluble of plasma proteins, it is isolated easily by relatively simple techniques. The plasma fractionation methods developed in World War II by E.J. Cohn and his associates allow the separation of plasma into multiple components (Ref. 12). Fraction I, separate at pH 7.2, temperature −3 °C with an 8 to 10 percent final concentration of ethanol, contains fibrinogen, factor VIII, and several other proteins (Ref. 12). Additional purification of the fibrinogen may be done with glycine (Ref. 13), ammonium sulfate (Ref. 14), or by other approaches. The preparation and purification of fibrinogen by these methods is relatively straightforward, and the assay of the final product can be accurately standardized.

4. *Clinical aspects of fibrinogen deficiency.* Fibrinogen is indicated for treatment of patients who are bleeding and have fibrinogen levels low enough to cause or contribute to the abnormal hemorrhage. Fibrinogen may also be used as prophylaxis in patients with abnormally low fibrinogen levels when a major stress to the blood coagulation system, e.g., surgery, is anticipated (Ref. 15). Because the fibrinogen to fibrin reaction is but one of a series of complex vascular and biochemical events leading to normal hemostasis, the fibrinogen level alone cannot be used to determine appropriate therapy. For the same reason, intravenous administration of fibrinogen is not, in most cases, adequate to reverse the hemorrhagic problem. In most cases, multiple abnormalities exist and simple infusion of fibrinogen will not produce normal coagulation.

The relationship of fibrinogen deficiency to abnormal bleeding is further confused by the presence, in many disease states, of abnormal activation of the fibrinolytic system. Thus, low fibrinogen may be a reflection of increased degradation of adequate amounts of fibrinogen; hence, attempts to correct the low level without simultaneously correcting the cause of the increased fibrinolytic activity may be deleterious rather than helpful (Ref. 16).

A similar dilemma occurs in the case of disseminated intravascular coagulation (DIC) (Ref. 17). The relatively recent konwledge that the hemorrhagic complications of many medical, surgical, and obstetrical disorders are related to widespread intravascular coagulation with consumption of coagulation factors, including fibrinogen, required that the treatmen of these problems be reevaluated. Disseminated intravascular coagulation can be acute or chronic and has been seen in such widely divergent states as gram-negative endotoximia, antigen-antibody reactions, abruptio placenta, ammotic fluid embolism, retained dead fetus in utero, hemolytic transfusion reaction, extracorporeal circulation, trauma, promyelocytic leukemia, thrombotic thrombocytopenic purpura, fat embolism, and poisonous snake bites. The laboratory findings vary in degree from patient to patient, but in all cases there is evidence of decreased levels of some coagulation factors, usually V, VIII, and fibrinogen, a low platelet count, and evidence of inceased fibrinolytic activity with the presence of circulating fibrinogen-fibrin degradation products. It is evident that many of the original theories of afibrinogenemia complicating various clinical conditions are better explained by widespread DIC. In this setting the previous emphasis on fibrinogen, both as an etiologic and therapeutic agent, requires reevaluaion (Ref. 17).

5. *Levels needed for coagulation.* Because fibrinogen deficiency is frequently associated with other coagulation abnormalities, it is difficult to assign a critical fibrinogen value below which the risk of abnormal bleeding is increased. In one patient with hereditary afibrinogenemia, bleeding from a cut tongue stopped when the level reached 78 mg per dL, (Ref. 18). Studies in this patient's plasma showed normal clot formation and retraction when fibrinogen values were as low as 50 mg per dL, although clot formation was slow. Other authors, usually reporting on bleeding in obstetrical patients, describe "unstable" clot formation when levels are in the range of 100 mg per dL but give no data (Ref. 19). Most review articles suggest that patients with plasma fibrinogen concentrations below 100 mg per dL have increased bleeding, but do not provide data to document the statement (Ref. 20).

6. *Specific indications*—a. *Hereditary afibrinogenemia.* Approximately 60 patients with hereditary afibrinogenemia have been reported, all with fibrinogen levels of essentially zero. Clinical features include a hemorrhagic tendency with bleeding after slight trauma. Menses are normal and hemarthroses are rare. There is a long bleeding time and evidence of platelet dysfunction. The abnormalities, both laboratory and clinical, are corrected by small amounts of fibrinogen (Ref. 18).

b. *Hereditary hypofibrinogenemia.* Approximately 25 patients with a disorder marked by moderate reductions in fibrinogen level, with or without a mild hemorrhagic tendency, have been reported. These patients have not been well classified and at least one, on careful reinvestigation, has been shown to have hereditary dysfibrinogenemia (see next paragraph) rather than hypofibrinogenemia. There are no data to substantiate the need for, or efficacy of, fibrinogen in this condition (Ref. 21).

c. *Hereditary dysfibrinogenemia.* Since the first report, in 1958, of congenital abnormality marked by the production of defective fibrinogen at least 10 different varieties of hereditary dysfibrinogenemia have been reported. Some are associated with a bleeding disorder, and in at least three families recurrent thromboembolism has been a problem. The role of fibrinogen therapy is not defined (Ref. 21).

d. *Disseminated intravascular coagulation.* Widespread intravascular coagulation with consumption of circulating coagulation factors, utilization of platelets, and activation of the fibrinolytic mechanism has been established as the etiologic process for the coagulation abnormality seen in a whole host of different clinical conditions (Refs. 22 and 23). Included among these are the serious coagulation abnormalities that accompany the obstetric complications of abruptio placenta, amniotic fluid embolism, retained dead fetus in utero, and induced abortion (Refs. 24, 25 and 26). The bleeding state in gram-negative septicemia, as well as that seen with many medical and surgical complications, is, in most cases, a manifestation of DIC (Ref. 27). Thus, nearly all hemorrhagic situations previously diagnosed and treated as acquired afibrinogenemia are now treated for consumption coagulapathy rather than by attempting to reconstitute the plasma level of fibrinogen with i.v. administration of concentrated fibrinogen. In general, the therapy of DIC is directed at the underlying pathologic problem rather than at attempts to replace deficient coagulation factors (Refs. 24, 25, 26, and 28). When the process is difficult or impossible to control, such as in metastatic cancer, heparin has been used (Refs. 29, 30, 31, and 32). The appropriate and judicious selection of anticoagulation (heparin), coagulation factor replacement, or therapy with fibrinolytic agents is a clinical decision of great difficulty. It is clear, however, that fibrinogen replacement is less important than had been previously believed, and that most patients do not need the infusion of fibrinogen concentrate.

(1) *Abruptio placenta.* The most frequent cause of severe bleeding during pregnancy is premature separation of the normally implanted placenta (Refs. 25, 26 and 33). The mechanism for the DIC is probably related to the destruction of the normal placental implantation with subsequent entry of decidual fragments, serum, and activated coagulation factors into the maternal circulation. Appropriate therapy includes prompt emptying of the uterus, treatment of shock, and blood transfusion (Ref. 24). Most patients do not require specific clotting factor replacement, and heparin, if indicated, is needed infrequently (Ref. 29). In those few cases where fibrinogen replacement is required, a dose of 4 g (Refs. 24 and 26) has been advised.

(2) *Intrauterine fetal death with prolonged retention of dead fetus.* In these cases these is slow continued absorption of thromboplastic materials from the retained dead fetus leading to chronic activation of the coagulation system in vivo. This produces a mild chronic DIC usually requiring about 5 weeks for full development. Appropriate therapy includes frequent monitoring by coagulation tests, including fibrinogen, along with prompt evacuation of the uterine contents as soon as significant abnormalities become evident. Intravenous administration of fibrinogen is rarely, if ever, required (Refs. 24 and 26).

(3) *Amniotic fluid embolism.* The entrance of amniotic fluid into the maternal circulation, usually about the time of delivery, can produce a sudden and catastrophic event marked by respiratory distress, cyanosis, shock, and acute DIC. In most cases the onset is sudden and death occurs within minutes. At times the shock develops more slowly, and widespread bleeding is noted before death (Refs. 25 and 26). Since amniotic fluid is rich in thromboplastic materials, the development of widespread consumption coagulopathy is not surprising (Ref. 26). These patients require immediate and massive treatment for shock, transfusion to replace blood loss, and fibrinogen replacement (Refs. 25 and 26). Four grams of fibrinogen have been recommended (Ref. 24).

(4) *Miscellaneous conditions.* Massive trauma, burns, incompatible transfusions, septicemia (particularly with gram-negative organisms), promyelocytic leukemia, carcinoma, hepatitis, virus infections and, indeed, almost any serious medical or surgical illness may, at times, be associated with DIC. Therapy in these cases varies, but the use of intravenous fibrinogen is not a major therapeutic modality (Refs. 17 and 34).

7. *Risks and complications.* Fibrinogen is prepared from the plasma of large numbers of donors. Because of this and because fibrinogen will not tolerate the 10 hours of heating at 60° C used to inactivate the hepatitis virus in other blood fractions, fibrinogen administration has been associated with a significant risk of transmitting viral hepatitis (Ref. 35). The actual current risk is, however, almost impossible to evaluate since:

a. Most studies do not have a careful followup of recipients.

b. In almost all cases, recipients of fibrinogen have also received other blood products.

c. There are no reports of the hepatitis incidence after fibrinogen prepared from donor plasma that is negative when tested for HBsAg by third generation methods. Since this is now a manufacturing requirement, reports from the 1950's and 1960's may not reflect the current risk.

Bearing these limitations in mind, the reported incidence of postfibrinogen hepatitis has ranged from 1.7 percent to 55 percent. The two most recent reports (Refs. 36 and 37), both from Michigan, give divergent hepatitis rates and also illustrate the difficulty of evaluating the published data. In one study (Ref. 36), the manufacturer received reports on 649 patients who had received an average of 2.2 units of Fibrinogen (Human) per patient. Of these, 452 were followed for 6 months. One case of hepatitis (1.7 percent incidence) was reported in the 50 recipients who received Fibrinogen (Human) alone, while 34 cases (8.6 percent incidence) were reported in the 394 patients who had also received an average of 7.0 units of whole blood. All the plasma from which the Fibrinogen (Human) had been prepared was from volunteer donors, but had not been tested for HBsAg. In addition, there was no effort to follow recipients, hence the reported incidence must be considered as the absolute minimum. A second study (Ref. 37), also from Michigan, where recipients were "followed at close intervals by careful physical examinations and laboratory tests," reported the incidence of hepatitis to be 55.5 percent in the 9 patients who received Fibrinogen (Human) and survived longer than 7 days. Unfortunately, the fibrinogen was partly from commercial donors and partly from volunteers. In addition, of course, the data were collected before HBsAg testing was required.

There are no data about the hepatitis risk from Fibrinogen (Human) prepared from HBsAg negative donors, but it is known that such donors may transmit hepatitis and that with current processing methods HBsAg is found in fibrinogen fraction (Refs. 38, 39 and 40). Thus it is probable, but not proven, that large plasma pools, even though prepared from HBsAg negative starting materials, will be infectious. There are no data for Fibrinogen (Human), but other fractions, such as Antihemophilic Factor (Human) and Factor IX Complex (Human), have been more widely used and studied. Since pool sizes and general processing methods are similar for all of these unheated fractions, it is reasonable to assume that the risk of hepatitis transmission is also similar and that risk is from 36 to 75 percent in recipients who have had little or no other contact with blood products (Refs. 41 through 45). Again, these data were collected before the requirement for HBsAg testing on each donor unit of starting material. This fact notwithstanding, the high hepatitis risk of pooled unheated material is evident. Elimination of HBsAg-positive donors will lower, but not eliminate, this risk, and lacking more current data the wisest course is to accept previous estimates of the hepatitis risk for fibrinogen of about 25 percent.

At least one death has been ascribed to diffuse intravascular thrombosis after fibrinogen administration in a surgical patient (Ref. 46), and several cases of severe pulmonary embolism have been seen (Refs. 47 and 48).

Coomb's positive hemolytic anemia, probably related to the presence of anti-A and anti-B antibodies in the product, has been seen after large doses of fibrinogen (Ref. 49). This complication has been reported only in patients with hemophilia who were treated with large doses of fibrinogen rich in Factor VIII. Although fibrinogen is no longer considered appropriate therapy for hemophilia, similar doses of fibrinogen administered for other indications could have the same effect.

Various side effects including hypotension, tachycardia, nausea, vomiting, paresthesias, urticaria, fever, chills, and headache have been noted occasionally but are difficult to evaluate since, in each case, the product was being administered to an extremely sick patient who had multiple complicating factors (Refs. 50 through 52).

8. *Other sources of fibrinogen.* Fibrinogen (Human) is a licensed product currently recommended for the indications stated above. Fibrinogen replacement, however, can be

accomplished with other blood components or fractions.
Cryoprecipitated Antihemophilic Factor (Human), (cryoprecipitate), while usually prepared as a source of Factor VIII for the treatment of hemophilia, is also an excellent source of fibrinogen, since each bag of cryoprecipitate contains approximately 250 mg of fibrinogen (Refs. 53 and 54).
Cryoprecipitate has been used in patients who were candidates for fibrinogen replacement (Refs. 55 and 56). The hepatitis risk is unknown, but is probably equal to or less than that associated with whole blood transfusion (Ref. 57).

9. *Recommendations.* Recent evidence including a multitude of well documented studies, has established disseminated intravascular coagulation as the major, or perhaps the only, etiological factor in the development of acquired hypofibrinogenemia. As such, therapy is appropriately directed at the underlying disease. Heparin is sometimes used, and fibrinogen replacement is almost always unnecessary. In those few patients with acquired hypofibrinogenemia or in the rare patient with hereditary a-, hypo-, or dysfibrinogenemia, cryoprecipitate is an adequate source of fibrinogen replacement.

The hepatitis risk of cryoprecipitate relative to Fibrinogen (Human) is unknown and, because of the relative infrequency of patients who require fibrinogen replacement, is not amenable to appropriate study. Thus, there are not and will not be, scientifically sound data from which to decide about the risk of hepatitis from Fibrinogen (Human). Traditionally the hepatitis risk from pooled products that cannot be heat treated is high. The exclusive use of HBsAg negative donors reduces, but does not eliminate, this risk. It is well known that even small amounts of virus can contaminate large pools and that the risk of infection increases as pool size increases. Thus, it seems logical to restrict therapy to components, fractions, and derivatives that supply the required factor with the lowest possible risk of exposure to potentially infectious materials. In the case of fibrinogen deficiency, the desired treatment can be achieved with cryoprecipitate. Even the most generous dosage schedules will expose the patient to relatively few donors. The substitution of cryoprecipitate, Single Donor Plasma (Human), or Single Donor Plasma (Human) Fresh Frozen for Fibrinogen (Human) in those few cases where fibrinogen is indicated will decrease donor exposure and should diminish hepatitis risk. Lacking definitive data about relative risks from cryoprecipitate and fibrinogen, the Panel recommends that cryoprecipitate be used as a source of fibrinogen in the few clinical situations when such therapy is indicated. The Panel recommends that Fibrinogen (Human) as presently prepared be placed in Category II.

The recommendations of the Panel were forwarded to the Commissioner of Food and Drugs following the January 14–15, 1977 meeting of the Panel, and all licenses for Fibrinogen (Human) were subsequently revoked as of December 7, 1977, as reported in the **Federal Register** of January 6, 1978 (43 FR 1131).

**References**


(1) Grannis, G.F., "Plasma Fibrinogen: Determination, Normal Values, Physiopathologic Shifts, and Fluctuations," *Clinical Chemistry*, 16:486–494, 1970.

(2) Goodwin, J., "An Evaluation of Technics for the Separation and Estimation of Plasma Fibrinogen," *Clinical Chemistry*, 11:63–73, 1965.

(3) Ratnoff, O.D. and C. Menzie, "A New Method for the Determination of Fibrinogen in Small Samples of Plasma," *Journal of Laboratory and Clinical Medicine*, 37:316–320, 1951.

(4) Ingram, G.I.C., "The Determination of Plasma Fibrinogen by the Clot-Weight Method," *Biochemical Journal*, 51:583–585, 1952.

(5) Jim, R.T.S., "A Study of the Plasma Thrombin Time," *Journal of Laboratory and Clinical Medicine*, 50:45–60, 1957.

(6) Class, A., "Gerinnungsphysiologische Schnellmethode Zur Bestimmung des Fibrinogens," *Acta Haemotologica*, 17:237–246, 1957.

(7) Parfentjev, I.A., M.L. Johnson and E.E. Cliffton, "The Determination of Plasma Fibrinogen by Turbidity with Ammonium Sulfate," *Archives of Biochemistry and Biophysics*, 46:470–480, 1953.

(8) Goodwin, J., "Estimation of Plasma Fibrinogen Using Sodium Sulfite Fractionation," *American Journal of Clinical Pathology*, 35:227–232, 1961.

(9) Podmore, D.A., "Rapid Turbidimetric Methods for the Determination of Plasma Fibrinogen," *Clinica Chimica Acta*, 4:242–245, 1959.

(10) Ellis, B.C. and A. Stransky, "A Quick and Accurate Method for the Determination of Fibrinogen in Plasma," *Journal of Laboratory and Clinical Medicine*, 58:477–488, 1961.

(11) Brittin, G.M., H. Rafinia, D. Raval, M. Werner and B. Brown, "Evaluation of Single Radial Immunodiffusion for Quantitation of Plasma Fibrinogen," *American Journal of Clinical Pathology*, 57:89–94, 1972.

(12) Cohn, E.J., L.E. Strong, W.L. Hughes, D.J. Mulford, J.N. Ashworth, M. Merlin and H.L. Taylor, "Preparation and Properties of Serum and Plasma Proteins. IV. A System for the Separation into Fractions of the Protein and Lipoprotein Components of Biological Tissues and Fluids," *Journal of the American Chemical Society*, 68:459–475, 1946.

(13) Blomback, B. and M. Blomback, "Purification of Human and Bovine Fibrinogen," *Arkiv for Kemi*, 10:415–443, 1956.

(14) Laki, K., "The Polymerization of Proteins: the Action of Thrombin on Fibrinogen," *Archives of Biochemistry and Biophysics*, 32:317–324, 1951.

(15) Tullis, J.L., *in* "Clot," Charles C. Thomas, Springfield, p. 215, 1976.

(16) Deykin, D., "The Clinical Challenge of Disseminated Intravascular Coagulation," *New England Journal of Medicine*, 283:636–644, 1970.

(17) Minna, J.D., S.J. Robboy and R.W. Colman, *in* "Disseminated Intravascular Coagulation in Man," Charles C. Thomas, Springfield, pp. 3–177, 1974.

(18) Pinniger, J.L. and F.T.G. Prunty, "Some Observations on the Blood-Clotting Mechanism. The Role of Fibrinogen and Platelets with Reference to a Case of Congenital Afibrinogenemia," *British Journal of Experimental Pathology*, 27:200–210, 1946.

(19) Weiner, A.E., D.E. Reid and C.C. Roby, "II. Incoagulable Blood in Severe Premature Separation of the Placenta: A Method of Management," *American Journal of Obstetrics and Gynecology*, 66:475–499, 1953.

(20) Rizza, C.R., "The Clinical Features of Clotting Factor Deficiencies," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," Edited by Biggs, R., Blackwell Scientific Publications, Oxford, p. 212, 1972.

(21) Jackson, D.P., "Congenital Disorders of Fibrinogen," *in* "Hematology," Edited by Williams, W.J., E. Beutler, A.J. Erslev, and R.W. Rundles, McGraw-Hill, New York, pp. 1209–1214, 1972.

(22) Merskey, C., A.J. Johnson, G.J. Kleiner and H. Wohl, "The Defibrination Syndrome: Clinical Features and Laboratory Diagnosis," *British Journal of Haematology*, 13:528–549, 1967.

(23) Kwaan, H.C., "Disseminated Intravascular Coagulation," *Medical Clinics of North America*, 56:177–191, 1972.

(24) Pritchard, J.A., "Treatment of the Defibrination Syndromes of Pregnancy," *Modern Treatment*, 5:401–422, 1968.

(25) Ratnoff, O.D., J.A. Pritchard and J.E. Colopy, "Hemorrhagic States During Pregnancy," *New England Journal of Medicine*, 253:63–68, 1955.

(26) Ratnoff, O.D., J.A. Pritchard and J.E. Colopy, "Hemorrhagic States During Pregnancy," *New England Journal of Medicine*, 253:97–102, 1955.

(27) Garner, R., B.V. Chater and D.L. Brown, "The Role of Complement in Endotoxin Shock and Disseminated Intravascular Coagulation: Experimental Observations in the Dog," *British Journal of Haematology*, 28:393–401, 1974.

(28) Bick, R.L., W.R. Schmalhorst and L. Fekete, "Disseminated Intravascular Coagulation and Blood Component Therapy," *Transfusion*, 16:361–365, 1976.

(29) van Doorm, J.M., H.J. Huisjes and C.T. Smit Sibinga, "Abruptio Placentae, Disseminated Intravascular Coagulation and the Use of Heparin: A Must?," Proceedings of the 7th European Conference on Microcirculation, Aberdeen 1972, Part II, Karger, Basel, 12:16–21, 1973.

(30) Kazmier, F.J., E.J.W. Bowie, A.B. Hagedorn and C.A. Owen, Jr., "Treatment of Intravascular Coagulation and Fibrinolysis (ICF) Syndromes," *Mayo Clinic Proceedings*, 49:665–672, 1974.

(31) Bachmann, F., "The Paradoxes of Disseminated Intravascular Coagulation," *Hospital Practice*, 6:113–126, 1971.

(32) Green, D., R.A. Seeler, N. Allen and I.A. Alavi, "The Role of Heparin in the Management of Consumption Coagulopathy," *Medical Clinics of North America*, 56:193–200, 1972.

(33) Sutton, D.M.C., R. Hauser, P. Kulapongs and F. Bachmann, "Intravascular Coagulation in Abruptio Placentae," *American Journal of Obstetrics and Gynecology*, 109:604–614, 1971.

(34) Horowitz, H.I., "Treatment of Defibrination Syndromes (other than those of pregnancy) and Fibrinolytic Disorders," *Modern Treatment*, 5:384–400, 1968.

(35) Barker, L.F. and J.H. Hoofnagle, "Transmission of Viral Hepatitis, Type B, by Plasma Derivatives," *Developments in Biological Standardization*, 27:178–188, 1974.

(36) Anderson, H.D., K.B. McCall, J.T. Sgouris and S.T. Gibson, "The Clinical Use of Dried Fibrinogen (Human) and the Risk of Transmitting Hepatitis by Its Administration," *Transfusion*, 6:234–246, 1966.

(37) Mainwaring, R.L. and G.G. Brueckner, "Fibrinogen-Transmitted Hepatitis," *Journal of the American Medical Association*, 195:437–441, 1966.

(38) Schroeder, D.D. and M.M. Mozen, "Australia Antigen. Distribution During Cohn Ethanol Fractionation of Human Plasma," *Science*, 168:1462–1464, 1970.

(39) Holland, P.V., H.J. Alter, R.H. Purcell, J.J. Lander, J.T. Sgouris and P.J. Schmidt, "Hepatitis B Antigen ($HB_sAg$) and Antibody (anti-$HB_sAg$) in Cold Ethanol Fractions of Human Plasma," *Transfusion*, 12:363–370, 1972.

(40) Leveque, P., J. Drouet, R. Schmitthaeusler, M.L. North, P. Amouch and J. Malgras, "$HB_sAntigen$ in Human Plasma Fractions," *Vox Sanguinis*, 28:1–8, 1975.

(41) Illinois Department of Health, *Monthly Report*, April 1975.

(42) Hellerstein, L.J. and D. Deykin, "Hepatitis After Konyne Administration," *New England Journal of Medicine*, 284:1039–1040, 1971.

(43) Faria, R. and N.J. Fiumara, "Hepatitis B Associated with Konyne," *New England Journal of Medicine*, 287:358–359, 1972.

(44) Oken, M.M., L. Hootkin and R.L. DeJager, "Hepatitis After Konyne Administration," *American Journal of Digestive Diseases*, 17:271–274, 1972.

(45) Sandler, S.G., C.E. Rath and A. Ruder, "Prothrombin Complex Concentrates in Acquired Hypoprothrombinemia," *Annals of Internal Medicine*, 79:485–491, 1973.

(46) Graham, J.H., C.P. Emerson and T.J. Anglem, "Postoperative Hypofibrinogenemia," *New England Journal of Medicine*, 257:101–104, 1957.

(47) Verstraete, M. in discussion of Schmitt, H., "Indications of Clinical Effect of Fibrinogen Preparations," *Vox Sanguinis*, 16:412–417, 1969.

(48) Roberts, L., "No Therapeutic Use for Fibrinogen," letter to editor, *New England Journal of Medicine*, 284:218, 1971.

(49) McMillan, C.W., L.K. Diamond and D.M. Surgenor, "Treatment of Classic Hemophilia: The Use of Fibrinogen Rich in Factor VIII for Hemorrhage and for Surgery," *New England Journal of Medicine*, 265:224–230, 1961.

(50) Lewin, J., M. Steinbuck and J.P. Soulier, "Statistical Survey on the Therapeutic Results Obtained With the Aid of Injectable Human Fibrinogen," *Pathologie et Biologie*, 7:2469–2475, 1959.

(51) Albrechtsen, O.K. and P. Skjodt, "Complications During Fibrinogen Therapy in a Case of Abruptio Placentae," *Acta Obstetricia et Gynecologica Scandinavica*, 43:129–140, 1964.

(52) Heaton, S.C., C. Solomon and E. Happel, "Afibrinogenemia: A Presentation of Cases," *American Journal of Obstetrics and Gynecology*, 70:320–327, 1955.

(53) Soloway, H.B. and C.E. Bereznak, "Plasma Fibrinogen Levels Following Cryoprecipitate Infusion," *Transfusion*, 10:326–328, 1970.

(54) Johnson, A., D. Aronson and W. Williams, "Clinical Use of Plasma and Plasma Fractions," *in* "Hematology," Edited by Williams, W.J., E. Beutler and A. Erslev, McGraw-Hill Book C., New York, p. 1345, 1972.

(55) Hattersley, P.G. and M.L. Dimick, "Cryoprecipitates in Treatment of Congenital Fibrinogen Deficiency," *Transfusion*, 9:261–264, 1969.

(56) Hattersley, P.G. and M. Kunkel, "Cryoprecipitates as a Source of Fibrinogen in Treatment of Disseminated Introvascular Coagulation (DIC)," *Transfusion*, 16:641–645, 1976.

(57) "Risk of Posttransfusion Hepatitis in the United States," National Transfusion Hepatitis Study, *Journal of the American Medical Association*, 220:692–701, 1972.

**15. Fibrinolysin (Human)**

*Generic Statement*

The coagulation system is complex and rigidly modulated. The "other side" of this system, the clot-lysing system, is apparently nearly as complex and as rigidly controlled, but is less well understood. Clinically, it is not less important. The ability to manipulate this system with certain agents is of potential therapeutic significance. References 1 through 3 support the basic discussion of the fibrinolytic system.

Plasminogen is a protein normally found in plasma. It is a single-chain beta globulin and can be purified from Cohn Fraction III. Its normal concentration is 200 micrograms/mL. Lower levels are found in infants and patients with cirrhosis. Higher levels are found in patients with infection, malignancies, or after injury. Two general forms have been identified, one with glutmatic acid in the N-terminal position (Glu-plasminogen) and one with lysine (Lys-plasminogen). The Glu form is slightly larger and is probably the natural circulating form. The Lys form, molecular weight 82,000–83,000, is probably a partially digested form. It has a shorter half-life after infusion into man (0.8 vs. 2–2. 5 days), and is more quickly activated and is more readily adsorbed to fibrin. This latter property may have therapeutic implications (Ref. 4). Plasminogen is rapidly synthesized, with plasma levels rising from none to normal within 12 to 24 hours after it has been depleted by infusion of an activator.

Plasminogen as it circulates is inactive. When it reacts with plasminogen activator, it is converted to plasmin, which lyses fibrin clots.

Plasminogen activators or precursors of activators are found in blood, many tissues (not liver), urine, saliva, and semen. There are high concentrations in vascular endothelium, more in veins than in arteries. The concentrations of activators in blood increase rapidly after vigorous exercise, emotional stress, injury, adrenergic stimulation, and following venous occulusion or ischemia of tissue or the infusion of various substances. The vascular endothelium may be the site of release of plasminogen activator into the circulation in response to many of these stimuli. Activated Factor XII promotes the formation of a plasminogen activator that may be different from the above. After injury or operation, the early rise in the levels of plasminogen activators in the blood is followed by at least several days of lower-than-normal levels.

The best-characterized plasminogen activator is urokinase. It is found in normal human urine and probably produced by renal parenchymal cells. Urokinase is a single chain beta globulin of molecular weight 54,000. It is not antigenic to humans. Many bacteria produce plasminogen activators, the best known of which is streptokinase. It is produced by beta-hemolytic Streptococci and is a protein with the mobility an *alpha*-2-globulin, and a molecular weight of 47,000. It is strongly antigenic in man.

When plasminogen and a plasminogen activator interact, plasmin is produced. The best defined reaction of this type is with urokinase. The product, plasmin, which forms has one heavy and one light chain linked by a single disulfide bridge. The light chain is the site of plasmin enzymatic activity. With streptokinase the reaction is less well understood, but a double-chain plasmin molecule is also formed. Streptokinase alone has no proteolytic activity. It combines with both

plasminogen and plasmin and undergoes structural rearrangements. The resulting complex acts as the "activator," and the streptokinase is partially fragmented in the process.

Plasmin is a serine protease, like many other enzymes formed from precursors. Like most such enzymes, it is fairly nonspecific and can digest a wide variety of substrates. In the coagulation system these include fibrin, fibrinogen, Factors II, V, VIII, and possibly VII. It also activates Factor XII and thereby can activate the coagulation, complement, and kinin systems (Ref. 35).

Such a powerful and nonspecific system must have a number of control mechanisms. Some of these have been identified. There are inhibitors to both plasmin and plasminogen activators. The anti-activators are found normally in the circulation, are probably *alpha*-2-globulins of molecular weight 75,000–80,000, and are fairly nonspecific (Ref. 37). Antibodies to streptokinase are specific anti-activators. These effectively neutralize infused streptokinase. They are found in almost all normal humans as the results of prior exposure ot streptococcal organisms. The level in the circulation varies widely, and will rise sharply in response to exposure to streptokinase through infection or infusion.

There are a rather large number of anti-plasmins. A fast-reacting inhibitor, highly specific for plasmin, may be the most important (Ref. 36). *Alpha*-2-macroglobulins are thought to be the principal secondary forms; they react rapidly but reversibly with plasmin in the circulation. Alpha-1-antitrypsin is also an anti-plasmin that reacts slowly but irreversibly. Other, perhaps less important, anti-plasmins are the anti-thrombin III-heparin complex, C 1 inactivator, inter-*alpha*-trypsin inhibitor, an inhibitor found in platelets, and inhibitors in granulocytes, arterial walls, and the placenta. The liver seems to be an important site of production of some anti-plasmins, and is also a site of inactivation of circulating activators. Patients with impaired hepatic function seem more prone to develop "out of control" fibrinolytic responses to various stimuli.

The products of the interaction of plasmin with both fibrinogen and fibrin can interfere with fibrin polymerization and can interfere with platelet function and therefore promote the development of clinical bleeding disorders (Ref. 1). Again the liver, or at least the reticuloendothelial system, seems to be an important site of clearance of fibrin or fibrinogen fragments from the circulation.

It is still not clear how the activity of plasmin, once formed, is limited to the area of need. There are a number of theories or hypotheses, but no real proof. The most widely accepted theory holds that plasminogen is adsorbed to fibrin. Plasminogen activator diffuses from the circulation into the clot, where plasmin, inhibitors are absent (Ref. 5). An alternate theory holds that plasmin-anti-plasim dissociates when in contact with fibrin and the plasmin becomes more tightly bound to the fibrin (Ref. 6). Another proposal suggests that plasminogen activators are selectively bound to fibrin (Ref. 7). In the background is preliminary evidence that fibrinolysis, not mediated by plasmin, may be clinically important.

There are marked differences among animal species in the activation and function of the plasminogen-plasmin system. Many laboratory animals respond to streptokinase with little or no activation of plasminogen. Man responds consistently by activating plasminogen when the proper dose is used. This has made evaluation of these agents, especially those containing streptokinase, almost impossible in controlled laboratory experiments and has required careful clinical study in man.

*Product Review*

1. *Description.* The Merck Sharp and Dohme Fibrinolysin (Human) "Thrombolysin™" product consists of a mixture of streptokinase (SK) and human plasminogen. Plasminogen is prepared from Cohn's Fraction III of human plasma. SK is prepared from the supernatant of cultures of streptococcus organisms. SK is added to the plasminogen, producing a mixture of SK, SK-plasminogen, SK-plasmin, plasmin, and other reaction products. It is not known if the plasmin is in the glutamic acid or lysine form. One vial of the substance containing "50,000 fibrinolytic units," contains about 40 units of plasmin and 20,000 units of SK. The manufacturer's "fibrinolytic units" relate to the ability of the active product to lyse a standard fibrin clot under certain conditions and in a specified period of time. The more commonly used units of measurement are determined by the ability of the active enzyme to hydrolyze casein (proteolytic activity) and the ability to convert additional plasminogen to plasmin as measured by resulting hydrolysis of casein (activator units). This review will refer to the latter two methods of measurement.

No known method of measurement relates simply and directly to human in vivo effects of this product. Most normal individuals have about five plasmin-inhibitory units per mL of plasma, or about 10,000 to 20,000 total circulating plasmin-inhibitory units. This obviously is vastly greater than the amount of plasmin usually infused with this product. Some investigators claim that the entire effect of this material is due to the in vivo activation of the recipient's plasminogen to plasmin by the streptokinase component, and that the preformed plasmin of the product is inconsequential. Most available evidence favors such an interpretation. There is a countervailing hypothesis that the inhibitor-plasmin complex formed almost immediately after infusion remains circulating for a time and is readily reversible. Fibrin forms a stronger bond with plasmin and is irreversible. Therefore, plasmin inactivated by inhibitor remains largely available by dissociation and active in in vivo fibrinolysis. There is little direct evidence to support this hypothesis; its main proponent has claimed therapeutic success with an SK-plasmin preparation from which the activator "had been removed" in a study involving five patients but without adequate controls (Ref. 8).

Normal individuals have about 3.8 plasminogen units per mL of plasma, so that the amount of activator (SK) infused with this product is potentially significant in activating the recipient's own plasminogen. Essentially all patients, however, have detectable levels of antistreptokinase, varying from 10,000 to 6 million circulating anti-SK units. Thus, even apart from the effects of plasmin inhibitors, there will be a wide range of effects from infusion of the SK of this product into a randomly selected population because of varying inactivation of this most important therapeutic component. Various investigators have proposed measuring anti-SK levels on all recipients and adjusting dosage accordingly, or titrating the dose to achieve a predetermined effect on a suitable laboratory test, such as prothrombin time, fibrinogen level, plasma recalcification time, or other tests, or both. Certainly, one of the major problems in evaluating the reported clinical experience is the lack of evidence that a physiologic effect upon the plasmin system was obtained in all patients with the dose used. Very few of the available studies contain satisfactory data in this regard.

The commercial product is supplied in dried form and must be mixed just before use. It should be kept cool during administration. At 4 °C loss of activity rarely exceeds 10 percent in 8 hours, but at room temperature, activity has been

reported as rapidly lost (up to 25 percent in 15 minutes) in freshly reconstituted products. The manufacturer adds a stabilizer and states that, when reconstituted, the product loses 10 percent of its activity in 2 hours and 25 percent in 4 hours at room temperature. It is not clear from clinical studies whether proper precautions were taken to guard against loss of activity.

2. *Safety.* The most recent reports of clinical use indicate a much lower incidence of febrile reactions than were common when the material was first marketed. This is now a fairly minor problem despite the known pre-immunization of almost every potential recipient to SK. This seems to have followed improvements in the purification of SK.

Anaphylaxis has been rare. The only reactions reported occurred following repeated parenteral administration of SK (Ref. 8). It is clear that careful consideration must be given before the repeated parenteral administration of a product containing SK. The need should be great, the circulating levels of anti-SK probably should be measured and an attempt be made to eliminate or lower the level of circulating antibody by administration of graded doses of SK before attempting a full therapeutic plasminogen-activating exposure.

Four instances of hepatitis were reported in a single series of patients early in the use of this product (Ref. 9). There have been no reported instances in the past 15 years. The product is heated at 60 °C for ten hours before release.

Hemorrhagic complications have been variously reported (Refs. 8 through 13). In general, the development of hemorrhage seems to parallel the induction of an active fibrinolytic state as detected by various laboratory tests; it occurs most easily at sites of recent injury, including venapuncture, and seems more common when anticoagulant drugs are used simultaneously (Refs. 8 and 12).

There is no generally agreed-upon method for monitoring the effects of this product on the recipient's coagulation system. Direct measurement of the components and activities of the plasminogen-plasmin system is technically demanding and is not routinely available. The "indirect" effects of the material have led various investigators to propose serially measuring bleeding time, whole blood-clotting time, thrombinclotting time, prothrombin time, fibrinogen concentration, thromboplastin generation, and plasma recalcification time among others. Fibrinogen concentration and one-stage prothrombin times seem the most consistently affected. Lengthening of the thrombin time or the prothrombin time seems to provide indirect evidence of the desired therapeutic effect at a state before severe effects which may result in bleeding are produced. Serious bleeding has followed the unintended induction of significant hypofibrinogenimia and digestion of other coagulation factors by plasmin with marked prolongation of the one-stage prothrombin time. Such patients have exhibited extensive activation of the plasminogin-plasminogen-plasmin system.

Other reported side effects include nausea, vomiting, abdominal pain, and, rarely, skin reactions or hypotension.

3. *Effectiveness.* The ability to dissolve clots intravascularly seems to vary with the age of the clot (easier when fresh), the circulating levels of fibrinogen and lipids (higher levels seem to impair efficacy) the status of inhibitors and anti-SK antibodies, hepatic function, perhaps the composition of the clot, and certainly the underlying condition(s) causing the intravascular thrombosis (Refs. 1 through 3 and 8). The benefit or harm to the patient from lysing an arterial clot, if such occurs, depends on the reversibility of tissue damage beyond the area of occlusion and the chances for harmful hemorrhage in the reperfused area. With venous clots, there is the theoretical danger of increasing the chances of pulmonary embolization by partially dissolving and "freeing up" thrombi. This seems not to occur.

The greatest problem in evaluating efficacy is the lack of properly controlled clinical trials, and the minimal value of studies on laboratory animals treated with this product. In addition, details of dosage and of handling the material and documentation of an effect on the proteolytic system are often lacking, as is angiographic evidence of the presence of thrombi before treatment and the dissolution of thrombi during treatment. The result is overall poor documentation of claimed benefits. Further, this product should be considered with closely related products, SK alone and urokinase from the point of view of safety and effectiveness.

4. *Specific clinical uses*—a. *Arterial thrombosis and embolization.* There were many reports of the use of this product alone or in conjunction with surgical intervention in the treatment of arterial thrombosis and embolization, mostly in the early 1960's (Refs. 14 through 17). By current standards, none of these studies were properly controlled. Often, there are underlying mechanical problems when an arterial thrombus develops, and the reports available are rather anecdotal and unconvincing. It is unlikely that surgery can be avoided by the use of this material, and there is no evidence that the outcome is improved. Techniques of vascular surgery such as better angiography, noninvasive flow measurements, better suture material, balloon catheterization, and extraction of clots have improved significantly since the earlier clinical studies and supplemental fibrinolysin now seems to be used rarely.

There is one important possible exception. Recent reports on the use of SK locally in structures used for vascular access for hemodialysis (shunts, fistulas, heterografts) have been impressive in that a number of patients who would otherwise have required surgical revision were carried for months after clotting of the devices had occurred and other usual means of restoring flow had failed. This is a small but important group of patients because these devices are literally life sustaining. Much of the time, thrombosis signifies an underlying mechanical problem which must be corrected. Some of the time local fibrinolysis seems to be effective. Since the material is used locally, systemic effects are minimal, making the technique even more attractive. Better-controlled studies are needed to indicate the proportion of such patients that can indeed be helped by this approach, but the reported experience to date is encouraging.

b. *Myocardial infarction.* The theoretical problems encountered when evaluating the effect of fibrinolysis in myocardial infarction are the uncertainty about how many myocardial infarctions are due to fibrin clots in the coronary arteries, and the problems of attaining reperfusion after infarction has occurred. The practical problems are those of establishing proper controls and demonstrating the presence of clots before treatment and their absence after treatment. Many reported studies are too small to draw conclusions or are uncontrolled. One very small study claimed less rise in SGOT in seven treated patients versus five controls (Ref. 18). Another claimed faster restoration toward normal of EKG abnormalities in 15 treated versus 40 historical "controls" (Ref. 19). Another series of papers dealing with a continuing series of patients claimed lower mortality in treated versus untreated patients, but the series was only partially controlled, and if the seemingly early uncontrolled group is removed, the differences disappear (Ref.

20). Three sizeable controlled studies with a total of 178 treated patients versus 182 control patients showed no differences in mortality (Refs. 9, 12 and 17).

c. *Cerebrovascular accidents.* Use of Fibrinolysis in ischemic strokes has not been shown to be beneficial in the best reported study to date (Ref. 21). This was a prospective double-blind study without angiography involving 20 treated patients and 20 control patients. In other smaller uncontrolled series the authors speculated as to benefit, but unconvincingly. The brain is one area where restoring blood flow rapidly to irreversibly damaged tissue undergoing necrosis conceivably could do more harm than good.

d. *Deep venous thrombosis.* This is one of the most troublesome therapeutic problems to evaluate. The recent resurgence of interest and investigation in this disease has clearly shown the inadequacy of relying on clinical criteria for either diagnosing the presence of clots or of detecting their dissolution. None of the early studies were properly documented by venography by modern standards, and very few were properly controlled even for clinical signs and symptoms (Refs. 8, 10, 11 and 17). Some compared such nebulous criteria as pain, disability, and duration of hospital stay with historical controls. In one of the few studies using simultaneous controls and three treatment groups, fibrinolysin, heparin, and rest and elevation only, the group treated with heparin seemed to fare better than the other two, which were indistinguishable from each other (Ref. 22). There was no angiographic documentation, and "superficial" phlebitis was included as were patients with underlying malignancy; this study is thus of doubtful merit. A more recent study indicated earlier lysis of deep venous clots with the infusion of SK and plasminogen separately (Ref. 4). This is not the same material as Thrombolysin™, but it is close.

The other problem with evaluating the treatment of deep vein thrombosis is in the selection of the criteria of success. Most pulmonary emboli result from clinically inapparent clots. The real problem with deep vein thrombosis is in the late sequelae. No study of fibrinolysis has adequately addressed this problem. The experience with ileofemoral thrombectomy indicates that early apparent benefit can disappear when late sequelae are evaluated at 5 to 10 years following the event (Ref. 23). Proof of efficacy in this disease will require a controlled study with angiographic documentation, and prolonged followup with double-blind evaluation of late sequelae.

e. *Pulmonary embolism.* The recent controlled trials with various fibrinolytic agents show that large pulmonary emboli can be lysed more rapidly when such agents are used (Refs. 24 and 25). Spontaneous lysis occurs at a significant rate also, so use of such agents should probably be limited to special circumstances, such as persisting hemodynamic changes or repeated embolization. One of the largest groups in which such criteria are likely to apply are patients soon after accidental or operative injury. This is the group in which the risks of significant hemorrhage are quite high following induced fibrinolysis. A better definition of benefit and risk is needed in such a group of patients before reliable conclusions can be drawn. For those patients without contraindications, use of lytic agents in the above circumstances seems warranted. These comments are based on the assumption that Thrombolysin™ is functionally similar to streptokinase, which was studied in some of these trials. Thrombolysin™ was not itself evaluated in these studies. Reports of the treatment of pulmonary emboli with Fibrinolysis (Human) are seriously lacking in either controls or angiographic documentation or both (Refs. 9, 17, 26 and 27).

f. *Thrombosis of the retinal artery or veins.* There seem to be only two reported instances in which there was significant return of vision following treatment of retinal arterial thrombosis with thrombolysin (Ref. 28). The oxygen demands of the retina are so high and the arterial supply so vulnerable, that it seems unlikely that a complete thrombotic occlusion could be lysed early enough to allow function to recover. It is not clear how often partial occlusions occur. There are more encouraging reports of improvement of vision after the treatment of occlusion of the central retinal veins, but none of these reports have presented proper controls (Refs. 10, 11 and 29).

g. *Traumatic hyphema.* Instillation of fibrinolysin into the eye to remove post-traumatic clots was reported with some frequency but with no controls. The closest to a controlled study seemed to show equal benefits from conservative treatment (Ref. 30). This use of fibrinolysins seems to have ceased in recent years and cannot be recommended.

h. *Priapism.* There have been several reports of the use of systemic and/or local fibrinolysin for the treatment of priapism, all without adequate controls (Refs. 10, 31 and 32). This is a disorder with a wide range of causes, some unlikely to be helped by fibrinolysin. Again, this does not seem to be a currently practiced method of treatment.

i. *Respiratory distress of the newborn.* One rather striking study showed a sharply increased mortality from the use of systemic fibrinolysin for the treatment of respiratory distress of the newborn in which 1 of 6 controls died versus 5 of 5 treated (Ref. 33). Autopsies yielded no clues as to the cause, but this experience suggests that this material should not be used parenterally in premature infants for any reason. Others have used it by pulmonary insufflation in respiratory distress of the newborn without such adverse results but also without apparent benefit.

j. *Intraperitoneal adhesions.* A single study in rats suggested fewer intraperitoneal adhesions after the use of intraperitoneal fibrinolysin (Ref. 34). The experimental model and the problems with extrapolating to another species makes this observation of uncertain significance for man. No clinical studies have been reported.

5. *Labeling.* The label available for review uses the manufacturer's dosage units, which differ from those commonly used in the literature. This can be misleading. The discussion in the labeling of published reports on the use of this product in various conditions does not refer to or properly emphasize some of the negative clinical trials, especially in patients with myocardial infarction and cerebrovascular accidents. The only indications listed for use are "phlebothrombosis, thrombophlebitis, pulmonary embolism, and thrombosis of arteries with exclusion of thrombosis of coronary arteries and cerebral arteries." The limitations of fibrinolytic therapy in such conditions, discussed in this review, are barely or not at all mentioned. There is perhaps an undue impression of accuracy of dosage, but in view of the uncertainty about proper dosage and monitoring, this is not an area in which definite statements can or should be made. The precautions do not list concurrent anticoagulation as probably increasing the risk of hemorrhage; this point seems well enough established to be included in the labeling.

6. *Summary.* Fibrinolysin (Human) was first evaluated clinically several years before the current resurgence of interest in the study of thromboembolic disease. As a result, its evaluation for effectiveness has been inadequate by modern standards. Improper or no controls and lack of angiographic

documentation are the two most serious and common defects. In many published studies, evaluation of hemostatic function was either not done or was inadequate to assess whether or not a fibrinolytic state had been induced. This is a particularly important point with a product containing streptokinase because of the variable level of inactivating antibodies in the human population. The extremely limited relevant data that can be obtained in animals with this product make careful human clinical studies mandatory.

The most likely clinical uses of value are for pulmonary embolism, deep venous thrombosis, and clotted vascular access devices in patients undergoing hemodialysis. The limitations and problems for these uses have been discussed. For all three uses, most of the pertinent data have been derived from studies using urokinase or streptokinase alone. One of the main problems the Panel faced was in deciding to what extent these data on SK could be applied to Thrombolysin™. It seems likely that most of them are applicable, but this is in fact a different product. There is little reason to expect much functional difference between these products, and the available data do indicate that Fibrinolysin (Human) can activate the plasmin system in human recipients. The Panel's first decision, then, was to treat this product in a manner similar to urokinase and streptokinase, and to allow market forces to decide its utilization, even though it seemed logical that if both a plasminogen activator and plasminogen itself were needed in specific circumstances, these should be provided separately in the doses indicated. The regulations in 21 CFR 601.25(d)(4) appear to require specific data supporting the need for each component of such a combination. The recommendation of the Panel follows the regulations, since the requirement for the plasminogen component cannot be documented by present data.

7. *Recommendations.* a. Fibrinolysin (Human) should be placed in Category IIIA, that is, to remain on the market pending proof of effectiveness, but requiring that such proof be presented to retain permanent licensure. A period of 3 years should be allowed for the recommended studies demonstrating the contribution of each component to the labeled indications.

b. During continued marketing, the only indications for which there is reasonable supportive evidence at present are for use in the treatment of pulmonary embolism, deep venous thrombosis, and clotted vascular access devices. Labeling for any of these indications should reflect the problems discussed in this review. Labeling should indicate that spontaneous lysis occurs with both pulmonary emboli and deep venous thrombi, that fibrinolytic agents appear to accelerate the early phases only, that there is no proof that late sequelae are lessened in patients with deep venous thrombosis, and that underlying mechanical factors are often the cause of thrombosis in vascular access devices.

c. All fibrinolytic agents should be rereviewed at a later date by a single panel of experts. Separate reviews of urokinase and streptokinase on one hand and Fibrinolysin (Human) on the other is artificial, duplicative, and could result in unfair inconsistencies.

d. The material should be named "Fibrinolysin."

8. *Other research.* The following are areas for which further research is recommended:

a. There is a great need for a practical laboratory test which can be used to monitor therapy with fibrinolytic agents.

b. The fibrinolytic system itself needs considerable further elucidation.

c. Plasminogen activators are needed which are effective, nonantigenic, and less expensive than urokinase as now produced.

d. The breakdown products of fibrin and fibrinogen need to be further defined, their effects and dynamics studied, and methods for their detection need to developed which will distinguish the various stages of fibrinolytic events in patients.

References

(1) Sherry, S., "Fibrinolysis," *Annual Review of Medicine*, 19:247–268, 1968.

(2) Kernoff, P.B. and G.P. McNicol, "Normal and Abnormal Fibrinolysis," *British Medical Bulletin*, 33:239–244, 1977.

(3) Kakkar, V.V. and M.F. Scully, "Thrombolytic Therapy," *British Medical Bulletin*, 34:191–199, 1978.

(4) Kakkar, V.V., S. Sagar and M. Lewis, "Treatment of Deep-vein Thrombosis With Intermittent Streptokinase and Plasminogen Infusion," *Lancet*, 2:674–676, 1975.

(5) Sherry, S., A.P. Fletcher and N. Alkjaersig, "Developments in Fibrinolytic Therapy for Thrombo-embolic Disease," *Annals of Internal Medicine*, 50:560–570, 1959.

(6) Ambrus, C.M. and G. Markus, "Plasminantiplasmin Complex as a Reservoir of Fibrinolytic Enzyme," *American Journal of Physiology*, 199:491–494, 1960

(7) Chesterman, C.N., M.J. Allington and A.A. Sharp, "Relationship of Plasminogen Activator to Fibrin," *Nature New Biology*, 238:15–17, 1972.

(8) Ambrus, J.L., C.M. Ambrus, J.E. Sokal, G. Markus, N. Back, L. Stutzman, D. Razis, C.A. Ross, B.H. Smith, A.C. Bekate, G.L. Collins, D.L. Kline, and J.B. Fishman, "Clinical Pharmacology of Various Types of Fibrinolytic Enzyme Preparations," *American Journal of Cardiology*, 6:462–475, 1960.

(9) Israel, H.L., G.R. Fisher, O. Mueller and D.A. Cooper, "Fibrinolysin Treatment of Thromboembolism," *Journal of the American Medical Association*, 188:628–631, 1964.

(10) Cliffton, E.E., "Review of Clinical Experience with Clot-lysing Agents," *American Journal of Cardiology*, 6:476–486, 1960.

(11) Mazel, M.S., R. Riera and J.R. Stern, "Clot Lysis of Fibrinolysin: Progress Report," *Journal of the American Geriatrics Society*, 15:87–94, 1967.

(12) Dewar, H.A., P. Stephenson, A.R. Horler, A.J. Cassells-Smith and P.A. Ellis, "Fibrinolytic Therapy of Coronary Thrombosis," *British Medical Journal*, 1:915–920, 1963.

(13) Wilson, W.L., F. Naso and E. Lippmann, "Dose Response Curves with Varying Doses of Fibrinolysin," *American Journal of Cardiology*, 6:503–506, 1960.

(14) Anlyan, W.G., "Fibrinolysis in Thromboembolic Disease," *New York State Journal of Medicine*, 62:3744–3746, 1962.

(15) Cliffton, E.E. and R.L. Clarke, "The Use of Fibrinolytic Agents in the Treatment of Arterial Occlusion," *American Journal of Surgery*, 103:173–179, 1962.

(16) Kartchner, M.M. and W.C. Wilcox, "Thrombolysis of Palmar and Digital Arterial Thrombosis by Intraarterial Thrombolysin," *Journal of Hand Survey*, 1:67–74, 1976.

(17) Richter, I.H., E.E. Cliffton, S. Epstein, F. Musacchio, A. Nassar, A.G. Favazza, G. Katabi, A.M. Derosas and H. Prado, "Fibrinolysin Therapy in Thromboembolic Diseases," *New York State Journal of Medicine*, 62:3746–3750, 1962.

(18) Boucek, R.J. and W.P. Murphy, "Segmental Perfusion of the Coronary Arteries with Fibrinolysin in Man Following a Myocardial Infarction," *American Journal of Cardiology*, 6:525–533, 1960.

(19) Datey, K.K., R.C. Hansoti and V.N. Pandya, "Value of Fibrinolysin in Management of Myocardial Infarction," *Journal of the American Medical Association*, 182:1078–1081, 1962.

(20) Richter, I.H., E.E. Cliffton, S. Epstein, F. Musacchio, A. Nassar, A.G., Favazza and G. Katabi, "Thrombolysin Therapy in Myocardial Infarction," *American Journal of Cardiology*, 9:82–85, 1962.

(21) Meyer, J.S., J. Gilroy, M.I. Barnhart and J.F. Johnson, "Therapeutic Thrombolysis in Cerebral Thromboembolism: Double-Blind Evaluation of Intravenous Plasmin Therapy in Carotid and Middle Cerebral Arterial Occlusion," *Neurology* 13:927–937, 1963.

(22) Sawyer, P.N., H.C. Schaefer, R.T. Domingo and S.A. Wesolowski, "Comparative Therapy of Thrombophlebitis," *Surgery*, 55:113–122, 1964.

(23) Lansing, A.M. and W.M. Davis, "Five-Year Follow-Up Study of Iliofermoral Venous Thrombectomy," *Annals of Surgery*, 168:620–628, 1968.

(24) Sasahara, A.A., T.M. Hyers, S. Cole, F. Ederer, J.A. Murray, N.K. Wenger, C.M. Sherry and J.M. Stengle, "The Urokinase Pulmonary Embolism Trial: A National

Cooperative Study," *Circulation*, 47:1-108, Supplement 2, 1973.

(25) Tibbutt, D.A., J.A. Davies, J.A. Anderson, E.W. Fletcher, J. Hamil, J.M. Holt, M.L. Thomas, G.D. Lee, G.A. Miller, A.A. Sharp and G.C. Sutton, "Comparison by Controlled Clinical Trial of Streptokinase and Heparin in Treatment of Life-threatening Pulmonary Embolism," *British Medical Journal*, 1:343-347, 1974.

(26) Cliffton, E.D., "Treatment of Pulmonary Embolism with Fibrinolytic Agents," *Bulletin of the New York Academy of Medicine*, 43:267-280, 1967.

(27) Wilcox, W.C. and T.L. Jarkowski, "Thrombolysin Therapy in Acute Main Pulmonary Thromboemboli," *Thrombosis et Diathesis Haemorrhagica*, Supplement 47:283-299, 1971.

(28) Hecker, S.P. and H.C. Zweng, "Central Retinal Artery Occlusion Successfully Treated with Plasmin," *Journal of the American Medical Association*, 176:1067-1069, 1961.

(29) Morton, W.R. and W. Turnbull, "An Unusual Case of Central Retinal Vein Occlusion, Treated Successfully with Intravenous Fibrinolysin," *Canadian Medical Association Journal*, 85:844-846, 1961.

(30) Cole, J.G. and H.M. Byron, "Evaluation of 100 Eyes with Traumatic Hyphema: Intravenous Urea," *Archives of Ophthalmology*, 71:35-42, 1964.

(31) King, L.M., D.P. McCune, J.J. Harris, and R.L. Buck, "Fibrinolysin Therapy for Thrombosis of Priapism," *Journal of Urology*, 92:692-695, 1964.

(32) Grace, D.A. and C.C. Winter, "Priapism: an Appraisal of Management of Twenty-three Patients," *Journal of Urology*, 99:301-310, 1968.

(33) Gomez, M.F. and S.N. Graven, "The Use of Fibrinolysin in the Treatment of Respiratory Distress Syndrome," *Pediatrics*, 34:877-880, 1964.

(34) Knightly, J.J., D. Agostino and E.E. Cliffton, "The Effect of Fibrinolysin and Heparin on the Formation of Peritoneal Adhesions," *Surgery*, 52:250-258, 1962.

(35) Murano, G., "The 'Hageman' Connection: Interrelationships of Blood Coagulation, Fibrino[geno]lysis, Kinin Generation, and Complement Activation," *American Journal of Hematology*, 4:409-417, 1978.

(36) Schreiber, A.D. and F. Austen, "Interrelationships of the Fibrinolytic, Coagulation, Kinin Generating and Complement System," *Seminars in Hematology*, 6:593-601, 1973.

(37) Aoki, N., M. Moroi, M. Matsuda and K. Tachiya, "The Behavior of Alpha-2-Plasmin Inhibitor in Fibrinolytic States," *Journal of Clinical Investigation*, 60:361-369, 1977.

### 16. $Rh_o$(D) Immune Globulin (Human)

*Generic Statement*

1. *Introduction.* Hemolytic disease of the newborn due to anti-$Rh_o$(D) was a significant problem prior to the advent of immunoprophylaxis in 1968. Milestones in the understanding and management of this problem include the discovery of the $Rh_o$(D) antigen, elucidation of the pathogenesis of the disease, the development of exchange transfusion in the neonate, the development of intrauterine diagnosis by amniocentesis and intrauterine transfusions. Despite these formidable achievements, it was estimated that in 1968, 2.7 deaths per 10,000 live births occurred in the United States as a result of this condition (Ref. 1).

The pathogenesis of Rh hemolytic disease of the newborn is well known. In a primigravid Rh-negative woman who has not been exposed previously to Rh-positive blood, primary immunization occurs most frequently during labor and delivery, particularly during the third stage of labor, when Rh-positive fetal red blood cells (RBC) cross the placenta and enter the maternal circulation in substantial numbers. The risk of immunization is related to the magnitude of feto-maternal hemorrhage: In the presence of ABO compatibility between mother and fetus, the risk is 3 percent when less than 0.1 mL of the fetal RBC are present in the mother, is 25 percent when 0.25 to 1 mL are present, and is 65 percent when more than 5 mL are present. Perhaps 75 percent of delivering women have less than a 0.1 mL feto-maternal hemorrhage while only 0.3 percent have feto-maternal hemorrhage of greater than 15 mL. Thus, the overall risk of Rh immunization in ABO compatible pregnancies is 13 to 15 percent per Rh incompatible pregnancy. In ABO-incompatible pregnancies the risk is 2 to 3 percent (Ref. 2).

A major development in the elimination of this problem occurred in the late 1960's when it was demonstrated by a number of investigators that active immunization of Rh-negative mothers carrrying Rh-positive fetuses could be prevented with the administration to the mother of an intramuscular injection of $Rh_o$ immune globulin within 72 hours after delivery (Refs. 3 through 6). Using the standard dose of 300 micrograms of Rh antibody, there has been a 90-percent reduction of the immunization rate from about 15 percent to about 1.5 percent (Refs. 2 and 7). The reasons for failure to achieve complete prophylaxis are not entirely clear and may reflect, in part, a lack of clear understanding of the mechanism by which prophylactic effect is achieved. Failures may result from a number of factors:

a. Immunization may have already occurred during pregnancy. Fetomaternal hemorrhage has been noted as early as during the early portion of the second trimester and increases in size and frequency as gestation proceeds (Ref. 2). Thus, some women may be immunized early in pregnancy. In recognition of this, some investigators have administered $Rh_o$ immune globulin during pregnancy in either single dose (300 μg) at 34 weeks gestation or twice at 28 and 34 weeks gestation. The evidence to date suggests that as many as 65 to 90 percent of all prophylaxis failures may be eliminated by antepartum administration of $Rh_o$ immune globulin (Refs. 8 and 9). These studies require demonstration that immunization has not occurred by evaluation subsequent pregnancies. Infants born after antenatal treatment show no evidence of increased red cell destruction resulting from the passive antibody administration to the mother, although many manifest a positive direct antiglobulin test of their red cells.

b. A large feto-maternal bleed may have occurred, and the standard 300 microgram dose is therefore inadequate. Studies indicate that 300 micrograms of Rh antibody are sufficient to prevent immunization when up to 15 mL of Rh-positive red cells have been infused into Rh-negative subjects (Refs. 10 and 11). As only 0.3 percent of all pregnancies will have feto-maternal bleeds of greater than 15 mL (Ref. 2), this factor cannot account for more than than a small number of all the $Rh_o$ immune globulin prophylactic failures. In most pregnancies, the dose of anti-$Rh_o$ is probably excessive.

c. It is possible that the intramuscular route of administration may not assure adequate uptake of antibody into the circulation. While there is no direct evidence on this point, European investigators have been using intravenous administration of a preparation prepared especially for intravenous use (Ref. 12). The World Health Organization has recommended that only half the usual dose is necessary if the intravenous route is used.

d. Rh-negative women born of Rh-positive mothers may have been actively immunized by a materno-fetal bleed when they were born ("grandmother theory"). When these women deliver an Rh-positive fetus, $Rh_o$ immune globulin would not be effective because of their prior immunization. Studies (Refs. 13 through 16) suggest this possibility, and a materno-fetal immunization rate of 5 to 11 percent has been observed (Refs. 14 and 16) Other studies have not confirmed these findings (Refs. 17, 18 and 38). Further studies are necessary to confirm the validity of the "grandmother theory." If proven, Rh-negative female children born of Rh-positive mothers might receive $Rh_o$ immune globulin to prevent

such immunization and later instances of hemolytic disease in their children.

While not a factor strictly relevent to the $Rh_o$ immune globulin prophylaxis failure rate, it is noteworthy that failure to administer $Rh_o$ immune globulin still occurs. Estimates by the Centers for Disease Control indicate that only 80 percent of women who should receive immunoprophylaxis actually do so (Ref. 1). Clearly, further educational efforts are needed in the total program aimed at eliminating Rh hemolytic disease of the newborn.

Other situations in which $Rh_o$ immune globulin may be useful include:

(1) *$Rh_o$ immune globulin in abortion.* In cases of abortion, a risk of maternal immunization exists. The overall rate of immunization has been estimated as between 3 to 5.5 percent where the Rh type of the fetus is unknown (Refs. 19 and 20). The method of inducing abortion may influence this rate (Ref. 19); hypertonic saline abortion results in a three times greater frequency of transplacental hemorrhage than does curettage abortion. The risk of immunization also increase directly with gestational age. On the basis of these considerations, Rh immunoprophylaxis has gained general acceptance in cases of abortion. While controlled studies demonstrating the effectiveness of immunprophylaxis in abortion case have not been performed, the argument for use of $Rh_o$ immune globulin in these cases is very compelling.

(2) *$Rh_o$ immune globulin in transfusion.* The third major clinical circumstance where $Rh_o$ immune globulin is used is when $Rh_o$(D) negative patients have accidentially received a transfusion of $Rh_o$ (D) positive blood. Studies in volunteers indicate up to an 80 percent immunization rate in these circumstances and, administration of 20 micrograms of $Rh_o$ immune globulin for each 1 mL of red blood cells affords total protection against immunization (Refs. 10 and 11). Other reports substantiate these observations (Refs. 21 through 24).

2. *Description of product.* $Rh_o$ immune globulin is manufactured from human plasma containing anti-$Rh_o$(D) antibody. The plasma undergoes fractionation and the globulin fraction is obtained. The material is tested for specificity and potency in vitro in the latter case, by comparison with an FDA, Bureau of Biologics reference material. The final product may be diluted with serum globulin which does not contain anti-$Rh_o$(D). Stabilizing and antibacterial materials are added.

The Bureau of Biologics' requirements are that at least 200 mL each of plasmas (or sera) from 20 different donors be represented in the original plasma pool. While this is an apparently arbitrary number, it does permit some confidence that all specificities of the $Rh_o$(d) mosaic and antibodies of different affinity constants are represented in the final material. The Bureau of Biologics has limits for the presence of red cell antibodies other than anti-$Rh_o$(D) and these appear prudent and not overly restrictive.

The amount of anti-$Rh_o$(D) antibody is determined by an antiglobulin titer which must be equal to or greater than the Bureau of Biologics' reference material. This procedure is open to question. Manual titration using doubling dilutions is a highly subjective test. A one tube difference in such an assay system could reflect a 50-percent error in antibody concentration. Further, it has been demonstrated that assay values for $Rh_o$(D) antibody obtained by either manual or automated methods may be inaccurate as the regression line for the assay depends on both the antigen, i.e., the Rh-phenotype of the test cell, and the heterogeneity of the antibody population being tested. Finally, since the critical literature on efficacy of $Rh_o$ immune globulin is expressed in doses described in micrograms of antibody, it would seem reasonable to demand consistency in standardization and expression of potency in the assay of manufactured lots.

Perhaps the best assay system for Rh antibody is the radioimmunoassay (Refs. 25 and 26). This test was the standard by which efficacy and dosage have been ascertained, and it has been demonstrably satisfactory. Radioimmunoassay procedures are difficult to carry out. A second quantitative technique that is acceptable is the Autoanalyzer™ titration method (Ref. 26). Since $Rh_o$ immune globulin is prepared from plasma pools representing at least 20 different donors, the problem of antibody heterogeneity is reduced. When using this test, dilutions within one log are usually employed, and errors or inaccuracies are minimized.

3. *Effectiveness.* a. There are three clinical situations where administration of $Rh_o$ immune globulin to prevent primary immunization to Rh antigen is currently used:

(1) *Postpartum in Rh-negative mothers who have delivered an Rh-positive child.* Administration within 72 hours after delivery affords 90-percent protection against primary immunization (Refs. 1 through 7).

(2) *After abortion in Rh-negative women.* Controlled studies are not available, but there is no reason to believe effectiveness is not equal to or greater than in term pregnancies.

(3) *After transfusion of Rh-positive blood to an Rh-negative individual.* Efficacy has been demonstrated in both controlled studies (Refs. 10 and 11) and clinical situations (Refs. 21 through 24).

b. There are a number of clinical situations where the use of $Rh_o$ immune globulin has been suggested to prevent primary immunization:

(1) *After transfusion of blood components containing Rh-positive erythrocytes to Rh-negative recipients.* Transfusion of platelet or granulocyte concentrates is usually associated with infusion of substantial numbers of red cells. Primary immunization to the Rh antigen may be prevented with $Rh_o$ immune globulin in those patients in whom it is desirable to do so, e.g., women in childbearing age. There is no evidence that cryoprecipitate from Rh-positive individuals can immunize Rh-negative recipients.

(2) *After abdominal trauma to an Rh-negative woman during pregnancy.* There is evidence that abdominal trauma, particularly amniocentesis, can be associated with feto-maternal bleeding (Refs. 28 through 32). It appears rational in these circumstances to administer intrapartum $Rh_o$ immune globulin, although controlled studies are not available to support this use.

(3) *Intrapartum administration to all Rh-negative women.* Current evidence in a relatively small number of pregnancies suggests that primary immunization may be prevented with this approach, although not completely, (Ref. 8) as determined by postpartum Rh antibody detection (Refs. 2, 8 and 9). However, firm documentation of efficacy would require demonstration of no immunization with subsequent Rh-positive pregnancies. These data are not currently available. Such a program is directed at the 1.5 percent of at risk women who currently fail to be protected by postpartum prophylaxis. As the number of doses of $Rh_o$ immune globulin would increase two- to three-fold with such a program, the impact on health care costs and on immunized plasmapheresis donors, the source of antibody-containing plasma, would be great if intrapartum prophylaxis were widely practiced. Thus, effectiveness should be established unequivocally before considering formal approval of this indication.

(4) *Administration to Rh-negative neonates born of Rh-positive mothers.* Current data do not support this use.

(5) *Administration to $D^u$ women.* There are case reports of $D^u$ women who developed "anti-D" with resulting

hemolytic disease of the newborn. This must be a rare event. Also, there is no evidence that administration of $Rh_o$ immune globulin in these women would be protective; much of the administered antibody would be adsorbed by maternal cells (Ref. 34). Of greater concern is the clinical situation where the mother's Rh status is unknown prior to delivery. In these cases, a postpartum maternal typing as $D^u$ might indicate the presence of a large feto-maternal hemorrhage of Rh-positive cells in an Rh-negative woman. In these cases, immune globulin should be given.

(6) *Administration later than 72-hours postpartum.* The 72-hour postpartum limit for $Rh_o$ immune globulin resulted from an artifact in the experimental design during the original studies on this material (Ref. 7). This time limit appears valid for optimal protection but, if the antibody has not been administered within this period, it should still be administered later, as protection, albeit to a lesser degree, may still be achieved at little risk (Ref. 39).

c. *Miscellaneous issues affecting efficacy*—(1) *Estimating the size of feto-maternal hemorrhage.* The risk of feto-maternal immunization increases with the size of the feto-maternal hemorrhage (Ref. 2). The standard dose of 300 μg of $Rh_o$ immune globulin protects against up to 15 mL of feto-maternal hemorrhage (Refs. 10 and 11). While hemorrhages greater than 15 mL occur in only 0.3 percent of pregnancies (Ref. 2), these women are at increased risk to become immunized and require more than the standard dose to be adequately protected. Provisions should be made in the labeling to recommend a screening or quantitative procedure for the detection of large (greater than 15 mL) feto-maternal hemorrhages. Appropriate upward adjustment of the dose of $Rh_o$ immune globulin should also be recommended in these cases.

(2) *Low dose $Rh_o$ immune globulin.* The current standard dose of $Rh_o$ immune globuli 300 micrograms, is excessive in most cases (Refs. 5, 10, 11 and 42), although the safety of the product is not affected by the excess. During abortions or abdominal trauma, where the transplacental hemorrhage is generally far less than at term gestations, a lower does of $Rh_o$ immune globulin may be equally efficacious. In Rh-negative male volunteers, it has been shown that 50 micrograms of $Rh_o$ immune globulin completely protects against primary Rh immunization from a dose of 2.5 mL of red blood cells (Ref. 37).

4. *Safety.* $Rh_o$ immune globulin has not been associated with severe toxicity. Localized reaction at the site of intramuscular injection is probably the most frequent side effect. A variety of complications have been reported in association with the administration of Rh immune globulin, but causal relationships are not always clear. Urticaria, temperature elevatio fever, myalgia, hyperbilirubinemia, splenomegaly, and rare sensitivities after repeated injections have been observed. Transmission of hepatitis has not been associated with this product.

Rh immune globulin administered during pregnancy to Rh-negative women carrying an Rh-positive fetus has not been associated with iatrogenic Rh hemolytic disease in the fetus (Refs. 2, 8, 9 and 33), although some infants show a positive direct antiglobulin test. Even when anti-$Rh_o$ is administered to Rh-positive adults, there appears to be little hazard (Ref. 35).

5. *Benefit/risk.* $Rh_o$ immune globulin is a highly effective product with few serious side effects.

6. *Recommendations.* a. The product should be placed in Category I for the currently approved indications.

b. In addition, $Rh_o$ immune globulin should be approved for the following indications:

(1) After transfusion of any blood product containing Rh-positive red cells to an Rh-negative recipient in whom it is desirable to suppress primary immunization; and

(2) After significant abdominal trauma, including amniocentesis, to a pregnant Rh-negative woman.

c. Estimation of a large feto-maternal hemorrhage (greater than 15 mL) of Rh-positive cells should be recommended in all labeling as part of regular postpartum evaluation, and the dose of $Rh_o$ immune globulin should be increased accordingly.

d. The 72-hour time limit for administering $Rh_o$ immune globulin after exposure to Rh-positive red blood cells should be encouraged as preferable for prophylaxis. If more than 72 hours have passed, $Rh_o$ immune globulin should still be given as soon as possible, up to 2 weeks after exposure to Rh-positive red blood cells, with the warning that efficacy may be reduced.

e. $Rh_o$ immune globulin should not be given to:

(1) Rh-positive individuals,

(2) Rh-negative individuals known to be immunized to the Rh antigen, and

(3) in an Rh-negative woman where the fetus is known to be Rh-negative.

f. The requirement for $Rh_o$ immune globulin crossmatch prior to administration should be eliminated.

g. Assay of all lots of $Rh_o$ immune globulin must be performed by an approved method.

h. Encourage educational efforts to eliminate instances of non-administration of $Rh_o$ immune globulin where it is indicated.

i. Further research is needed on (1) intrapartum prophylaxis, (2) immunization of Rh-negative newborns of Rh-positive mothers, (3) low-dose prophylaxis in abortion, (4) low-dose prophylaxis in abdominal trauma, and (5) the use of $Rh_o$ immune globulin for intravenous use when large doses are required.

j. *Labeling recommendations.* (1) Add the new indications noted above.

(2) Add a recommendation for screening or quantitating the size of the feto-maternal bleed.

(3) Change the wording on the 72-hour time limit to permit administration for up to 2 weeks after exposure (Ref. 39).

(4) Eliminate the instructions for the crossmatch.

(5) Eliminate any statement directed specifically at administration to the infant.

(6) Eliminate the statement that $Rh_o$ immune globulin should not be administered to "an Rh-negative woman who has received an Rh-positive transfusion within three months of delivery."

**References**

(1) "Rh Hemolytic Disease Surveillance 1974," Center for Disease Control, Issued August 1976.

(2) Bowman, J.M., "Rh Erythroblastosis Fetalis 1975," *Seminars in Hematology*, 12:189–207, 1975.

(3) Freda, V.J., J.G. Gorman, W. Pollack, J.G. Robertson, E.R. Jennings and J.F. Sullivan, "Prevention of Rh Isoimmunization. Progress Report of the Clinical Trail in Mothers," *Journal of the American Medical Association*, 199:390–394, 1967.

(4) Pollack, W., J.G. Gorman, V.J. Freda, W.Q. Ascari, A.E. Allen and W.J. /Baker, "Results of Clinical Trails of $Rh_oGAM$ in Women," *Transfusion*, 8:151–153, 1968.

(5) Chown, B., et al., "Prevention of Primary Rh Immunization: First Report of the Western Canadian Trail, 1966–1968," *Canadian Medical Association Journal*, 100:1021–1024, 1969.

(6) Clarke, C.A., W.T.A. Donohue, R.B. McConnell, J.C. Woodrow, R. Finn, J.R. Krevans, W. Kulke, D. Lehane and P.M. Sheppard, "Further Experimental Studies on the Prevention of Rh Haemolytic Disease," *British Medical Journal*, 1:979–984, 1963.

(7) Freda, V.J., J.G. Gorman, W. Pollack and E. Bowe, "Prevention of Rh Hemolytic Disease. Ten Years' Clinical Experience with Rh°(D) Immune Globulin (Human)." *In* "Rh Antibody Mediated Imunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ, pp. 71–75, 1975.

(8) Davy, M.G., "Antenatal Administration of Anti-Rh: Australia 1969–1975," *In* "Rh Antibody Mediated Immunosuppression,"

Ortho Research Institute of Medical Sciences, Raritan, NJ. pp. 59–62, 1975.

(9) Bowman, J., "Winnipeg Antenatal Prophylaxis Trail," *In* "Rh Antibody Mediated Immunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ pp. 55–58, 1975.

(10) Pollack, W., W.Q. Ascari, R.J. Kochesky, R.R. O'Connor, T.Y. Ho and D. Tripodi, "Studies on Rh Prophylaxis. I. Relationship Between Doses of Anti-Rh and Size of Antigenic Stimulus," *Transfusion*, 11:333–339, 1971.

(11) Pollack W., W.Q., Ascari, J.F. Crispen, R.R. O'Connor and T.Y. Ho., "Studies on Rh Prophylaxis. II. Rh Immune Prophylaxis After Transfusion with Rh-Positive Blood," *Transfusion*, 11:340–344, 1971.

(12) Hoppe, H.H., T. Mester, W. Hennig, and H.J. Krebs, "Prevention of Rh-Immunization. Modified Production of IgG Anti-Rh of Intravenous Application by Ion Exchange Chromatography (IEC).," *Vox Sanguinis*, 25:308–316, 1973.

(13) Taylor, J.F., "Sensitization of Rh-Negative Daughters by Their Rh-Positive Mothers," *New England Journal of Medicine*, 276:547–551, 1967.

(14) Bowen, F.W. and M. Renfield, "The Detection of Anti-D in $Rh_o$(D)-Negative Infants Born of $RH_o$(D)-Positive Mothers," *Pediatric Research*, 10:213–215, 1976.

(15) Scott, J.R., "Immunologic Risks to Fetuses from Maternal to Fetal Transfer of Erythrocytes," *In* " Rh Antibody Mediated Immuosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ. pp. 19–22, 1975.

(16) Hindermann, P., "Maternofetal Transfusion During Delivery and Rh-Sensitization of the Newborn," *Lancet* i:46, 1973.

(17) de Almeida, J.M.R. and L. Rosado, "Rh Blood Group of Grandmother and Incidence of Erythroblastosis," *Archives of Disease in Children*, 47:609–612, 1972.

(18) Jennings, E.R., "Maternal-Fetal Hemorrhage: Its Incidence and Sensitizing Effects," *In* "Rh Antibody Mediated Immunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ. pp 23–32, 1975.

(19) Queenan, J.T., S.F. Kubarych, S. Shah and B. Holland, "Role of Induced Abortion in Rhesus Immunisation," *Lancet*, i:815–817, 1971.

(20) Freda, V.J., J.G. Gorman, R.S. Galen and N. Treacy, "The Threat of Rh Immunization from Abortion," *Lancet*, ii:147–148, 1970.

(21) Bowman, J.M. and B. Chown, "Prevention of Rh Immunization after Massive Rh-Positive Transfusion," *Canadian Medical Association Journal*, 99:385–388, 1968.

(22) Keith, L., A. Cuva, K. Houser and A. Webster, "Suppression of Primary Rh Immunization by Anti-Rh," *Tranfusion*, 10:142–147, 1970.

(23) Keith, L.G. and G.H. Houser, "Anti-Rh Immune Globulin After a Massive Transfusion Accident," *Transfusion*, 11:176, 1971.

(24) Bowman, H.S., J.F. Mohn and R.M. Lambert, "Prevention of Maternal Rh Immunization After Accidental Transfusion of D ($Rh_o$)-positive Blood," *Vox Sanguinis*, 22:385–396, 1972.

(25) Pollack, W. and R.J. Kochesky, "The Importance of Antibody Concentration, Binding Constant, and Heterogeneity in the Suppression of Immunity to the Rh Factor," *International Archives of Allergy and Applied Immunology*, 38:320–336, 1970.

(26) Hughes-Jones, N.C., "The Estimation of the Concentration and Equilibrium Constant of Anti-D," Immunology, 12:565–571, 1967.

(27) Rosenfield, R.E., E.M. Berkman, J. Nusbacher, C. Dabinsky and S. Kochwa, "Immunochemistry of the Rh System. V. Determination of Rh Agglutinating Activity and IgG Content of Sequential Eluates for the Assay of Rh Antibody," *Annals of the New York Academy of Sciences, 190:519–528, 1971.*

(28) Queenan, J.T. and D.W. Adams, "Amniocentesis: A Possible Immunizing Hazard," *Obstetrics and Gynecology, 24:530–532, 1964*

(29) Zipursky, A. J. Pollock, B. Chown and L.G. Israels, "Transplacental Foetal Hamorrhage after Placental Injury During Delivery or Amniocentesis," *Lancet*, ii:493–494, 1963.

(30) Aickin, D.R., "The Significance of Rises in Rhesus Antibody Titre Following Amniocentesis," *The Journal of Obstetrics and Gynacology of the British Commonwealth, 78:149–154, 1971.*

(31) Henry, G., P. Wexler and A. Robinson, "Rh-Immune Globulin After Amniocentesis for Genetic Diagnosis," *Obstetrics and Gynecology, 48: 557–559, 1976.*

(32) Wang, M.Y.F.W., E. McCutcheon and J.F. Desforges, "Fetomaternal Hemorrhage from Diagnostic Transabdominal Aminocentesis," *American Journal of Obstetrics and Gynecology*, 97:1123–1128, 1967.

(33) Pollock, J.M. Lewis, H. Kaita, B. Chown and J. M. Bowman, "Rh Prophylactic Treatment During Pregnancy. An Attempt to Select for Treatment Those at Possible Risk," *Vox Sanguinis*, 26:26–33, 1974.

(34) Schneider, J., "German Trials," *In* "Rh Antibody Mediated Immunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ. pp. 63–66, 1975.

(35) Chown, B., J.M. Bowman, J. Pollock B. Lowen and A. Pettett, "The Effect of Anti-D IgG on D-positive Recipients," *Canadian Medical Association Journal*, 102:1161–1164, 1970.

(36) Hughes-Jones, N.C., "Clinical Trial of Anti-D Dosages in the Prevention of Rh Immunization," *In* "Rh Antibody Mediated Immunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ. pp. 37–42, 1975.

(37) Crispen, J., "Immunosuppression of Small Quantities of Rh Positive Blood with MICRh$_o$GAM in Rh Negative Male Volunteers," *In* "Rh Antibody Mediated Immunosuppression," Ortho Research Institute of Medical Sciences, Raritan, NJ. pp. 51–54, 1975.

(38) Scott, J.R., A.E. Beer, L.R. Guy, M. Liesch and G. Elbert, "Pathogenesis of Rh Immunization in Primigravidas. Fetomaternal Versus Maternofetal Bleeding," *Obstetrics and Gynecology*, 49:9–14, 1977.

(39) Samson, D. and P.L. Mollison, "Effect on Primary Rh Immunization of Delayed Administration of Anti-Rh," *Immunology*, 28:349–357, 1975.

### 17. Thrombin

*Generic Statement*

Thrombin is a proteolytic enzyme that initiates the conversion of fibrinogen to fibrin by splitting arginyl-glycyl bonds at the N-terminal end of the fibrinogen molecule (Ref. 1). As a result of this enzymatic action, two pairs of peptides, fibrinopeptides A and B, are released and the fibrinogen molecule becomes fibrin monomer. The molecules of fibrin monomer polymerize to form a fibrin clot. Thrombin has been reported to cause proteolytic activation of other enzymes and has esterolytic action on a number of synthetic amino acid esters as well (Refs. 2 through 5).

Thrombin activity can be determined by its ability to convert fibrinogen to fibrin, i.e., to form a visible clot or by its esterolytic activity (Ref. 3). It is derived from an inactive precursor, prothrombin, through the interaction of plasma procoagulants, calcium phospholipids (thromboplastin) (Refs. 6 through 8). Active thrombin is rapidly neutralized by several substances known collectively as antithrombins (Ref. 3). Even though considerable thrombin activity may be formed at a site of tissue injury, very little is present in the circulation.

Since thrombin acts directly on fibrinogen, it might appear that it would be an effective therapeutic agent for hemostatic disorders that are the result of defective conversion of prothrombin to thrombin. Thrombin has been found to be both upsafe and ineffective when given parenterally (Ref. 10). Under experimental conditions, dilute solutions of thrombin introduced into the circulation will produce disseminated intravascular coagulation (Ref. 10). When given intravascularly in more concentrated form, thrombin will cause thrombosis at the site of injection (Ref. 10).

Thrombin has been used topically as an aid to hemostasis (Ref. 10). There are several anecdotal reports indicating benefit from its use topically in accessible areas of bleeding from cancellous bone, dental extraction sites, skin-grafting sites, and sites of nasopharyngeal surgery. A few reports suggest that thrombin given orally along with a buffering agent is helpful in controlling bleeding of the upper gastrointestinal tract. No recent or comprehensive data were found concerning this clinical use.

Hemostasis results from interactions of platelets, the fibrin clotting system, and the vascular system (Refs. 11 and

12). At the site of vascular injury platelets clump together and adhere to the vessel wall to form a hemostatic plug. If the vascular defect is not too large, this platelet plug temporarily serves to prevent further bleeding. Later, the platelet plug is reinforced by a fibrin clot. Although the fibrin-clotting mechanism plays an inportant role in hemostasis and eventual repair of an injury, the platelet-vascular response is of primary importance for the prompt control of bleeding. Thrombin has been shown to play a role in platelet aggregation in vitro (Refs. 11 and 12), but there is no evidence that topically applied thrombin plays a direct role in the platelet reaction in vivo. It is well recognized that blood excaping from a denuded surface will promptly clot following the application of thrombin (Ref. 10).

However, the clot that is formed does not appear to prevent the loss of additional blood. Unless pressure is also applied, the clot formed in this way tends to be floated away by the escaping blood.

To provide a mechanism to apply pressure and to apply thrombin directly to the denuded surface, one technique employs a biodegradable sponge which is saturated with thrombin and applied to the surface of a wound (Ref. 23). Although this technique appears to aid in hemostasis, the Panel found no controlled clinical study to indicate whether hemostasis is achieved as a result of the use of the biodegradable sponge alone or as an effect of the thrombin or to both.

Thrombin is useful as a diagnostic reagent and as a reagent for research. The speed with which a visible clot forms is dependent on the concentration of fibrinogen and thrombin (Ref. 13). Under controlled conditions, the speed with which a visible clot forms after the addition of a standardized thrombin solution is a measure of the amount of fibrinogen present. This provides a rapid semiquantitative test for fibrinogen. It has been reported that individuals prone to have thromboemobolic disorders are deficient in antithrombin (Ref. 14). Thrombin is used as a reagent for the measurement of these antithrombins (Ref. 16). Although this test is promising, it is still experimental in nature.

Thrombin is prepared by separating prothrombin from plasma and then converting it to thrombin. Various methods have been used to obtain prothrombin; the principles of isoelectric precipitation, adsorption and elution, salt and alcohol fractionation, and chromatography have been utilized (Ref. 16). Prothrombin can be adsorbed from oxalated plasma by several poorly soluble salts such as barium sulfate, barium carbonate, aluminum hydroxide, and tricalcium phosphate. Prothrombin, along with other coagulation factors, can be eluted with sodium citrate from the adsorbents. The first high quality thrombin was prepared from bovine prothrombin by Seegers, et al. (Ref. 19), who used magnesium hydroxide as the adsorbing agent. Prothrombin was obtained by decomposing the magnesium hydroxide with carbon dioxide. Regardless of the method used, it is essential to separate prothrombin from the antithrombins that are present. Once this has been achieved, the prothrombin can be converted to thrombin by the addition of calcium and tissue thromboplastin. Unless further purified, these thrombin preparations contain at least trace amounts of other proteins. Commercial bovine thrombin has been used extensively as the starting material for the preparation of more purified thrombin (Refs. 18 through 21). In concentrated, lyophilized form, thrombin preparations are stable; once reconstituted to the liquid state, activity rapidly decreases (Ref. 15). If one is to rely on the unitage indicated on the label, freshly reconstituted solutions are essential.

*Product Review*

1. *Product.* Thrombin (Human) by Ortho Diagnostics, Inc. is a reagent for the qualitative determination of fibrinogen in human plasma. It is packaged in sealed ampules each containing 50 units of thrombin. It is to be reconstituted with 1.0 mL of saline. The recommended procedure is to add 0.2 mL of the reconstituted product to a 0.2 mL sample of plasma in a test tube. With normal plasma a visible clot will form in 15 seconds after the addition of thrombin, and the clot will adhere to the walls of the test tube. If the test plasma contains less than 100 mg/dL fibrinogen, the clot will be slower to form.

2. *Effectiveness.* Effectiveness is readily demonstrated by the routine laboratory control tests (Ref. 22).

3. *Safety.* The label carries a specific warning that this material is not for human administration and that it should be handled as if capable of transmitting hepatitis.

4. *Recommendations.* This product should be placed in Category I for in vitro diagnostic use only.

*Product Review*

1. *Description.* Thrombin Topical (Bovine) by Parke, Davis & Co. is supplied as a dried powder for solution containing 5,000 units of bovine thrombin, calcium chloride, sodium chloride, glycine, and benzethonium chloride. The potency is measured by determining its activity in clotting a standardized fibrinogen solution.

2. *Effectiveness.* Thrombin Topical (Bovine) is recommended for human use topically wherever oozing blood from capillaries and small venules is accessible to act an as aid to hemostasis. It may be used in conjunction with an absorbable gelatin sponge to aid hemostasis. Information submitted by the manufacturer (Ref. 23) tends to support this general indication. It should be pointed out that adequate, well-controlled clinical studies are not available in support of many of the specific indications mentioned in labeling or in the supporting literature. Much of the supporting data is anecdotal, but is based upon widely accepted clinical practices.

3. *Safety.* The label carries a warning that Thrombin Topical (Bovine) is not to be injected. When used as directed it appears to be safe.

4. *Recommendations.* a. The labeling should be modified to define more precisely the indications for clinical use. The manufacturer has suggested:

> Thrombin is indicated as an aid in hemostasis wherever oozing blood from capillaries and small venules is accessible. In various types of surgery, solutions of thrombin may be used in conjunction with absorbable gelatin sponge, USP, for hemostasis.

This statement is appropriate.

b. There are inadequate data to support the usefulness of thrombin administered orally for the treatment of bleeding peptic ulcer. The labeling should be modified to delete this as an indication for use.

c. With appropriate modifications of the labeling, it is recommended that this product be placed in Category I.

**References**

(1) Laki, K. and J.A. Gladner, "Chemistry and Physiology of the Fibrinogen-Fibrin Transition," *Physiological Reviews*, 44:127–160, 1964.

(2) Sherry, S. and W. Troll, "The Action of Thrombin on Synthetic Substrates," *Journal of Biological Chemistry*, 208:95–105, 1954.

(3) Lanchantin, G.F., C.A. Presant, D.W. Hart and J.A. Friedmann, "A Comparison of the Esterase (TAMe) and Clotting Activities of Human and Bovine Thrombin Preparations," *Thrombosis et Diathesis Haemorrhagica*, 14:159–175, 1965.

(4) Cole, E.R., J.L. Kopple and J.H. Olwin, "Multiple Specificity of Thrombin for Synthetic Substrates," *Nature*, 213:405–406, 1967.

(5) Seegers, W.H., L. McCoy, R.K. Kipfer and G. Murano, "Preparation and Properties of Thrombin," *Archives of Biochemistry and Biophysics*, 128:194–201, 1968.

(6) Davie, E.W. and O.D. Ratnoff, "Waterfall Sequence for Intrinsic Blood Clotting," *Science*, 145:1310–1312, 1964.

(7) Macfarlane, R.G., "An Enzyme Cascade in the Blood Clotting Mechanism and its Function as a Biochemical Amplifier," *Nature*, 202:498–499, 1964.

(8) Seegers, W.H., "Basic Enzymology of Blood Coagulation," Thrombosis et Diathesis Haemorrhagica, 14:213–228, 1965.

(9) Biggs, R. and K.W.E. Denson, "Natural and Pathological Inhibitors of Blood Coagulation," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," 2nd Edition, Edited by Biggs, R., Blackwell Scientific, Oxford, p. 143, 1976.

(10) Warner, E.D., K.M. Brinkhous, W.H. Seegers and H.P. Smith, "Further Experience with the Use of Thrombin as a Hemostatic Agent," *Proceedings of the Society of Experimental Biology and Medicine*, 41:655–657, 1939.

(11) Mason, R.G. and H.I. Saba, "Normal and Abnormal Hemostasis—An Integrated View," *American Journal of Pathology*, 92:775–811, 1978.

(12) Macfarlane, R.G., "Haemostasis," *in* "Human Blood Coagulation, Haemostasis and Thrombosis," 2nd Edition, Edited by Biggs, R., Blackwell Scientific, Oxford, p. 608, 1976.

(13) Warner, E.D., K.M. Brinkhous and H.P. Smith, "A Quantitative Study on Blood Clotting: Prothrombin Fluctuations Under Experimental Conditions, *American Journal of Physiology*, 141:667–675, 1936.

(14) Egeberg, O., "Inherited Antithrombin Deficiency Causing Thrombophilia," *Thrombosis et Diathesis Haemorrhagica*, 13:516–530, 1965.

(15) Klein, P.B. and W.H. Seegers, "The Nature of Plasma Antithrombin Activity," *Blood*, 5:742–752, 1950.

(16) Murano, G., "Purification of Prothrombin," *in*, "Thrombosis and Bleeding Disorders—Theory and Methods," Edited by Bang, N.U., F.K. Beller, E. Deutsch and E.F. Mammen, Academic Press, New York, p. 101–120, 1970.

(17) Seegers, W.H., E.C. Loomis and J.M. Vandenbelt, "Preparation of Prothrombin Products: Isolation of Prothrombin and Its Properties," *Archives of Biochemistry*, 6:85–95, 1945.

(18) Kerwin, D.M. and J.H. Milstone, "Removal of Thrombokinase from Commercial Thrombin," *Thrombosis et Diathesis Haemorrhagica*, 17:247–255, 1967.

(19) Yin, E.T. and S. Wessler "Bovine Thrombin and Activitated Factor X," *The Journal of Biological Chemistry*, 243:112–117, 1968.

(20) Lundblad, R.L., "A Rapid Method for Purification of Bovine Thrombin and the Inhibition of the Purified Enzyme with Phenylmethylsulfonyl Floride," *Biochemistry*, 10:2501–2506, 1971.

(21) Baughman, D.Y. and D.F. Waugh, "Bovine Thrombin," *The Journal of Biological Chemistry*, 242:5252–5259, 1967.

(22) BER Volume 6091.

(23) BER Volumes, 6005, 6005A and 6005B.

**18. Fibrinolysin and Desoxyribonuclease, Combined (Bovine), and Fibrinolysin and Desoxyribonuclease, Combined (Bovine) With Chloramphenicol**

*Product Statement*

Product Reviews

1. *Introduction*—a. *Products.* Fibrinolysin and Desoxyribonuclease, Combined (Bovine), marketed by Parke, Davis and Company as Elase™ brand powder for solution and as Elase™ ointment.

Fibrinolysin and Desoxyribonuclease, Combined (Bovine) with Chloramphenicol, marketed by Parke, Davis and Company as Elase-Chloromycetin™ ointment.

For the purpose of this document, the brand name "Elase" will be used indicating the combination of Fibrinolysin and Desoxyribonuclease. Elase was issued a biological license in April 1960, and the Elase ointment with chloramphenicol was licensed in September 1963.

b. *Indications.* Elase lyophilized powder for solution is labeled by the manufacturer for topical use as a debriding agent in a variety of inflammatory and infected lesions. These include: (1) General surgical wounds; (2) ulcerative lesions—trophic, decubitus, stasis, arteriosclerotic; (3) second- and third-degree burns; (4) circumcision and episiotomy. Elase is used intravaginally in: (1) Cervicitis—benign, postpartum, and postconization and (2) vaginitis. Elase is also used as an irrigating agent in the following conditions: (1) Infected wounds—abscessed, fistulae, and sinus tracts; (2) othorhinolaryngologic wounds; (3) superficial hematomas (except when the hematoma is adjacent to or within adipose tissue).

Elase ointment is labeled for topical use as a debriding agent in a variety of inflammatory and infected lesions. These include: (1) General surgical wounds; (2) ulcerative lesions—trophic, decubitus, stasis, arteriosclerotic; (3) second and third degree burns; (4) circumcision and episiotomy. Elase is used intravaginally in: (1) Cervicitus—benign, postpartum, and postconization and (2) vaginitis.

Elase-Chloromycetin ointment is labeled for use in the treatment of infected lesions such as burns, ulcers, and wounds where the actions of both a debriding agent and a topical antibiotic are desired.

c. *Manufacturing.* Fibrinolysin is prepared from bovine plasma, isolated by ammonium sulfate fractionation, activated with chloroform, and precipitated by adjusting the pH to the isoelectric point. The desoxyribonuclease is prepared from bovine pancreas by a chromatographic isolation technique. Potency standardization for each ingredient is done on the raw material and on the final product. Proteolytic activity is measured by a fibrinolytic assay measuring the time that it takes for a clot of bovine fibrinogen to be lysed. Desoxyribonuclease is measured by a viscometric assey in which the product is allowed to act upon desoxribonucleic acid (DNA) substrate.

d. *Pharmacology.* The pharmacologic rationale for the combination of these two enzymes is based on the observation that purulent exudates consist largely of fibrinous material and nucleoprotein. Desoxyribonuclease attacks the DNA and also chromatin; therefore, theory would predict that it should lyse exudate that is rich in cell nuclei. Fibrinolysin is an endo-peptidase which ruptures peptide bonds in proteins in which lysine is the amino acid and should thus lyse any clotted protein of plasma origin. Chloramphenicol, a broad-spectrum antibiotic, is included in the Elase-Chloromycetin ointment for use in the treatment of infected lesions where the action of a topical antibiotic "may be helpful."

2. *Evidence of effectiveness.* Data supporting the effectiveness of Elase covers a wide variety of conditions and types of studies. The primary rationale for use is based on the theory that lesions needing debridement might heal better with enzyme therapy. The clinical trials vary from double-blind, controlled studies to anecdotal reports on a few patients.

The most convincing data supporting the effectiveness of Elase comes from the study of Friedman et al. (Ref. 1) on the treatment of post-partum cervicitis. When Elase was used as a solution at each of two dose levels, and compared with a placebo, there was no difference in results. However, when Elase was incorporated in an ointment base and administered more frequently, there was a significant difference between the placebo ointment and Elase ointment in favor of the Elase. This was reflected in a decreased need for post-partum cervical cauterization as well as improvement in other parameters which were evaluated. In these studies there was no additional benefit evident from including chloramphenicol in the ointment.

The other controlled and blinded trial was by Glick et al. (Ref. 2) on postconization cervices. The

investigators reported little difference between Elase and placebo but found the inclusion of chloramphenicol to be beneficial. Since no group was treated with chloramphenicol alone, it was not known whether Elase is of any benefit for this indication.

Kaufman et al. (Ref. 3) in an unpublished study investigated the effect of Elase, Elase plus chloramphenicol, and a placebo upon "postpartum" bacterial cervicitis. There was no statistical difference between the three groups according to a Parke-Davis memorandum (Ref. 3), although it is not clear how the therapeutic results were evaluated. Chloramphenicol did not seem to have any effect on the type of flora seen after treatment.

The other uncontrolled gynecologic studies are of little help in evaluating drug effectiveness. It was noted that in one unpublished study of the chloramphenicol-containing ointment, there seemed to be an increased incidence of vaginal moniliasis (Ref. 4). In this report, 10 percent of the patients were dropped from the study because their white blood count (WBC) had dropped below normal after 2 days of treatment. No mention of this phenomena was made in other studies, although this may be because serial WBC's were not done.

The evaluation of Elase treatment on other surgical lesions has not been reported in well-controlled clinical studies. Several investigators have reported the effect of these agents on chronic lesions unresponsive to standard therapy and have concluded that there is a beneficial effect. The report of Coon et al. (Ref. 5) is an example of this type of study. Patients with chronic ulcers or abscesses were treated with Elase solution or ointment. Ulcers associated with arteriosclerosis showed little response to treatment and none of these healed, whereas trophic and decubitus ulcers were reported to be treated successfully. Four burn patients also were reported as responding well to Elase ointment. Similarly, Connell and Rousselot (Ref. 6) discussed treatment of 125 patients of whom 90 percent were judged to respond to this treatment in 24 to 72 hours. The authors of other studies of this nature all conclude that enzymatic debridement is a useful treatment.

The only available data on the use of Elase in circumcision and episiotomy were found in one table in the paper of Margulis et al. (Ref. 7). In this report, all of the 30 standard treated circumcision patients are classified as healing more slowly than patients treated with Elase ointment for 4 to 6 days. This same report lists eight patients with "inflamed" episiotomy wounds which "healed" quickly when enzyme ointment was applied.

The recommendation for use in otolaryngology is supported by several letters from Dr. Sylvester Daly (Ref. 8) which discuss the use of Elase in a few patients. Analysis of these data is not possible.

One article reports on the treatment of 107 ophthalmic lesions with Elase (Ref. 9). The author concludes "in no instance was healing impaired——. In dendritic keratitis and severe trauma healing was speeded up and morbidity diminished."

During the original licensing of this family of products, the then current regulatory agency, the Division of Biologics Standards of the National Institutes of Health felt the controlled trial indicated fibrinolysin with desoxyribonuclease to be effective, although no clinical data supported the advantage of the combination of fibrinolysin and desoxyribonuclease as compared with the individual components. As shown by the correspondence between the regulatory agency and Parke-Davis (Ref. 10), there was concern about the usefulness of incorporating chloramphenicol into this same ointment. None of the studies then available supported this view. The later report of Glick et al. (Ref. 2) seems to support this contention after conization of the cervix. However, there is no evidence to support the effectiveness of Elase in this investigation. Chloramphenicol ointment alone might have given the same results without the reported side effects of increased bleeding. The Friedman study (Ref. 1) shows no significant difference in favor of chloramphenicol nor does the study at Baylor (Ref. 3).

3. *Evidence of safety.* A review of the studies referenced above indicates that the fibrinolysin-desoxyribonuclease combination exhibits a high degree of safety. During the original licensing there was concern about sensitization of patients to the enzyme proteins of bovine origin. From the data submitted this does not seem to be a problem. Bleeding after conization is an expected sequela of this type of treatment. The report of decreased WBC's in several patients receiving the ointment containing chloramphenicol should be further investigated. There is a report of at least one case of a blood dyscrasia associated with an ophthalmic chloramphenicol ointment, and there is probably significant absorption of chloramphenicol through mucosal and damaged wound surfaces.

4. *Benefit/risk evaluation.* Published studies about Elase and experience with the product indicate that it is probably effective as a general debriding agent. The data on circumcision, episiotomy, and certain other specific indications are still not convincing. The inclusion of chloramphenicol in the ointment remains of concern. None of the studies offer significant evidence of benefits from the combined enzyme-antibiotic compared to the separate ingredients.

The following conclusions were reached:

a. For the Elase ointment with chloramphenicol, there was relatively little bacteriologic data indicating that there is a need for the antibiotic or demonstrating its effectiveness. The only bacteriological studies reported were essentially surface cultures. Newer methods, such as punch biopsies of eschars, were not done to find out whether the chloramphenicol does anything more than cause the surface contamination to be somewhat suppressed.

b. Systemic absorption of the chloramphenicol component and its potential adverse reactions were a cause of concern. Some of the recommended indications would allow a large amount of the ointment to be placed in a body cavity where significant amounts of chloramphenicol could be absorbed, particularly if the application is repeated frequently over a period of several days. It was noted that no hematologic studies have been done on absorption or systemic effects of Elase with chloramphenicol. White blood counts concurrent with treatment may be indicative of a reaction to chloramphenicol even though the development of aplastic anemia may not be detectable until some time after cessation of therapy.

c. The safety of the two enzyme ingredients either in the ointment or in the solution were not questioned. There was no evidence of sensitization resulting from the enzymes.

d. Regarding effectiveness, there are only one or two well-controlled trials. Most of the other reports were more of a testimonial nature. Also, most of the studies were conducted some years ago. With the variety of conditions treated with these products, the progress of wound healing is difficult to assess unless there are adequate controls. Factors such as degree of surgical debridement, frequency of dressing changes, proper cleansing, and other nursing care practices affect the outcome and must be well controlled to provide an objective evaluation. Many of the indications in the current labeling may be treated by alternate methods, some of which have been developed

since the original studies were done with these products.

e. Therefore, the benefit-to-risk ratio may not be as favorable now as it was at that earlier time. Although there has been extensive use of the products and sales have been increasing over the years, this is not significant evidence of effectiveness. However, it may have some relevance in the judgement of safety.

5. *Recommendations*—a. At the request of the Panel on Review of Blood and Blood Derivatives the Bureau of Biologics, the Surgical Drugs Advisory Committee of the Bureau of Drugs first reviewed the Elase products at meetings held December 15–16, 1977 and March 17, 1978. Although it was recommended by the Surgical Drugs Advisory Committee that Elase powder for solution and Elase ointment be placed in Category I (with the provision that the labeling be modified to remove those specific indications for which there are insufficient data), the Panel on Review of Blood and Blood Derivatives does not concur with this recommendation, but rather recommends that these products be placed in Category IIIA. This recommendation is based upon the combination policy stated in 21 CFR 601.25(d)(4) and is consistent with recommendations made for other combination products. Evidence should be developed by appropriate in vivo or in vitro tests to demonstrate that each component makes a contribution to the claimed effects. A period of 3 years is recommended for the completion of these studies.

b. Indications which are recommended to be deleted if the products remain on the market pending the completion of studies inlcude:

(1) Trophic, decubitus, stasis, and arteriosclerotic ulcers.

(2) Second- and third-degree burns.

(3) Circumcision and episiotomy.

(4) Vaginitis.

(5) Specific use as an irrigating agent in: Abscesses, fistulae, and sinus tracts; otorhinolaryngologic wounds; and superficial hematomas.

c. Elase ointment with chloramphenicol [Elase-Chloromycetin™] should be placed in Category IIIA because there are insufficient data demonstrating effectiveness of this combination product. Additional studies should be completed to demonstrate the effectiveness of the combination product. It is recommended that a period of 3 years be permitted for completion of the studies. The primary study should be a double-blind clinical trial to compare the safety and effectiveness of Elase-Chloromycetin ointment to Elase ointment and to a placebo in a management of a variety of infected skin lesions. The study should be designed to show that each individual ingredient contributes to the claimed effects of the combination. During the period the studies are being conducted, the labeling should be modified to remove the indication for use in burns.

During the deliberations of the Surgical Drugs Advisory Committee, Parke-Davis and Company provided details of a suggested protocol and suggested modified labeling (Ref. 11). It is recommended that the Bureau of Biologics review these submissions. In addition to the application of the protocol suggested by the manufacturer, it is recommended that more objective means to measure wound healing be employed.

This should include photographs taken under controlled conditions and the use of tracings which may be transferred directly to records. Also, wound culture methods should be designed to detect the presence of anaerobic organisms. Swab cultures alone are considered to be inadequate. There is also a need for thorough follow-through of all patients accepted into the study and for careful design for the evaluation of results.

d. Regarding the potential for adverse reactions from chloramphenicol absorption from the wound into the systemic circulation, a separate, smaller study is recommended, selecting patients with more extensive wounds which require larger amounts of the Elase-Chloramphenicol ointment.

**References**

(1) Friedman, E.A., W.A. Little and M. Sachtleben, "Enzymatic Debridement of Cervical Erosions," *American Journal of Obstetics and Gynecology*, 79(3):474–479, 1960.

(2) Glick, H.L. I.M. Kiem and D. Cavanagh, "Topical Enzymatic Therapy in the Postconization Cervix," *American Journal of Obstetrics and Gynecology*, 85(1):112–118, 1963.

(3) BER Volume 6003, pp. 183–193.

(4) BER Volume 6003, pp. 276–280.

(5) Coon, W.W., E.F. Wolfman, Jr., J.A. Foote and P.E. Hodgson, "Enzymatic Debridement with Bovine Fibrinolysin," *American Journal of Surgery*, 98:4–81959.

(6) Connell, J.F., Jr. and L.M. Rousselot, "Development of a New Fibrinolytic Enzyme and Its Use in Surgical Lesions, "*Surgery*, 47:709–715, 1960.

(7) Margulis, R.R., J.E. Ladd, M.F. Fahey and H.C. Walser, "Use of Proteolytic Enzymes in Surgical Complications, Obstetrics and Gynecology," *American Journal of Obstetrics and Gynecology*, 81(5):840–847, 1961.

(8) BER Volume 6002, pp. 296–303.

(9) Webb, E.F., "Enzyme Therapy of Dendritic Keratitis," *Illinois Medical Journal*, 127(2):176–179, 1965.

(10) BER Volume 6003, pp. 148–165.

(11) BER Volume 6003A.

**19. Blood Grouping Diagnostics**

*Generic Statement*

1. *Introduction.* The clinical and laboratory investigations that followed discovery of the ABO and Rh blood groups have shown clearly that blood almost always can be infused without acute hemolytic reactions if certain laboratory tests are done before transfusion. These are (1) ABO grouping, (2) Rh typing, (3) testing of donor and recipient for selected blood group antibodies and (4) testing, by means of a crossmatch procedure, for potential incompatibility between donor and recipient. Licensed reagents for these tests include (1) blood grouping serums, (2) reagent red blood cells (human) and anti-human serum. These are used with samples of serum or red cells to do the testing required for some of the processing of donor blood, typing of recipient blood, detecting antibodies in donor serum, and finally, crossmatching between the intended donor and the recipient. All these tests are based on the principles of immunologic reactions involving antigens and antibodies.

The blood group antigens are complex biochemical structures that make up part of the red cell membrane. The corresponding antibodies are similar to other antibodies in that they are formed as a result of previous exposure to a specific antigen and, like other antibodies, they react with these antigens under appropriate conditions. The resulting antigen-antibody complex provides an indicator for the blood typing, antibody detection, or crossmatching tests.

In the laboratory a reaction between red cell antigens and the appropriate antibodies results in one or more of the following events (Ref. 1): (1) Hemolysis (destruction) of the cells, (2) agglutination (clumping) of the cells and/or (3) coating of red blood cells with antibody without demonstrable hemolysis or agglutination.

When hemolysis or agglutination occurs in a crossmatch test for example, positive tests are easily noted and are clear indiators that the recipient's antibody involved may be clinically important. Not all dangerous antibodies, however, react with red cells to produce such obvious evidence of their hazardous potential. In many cases, red cells become coated with antibody (i.e., are sensitized) without demonstrable hemolysis or agglutination. When this

sensitization occurs in vivo the antibody coated cells are frequently recognized by the body as incompatible and are removed rapidly (Ref. 2). Such antibodies can usually be detected by the antiglobulin or Coombs test. This test depends upon the fact that the reaction between red blood cells and these antibodies leaves the cells coated with antibody protein, or with various complement components, or with both. These red cell-bound proteins are detected most easily and reliably by the antiglobulin test in which the cells are reacted with Anti-Human Globulin Serum as discussed later in this section.

2. *The complement system.* Immunologic reactions between red blood cell antigens and their corresponding antibodies involve, at times, a family of plasma proteins known as the complement system (Ref. 3). In the blood stream the complement-antibody-red cell interaction often causes antibody coated red blood cells to be removed from the circulation. In the test tube a reaction between antibody and red blood cells can also involve proteins of the complement system when they are present in active form.

In vitro, complement-antibody-red cell interactions lead to two possible consequences (Ref. 4).

a. If the antibodies are of the complement-fixing variety, red cell hemolysis may occur. Such antibodies are usually IgM, but some antibodies, especially anti-A, in the IgG class also cause hemolysis in this way.

b. Certain antibodies, particularly IgM cold agglutinins, may react with red cells and, as part of this reaction, fix some complement proteins to the red cell membranes. Under some conditions, the bond between the two blood cells and the antibody is subsequently broken, leaving the cells free of antibody but coated with complement components. Hence, a test under these circumstances to detect the original antibody-red cell interaction will be negative unless it is also capable of detecting the presence of the appropriate complement components on the red cells.

*The Complement Reaction Sequence*

The complement system consists of at least 11 different proteins that interact in a sequential fashion. Complement components are abbreviated by the capital letter C and an appropriate numeral from 1–9, e.g., C1, C2, C3, etc. The addition of a lower case letter, e.g., C3a, C3b, indicates fragments of the components and a bar over the term indicates the activated form, e.g., $\overline{C1}$, $\overline{C2}$, $\overline{C3}$, etc. These components interact in a numerical sequential fashion except for C4 which reacts with $\overline{C1}$ so that the reaction sequence becomes C1, C4, C2, C3, C5 through C9.

This reaction sequence, the so-called classical pathway, can be initiated by diverse biochemical or immunological reactions, but only those related to red cells and blood group antibodies will be considered here. A second reaction sequence, called the alternative pathway, has been described but will not be included in this discussion since current evidence indicates that it is not related to immunological reactions that are important in blood transfusion practice. The reactions can occur in vivo or in vitro and do not always involve the complete sequence of complement proteins. Three phases of the reactions, recognition, attack, and lysis, have been defined. In addition, reaction control mechanisms are present and include either decay of selected components or inhibition of further reactions by specific inhibitors.

a. *Recognition.* The binding of one IgM or two adjacent IgG blood group antibody molecules to a red cell membrane is sufficient to initiate the complement reaction sequence. Calcium links C1q, C1r, and C1s into a macromolecular complex. The C1q fragment of this complex reacts with cell bound antibody and is activated to form $\overline{C1}$ which, in turn, acts on C4.

b. *Activation.* The action of C1, particularly the C1s fragment, converts C4 to C4b by splitting off a fragment known as C4a. C4b, in conjunction with the previously established C1qrs-antibody-red cell complex binds to an adjacent location on the red cell membrane. Here the C4b combines with C2a which had been previously generated by the action of $\overline{C4b}$ on circulating C2. C4b, C2a and magnesium establish the $\overline{C4b,2a}$ activation enzyme which next acts on C3.

c. *Lysis.* C3, under the influence of $\overline{C4b,2a}$ is activated to C3b by enzymatic removal of the C3a peptide. Some C3b molecules join the $\overline{C4b,2a}$ complex to establish a new complex $\overline{C4b,2a,3b}$, which reacts with C5, activating it to the C5b form and releasing C5a. Other C3b molecules do not participate in the formation of $\overline{C4b,2a,3b}$ complexes but instead are acted upon by C3 inactivator and converted to C3d (Ref. 5). C3d is a cell-bound component. Although it is apparently biologically inert, its presence can be used as a reliable indicator of previous antibody-red-cell interactions (Ref. 6). When the $\overline{C4b,2a,3b}$ complexes bind to cells there may be a progression of the activation sequence through the C9 state ending in cell lysis. In some cases, the sequence stops at C3, so that red cells are coated with C proteins but not lysed.

3. *Blood grouping serum*—a. *Introduction.* In 1900 Karl Landsteiner observed that the serum of normal humans frequently agglutinated the red blood cells of other individuals. A year later he reported that the reactions showed a "peculiar regularity" which separated human blood into three phenotypes. It is now known that these agglutination reactions were the visible indication of interactions between antibodies in the serum of one individual and the homologous red blood cell antigens of another. The phenotypes he described were A, B and O, although these letter designations were not universally accepted until many years later.

Immediately, Landsteiner and others suspected that human red cells might possess more than the two unique antigens, A and B, already observed and began a search for new blood groups. Looking for additional blood group antibodies, these early workers tested many serums from normal persons, but none were discovered by the methods available at that time. They turned, then, to the injection of human red cells into laboratory animals in an effort to stimulate production of antibodies that would identify new blood groups. These experiments were successful, and the P and MN blood groups were detected and reported in 1926. Shortly thereafter, antibodies specific for P and M were also found in human serum, but it was not until 1940 that the important Rh blood group system was recognized. The Rh antigens, like nearly all of the 400 or more blood group antigens now known (Ref. 7), were detected because the corresponding antibodies were found in the serum of a patient. The Rh antibodies are almost always stimulated by transfusion or by pregnancy. In the latter case, small numbers of fetal red blood cells cross the placenta, enter the maternal circulation, and induce production of one or more blood group antibodies.

b. *Source.* Blood Grouping Serum is serum containing a blood group antibody which, when used as directed by the manufacturer, will detect the presence or absence of one or more specific blood group antigens. Most Blood Grouping Serum is prepared from human rather than animal sources, although some reagents prepared in rabbits and goats are currently licensed. In some cases, plasma is harvested from persons who have been immunized by pregnancy or transfusion and have produced antibodies that can be processed into a suitable reagent.

Nearly all of the less widely used and less important blood grouping serums (e.g., Anti-Kp$^a$, Anti-Kp$^b$, Anti-S, Anti-s, Anti-Di$^a$, etc.) are prepared from such starting material. Other blood grouping serums (e.g., Anti-A, Anti-B and Anti-D) are needed in such large quantities or must be of such potency (see below) that additional stimulation of selected donors is required. In such cases, donors are stimulated by injection with blood group substances or appropriate red cells and, if suitable antibodies result, these donors are then plasmapheresed on a regular schedule to obtain Source Plasma (Human) for further processing into Blood Grouping Serum. As mentioned earlier, only a few blood-grouping serums, such as anti-M, anti-N, anti-$P_1$, anti-Le$^a$ and anti-Le$^b$, are prepared by immunization of laboratory animals.

c. *Indications for use*—(1) *Pretransfusion testing of recipients.* Before transfusion, it is essential to test the red blood cells of the recipients with anti-A, anti-B, and anti-D to determine their ABO groups and Rh(D) types. Many other Rh blood antigens are known, and Blood Grouping Serums for some of these are easily available (anti-C, anti-E, anti-C$^w$, anti-c, anti-e, etc.), but only tests for the D antigen are required for routine purposes. The reasoning for this decision has been developed in the section on Rh typing under Whole Blood (Human).

(2) *Testing of donor blood.* All donor blood must be characterized as to ABO group and Rh(D) type. To accomplish this, the donor red blood cells must be tested with anti-A, anti-B and anti-D. Routine tests for other blood groups are neither required nor advised.

(3) *Pretransfusion testing of donor red cells when the recipient has been previously immunized.* The serum of certain recipients who have been previously transfused or pregnant will contain one or more blood group antibodies. Such persons must be transfused with blood lacking the corresponding antigen if a transfusion reaction is to be avoided. The compatibility test or crossmatch is an important procedure because it can usually detect evidence of potentially dangerous antibodies in the recipient's serum. When the specificity of the antibodies is known and an appropriate blood-grouping serum of the same specificity is available, it is useful to test red cells from the intended donor to be certain that they lack the antigen in question. Such tests, of course, depend upon previous identification of the recipient's serum antibody (see section on Reagent Red Blood Cells).

(4) *Testing of red blood cells for genetic, medicolegal, or research purposes.* Because red blood cell antigens are inherited characteristics and because they do not, for all practical purposes, change throughout life, their presence or absence can serve as useful genetic markers. Red cell antigens, for example, have been used to exclude paternity, identify blood stains, determine twin zygosity, and establish family relationships. Such studies and others rely on blood grouping serums.

d. *Safety and effectiveness.* The effectiveness of any blood-grouping serum is evaluated by its ability, when used as directed by the manufacturer, to type correctly the blood cells being tested. A positive test result is indicated by agglutination (i.e. clumping) of the red cells. An ideal serum is one that is both highly specific and sensitive. Specificity refers to the ability of the serum to react with a given blood group antigen but with no other. Since Blood Grouping Serum is nearly always derived from the plasma of individuals who possess antibodies against more than one blood group antigen, a manufacturing process is required to remove or neutralize the unwanted antibodies. Appropriate tests on the final product are essential to show that unwanted antibodies have been removed and additional tests are required to show that the original specificity is retained at the end of the dating period. In some very rare cases the desirable antibodies do not maintain adequate reactivity throughout the storage period, while activity of antibodies that originally had been adsorbed or inactivated return.

Sensitivity, the capability of a blood grouping reagent to detect the weaker reacting red cell antigens of the claimed specificity, is an equally important characteristic of licensed Blood Grouping Serums.

While many individuals develop blood-group antibodies as a consequence of transfusion or pregnancy, only a few produce serums with sufficient potency to be useful as blood grouping reagents. Unlike chemical reagents that can be measured in absolute terms, standards of potency for blood-grouping serum can be established only by comparing the test serum with a reference serum by titration, a test that applies subjective criteria concerning the strength of the agglutination produced by increasing dilutions of serum. In the usual titration a series of tests is done; each succeeding tube in the series contains half the amount of serum present in the previous tube. The end point is recorded as the greatest serum dilution (e.g., 1:2, 1:4, 1:8, 1:16, 1:32, etc.) in which test cells are agglutinated. The reaction strengths are scored by one of several arbitrary grading systems. Federal regulations (Ref. 8) mandate that actions be graded as follows:

4+—cell button remains in one clump;
3+—cell button dislodges into several clumps;
2+—cell button dislodges into many small clumps of equal size;
1+—cell button dislodges into finely granular, but definite small clumps; and,
D—cell button dislodges into fine granules but not definite small clumps. Results shall be recorded as doubtful.

Requirements for both sensitivity and specificity of Blood Grouping Serums are arbitrary but have resulted in reagents that are reliable and effective. For some reagents (e.g., anti-A, anti-B, anti-D, anti-A,B, anti-CD and others) reference serums are available from the Bureau of Biologics. Manufacturers must demonstrate that their reagents are at least as potent as these reference standard serums. For other blood grouping serums reference standards are not supplied but regulations define minimum potency standards that such serums must meet. These standards are expressed in terms of the titration value that a serum must reach to be acceptable. Reagents that are generally in good supply such as anti-K, anti-k, anti-Fy$^a$, and anti-C$^w$ must show at least a 1+ reaction with a 1:8 dilution of the antiserum. Others, such as anti-S, anti-s, anti-$P_1$, anti-M, anti-I, anti-e (saline), anti-c (saline) and anti-$A_1$, need react only at a 1:4 dilution; antibodies in even shorter supply are acceptable if a 2+ reaction is seen with undiluted serum. Clearly these regulations suggest that weaker reactions are acceptably safe, at least for reagents that are used infrequently and in special circumstances. There are no controlled studies to show that blood grouping serums which meet current regulations are effective, nor are any now needed. The vast clinical experience gained from the millions of accurate blood typing tests done each year indicates a high level of effectiveness for the reagents, as currently prepared.

Whether reagents meeting a different standard, for example, more diluted, would be equally acceptable is unknown. The question is important since the starting material for production of Blood Grouping serum almost always requires hyperimmunization of donors, a procedure not without risk as discussed

elsewhere in this report (See Donor Immunization and Hyperimmunization). If satisfactory reagents can be prepared using smaller amounts of starting plasma, the benefit will be obvious. Unfortunately, the required data relating to effectiveness are not available.

The Panel recommends that studies be designed and instituted to determine the lowest titer of antibody that will produce an effective agent. Such studies should especially address the production of anti-A, anti-B, anti-A,B, anti-D and other Rh antiserums.

Current Federal regulations (21 CFR 660.26(c) (1), (2) and (3)) define specificity tests to ensure that Blood Grouping Serums are free from unwanted or contaminating antibodies. The Panel believes that requirements to test candidate serums against red blood cells containing some antigens, e.g., $Co^b$, $Do^a$, $Do^b$, $Yt^b$, and $M^g$, will be difficut to meet since antiserums to prove that test cells possess these antigens are not easily available. Thus, it is recommended that these requirements be reviewed and modified.

e. *Methodological considerations.* (1) There are several commonly used methods for testing blood types. Serums prepared and standardized to produce acceptable results by one method may, when used by another, give weak or even incorrect answers.

(a) *Slide or rapid tube tests.* Blood grouping serums for these tests must react appropriately when tests are done on slides or in tubes. When slides are used, a red cell suspension of approximately 50 percent in autologous or compatible serum or plasma usually is required, although some manufacturers specify cell concentrations of 5 to 15 percent. For some serums (e.g., anti-C, anti-D and others) results must be interpreted by observing the test over a heated viewbox. Such serum usually contains a potentiating agent such as bovine serum albumin. Slide tests are generally less sensitive than tube tests and are not frequently done. There is no evidence, however, that properly performed slide tests are inaccurate, and there is no reason to suggest that reagents for slide tests are unsafe.

When blood from some *patients* is tested with anti-D by slide tests, false-positive results may be seen. Similar considerations apply to modified tube tests. These false results are caused by clumping of the patient's cells by his or her own serum or by some component of the reagent other than the antibody itself. It is essential to provide a control for these false positive results by simultaneously testing the individual's blood alone and with the diluent medium of the blood grouping serum. Recently it has become clear that bovine serum albumin solutions are not ideal for this control purpose (Ref. 9) probably because some marketed reagents contain agglutination-potentiating substances other than albumin. The appropriate control material is the serum diluent medium itself added to serum lacking the specific antibody. Such control materials add a small but definite measure of safety to blood-grouping tests. Manufacturers should be required to make appropriate control materials available for use with their anti-D serum.

When testing donors it is also possible to get false-positive results by the same mechanism. Because donors are almost always healthy, such problems are infrequent. Furthermore, they do not compromise patient safety since the worst that can happen is the classification of an Rh negative donor as Rh positive. As such his/her blood will be given to an Rh positive recipient. But, as is well known, the use of Rh negative blood in Rh positive recipients is without added risk. Hence the Panel does not believe that the added cost of an Rh control is justified in the testing of donor blood.

"Modified tube" tests are done using red cells suspended in serum or plasma. While the relative amounts of cells and serum in the mixture are not critical, acceptable ranges should be defined in the instructions to the user. False-positive reactions, as described above, may be seen and a control reagent lacking the antibody should be available.

(b) *Tube tests.* Red blood cells, suspended in saline or in compatible or autologous plasma, may be tested by any of several methods including:

(i) Incubation at 37°C and centrifugation,

(ii) Incubation at 4°C and centrifugation,

(iii) Incubation at room temperature without centrifugation,

(iv) Immediate centrifugation and reading without incubation,

(v) Incubation at 37°C, washing, and testing with Anti-Human Serum (see below), and

(vi) Some combination of above.

Tube tests are commonly used for most blood bank work. Methods that can be completed without long incubation times or additional procedures such as the use of Anti-Human Serum are preferred for routine tests such as those for A, B, or D. Other methods, including those that use Anti-Human Serum, are used when simpler procedures are not sufficiently sensitive.

(c) *Tests with automated equipment.* Two automated blood-typing machines are currently available. These machines require reagents that are prepared specifically for this purpose since reagents that meet standards for tube or slide tests may not yield satisfactory results when used by automated methods. Licensed reagents for such equipment must, after a two-fold dilution, be potent enough to detect the antigen on heterozygous red cells.

f. *Labeling and packaging*—(1) *Packaging.* Blood grouping serums, excluding those intended for use in automated equipment, are packaged in dropper vials containing between 1 and 10 mL of reagent. Suggestions that packaging should be permitted in amounts greater than 10 mL have been rejected (Ref. 10) because of the potential for error that accompanies the transfer of reagents from larger to smaller containers. The Panel recommends that bulk packaging for some reagents, e.g., anti-A or anti-B, is reasonable for some large users and should be allowed.

The dropper bulb must be black or color matched with labels of reagent bottles that allow for color coding. Suggestions that white dropper bulbs be allowed have been rejected (Ref. 10) because of the desire to restrict the use of white dropper bulbs to Anti-Human Serum. The Panel agrees that these cautions are justified and supports the current regulations as written.

(2) *Labeling.* Labeling for blood grouping serums includes the vial label, the package label if a package is provided, and the package insert. Since some vials contain only 1 or 2 mL of serum, the amount of space on the label itself is restricted and regulations require that only a limited amount of information appear on the label. Additional information may appear either on the container label or the package label. The remainder of the information, including directions for use, may be provided in the package insert. This procedure is satisfactory, and the Panel sees no need to suggest major revisions.

g. *Other recommendations.* (1) The Panel concludes that the reviewed Blood Grouping Serum products should be placed in Category I.

(2) Current labeling arrangements with some information on the vial label, some on the package, and some included in the package insert are appropriate. The Panel recommends that the vial label, because of its small size, be reserved for critical information concerning product identification and

safe storage procedures, the lot number, and the manufacturer's name.

4. *Reagent Red Blood Cells*—a. *Introduction.* Reagent Red Blood Cells are prepared from selected human red blood cells and are intended to detect or identify human blood group antibodies. The blood from which these cell preparations are made is collected, diluted with an anticoagulant preservative solution, packaged, and distributed. The blood types of the red cells, the packaging, and the circular of instructions determine, to a large extent, the ultimate use of the cells. For example, A and B cells are universally used in the reverse-typing or serum-grouping test to confirm the ABO type determined by cell-typing methods, while O cells are used for either antibody detection or antibody identification outside the ABO blood group system.

b. *Source.* Reagent Red Blood Cells from adults are collected by producers that meet applicable regulations applied to donors of human blood for transfusion. These regulations ensure the safety of both donor and product. Since the same procedures cannot be applied to the collection of blood from newborn infants, manufacturers of cord red cells, which are used for tests of specificity in the $I_i$ blood group system, must collect them in institutions that have large obstetrical services. One donor (i.e., one umbilical cord) can provide only a limited number of red blood cells; thus, products prepared from cord red cells, unlike those from adults, consist of pools from many infants.

c. *Indications for use.* (1) *As reagents to assist in determination of the ABO group of patients or blood donors.* Almost all adults normally have, in their plasma, antibodies against the A and B antigens that are absent from their own red blood cells. For example:

| Blood group | Red blood cell antigens | Serum antibody |
|---|---|---|
| A | A | Anti-B |
| B | B | Anti-A |
| O | Neither A nor B | Anti-A, anti-B |
| AB | A and B | Neither anti-A nor anti-B |

It is appropriate to confirm the ABO typing of patients or of blood donors by testing their serums for the expected antibody. Reagent Red Blood Cells of type A and type B are used for this purpose. The Type A cells must be of the $A_1$ subtype since the anti-A antibodies in the plasma of group B and group O persons always possess this specificity. Rarely, persons of type $A_2B$ and even more rarely persons of type $A_2$, have antibodies that react specifically with cells of the $A_1$ subtype. In such cases, additional testing with $A_2$ cells may be helpful but is not essential.

(2) *As reagents for the detection of unexpected blood group antibodies.* It is common practice to test the serums of patients and blood donors for clinically important blood group antibodies. This testing, also known as "antibody screening," is done by mixing the serum to be tested with Reagent Red Blood Cells intended for this purpose and subjecting the mixture to one or more tests for an antigen-antibody reaction. These "screening cells" must be of type O since antibodies of other than A or B specificity are being sought by this test.

Issitt and Issitt (Ref. 7) estimate that there are at least 400 different blood group antigens. The red blood cells of any one blood donor can be expected to posses only a proportion of these, although antibodies to most may be dangerous. Blood group antibody screening tests of patients should be able to detect as many as possible of the antibodies that can occur and, of course, must detect those that are clinically most important.

Federal regulations require that Reagent Red Blood Cells used for detection of unexpected blood group antibodies must contain at least the following antigens: D, C, E, c, e, K, k, $Fy^a$, $Fy^b$, $Jk^a$, $Jk^b$, $Le^a$, $Le^b$, $P_1$, M, N, S, and s. Because it is impractical to find one donor whose cells have all these antigens, tests for antibody detection must be done using cells from two or more donors. These cells may be pooled or used individually, but in either case must together provide all the required antigens. If the test cells are pooled, the final pool must be prepared from equal volumes of cells from no more than two donors. If reagent cells are provided individually, each lot, but not each cell sample in the lot, must have cells positive for each of the listed antigens.

The Panel believes that the goal of having each required antigen present on half of the cells in the final pool is appropriate. Limiting the pool of cells to two donors, as currently is done, is the best way to do this since it reduces the possibility of weak and misleading mixed field reactions.

Because there is a general opinion, unsubstantiated by data, that weakly reacting antibodies are more easily detected using individual rather than pooled cells, the use of pooled cells for testing patient serums has become infrequent. The disadvantage of using individual cells is that each patient's serum must be tested at least twice with the resultant increase in cost and labor. In the case of tests of donors, there is good evidence (Ref. 11) that problems caused by antibodies in donor serum are so infrequent as to warrant a different approach, and antibody testing with pooled cells is acceptable in this situation. This is in part because donor blood, when transfused, results in an immediate dilution of the donor antibodies by the recipient's plasma; this leads to at least a give-fold diminution in their concentration. In addition, the transfused antibodies encounter a large excess of antigen-bearing red cells. As a result, rarely, if ever, is the blood cell antigen to antibody ratio such that the induction of dangerous hemolysis will occur. Finally, healthy donors do not usually have dangerous blood-group antibodies except, of course, for anti-A or anti-B. The Panel believes that testing of donor serum for unexpected antibodies using pooled cells is adequate. This subject is discussed further in the section on stored red cell products, testing of donor blood and antibody detection tests.

For testing of patients' bloods, the circumstances are significantly different. A transfusion of incompatible red blood cells into a patient who has even weak blood-group antibodies may lead to a serious hemolytic reaction. In addition, patients are far more liable to have blood group antibodies than are normal healthy blood donors; many of them have been transfused previously. Thus while pooled test red cells are acceptable for donor testing, they may or may not be acceptable for recipient testing. The Panel believes that the current practice, which allows the use of pooled cells for recipient serum screening, is safe provided tests are read microscopically, although perhaps not as sensitive as tests in which the cells are used individually. Studies are needed to clarify this significant problem.

(3) *As reagents for the identification of unexpected blood group antibodies.* When unexpected red cell antibodies are found in the serum of a patient, it is good practice to identify their specificities. This requires testing the patient serum with a panel of Reagent Red Blood Cells of known antigenic constitution. These red cell panels are prepared by individually packaging from 2 to 5 mL of diluted suspended cells obtained from each donor of a panel usually composed of 8 or 10 selected donors. The user is provided with information in the form of a graphic worksheet that lists the major antigens present or absent on the cells of each donor and a package insert with appropriate instructions.

Each manufacturer is required to establish a dating period beyond which the test red cell product cannot reasonably be expected to give satisfactory results. The dating period, from 21 days to 45 days after phlebotomy, is based upon data filed by each manufacturer with the Bureau of Biologics. The Panel believes that these products are, at times, used beyond the specified dating period and suggests that an appropriate caution against this practice be included in the package insert. The Panel has concerns about the stability of cell reactivity for periods of up to 45 days, in view of published data (Refs. 12 and 13) about the weakening of some antigens during storage. The Bureau of Biologics should review all current license applications to ensure that the data are adequate to support current dating periods for Reagent Red Blood Cells in view of these new studies.

Regulations specify that Reagent Red Blood Cells must have a cell concentration of no less than 2 percent, but specify no upper limit of concentration. It is common practice to provide this product with cell concentrations of approximately 5 percent. Some users, however, prefer to use a more dilute suspension of cells and routinely dilute the product before use. Because of this, the Panel believes that manufacturers should include instructions about how to dilute these test cells before use and the expected useful life of such diluted cells.

d. *Safety and effectiveness.* When shipped appropriately, stored and used as directed, and when the test results are interpreted properly, Reagent Red Blood Cells are safe and effective for all recommended indications.

e. *Labeling analysis.* Labeling of the vial and the package are appropriate. The package insert should be more specific about loss of reactivity with storage, should caution against use after the end of the dating period, and should indicate how additional information about the test cells can be obtained.

f. *Recommendations.* (1) Reagent Red Blood Cells (Human) should be placed in Category I.

(2) Appropriate studies are needed to evaluate whether pooled test red cells are adequate for antibody detection tests in patients.

(3) Package inserts should give specific instruction about how to obtain additional information about the test cells if it is needed.

(4) Manufacturers should provide information about how to dilute test cells if a lower cell concentration is desired and the useful life of the cells so diluted.

(5) The product name should be "Reagent Red Blood Cells."

5. *Anti-Human Serum*—a. *Introduction.* In 1908, C. Moreschi (Ref. 14) described the principal of a test that could be used to demonstrate the presence of antibody molecules on the surface of cells. Thirty-seven years later that test was rediscovered by Coombs, Mourant, and Race (Ref. 15) who used it to detect what were then known as blood-group blocking antibodies. These antibodies, found in the serum of some Rh-negative women, had been previously identified as the cause of hemolytic disease in Rh-positive newborn infants (Ref. 16). A year later Coombs and his coworkers used the same test to show that in some babies the disease was accompanied by an in vivo reaction between the infant's red blood cells and transplacentally acquired maternal antibodies. Later applications of the same test, now called the antiglobulin test, have included its use in the diagnosis of autoimmune hemolytic disease, the detection of drug-antibody-red cell interactions, the detection and identification of a multitude of blood-group antigens with nonagglutinating alloantibodies, the investigation of suspected transfusion reactions and pretransfusion compatibility testing. The antiglobulin test depends upon the fact that the reaction between red blood cells and some blood group antibodies leaves the cells coated with antibody protein (IgG), with various complement components, or with both, but does not result in agglutination or hemolysis. These red-cell bound proteins are best detected by the antiglobulin test in which the cells are reacted with Anti-Human Serum.

b. *Anti-Human Serum.* Rabbits or other animals such as goats injected with human plasma proteins produce antibodies against these proteins. The injection of human globulin leads to the production of anti-human globulin. When suitably processed, this anti-human globulin serum becomes a reagent capable of reacting with the same categories of human globulins that were present in the original immunizing material. Since a significant proportion of the human globulins are antibodies of the immunoglobulin G class, the reagent is a useful tool for detection of human IgG antibody. IgG molecules that have coated human red cells without causing agglutination will react with the anti-human globulin serum and cause visible agglutination of the antibody-coated red cells. As mentioned previously, antibody coating alone is often not adequate to cause agglutination of the cells, but does alter the red cells sufficiently so that they are recognized as abnormal by the body and are rapidly destroyed.

The injection of almost any human protein into a suitable animal will bring about antibody production. In this way reagents such as anti-IgA, anti-IgM, anti-IgG and antibodies against the various components of the complement system can be produced.

c. *Complement.* As related to the use of antiglobulin reagents in transfusion practice, the salient points about the red blood cell-antibody-complement interaction are:

(1) Some blood group antibodies react with blood cells by binding complement to the cell membrane. The antibodies then elute from the red cells leaving them coated with complement components but very little antibody. In vivo such reactions lead to hemolysis. In vitro they can be detected only by techniques that are sensitive to the presence of complement coating. The complement component that is present when such reactions occur in vitro is initially C3 and eventually C3d.

(2) Antiglobulin reagents intended to detect such complement-coated red blood cells must contain adequate amounts of either anti-C3 or anti-C3d activity (Ref. 17).

(3) The plasma from all normal persons contains small amounts of an IgM cold-reacting antibody called the normal, or naturally occurring, cold autoagglutinin. The amount of this antibody usually present in normal serum does not cause hemolysis of red blood cells. It may, however, lead to complement activation and fixation of C3 and C4 to red blood cells (Ref. 18). Such reactions have no clinical importance. These "false positive" tests can be avoided by limiting the amount of anticomplement in antiglobulin reagents intended for routine blood bank work (Ref. 6).

(4) C3d coated red cells are found in some patients with hemolytic anemia and in some cases of hemolysis associated with drug hypersensitivity (Refs. 5, 18 and 19). In some of these patients the test for complement coating of the red cells is the only one that will be positive (Ref. 5). Thus, the antiglobulin test has diagnostic value besides its usefulness in blood transfusion serology.

(5) Clinically important IgM blood group antibodies that fix complement almost always agglutinate or hemolyze red blood cells as well (Ref. 20). In these cases direct detection of complement by the antiglobulin procedure is rarely, if ever, necessary to prove that an antibody-red cell interaction has occurred, although it may be helpful.

(6) Clinically important IgG blood group antibodies almost always bind directly to red blood cells. If adequate tests for the presence of IgG are done, tests for complement binding usually add nothing (Ref. 21). Occasional exceptions are known.

d. *Direct and indirect antiglobulin tests.* The antiglobulin test is used to demonstrate that red blood cells have reacted with immunoglobulin molecules and are coated by either antibodies or some component of the complement system. The red cell-antibody intereaction may take place while the red cells are circulating (in vivo) or it may occur as part of a laboratory test (in vitro) in which serum to be tested for antibodies is mixed with normal red blood cells which carry the antigen(s) in question.

The direct antiglobulin test detects coating in vivo. Red cells from the patient are washed to remove unbound plasma protein and then reacted with Anti-Human Serum. No intermediate steps are involved.

The indirect antiglobulin test is used to detect alloantibodies or autoantibodies in a patient's serum or plasma. In performing the indirect test, patient's serum is mixed with antigenically appropriate red blood cells and allowed to incubate, usually at 37°C, for from 5 to 120 minutes. The cells are then washed and tested with Anti-Human Serum.

When positive, either test shows that antibody and red cells have reacted together. In the case of the direct test, the reaction occurred in vivo; in the indirect test it occurred in vitro.

e. *Indications*—(1) *Direct antiglobulin test*—(a) *hemolytic disease of the newborn.* In Hemolytic disease of the newborn (also known as erythroblastosis fetalis), antibody produced by the mother crosses the placenta and reacts with the unborn infant's red blood cells. This can occur only if certain conditions are met.

(i) Maternal antibody must be directed against a blood group antigen present on the fetal red cells.

(ii) The maternal antibody must be of the class (IgG) that is readily secreted across the placenta.

When these conditions are met the blood group antibody reacts with the unborn infant's red blood cells and may destroy a variable number of these fetal red cells before the child is delivered. At birth, antibody coating of fetal red cells is evidenced by a positive direct antiglobulin test.

While hemolytic disease of the newborn can result from almost any blood group incompatibility, the cases that occur when an immunized Rh-negative mother delivers an Rh-positive infant are best know. In this disease the infant's red blood cells are always coated with maternally derived IgG antibodies; for that reason only, antibodies with anti-IgG specificity need be present in the Anti-Human Serum reagents used for antibody detection caused by Rh incompatibility. The findings are identical for almost all cases of hemolytic disease of the newborn caused by other antibodies. A very few cases have been reported in which the antibodies are detected by anticomplement reagents but not by anti-IgG (Refs. 22 through 24). Such cases are rare, have been reported only from outside the United States, and were tested only by the less sensitive slide method which is not used much in the United States.

In hemolytic disease of the newborn caused by materno-fetal ABO incompatibility, the mother is usually type O and the child type A or B. In this disease, reactions with some United States licensed Anti-Human Serum reagents are negative, while others are positive. Reasons for these differences are obscure (Refs. 25 and 26).

Anti-Human Serum is an effective reagent when used for the diagnosis of hemolytic disease of the newborn. Lebeling of the reagent should indicate that a negative test does not always rule out the disease, especially when ABO incompatibility is suspected. Anti-Human Serum reagents containing antibodies in addition to anti-IgG are not necessary for this purpose, but can be used if the anti-IgG reactivity is adequate to detect IgG-coated cells using an accepted in vitro test system. Anti-Human Serums that do not contain anti-IgG activity are unsatisfactory for detecting infant red cell sensitization in hemolytic disease of the newborn and should be so labeled.

(b) *Autoimmune hemolytic disease.* The term autoimmune hemolytic disease (AHD) is often considered to be synonomous with autoimmune hemolytic anemia. Since all patients with AHD do not have anemia, the more general term will be used here. Patients with AHD can be classified as follows:

(i) *AHD warm antibody type.* This is a pathological condition in which circulating red blood cells react in vivo with autoantibodies. This reaction, at times in association with complement fixation, leads to variable rates of destruction of circulating red blood cells. Red cells are usually coated in vivo with IgG, rarely with IgA, and/or complement components. The responsible autoantibodies are produced by the patient himself/herself, and react with his/her own red blood cells. Normally a person does not produce antibodies that react with his/her own tissues. In approximately 80 percent of cases of AHD with significant hemolysin the direct antiglobulin test is positive with Anti-Human Serum containing only anti-IgG. In some cases, only complement components, especially C3d, are present on the red blood cells; in other patients both IgG and C3d can be detected (Ref. 27). The pattern of coating protein, i.e., IgG alone, C3d alone, or both, may be of diagnostic value (Ref. 28).

Use of Anti-Human Serum and the direct antiglobulin test is indicated in patients suspected of having AHD of the warm antibody type. An Anti-Human Serum reagent must contain a mixture of anti-C3d and anti-IgG, each in adequate amounts, to be satisfactory for this purpose. For a more definitive diagnosis, separate reagents, one pure anti-IgG and the other without anti-IgG but with adequate anti-C3d activity, are needed.

(ii) *Autoimmune hemolytic disease, cold antibody type.* This disorder is a pathological condition in which circulating red blood cells react in vivo with autoantibodies that react as cold agglutinins in vitro (Ref. 27). The autoantibodies involved are almost always IgM and are characterized by optimum reactivity at temperatures lower than 37° C (Ref. 28). In vivo, therefore, reactions between red cell and cold reactive autoantibodies probably occur predominately in areas of the body where temperature is lowest, for example, finger tips, skin, etc. where temperatures may reach 30–32 °C. These reactions invariably involve red blood cells, autoantibodies, and complement (Ref. 5). As the red blood cells, now coated with both antibodies and complement, circulate through warmer areas of the body, some are taken up by reticuloendothelial tissues and hemolyzed. Others have the unstable bond between the antibodies and red cells broken. This leaves circulating red blood cells coated with C3 which eventually converts into the C3d component of complement (Ref. 29). Because most red cells become coated with C3d by this mechanism, the direct antiglobulin test will be positive only if the Anti-Human Serum contains anti-C3d activity. Reagents intended for screening purposes must contain anti-C3d with or without anti-IgG. Reagents for definitive diagnostic purposes should be monospecific, that is, contain, anticomplement activity, particularly anti-C3d, and no anti-IgG. If anti-C4 is present, the amount should be such that reactions with normal red cells stored in the refrigerator as clotted samples will

be negative. Red cells stored in this way may become sensitized with C components by the small amount of so-called normal cold agglutin present in most samples of human serum.

(iii) *Autoimmune hemolytic disease, drug induced.* Autoimmune hemolytic disease, with or without anemia, is a relatively uncommon complication of therapy with many drugs in common use. Mechanisms by which drugs bring about the autoimmune state include (Ref. 18): Immune complex adsorption to circulating red blood cells; adsorption of drug to red cells followed by in vivo reaction of anti-drug antibodies with drug-coated red blood cells; drug-induced alterations of the red cell membrane causing it to adsorb plasma proteins, including IgG; unknown mechanisms which, in some cases lead to serological findings indistinguishable from AHD, warm antibody type. The direct antiglobulin test is essential for diagnosis of these drug-induced diseases and, as in other types of AHD, the Anti-Human Serum used for screening purposes must contain both anti-IgG and anticomplement activity (Ref. 18). While IgG is the protein most often found in drug-induced AHD, cases are known in which complement occurs either alone or in combination with IgG. A reagents containing a mixture of both anti-IgG and anti-C3d is adequate for screening, but IgG and C3d monospecific reagent are needed for optimum testing in these cases.

(c) *Evaluation of suspected incompatible transfusions.* The infusion of incompatible blood is a serious and occasionally fatal complication of transfusion therapy. Incompatible red cells react promptly with circulating antibodies and either are destroyed immediately in the vascular system or hemolyzed more slowly by the body's reticuloendothelial tissues. In the latter case, antibody-coated red cells may circulate for a variable time before they are destroyed and can be detected in the recipients since they cause a positive reaction in the direct antiglobulin test. This is called a "mixed field" reaction, which is a mixture of agglutinated incompatible donor red cells and unagglutinated recipient cells. The evaluation of suspected incompatible transfusions is an accepted and valid indication for the use of Anti-Human Serum. Reagents for this purpose must contain anti-IgG activity either alone or with anticomplement. Pure anticomplement reagents are unsatisfactory.

(2) *Indirect antiglobulin test.* When red blood cells are incubated in plasma or serum which contain antibody, a reaction will occur if the red cells contain an antigen against which the antibodies are directed. The cells, now coated with antibody, can be detected by any of several methods. The use of Anti-Human Serum is among the best of these, particularly for IgG antibodies that do not bring about agglutination or hemolysis of red cells after the original in vitro reaction (Ref. 30).

(a) *Antibody detection tests (antibody screening).* Serum from patients or blood donors can be tested for blood-group antibodies by mixing their serum with normal red cells selected for their antigen content and then testing these cells with Anti-Human Serum. The red blood cells used cannot possibly bear all of the known blood group antigens, but must possess those antigens considered to be most dangerous to potential blood recipients whose serums contain the corresponding antibodies. To achieve this goal usually requires testing a serum against two or three selected type O red cells, either individually or pooled. The exact techniques employed, for example, the ratio of serum to cells, the incubation time, the incubation medium (saline, normal serum, albumin, etc.) influence the sensitivity of the test. After incubation, the cells are washed and tested with Anti-Human Serum to see if an antigen-antibody reaction had occurred. A positive result indicates that the serum being tested contains blood group antibodies. The specificity of the detected antibody can be established by another series of tests.

Nearly all blood group alloantibodies that require the use of Anti-Human Serum for detection require only a reagent with anti-IgG activity. Such blood-group alloantibodies sometimes also lead to complement coating of the red blood cells, but in nearly all instances the IgG antibody itself is also bound to the cell, usually in greater quantity and more readily detectable than the complement. Occasionally, antibodies that are detected by anticomplement but not anti-IgG have been reported (Refs. 22 through 24 and 31 through 37). However, such antibodies must be very rare. Abelson and Wurzel (Ref. 38) in a communication to this Panel report studies of 4,980 specimens. They found no reactions with "broad spectrum reagents" which were not also found with anti-IgG. Beck and Marsh (Ref. 39) report a combined experience of patient transfusion problems from 500 metropolitan New York hospitals along with blood donor antibody testing on more than 5.5 million units. In no case was a blood-group alloantibody detected solely because of its complement-binding capability. Petz (Ref. 40) has tested 113 sera selected because they contained antibodies with presumed complement-binding ability. Of this group, there were only one specimen, an anti-S, in which the antibody could be detected by anticomplement alone. Applying these statistics to usual transfusion practice, Petz estimates that the largest hospital in the San Francisco Bay area can expect to find such an antibody only once in 12.5 years, while the average-sized hospital will encounter such antibodies only once in 107 years.

While neither of these studies has shown the need for anticomplement activity, the results are preliminary and must be interpreted in light of the more than 20 years of experience with the antiglobulin test. An early report by Millison and Cutbush (Ref. 36) pointed out that to cause a positive antiglobulin reaction, some alloantibodies required an Anti-Human Serum with anticomplement activity. Reports from Stratton's laboratory (Refs. 24, 31 and 33), as mentioned earlier, suggest an important role for anticomplement as component of Anti-Human Serum. Pollack, Reiss and Treacy (Ref. 37) showed that in some cases a large amount of complement was attached to a red cell surface that was only weakly sensitized with IgG. Pollack (Ref. 41) has reported to this Panel that he has studied alloantibodies which caused severe transfusion reactions which were detected only by anticomplement. Finally, Sherwood, Haynes and Rosse (Ref. 34) have reported a hemolytic transfusion reaction caused by the failure of commercial antiglobulin reagent to detect complement. These reports document cases in which antibodies were detected by reagents containing anticomplement but not by anti-IgG alone. While cases where only complement is present on red cells are infrequent, there is little doubt that some blood group antibodies both bind to red cells and fix complement. In these cases, the amount of red cell-bound protein detected by a reagent containing both anti-IgG and anticomplement must be greater than the amount detected by either antiserum alone. Hence, broad spectrum reagents can be expected at times to yield stronger reactions which are easier to interpret that either anti-IgG or anticomplement alone. This appears to be a reason to require the use of reagents with boty specificities, but data to support this contention are inadequate. For the present, the Panel believes that reagents lacking antibodies against complement may be used for detection of red cell alloantibodies provided the package

insert warns that some antibodies may not be detected optimally. A multcenter study is underway to evaluate the requirement for anticomplement activity in the Anti-Human Serum used for this indication. This study should also evaluate the frequency and nature of the problems ("false positive") associated with reagents containing anticomplement.

(b) *Compatibility testing (crossmatching).* Compatibility testing, also known as crossmatching, is done before transfusion to ensure that the red blood cells intended for transfusion will be compatible. The usual procedure (Ref. 42) involves mixing the red blood cells of the intended donor with the serum of the recipient. After incubation the mixture is washed and Anti-Human Serum is added. The procedure is identical to that used for antibody detection tests except that cells of the intended donor replace the selected screening cells used in the latter procedure. Since both antibody detection testing and compatibility testing are identical procedures except for the choice of cells, similar considerations apply to both.

The Panel concludes that Anti-Human Globulin Serum is appropriately used in the indirect antiglobulin procedure as a part of donor-recipient compatibility testing. Anti-IgG is essential in this test. Until more definitive data are available to the contrary, the Panel concludes that additional anticomplement activity is not required. If antiglobulin serum contains anticomplement it must have adequate ant-C3 or C3d. Anticomplement (especially ant-C4), if present, should not be in such amounts that false-positive reactions occur. If antibodies to C3 or C3d are absent in a reagent serum, the package insert should state that some blood group alloantibodies may not be optimally detected. These recommendations are the same as those for the use of Anti-Human Serum in the antibody detection procedure.

(c) *Detection of $D^u$.* The presence of absence or the D blood group antigen of the Rh blood group system is important since the differentiation of donors and recipients into Rh-positive and Rh-negative groups is based on the presence or absence of this one Rh factor. Some variants of the Rh antigen, termed $D^u$, react weakly or not at all when tested with usual procedures (Ref. 43). Despite these weak reactions these bloods are antigenically Rh positive and, if transfused into Rh negative recipients with high titered anti-Rh antibodies, could cause serious reactions. The $D^u$ antigen can be detected by several techniques, one of which involves the use of Anti-Human Serum. Cells to be tested are incubated with a reagent antiserum specific for the D blood group antigen. The cells, if $D^u$ positive, react with and become coated by the anti-Rh but are not agglutinated. The addition of Anti-Human Serum after the cells are washed agglutinates these cells, thus showing them to be $D^u$ positive.

The Panel concludes that Anti-Human Serum is indicated for use in the test for $D^u$. The reagent needs to contain only anti-IgG for this purpose since all anti-Rh reagent antiserums used for $D^u$ testing are of IgG class and do not fix complement.

(d) *Red blood cell typing.* Red-cell typing is done by mixing the cell to be tested with antiserums of known specificity and examining the mixture for evidence of a reaction. In many cases, the antiserums used do not agglutinate the red cells directly, and the fact that an antigen-antibody reaction has occurred (a positive test) can be determine most efficiently using the indirect antiglobulin test. This type of testing is required for many of the reagents now licensed for red-cell typing. These include anti-$Fy^a$ serum, anti-K serum, anti-$Lu^a$ serum, and many others. The Anti-Human Serum used for these tests needs to contain only anti-IgG activity since complement components are not ordinarily involved in these reactions. The use of Anti-Human Serum in the indirect antiglobulin test is appropriate in these tests.

f. *Labeling analysis.* The major portion of the labeling for Anti-Human Serum reagents is not on the package but in the package insert. This circular should provide the laboratory worker with sufficient information to use, store, and evaluate the product. For the sake of uniformity, package inserts should use similar terminology. For example, either of the terms "crossmatching" or "compatibility testing" are appropriate, but one should be selected as the proper one with appropriate synonyms in brackets. In a like manner, terms for the various immunoglobulins, complement components, and diseases (autoimmune hemolytic anemia versus acquired hemolytic anemia versus autoimmune hemolytic disease) should be standardized.

A paragraph containing information about the specific antiglobulin activities present or absent in the reagent should be included. Methods used to determine these activities should be given in enough detail to allow the user to evaluate the product if necessary. In addition, the vial label should give specific information about the antibody activities included in the product.

Detailed instructions for the use of the product should be included. Information about how to set up necessary controls is essential.

g. *Summary.* Anti-Human Serum is a valuable reagent for blood bank work. The Panel recommends that it be placed in Category I. The use of Anti-Human Globulin Serum is indicated for:

*Direct antiglobulin test.*

(1) Diagnosis of hemolytic disease of the newborn.

(2) Diagnosis of autoimmune hemolytic disease.

(3) Evaluation of suspected incompatible transfusion reactions.

*Indirect antiglobulin test.*

(1) Antibody detection.

(2) Compatibility testing.

(3) Detection of $D^u$.

(4) Red blood cell typing.

Anti-Human Serum may contain antibodies against any of the human plasma proteins; however, reagents for use in blood banks, transfusion services, or laboratories involved in the diagnosis of immunohematologic disorders should contain antibodies specific for immunoglobulin G and selected components of the complement system. These may be present as individual components or may be mixed to produce Anti-Human Serum that has more than a single reactivity. Anti-Human Serum intended to screen patients for autoimmune hemolytic disease must contain activity against IgG and the C3d component of complement. More definitive characterization of these disorders requires reagents with either pure anti-IgG or pure anti-C3d activity. Reagents for all other indications must contain anti-IgG activity and may also have anti-C3 or C3d activity. In all cases the labeling must specify the antibody activities present, how tests for this were done, and the indications for which the reagent is suitable. Sufficient information must be included to allow the user to test the reagent to determine which antibody activities are present.

**References**

(1) Huestis, D.W., J.R. Bove and S. Busch, "Practical Blood Transfusion," 2nd Ed., Little, Brown & Co., pp. 87–110, 1976.

(2) Mollison P.L., "Blood Transfusion in Clinical Medicine," 5th E., Blackwell Scientific Publications, Oxford, pp. 482–483, 1972.

(3) Muller-Eberhard, H.J., "Chemistry and Function of the Complement System," *Hospital Practice*, 12:33–43, 1977.

(4) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publications, Oxford, pp. 471–477 and 480–482, 1972.

(5) Engelfriet, C.P., K.W. Pondman, G. Wolters, A.E.G. Kr. von dem Borne, D. Beckers, G. Misset-Groenveld and J.J. van Loghem, "Autoimmune Haemolytic Anaemias: III. Preparation and Examination of Specific Antisera Against Complement Components and Products, and Their Use in Serological Studies," *Clinical and Experimental Immunology*, 6:721–732, 1970.

(6) Garratty, G. and L.D. Petz, "The Significance of Red Cell Bound Complement Components in Development of Standards and Quality Assurance for the Anti-Complement Components of Antiglobulin Sera," *Transfusion*, 16:297–306, 1976.

(7) Issitt, P.D. and C.H. Issitt, "Applied Blood Group Serology," 2nd Ed., Becton, Dickenson and Co., p. 1, 1975.

(8) 42 FR 54543; October 7, 1977.

(9) White, W.D., C.H. Issitt and D. McGuire, "Evaluation of the Use of Albumin Controls in Rh Phenotyping," *Transfusion*, 14:67–71, 1974.

(10) 42 FR 53535, October 7, 1977.

(11) Giblett, E.R., "Blood Group Alloantibodies An Assessment of Some Laboratory Practices," *Transfusion*, 17:299–308, 1977.

(12) Greendyke, R.M. and J.C. Banzhaf, "Effects of *In Vitro* Storage on Red Blood Cell Agglutinogens," *Transfusion*, 14:365–371, 1974.

(13) Sussman, L.N. and J. Butler, "Antigen Reactivity in Pilot Tube Blood Specimens: Clotted Blood vs. Blood Stored in Acid-Citrate-Dextrose," *Transfusion*, 4:195–199, 1964.

(14) Moreschi, C., "Neue Tatsachen über die Blutkörperchenagglutination," *"Centralblatt für Bakteriologie, Parasitenkünde, Infektionskrankheiten und Hygiene*, 46:49–51, 1908.

(15) Coombs, R.R.A., A.E. Mourant and R.R. Race, "A New Test for the Detection of Weak and 'Incomplete' Rh Agglutinins," *British Journal of Experimental Pathology*, 26:255–266, 1945.

(16) Levine, P., E.M. Katzin and L. Burnham, "Isoimmunization in Pregnancy, its Possible Bearing on the Etiology of Erythroblastosis Fetalis," *Journal of the American Medical Association*, 116:825–827, 1941.

(17) Chaplin, H., "Clinical Usefulness of Specific Antiglobulin Reagents in Autoimmune Hemolytic Anemias," *in* "Progress in Hematology," Vol. VIII, Edited by Brown, E., Grune and Stratton, New York, pp. 25–49, 1973.

(18) Garratty, G. and L.D. Petz, "Drug-Induced Immune Hemolytic Anemia," *The American Journal of Medicine*, 58:398–407, 1975.

(19) Croft, J.D., S.N. Swisher, B.C. Gilliland, R.F. Bakemeier, J.P. Leddy and R.I. Weed, "Coombs'-Test Positivity Induced by Drugs—Mechanisms of Immunologic Reactions and Red Cell Destruction," *Annals of Internal Medicine*, 68:176–187, 1968.

(20) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publications, Oxford, p. 183, 1972.

(21) Mollison, P.L., "Blood Transfusion in Clinical Medicine," 5th Ed., Blackwell Scientific Publications, Oxford, p. 184, 1972.

(22) Dorner, I., J.A. Moore and H. Chaplin, "Combined Maternal Erythrocyte Autosensitization and Materno-Fetal Jk$^a$ Incompatibility," *Transfusion*, 14:212–219, 1974.

(23) Stratton, F., D.S. Smith and V.I. Rawlinson, "19S M, Followed by 7S G Anti-Jk$^a$ Antibodies Associated with Pregnancy," *Clinical Experimental Immunology*, 3:81–90, 1968.

(24) Stratton, F., H.H. Gunson and V.I. Rawlinson, "Complement Fixing Antibodies in Relation to Hemolytic Disease of the Newborn," *Transfusion*, 5:216–222, 1965.

(25) Voak, D. and M.A. Williams, "An Explanation of the Failure of the Direct Antiglobulin Test to Detect Erythrocyte Sensitization in ABO Haemolytic Disease of the Newborn and Observations on Pinocytosis of IgG Anti-A Antibodies by Infant (Cord) Red Cells," *British Journal of Haematology*, 20:9–23, 1971.

(26) Romano, E.L., N.C. Hughes-Jones and P.L. Mollison, "Direct Antiglobulin Reaction in ABO-Haemolytic Disease of the Newborn," *British Medical Journal*, 1:524–526, 1973.

(27) Issitt, P.D., "Autoimmune Hemolytic Anemia and Cold Hemagglutinin Disease: Clinical Disease and Laboratory Findings," *Progress in Clinical Pathology*, 7:137–163, 1977.

(28) Chaplin, H., "Automimmune Hemolytic Anemia," *Archives of Internal Medicine*, 137:346–351, 1977.

(29) Engelfriet, C.P., A.E.G. Kr. von dem Borne, D. Beckers, E. Reynierse and J.J. van Loghem, "Autoimmune Haemolytic Anaenias. V. Studies on the Resistance Against Complement Haemolysis of the Red Cells of Patients with Chronic Cold Agglutinin Disease," *Clinical and Experimental Immunology*, 11:255–284, 1972.

(30) Huestis, D.W., J.R. Bove and S. Busch, "Practical Blood Transfusion," 2nd Ed., Little, Brown & Co., p. 110, 1976.

(31) Stratton, F., D.S. Smith and V.I. Rawlinson, "Value of Gel Filtration on Sephadex G 200 in the Analysis of Blood Group Antibodies," *Journal of Clinical Pathology*, 21:708–714, 1968.

(32) Adinolfi, M., M.J. Polley, D.A. Hunter and P.L. Mollison, "Classification of Blood-Group Antibodies as $B_2M$ or Gamma Globulin," *Immunology*, 5:566–579, 1962.

(33) Stratton, F., "Recent Observations on the Antiglobulin Test," *Wadley Medical Bulletin*, 5:182–203, 1975.

(34) Sherwood, G.K., B.F. Haynes, and W.F. Rosse, "Hemolytic Transfusion Reactions Caused by Failure of Commercial Antiglobulin Reagents to Detect Complement," *Transfusion*, 16:417–420, 1976.

(35) Petz, L.D. and G. Garratty, "Complement in Immunohematology," *Progress in Clinical Immunology*, 2:175–190, 1974.

(36) Mollison, P.L. and M. Cutbush, "Use of Isotope-Labeled Red Cells to Demonstrate Incompatibility *In Vivo*," *Lancet*, 1:1290–1295 (cases 2, 3, p. 1295), 1955.

(37) Pollack, W., A. Reiss and M. Treacy, "The Use of Complement in the Serological Diagnosis of Hemolytic Disease of the Newborn," Proceedings of the Seventh Congress of the International Society of Blood Transfusion, Rome, p. 124, 1958.

(38) Abelson, N.M. and H.A. Wurzel, letter to the Panel received January 6, 1977, BER Volume 6144.

(39) Beck, M.L. and W.L. Marsh, "Complement and the Antiglobulin," (letter), *Transfusion*, 7: 529–530, 1977.

(40) Petz, L.D., "Complement in Immunohematology and Neurologic Disorders," in an International Symposium on "The Nature and Significance of Complement Activation," Otho Research Institute, pp. 87–94, 1976.

(41) Pollack, W., letter to the Panel dated December 6, 1977, BER Volume 6144.

(42) Miller, W., "Technical Manual of the American Association of Blood Banks," J.B. Lippincott, Philadelphia, pp. 192–193, 1977.

(43) Miller, W., "Technical Manual of the American Association of Blood Banks," J.B. Lippincott, Philadelphia, pp. 100–102, 1977.

### 20. Hepatitis B Testing

1. *Introduction.* Post-transfusion hepatitis has long been a serious medical problem. In 1970 the National Research Council estimated that there were approximately 30,000 cases of clinical post-transfusion hepatitis annually with a mortality rate of approximately 10 percent (Ref. 1). It was also estimated that there may be up to five times that many cases that are not clinically detectable. Other studies (Ref. 2) estimated the risk at 6.4 cases per 1,000 units of blood transfused, with one-third of these being icteric, but more recent studies suggest a higher risk, of between 7 and 10 percent of all blood recipients (Ref. 20).

The discovery of the hapatitis B surface antigen (HBsAg), previously called Australia antigen (Au) or hepatitis-associated antigen (HAA) was a major scientific breakthrough toward characterizing the hepatitis B virus and decreasing the incidence of post-transfusion hepatitis (Refs. 3 and 4). HBsAg, which is thought to be the outer coat or surface protein of the hepatitis B virus, is released into serum in three major morphologic forms available on electronmicroscopy: as a 20-nm sphere, as an elongated tubular form, and as an outer coat component fragment of the complex 42-nm Dane particle (Refs. 5 and 6). The presence in serum of HBsAg and studies of transfusion hepatitis have demonstrated an association between HBsAg and infectivity (Refs. 7 and 8). Testing all donor blood for HBsAg was mandated the Bureau of Biologics in 1972 (Ref. 9) and has resulted in a significant reduction of hepatitis B related post-transfusion hepatitis (Refs. 8 and 10). Other forms of hepatitis, including hepatitis A, but particularly the group of so-called non-A, non-B hepatitis now comprise the majority of post-transfusion cases (Refs. 12 and 13). However, there continue to occur cases

of type B post-transfusion hepatitis caused by blood found to be negative by the most sensitive tests currently available. New tests for other markers of hepatitis B infectivity, such as detection of antibody to the hepatitis B core antigen (HBcAg) may permit detection of potentially infective donor blood in some of these cases (Ref. 14).

Test methods for HBsAg have improved rapidly. HBsAg was initially detected by agar gel diffusion, a test of low sensitivity requiring a long incubation time. When HBsAg testing of blood donors became mandatory in 1972, second generation tests were required, that is, tests equal to or greater in sensitivity than counter-immunoelectrophoresis. These tests were more rapid to perform and had greater sensitivity than agar gel diffusion. In 1974, this category of tests was superseded by third-generation tests which are more reliable and reported to be 50 to 1,000 times more sensitive than counter-electrophoresis. Current third generation tests include radioimmunioassay (RIA), reverse passive hemagglutination (RPHA), and ezyme-linked immune adsorbant assay (ELISA).

As set forth by the Bureau of Biologics, third generation tests for HBsAg are defined by the ability to detect certain HBsAg-positive serum samples in a Bureau of Biologics reference panel. This panel is comprised of HBsAg positive and negative samples and includes samples with greater and lesser amounts of the antigen. Both antigen subtypes, adw and ayw, are included. The reference panel also includes a variety of HBsAg positive specimens variously diluted, both to the current limits of detectability by available tests and to dilutions that are not detectable by any currently available method. New tests that may be introduced, must perform acceptably against this Bureau of Biologics' serum panel.

2. *Test methods*—a. *Radioimmunoassay tests (RIA).* Polyethylene tubes or another suitable "solid-phase" carrier such as a bead supplied by the manufacturer are coated with specific anti-HBsAg. When serum containing HBsAg is added to the anti-HBsAg coated "solid-phase," the HBsAg will "attach" to the antibody. Excess serum is removed, and the solid-phase complex is washed, and radiolabeled anti-HBsAg is added. The anti-HBsAg becomes fixed to the "bound" HBsAg forming a (solid-phase) antibody antigen-$^{125}$I-labeled antibody "sandwich". The radiolabeled antibody remains in the tube or on the "solid-phase" after a series of washes, producing a strongly radioactive tube or "solid-phase". A serum nonreactive for HBsAg will not provide a site for binding of the readioactive antibody. Radioactive anti-HBsAg is therefore removed by the subsequent washes, resulting in a test with low radioactivity.

RIA tests results are determined by counting radioactive emissions in a gamma counter and comparing test samples with control standards. Reading of this test is thus objective.

b. *Reversed passive hemagglutination tests (RPHA).* Reagent human erythrocytes are coated with specific antibody (anti-HBsAg) and stabilized by lyophilization. In the presence of HBsAg, the antibody-coated erythrocytes form a complex leading to a visible hemagglutination. If the antibody coatd cells are not agglutinated because HBsAg is absent or there is insufficient HBsAg in the sample, the antibody-coated erythrocytes settle in a recognizable nonagglutinated pattern, a sharp compact button. The interpretation of this test is subjective; it requires distinguishing agglutinated-positive tests from unagglutinated-negative results.

c. *Enzyme-linked immune absorbent assay (ELISA).* This test is similar in principle to "solid-phase" RIA tests except that enzyme-linked reagent antibodies of anti-HBsAg specificity are employed at the final stage to form a solid-phase antibody-antigen-enzyme-linked antibody "sandwich."

Instead of direct transfer to a gamma counter, a colorless enzyme substrate, *p*-nitrophenyl, is added to the "sandwich." Hydrolysis of the colorless substrate by the enzyme linked to the anti-HBsAg forms a yellow end product. The intensity of the color, measured spectrophotometrically, defines the presence of HBsAg when appropriate controls are employed. Interpretation of this test is also objective.

3. *Antibody used for testing.* Antibodies used for the detection of HBsAg in third generation tests vary considerably among the current licensed procedure. Antibodies raised in a variety of animals immunized with HBsAg as well as antibodies from humans are used. These are summarized in Table 1 below. As all test procedures have a significant incidence of false-positive reactions, some due to the presence of heterospecific antibodies, all manufacturers recommend a neutralization test for confirmation of specificity. For confirmatory testing, all manufacturers provide human anti-HBsAg (with one exception where chimpanzee anti-HBsAg is used) to neutralize specifically the presumed antigen prior to the perfomance of the confirmatory detection test, which should become negative. Antibodies in all test procedures must also contain specificities to the two major subclasses of HBsAg, ay and ad.

In some cases manufacturers offer alternative test procedures employing different temperatures of incubation to shorten the time required for the test. These are to be used when the usual time required for performing the test is too great, and the need for the particular blood product is immediate. Short incubation time tests are usually less sensitive than tests performed in the standard manner with material from the same manufacturer.

TABLE 1.—SOURCE OF ANTIBODY FOR LICENSED TESTS FOR HBSAG

| | Bound to solid phase | Label | Neutralization |
|---|---|---|---|
| RIA | | | |
| RIA International | Goat | Human | |
| Electronucleonics | do | Goat | Human. |
| Abbot | Guinea pig | Human | Do. |
| Hyland | do | Chimpanzee | Do. |
| RPAH | | | |
| Abbott | do | do | Do. |
| Ortho | Chimpanzee | do | Chimpanzee. |
| ELISA | | | |
| Cordis | Horse | Horse | |

4. *Test sensitivity and performance.* Direct Comparisons of test sensitivity between RIA and RPHA have been made. In one study (Ref. 15), when comparisons were made by parallel testing of serial dilutions of HBsAG positive samples, RIA was able to detect one-fourth the quantity of HBsAg subtype ad and one-sixteenth the quantity of a subtype ag antigens when compared with RPHA. Another study, performed by the Bureau of Biologics and shown in Table 2 below, also indicates that RIA, in general, is more sensitive than RPHA. However, a third study (Ref. 16) indicates that the sensitivity of RPHA is comparable to RIA.

TABLE 2.—COMPARATIVE SENSITIVITIES OF LICENSED THIRD GENERATION TESTS*

| HBsAg Sample No. (subtype) | RIA-1 | RIA-2 | RPHA-1 | ELISA-1 | RPHA-2 |
|---|---|---|---|---|---|
| 4 (ay) | 32 | 16 | 16 | 8 | 16 |
| 12 (ay) | 32,768 | 16,384 | 16,384 | ,096 | 8,192 |
| 19 (ay) | 2,048 | 2,048 | 512 | 512 | 512 |

TABLE 2.—COMPARATIVE SENSITIVITIES OF LICENSED THIRD GENERATION TESTS*—Continued

| HBsAg Sample No. (subtype) | RIA-1 | RIA-2 | RPHA-1 | ELISA-1 | RPHA-2 |
|---|---|---|---|---|---|
| 37 (ay) | 64 | 64 | 64 | 16 | 32 |
| 6 (ad) | 8,192 | 8,192 | 8,192 | 2,048 | 2,048 |
| 18 (ad) | 128 | 64 | 128 | 32 | 32 |
| 20 (ad) | 2,048 | 1,024 | 1,024 | 256 | 512 |
| 27 (ad) | 16,384 | 16,384 | 8,384 | 8,192 | 4,096 |
| 32 (ad) | 128 | 128 | 128 | 64 | 64 |
| 33 (ad) | | | 64 | 64 | 64 |

*End-point dilution titers.

When comparing RIA and RPHA in their ability to detect HBsAg positive samples in populations containing antigen positive and negative individuals, RIA testing results in a slightly higher detection rate. Some of the published data are summarized in Table 3 below.

TABLE 3

| No. tested | No. RPHA positive | No. RIS positive | (Reference) |
|---|---|---|---|
| 7,067 | 34 | 34 | (17) |
| 3,189 | 5 | 6 | (16) |
| 25,357 | 173 | 176 | (15) |

Proficiency testing indicates superior performance of RIA when compared with RPHA in most cases. The AABB–CAP survey (Ref. 19), including eight proficiency test panels distributed over a 3-year period gave the following results: The percentage of correctly identified positive samples by RIA was between 98.5 and 99.8; by RPHA it was between 79.5 and 98.1. The differences between the two test methods was magnified if only weakly reactive positive samples were compared. This study also reported that in panels of HBsAg positive and negative samples, 87.8 percent of participants correctly identified all samples by RIA but only 55.8 percent by RPHA.

In two more recent AABB–CAP proficiency test panels studied in February 1977 and February 1978, RIA also gave higher detection rates and correct response rates than did RPHA. These data can be summarized as follows:

1977 (AABB–CAP PANEL)

| | HBsAg Pos. (15), number of correct responses/total responses | Percent | HBsAg Neg. (5), number of correct responses/total responses | Percent |
|---|---|---|---|---|
| RIA | 5243/5493 | 95.5 | 1776/1845 | 96.3 |
| RPHA | 829/961 | 86.3 | 315/320 | 98.4 |

1978 (AABB–CAP PANEL)

| | HBsAg Pos. (7), number of correct responses/total responses | Percent | HBsAg Neg. (3), number of correct responses/total responses | Percent |
|---|---|---|---|---|
| RIA | 3179/3207 | 99.1 | 1293/1317 | 98.2 |
| RPHA | 497/519 | 95.8 | 211/220 | 95.9 |

Proficiency tests sponsored by the Centers for Disease Control (CDC) gave inconsistent results. In the first CDC Panel (Diagnostic Immunology 1977 I, Hepatitis B, September 1977), RIA gave a 99-percent correct response rate as compared with RPHA which had a 93-percent correct response rate. In the second CDC Panel (November 1977), RIA and RPHA had equally good performance, both 99-percent correct, but RIA showed a higher false-positive rate.

Evaluations of ELISA in comparison with RIA and RPHA have been few. In one study, in titration of HBsAg positive samples, ELISA gave results comparable to RIA (Ref. 19). Titration studies performed by the Bureau of Biologics indicate ELISA to be less sensitive than RIA but comparable to RPHA (Table 2). In field tests, ELISA also gave results comparable to other third-generation tests, although the type of tests is not identified (Ref. 19). ELISA seems to be associated with a relatively high incidence of false-positive results (Ref. 19).

These data must be considered with caution. As there are a number of manufacturers of both RIA and RPHA test kits, it is possible that not all RIA or RPHA products are of equal sensitivity or performance. Although the currently available data are few, there is reason to believe this is correct. Thus, comparisons of tests on a generic basis, e.g., RIA versus RPHA, may not be an entirely valid basis for drawing conclusions with regard to test efficacy. Finally, it must be appreciated that all data agree that any third-generation test is far superior to second-generation tests for screening blood donors for HBsAg.

7. *Summary.* a. Third-generation tests for the detection of HBsAg in blood donors are far more sensitive and proficient than second-generation tests, and their mandated use has reduced the occurrence of hepatitis B in blood recipients.

b. Among third-generation tests, RIA is most sensitive for the detection of small amounts of HBsAg. There are no data that relate such sensitivity to possible infectivity.

c. In general, proficiency testing has demonstrated that RIA detects more HBsAg positive samples than other third generation tests.

d. All currently available licensed third-generation tests meet minimal standards for safety and efficacy.

e. There is some evidence that among RIA or RPHA tests there may be some variability in sensitivity and performance.

f. There is evidence that short-incubation RIA is less sensitive than overnight incubation RIA.

8. *Recommendations.* a. The licensed third-generation hepatitis testing reagents are recommended to be placed in Category I.

b. A workshop should be organized to attempt to redefine third generation tests on the basis of an absolute minimal standard amount of HBsAg that must be detected by any method. All tests must be able to detect this minimal quantity consistently without an inordinate number of false-positive results, in order to be designated a third generation test.

c. Studies relating test sensitivity with infectivity should be encouraged.

d. The standard should be reviewed periodically to reflect new advances in the field which might result in tests of even greater sensitivity.

**References**

(1) Panel of The Committee on Plasma Substitutes of The Division of Medical Science, National Academy of Sciences, National Research Council: Statement on Laboratory Screening Tests for Identifying Carriers of Viral Hepatitis in Blood-banking and Transfusion Services, *Transfusion*, 10:1-2, 1970.

(2) Alter, H.J., P.V. Holland, A.G. Morrow, R.H. Purcell, S.M. Feinstone and Y. Moritsugu, "Clinical and Serological Analysis

of Tranfusion-Associated Hepatitis." *Lancet*, ii:838–841, 1975.

(3) Blumberg, B.S., A.I. Sutnick and W.T. London, "Hepatitis and Leukemia: Their Relation to Australia Antigen." *Bulletin of the New York Academy of Medicine*, 44:1566–1586, 1968.

(4) Prince, A.M., "An Antigen Detected in The Blood During the Incubation Period of Serum Hepatitis," *Proceedings of the National Academy of Sciences*, 60:814–821, 1968.

(5) Bayer, M.E., B.S. Blumberg and B. Werner, "Particles Associated with Australia Antigen in the Sera of Patients with Leukemia, Down's Syndrome and Hepatitis," *Nature*, 218:1057–1059, 1968.

(6) Dane, D.S., C.H. Cameron and M. Briggs, "Virus-like Particles in Serum of Patients with Australia-Antigen-Associated Hepatitis," *Lancet*, i:695–698, 1970.

(7) Gocke, D.J., "A Prospective Study of Post-transfusion Hepatitis: The Role of Australia Antigen," *Journal of the American Medical Association*, 219:1165–1170, 1972.

(8) Goldfield, M., J. Bill, H. Black, W. Pizzuti and S. Srihongse, "Hepatitis Associated with the Transfusion of HBAg-negative Blood," *in* "Hepatitis and Blood Transfusion." Edited by Vyas, G.N., H.A Perkins and S. Schmid, Grune and Stratton, New York, pp. 353–361, 1972.

(9) 42 CFR 73–755, Federal Register, 37 FR 10937, 1972.

(10) Alter, H.J., P.V. Holland, R.H. Purcell, J.J. Lander, S.M. Feinstone, A.G. Morrow and P.J. Schmidt, "Posttransfusion Hepatitis After Exclusion of Commercial and Hepatitis-B Antigen-Positive Donors," *Annals of Internal Medicine*, 77:691–699, 1972.

(11) Koretz, R.L., D.R. Klahs, S. Ritman, K.H. Damus and G.L. Gitnick, "Post-Transfusion Hepatitis in Recipients of Blood Screened by Newer Assays," *Lancet*, ii:694–696, 1973.

(12) Purcell, R.H., S.M. Feinstone and A.Z. Zapikian, "Recent Advances in Hepatitis A Research," *In* "Transmissible Diseases and Blood Transfusion", Edited by Greenwalt, T.J., and G.A. Jamieson, Grune and Stratton, New York, pp. 11–26, 1974.

(13) Feinstone, S.M., A.Z. Zapikian, R.H. Purcell, H.J. Alter and P.V. Holland, "Transfusion-Associated Hepatitis Not Due to Viral Hepatitis Type A or B," *New England Journal of Medicine*, 292:767–770, 1975.

(14) Hoofnagle, J.H., R.J. Gerety, L.Y. Ni and L.F. Barker "Antibody to Hepatitis B Core Antigen, A Sensitive Indicator of Hepatitis B Virus Replication," *New England Journal of Medicine*, 290:1336–1340, 1974.

(15) Abbott Laboratories, Ausria II—125, Package insert.

(16) Ortho Diagnostics, Ruphadex B, Package insert.

(17) RIA International, Hepria B, Package insert.

(18) Polesky, H.F. and M.R. Hanson, "Results of HB$_s$Ag Testing of AABB–CAP Survey Samples," *American Journal of Clinical Pathology*, 68:210–212, Supplement 1977.

(19) Cordis Corporation, Cordia H, Package insert.

(20) "Viral Hepatitis," Edited by Vyas, G.N., S.N. Cohen and R. Schmid, Franklin Institute Press, Philadelphia, p. 359, 1978.

**21. Antivenins**

*Generic Statement and Product Reviews*

1. *Introduction.* This statement reviews the licensed antivenins and the associated horse serum control materials. The products are Antivenin (*Crotalidae*) Polyvalent and Antivenin (*Micrurus fulvius*) manufactured by Wyeth Laboratories, Inc., and Antivenin (*Latrodectus mactans*) manufactured by Merck Sharp and Dohme.

Therapeutic antivenins are the fractionated globulins from the serum of horses which have been immunized with a clinically important toxic venom. Three major preparations are available: (1) Polyvalent antivenin, (*Crotalidae*), the North American pit vipers, (2) antivenin (*Micrurus fulvius*), the North American Coral Snake, and (3) antivenin (*Latrodectus mactans*), the Black Widow Spider. These antivenins have a long history of development and clinical use and have well-established indications for treatment of the respective envenomations, which include toxic bites of most of the significant indigenous North American animals from which life may be at risk.

It is of note that many toxic animals from throughout the world have been imported into the United States into zoos, research institutes, and, in some instances, private collections. Occasional accidental bites from these animals constitute a small but serious health problem for the involved individuals. A volunteer organization has developed a network of information centers and repositories for antivenins appropriate to these exotic toxic animals, situated through the United States. These materials come from primarily foreign origins and are imported into the United States under individual IND exemptions at the present time, since their distribution is not regarded as primarily commercial in nature.

Most animal venoms are complex mixtures of proteins and peptides that have a wide variety of biochemical and physiological activities which result in their toxic effects (Refs. 25 and 26). In the case of the venom of *Crotalidae*, several of the venom fractions have primarily local effects, resulting in inflammation, tissue necrosis, and vascular thrombosis. Other fractions have more general systemic effects, particularly the so-called "lethal fraction" which is primarily responsible for death of man or test animals. Other prominent systemic effects are induction of hemolysis and activation of the blood coagulation system (Refs. 3 through 10).

This discussion will not include comprehensive consideration of the management of toxic bites, but will focus on the use of antivenins. It is important to recognize the need for comprehensive understanding of the problems prior to treatment of such a patient.

Antivenin is standardized by a biological test in mice for its protective effect primarily against the lethal factor. The components of these venoms which act locally may be variably neutralized by antivenin. Local injury may already have been produced by the time venom neutralization is attempted; and the antivenins themselves are not standardized for their action against these locally injurious components. Thus, it should be recognized that the *Crotalidae* polyvalent antivenin is a useful therapeutic agent primarily for its life-saving effect and that local injuries at the site of a bite may be quite severe even in face of adequate antivenin administration. It is important that the total management of these bites is understood by the person responsible for their treatment and that actions not be taken, such as excessive tissue cooling, obstruction of the arterial circulation, or widespread incision which may well increase the local tissue damage without any therapeutic effect; corticosteroid therapy should not be employed except on very specific indications. By contrast, the venoms of the North American Coral Snake and the Widow Spiders act predominantly against the central nervous system, frequently with little or no local reaction which predicts the degree of envenomation. The first symptoms suggesting that envenomation has occurred may be rapidly developing paralysis, including respiratory paralysis. The administration of antivenin in this situation is quite specific, but again it must be integrated into a program of management which includes support of the patient, with maintenance of adequate respiratory function and oxygen uptake (Refs. 11 through 23).

A wide variety of other systemic effects occur primarily in association with bites of pit vipers and to a lesser extent coral snake envenomations. Many of these appear to be related to activation of the coagulation system with associated fibrinolysis, thrombocytopenia, a variety of hemorrhagic manifestations, hemolysis and impairment of renal function. Maintenance of adequate hydration, blood pressure, and urinary output during recovery from a bite is important for successful outcome. These effects are relatively short lived and commonly begin to correct themselves following

adequate treatment with antivenin during the first 48 to 72 hours of treatment. In some instances, specific interventions such as red cell transfusions or correction of severe hemostatic defects may be indicated on the merits of the specific problem itself (Ref. 2).

a. *Nature and sources of immunizing antigens.* A number of problems exist with regard to the sources and standardization of the immunizing antigens used in the preparation of antivenins. As noted previously, venoms are a complex mixture of materials with wide range of biochemical effects primarily due to their enzymatic activities. There appear to be variations between species and subspecies in the quantitative and qualitative characteristics of the venoms. There are also variations within a species over different geographic ranges and seasonal variability as well. There may well be variability in the venom obtained from a single individual animal depending upon the conditions under which the animal is kept, the frequency of venom removal and other factors not well understood (Refs. 12 and 16).

In general there is not a serious problem of supply of snake venoms since these are available commercially from a number of serpentariums. This, however, does not eliminate the kinds of variability just mentioned.

In the case of the venoms of the widow spiders, the problem is more serious. It should be noted that in most instances the venom is not a secreted product of the animals, but rather an extract of the removed venom sacs of a large number of individual animals. Thus it will contain materials derived from the venom producing apparatus in addition to the venoms themselves. There have been significant problems in obtaining reliable supplies of standardized venoms for the widow spiders. It is probable that little of the currently available antigenic venom is actually derived from the Black Widow Spider itself; rather it is derived from a variety of related spiders from both North and South America, the venom of which has a high degree of cross-reactivity with that of the Black Widow Spider. Since the antivenin produced with these antigens is useful in the treatment of toxic bites from this group of related spiders, it seems reasonable to rename the material to reflect this fact (Ref. 27).

Not only must venoms be obtained for purposes of immunization of horses, but they must also be available in standardized and stable form for subsequent testing of the potency of the antibody that has been produced. This must be done both by immunochemical means and more importantly by in vivo mouse protective tests conducted by both the manufacturer and by the Bureau of Biologics which also tests the material for potency before release. Thus the secretion, procurement, storage and stability of the antigenic venoms is a crucial problem in the production of these materials. At the present time, the situation with regard to sources of appropriate venoms seems adequate, but one might easily envision situations in which particularly the venoms of the widow spider may be in very short supply.

b. *Antivenins prepared in other species.* Because the products reviewed here are prepared in horses, their principle toxicity relates to horse serum sensitivity of the recipient. This has lead to a number of efforts to develop antivenins in other species, particularly in goats, so that at least small supplies may be made available to patients who are highly sensitive to horse serum, possibly as a result of previous treatment with antivenin. These efforts have not been commercially supported and at the present time there is no such alternative source of antivenin available in the United States. Nevertheless there remains a need for such products. Attention should be given to a variety of ways in which they might be produced, distributed, and utilized for the treatment of these seriously compromised patients in whom desensitization to horse serum may be very hazardous, particularly if it is not carried out by someone thoroughly familiar with the procedure and who has adequate monitoring capability and understanding of the management of anaphylaxis (Ref. 24).

2. *Indications.* The primary indication for administration of antivenin is envenomation as the result of a bite. This deceptively simple criterion has many difficulties in its application. First, as many as 20 percent of toxic snake bites may not be accompanied by the injection of venom (Refs. 3 and 4). Thus, the presence of a bite alone does not provide an indication for the administration of antivenin. In the case of pit viper bites, usually local reactions promptly signal the occurrence of envenomation. Under some circumstances where venom is injected deeply into muscle or into a vascular structure, local reaction may be minimal or absent, and the first indications of envenomation are systemic symptoms. Furthermore, it is important to estimate the degree of envenomation in order to administer an adequate amount of antivenin.

Close observation of the patient and the site of the bite with periodic revisions of the estimate of the degree of envenomation and reassessment of the amount of antivenin administered are thus indicated in the management of these injuries. In general, underestimation of the degree of envenomation is more hazardous than overestimation, although maximum treatment with antivenin in every case cannot be justified on this basis.

A number of grading systems for evaluating the degree of envenomation have been employed in the past. These systems may require a period of up to 12 hours to permit accurate evaluation. This is of course well beyond the period of up to 4 hours when antivenin has its maximum therapeutic effectiveness. These delayed grading systems of the amount and/or severity of envenomation may have utility in predicting or evaluating ultimate clinical outcomes, or in clinical investigation, but they should not be employed in labeling as a guide to therapeutic antivenin administration and dosage. Emphasis must be given to the necessity of an early clincial judgment about degree of envenomation as the basis for prompt administration of antivenin. Labeling material should reflect this position.

The bite of the Coral Snake, as noted previously, may be associated with no local symptomatology other than the superficial injury of the bite itself. In these patients, very close attention to clinical manifestations are necessary to judge the degree of envenomation and the appropriate amount of antivenin for administration (Ref. 13). Widow spider bites can be regarded in the same way (Ref. 17).

It is of great importance that the exact identification of the animal responsible for the bite be made if possible. The probable severity of envenomation can be predicted to some degree both by the species and the size of the responsible animal. These judgments must of course be made in the light of the body size of the victim, with the recognition that equivalent amounts of envenomation are much more serious in children, particularly small children. For example, bites of the so-called "pygmy rattlesnake" are rarely lethal in adults but may be severe in small children. The same may be said of Copperhead and Water Moccasin bites. By contrast the venom of the Mojave rattlesnake (*C. scutulatus*) is extremely toxic (Ref. 2).

It should be recognized that the judgment required to estimate the degree of envenomation is not simply acquired, and the help of persons

experienced in the management of toxic bites should be sought where it is available. The always confused and sometime hysterical situation surrounding the management of the snake bite victim should not lead to precipitous and unwise intervention. Rather, a calm and thoughtful examination of the entire situation and an evaluation of the severity of the injury is always preferable to a hurried, routinized intervention. Although these are emergency situations, time is always available to make such an evaluation. It should be recognized that the unwarranted administration of antivenin to a patient, who because of occupational reasons or other factors affecting his/her exposure has a high likelihood of repeated bites, will certainly produce a serious problem if that patient is bitten subsequently. The decision to administer antivenin can be lifesaving and frequently is, but its consequence will almost certainly be a lifetime sensitivity in varying degree to horse serum and possibly related materials.

3. *Effectiveness.* A large volume of literature supports the effectiveness of antivenins in the management of these toxic bites. The principle limitations on effectiveness are the time interval from the occurrence of the bite to the administration of antivenin. Treatment within 4 hours of the bite once the presence of envenomation has been determined appears to be optimal, with declining effectiveness over the following 16 hours. In severe envenomation administration of antivenin has been recommended even if a 24 or more hour interval has occurred since the injury (Ref. 24).

A second limitation on effectiveness appears to be undertreatment. Present package sizes provide 10 mL of reconstituted dry antivenin as the therapeutic dosage unit. Since two to four vials of antivenin are recommended for even mild envenomation and 10 to 20 vials where severe envenomation has occurred, it might be reasonable to increase the individual package size by a factor of at least two.

4. *Safety.* The hazard associated with all of these antivenins is that of horse serum sensitivity of the recipient. Great care must be taken in determining the recipient's status from this point of view both by a carefully obtained history and by appropriate testing with horse serum. Carefully done intradermal testing is mandatory. Severely hypersensitive individuals may have severe reactions to even the small quantities of antigens in the intradermal test. Intradermal testing should not be done unless preparations have been made to manage anaphylaxis. A conjunctival test, whereas it may be of use in detecting severely hypersensitive people, also is subject to significant false positives unless it is very carefully carried out and supervised. The conjunctival test may provoke severe conjunctivitis in severely hypersensitive people, sometimes with threats to vision. Since an intradermal test should be done, there is little reason to carry out the conjunctival test.

Even in the absence of positive skin tests, an anaphylactic reaction may occur shortly after the administration of antivenin, and its immediate management with appropriate measures will be lifesaving. Delayed reactions of the serum sickness type generally occur within 5 to 25 days after administration in patients receiving horse serum for the first time and somewhat earlier in patients who have been immunized to this material previously.

Patients may be sensitive to horse serum in the absence of prior horse serum injections. Contact with horses, possibly by inhalation of horse dander and other exposures, appears to be capable of sensitizing susceptible individuals. In other instances, patients may be sensitive without any known or remembered contact with horses or horses proteins. The history given by patients who must receive horse serum products is thus of limited value. A valid history of prior horse serum administration should always be regarded as strong evidence of presumed hypersensitivity. The absence of such a history cannot be relied upon to indicate lack of sensitivity.

Hypersensitive patients will require desensitization prior to the administration of antivenin. This can be accomplished according to a standard dosage regimen in almost every patient, with little risk in experienced hands. The procedure does clearly have a significant associated risk when it must be carried out by people with inadequate experience or facilities to monitor and support the patient during desensitization. In general, the existence of hypersensitivity in the envenomated patient is not a contraindication for the administration of the antivenin, but it should be recognized that this situation increases the risk to the patient of antivenin treatment. The details of an adequate procedure for desensitization will not be discussed here, although the general procedure is considered in the labeling (package insert) provided with all of these products.

Antivenins should not be injected at the site of a bite, or distal to the wrist or ankle. They are maximally effective when delivered to the envenomated tissues by the circulation.

5. *Benefit/risk evaluation.* An abundant literature supports the position that the benefits of antivenin therapy, appropriately used, markedly outweight the risks involved.

6. *Recommendations.* a. These products are recommended to be placed in Category I.

b. Antivenins from alternative animal sources should be made available in the United States to treat patients who have severe horse serum hypersensitivity, particularly for patients who are at high risk of repeated bites.

c. Package dosage sizes should be increased by a factor of two.

7. *Labeling recommendations.* a. Easily recognizable common names should be included in the official name for the Crotalidae antivenin as is done for the Coral Snake antivenin. The addition of the words "Rattlesnake, Copperhead and Moccasin" is recommended.

b. Since it is likely that the antigen used for the preparation of the "Black Widow Spider Antivenin" is not actually derived from the Black Widow Spider but from closely related species, the name of this product should be changed to reflect this fact. An appropriate common name would be "Widow spider Spp. antivenin". These changes in title would have the purpose of improving the identification of the product for personnel with less training who may be called upon to handle them.

c. Antivenin should be administered intravenously, except in circumstances where this is not possible. Intramuscular administration results in delayed absorption and may well result in inadequate treatment, particularly in severe envenomations. At the persent time, intramuscular administration is still recommended in labeling. The labeling should be revised to remove the recommendation for intramuscular injection, except in circumstances where intravenous administration is impossible.

d. All references to delayed or deferred determination of the degree of envenomation as a basis for determining the appropriate dose of antivenin should be eliminated from labeling materials. Guidelines should be given for estimation of severity of the bite based upon initial observations and further observation over a short time period, an hour or two at most. Emphasis should be placed on prompt treatment, rather than precise calculation of the degree of envenomation.

e. The limited usefulness and possible hazard of the traditional conjunctival test for horse serum sensitivity should be made explicit in labeling materials. Emphasis should be placed upon proper performance of a skin test and its interpretation. Emphasis should be given to the possibility that anaphylaxis may occur after even a test dose of horse serum in severely hypersensitive patients.

f. Package inserts should be printed in more durable booklet form if possible and the material reorganized in such a fashion as to provide a primer on the management of victims of the specific toxic bit. The most important clinical material should be printed in somewhat larger type to provide inexperienced people with an easily comprehended guide to management of the envenomated patient. Package inserts of this type might have a lasting value as readily available instructional materials in emergency rooms, isolated aid stations, and other places where bitten patients are treated. The assistance of experienced clinicians in this field should be sought in the reorganization and preparation of this material.

**References**

(1) Parrish H.M., "Incidence of Treated Snakebites in the United States," *Public Health Reports*, 81:269–276, 1966.

(2) Russell, F., R.W. Carlson, J. Wainschel and A.H. Osborne, "Snake Venom Poisoning in the United States. Experiences with 550 Cases," *Journal of the American Medical Association*, 233:341–344, 1975.

(3) Russell, F.E., "Venomous Bites and Stings: Poisonous Snakes," *The Merck Manual of Diagnosis and Therapy*, 13th Ed., pp. 1982–1987, 1977.

(4) Wangert, W.A. and J. Wainschel, "Diagnosis and Management of Envenomation of Poisonous Snakes," *Southern Medical Journal*, 68:1015–1026, 1975.

(5) Parrish, H.M. and R.H. Hayes, "Hospital Management of Pit Viper Venenations," *Clinical Toxicology*, 3:501–511, 1970.

(6) McCollough, N.C. and J. Gennaro, Jr. "Diagnosis, Symptoms, Treatment and Sequelae of Envenomation by Crotalus Adamanteus and Genus Ancistrodon," *Journal of the Florida Medical Association*, 55:327–329, 1968.

(7) Watt, C. and J. Gennaro, "Pit Viper Bites in South Georgia and North Florida," *Transactions, Southern Surgical Association*, 77:378–386, 1966.

(8) Minton, S.A., "Venom Diseases: Snakebite," *in* "Textbook of Medicine," Edited by Beeson, P. and W. McDermott, Saunders, Philadelphia, pp. 88–92, 1975.

(9) Van Mierop, L. H.S., "Poisonous Snakebite: A Review. Snakes and Their Venom," *Journal of the Florida Medical Association*, 63:191–200, 1976.

(10) Arnold, R.E., "Treatment of Snakebite," *Journal of the American Medical Association*, 236:1843, 1976.

(11) McCollough, N.C. and J.F. Gennaro, Jr., "Coral Snake Bites in the United States," *Journal of the Florida Medical Association*, 49:968–972, 1963.

(12) Fix, J.D. and S.A. Minton, Jr., "Venom Extraction and Yields from the North American Coral Snake, Micrurus Fulvius," *Toxicon*, 14:143–145, 1976.

(13) Parrish, H.M. and M.S. Khan, "Bites by Coral Snakes: Report of 11 Representative Cases," the American Journal of the Medical Sciences, 253:561–568, 1967.

(14) Moseley, T., "Coral Snake Bite: Recovery Following Symptoms of Respiratory Paralysis," *Annals of Surgery*, 163:943–948, 1966.

(15) Ramsey, G.F. and G.D. Klinckstein, "Coral Snake Bite. Report of a Case and Suggested Therapy," *Journal of the American Medical Association*, 182:949–951, 1962.

(16) Neill, W., "Some Misconceptions Regarding the Eastern Coral Snake. Micrurus fulvius," *Herpetologica*, 13:111–118, 1957.

(17) Russell, F.E., "Bites by the Sonoran Coral Snake, Micruroides Euryxanthus," *Toxicon* 5:39–42, 1967.

(18) Barron, W.E., "Spider Bites," *Journal of the Medical Association of Georgia*, 49:511–512, 1960.

(19) Micks, D.W., "Insects and Other Arthropods of Medical Importance in Texas," *Texas Reports on Biology and Medicine*, 18:624–635, 1960.

(20) Price, G.E., "Arachnidism in Children," *Journal of Pediatrics*, 49:101–108, 1956.

(21) Russell, F.E., "Injuries by Venomous Animals in the United States," *Journal of the American Medical Association*, 177:903–907, 1961.

(22) Russell, F.E., "Muscle Relaxants in Black Widow Spider (Latrodectus mactans) Poisoning," *American Journal of the Medical Sciences*, 243:159–162, 1962.

(23) Russell, F.E., "Venom Poisoning," *Rational Drug Therapy*, (5)8:1–7, 1971.

(24) Russell, F.E., Testimony Contained in Transcripts of the January 6, 1978 meeting of the Panel on Review of Blood and Blood Derivatives.

(25) Russell, F.E. and P.R. Sanunders, (Ed's), "Animal Toxins. First International Symposium on Animal Toxins," Pergamon Press, New York, 1966.

(26) Bucherl, W. and E.E. Buckley, "Venomous Animals and Their Venoms," *in* "Venomous Invertebrates," Vol. III, Academic Press, New York, 1971.

## 22. Normal Horse Serum

*Generic Statement*

Normal Horse Serum, a 1:10 dilution of sterile unfractionated normal horse serum is employed in human use as a test antigen to determine the presence or absence of horse serum sensitivity of potential recipients of other injectable products derived from horse serum. Normal Horse Serum is provided as a test antigen with some of these products particularly the antivenins. The details of sensitivity testing procedures are specified in the labeling provided with the individual products. Both conjunctival and skin tests are described.

This test antigen is provided as normal unfractionated horse serum, whereas most horse serum therapeutic products are gamma globulin fractions of the native antibody-containing horse serum. Positive reactions are a common clinical experience in known horse serum sensitive patients. There is no evidence that normal horse serum is in any way inadequate as a test antigen for horse serum sensitivity of recipients, or that the use of the globulin fraction of normal horse serum would provide a better, more specific, more sensitive, or more reliable test antigen. Effectiveness has been demonstrated by the patients' responses to the subsequently administered horse serum products.

The product labeling does not contain warning statements with regard to the interpretation of conjunctival tests, particularly in children. Unless the person being tested by this method is watched continuously during the entire period of the test and irritation by rubbing of the eye is prevented, test results may be falsely interpreted as positive, particularly by inexperienced observers. This problem is most significant in children who tend to react to the instillation of anything into the eyes by rubbing them. This may delay or possibly prevent a therapeutic administration of a horse serum product. Also, severe conjunctivitis can be produced in hypersensitive people by the test. Informed opinion generally indicates that horse serum products should rarely if ever be injected without prior performance of a skin test. Thus the utility of the conjunctival test is low. At most, it may provide confirmation by a less sensitive means of the results of the skin testing procedure which provides a significantly better method of objective evaluation and control.

*Recommendations.* This material is safe, effective, and necessary for the sefe therapeutic use of horse serum products. Normal Horse Serum should be placed in Category I.

Labeling for horse serum products should call attention to the limitations of conjunctival tests if they are to be mentioned and should require performance of an appropriate skin test with Normal Horse Serum or the horse serum product itself prior to therapeutic administration of any horse serum based product, as noted in the discussions of the antivenins.

**23. Blood Group Substances, A, B, and AB**

*Generic Statement*

Review of Products Manufactured by Armour Pharmaceutical Co. and Pfizer, Inc.

1. *Introduction.* The blood group characteristics of red cells are inherited by Mendelian laws and are almost always constant throughout life. The ABO blood groups are defined by the presence or absence of antigens A and B or the red cell surface and the reciprocal presence or absence of two antibodies, anti-A and anti-B, which occur in the plasma when the corresponding antigen is mission. Blood group A and B antigenic substances are not confined to the red cell; they occur on the cell surfaces of probably all endothelial cells and of many epithelial cells. Substances capable of inhibiting either anti-A or anti-B activity are also found in water soluble form in body secretions. The ability to secrete or not secrete these materials is inherited in Mendelian fashion. Secretions such as saliva, gastric juice, seminal fluid, urine, and meconium, as well as pathological secretions, e.g., ovarian cyst fluid, contain A and/or B substance on the basis of this genetic mechanism. Horse and swine gastric secretions, and the mucosae from which they are derived, contain polysaccharide substances which are immunochemically almost identical to the A and B substances of human origin. Indeed, A and B-like substances are widely distributed in nature.

a. *Isolation.* These materials are usually extracted from pepsindigested horse or swine gastric material using cold 95-percent phenol followed by ethanol precipitation. Normally, several successive extraction-precipitation cycles are employed. Sometimes, further precipitation is accomplished with saturated ammonium sulfate at 60° C and even further purification can be performed using column chromatography.

b. *Chemistry.* The blood group substances derived in this way are macromolecules, classified as glycopeptides with molecular weights ranging from $2 \times 10^5$ to several million daltons. Approximately 85 percent of the weight of these molecules is carbohydrate. Both the A and B substances contain the five sugars, L-fucose, D-galactose, *N*-acetyl-D-glucosamine, *N*-acetyl-D-galactosamine and *N*-acetylneuraminic acid.

c. *Immunological characteristics.* Because of their marked immunochemical similarity to human blood group substances, porcine blood group substance A can be used to stimulate anti-A production in blood group B or O individuals and equine blood group substance B can be used to stimulate anti-B antibodies in blood group A or O individuals. Equine blood group substance B preparations usually also contain measurable quantities of blood group substance A activity.

2. *Uses.* The present principal use of blood group substances A and B is for the in vivo stimulation of anti-A and/or anti-B antibodies in donors whose plasma is to be used for the preparation of diagnostic anti-A and/or anti-B reagents. Former uses of A and B substances were for specific neutralization of anti-A or anti-B antibodies in vitro for out-of-group blood transfusions, and for in vitro neutralization of unwanted anti-A or anti-B antibodies in the preparation of anti-Rh and other similar diagnostic reagents. These are no longer valid uses for the licensed biological blood group substance products.

When blood group substances A and/or B were used to neutralize A and/or B antibodies in Group O blood transfusions given to A, B, or AB recipients, 3-, 10-, or 25-mg doses were ordinarily employed. Between 1956 and the general discontinuation of this use in 1965 and last manufacture in 1969, approximately 100,000 3-mg doses were estimated to have been distributed by one firm for administration to recipients by this route without record of adverse effects (Ref. 5). Blood group substance products, not subject to licensure as biological drugs, are currently sold for use in anti-A or B neutralization steps in the in vitro processing of diagnostic reagents.

3. *Potency.* Licensed materials must have a potency sufficient to neutralize specifically anti-A or anti-B antibodies in vitro as outlined in the procedure in Ref. 8.

Although it was originally thought that differences between naturally occurring and hyperimmune anti-A or B antibodies could be discerned by their patterns of absorption or neutralization by soluble blood group substances, this no longer appears to be the case. Licensed blood group substance products must, however, satisfactorily meet arbitrary minimum potency test requirements. This test determines their immunologic reactivity on the basis of their capacity to inhibit the agglutination of group A red blood cells by anti-A or group B red blood cells by anti-B. In the future, test methods for licensed blood group substances may be developed wherein the products will be compared to reference standards which have been selected to meet the defined conditions.

4. *Safety and effectiveness.* Between 1967 and 1970, 117 donors received A, B, or AB substances for immune stimulation; 25 were successfully stimulated, of whom 17 were strong responders. There was no mention of any adverse reaction (Ref. 4).

In a review (Ref. 5) of 341 immunized subjects the following was observed:

One subject had slight fever with pain at the injection site; two of 219 subjects had mild systemic reactions following the injection; one subject had a nonfatal anaphylaxis.

In general, there were no significant reactions in subjects receiving 30 mg of A or B substance. The manufacturer estimated that a few thousand persons are deliberately immunized each year.

Until early 1977 when the Bureau of Biologics published immunization guidelines, two or three subcutaneous injections of 1- to 3-mg doses were often given at intervals ranging from 2 to 4 weeks (Ref. 7). Approximately 15 percent of the immunized subjects responded with insignificantly elevated isoagglutinin titers. Minor side effects, such as cutaneous wheal reactions, occurred in 1.8 to 3.6 percent of these subjects and were easily treated with an antihistamine.

TABLE 1.—ANTIBODY STIMULATION BY BLOOD GROUP SPECIFIC SUBSTANCES (REF. 5)

| Site | Stimulus used | Route of admin. | Number of subjects | Percent satisfactory response | Percent minor side effects | Source of stimulating substance |
|---|---|---|---|---|---|---|
| Knickerbocker Laboratories | A | IM | 1,000 | 15 | 1.8-3.6 | Pfizer |
| Bio-Lab, Inc. | A, B | IM | 673 | 58 | 3 | Matrix |
| Plasma Derivatives | B | IM,SC | 25 | 82 | 4 | Other |

More recent data indicate that a relatively high proportion of subjects will make adequate immune responses if they are not immunized too frequently.

Armour Pharmaceutical Company in studies cited below (Ref. 4) required an eight-fold increase of anti-A or B titer above baseline or a response titer equal to or greater than 1/256 as a definition of an acceptable immune response.

In one study, Armour's objective was to elicit increased anti-A production

using 1 mg/mL intramuscular injections of blood group substance A into group B subjects. Of 89 recipients, 32 of whom were lost to followup, 63 percent had good responses. The rest yielded unacceptable titers even with a second injection given on the third to eleventh day. Of these subjects, 19 had been previously immunized (mean of 22 months earlier; range 6 to 32 months earlier). Thirty-eight subjects had had no prior immunization. Evaluation of subgroup responses within this study revealed the following:

a. Subjects with no prior immunization who were given one injection yielded 100-percent acceptable responses.

b. Subjects with no prior immunization who were given two injections yielded 88-percent acceptable responses.

c. Subjects with prior immunization who were given one more injection yielded 50-percent acceptable responses.

d. Subjects with prior immunization who were given two more injections yielded only 23-percent acceptable responses.

These data indicate that there was no improvement in responsiveness following two closely spaced injections of blood group substances and that the best responses occurred in subjects who had no prior immunization.

In a parallel study by the Armour Company designed to elicit increased anti-B production in group A subjects, a 0.9-mg intramuscular injection was preceded 2 to 21 days earlier by a 0.1-mg intradermal test injection. Of 97 recipients in this study, 29 of whom were lost to followup, 64 percent had acceptable responses.

The subgroup responses were as follows: In all instances the first does was 0.1 mg. When the second 0.9-mg dose was given 2 to 3 days later, 81 percent of the subjects had an acceptable response. If the second injection was given 4 days later, 52 percent had acceptable responses, and if it was given 5 to 21 days later, only 32 percent had an acceptable response.

These data suggest that waiting for more than 3 days between the skin test and the intended immunization caused the skin test dose to interfere with the response to intramuscular immunization.

In another pair of studies by Armour using A and B blood group substances for immunization of group O subjects, 1 mg of each substance was given in divided doses, both on the same day (0.1-mg intradermal plus 0.9-mg intramuscular) to a group of recipients with no prior immunization with these antigens. In 55 group O subjects, with 15 lost to followup, there were 75 percent who had good responses with anti-A. With anti-B, with 14 subjects lost to followup, there were 68 percent who had good responses. In a second similar study these responses in group O subjects were observed: With anti-A, of 51 subjects with 13 lost to followup, 78 percent had good responses; with anti-B, of 51 subjects with 14 lost to followup, 56 percent had good responses. In these studies, there were no adverse reactions noted except for occasional pain and swelling at the injection site.

From these studies, it appears that blood group substances A and B can elicit simultaneous anti-A and anti-B responses in group O subjects. Blood group substance A appears to be slightly more immunogenic than substance B. Both products are relatively safe.

Other data from Ortho Diagnostics, for a recently licensed product not subject to this review, further indicates the safety and effectiveness of these substances in stimulating anti-A and anti-B antibodies (Ref. 6).

Some data also exist about the use of A, B, or AB substance in vivo for neutralization of anti-A and B antibodies in factor VIII concentrate preparations. This is not an indication in the labeling of these products. Although significant hemolysis is recognized when large amounts of factor VIII materials (wet and/or dry) are administered, only anecdotal data are available about the effectiveness and safety of in vivo use of A and B substance to prevent such hemolysis. Preliminary observations have revealed that the substances can be mixed with factor VIII preparations in vitro given to reduce or eliminate in vivo hemolysis without observed adverse reactions (Ref. 7).

5. *Label analysis.* Pfizer, Inc., made no request to update labels, nor has it submitted any product lots for release for several years. Their production is, therefore, essentially defunct and their labeling is obsolete. Their labels have no clear information on actual dosage, side effects, precautions (such as asepsis), contraindications (regarding allergy in general or specifically regarding equine or porcine proteins), or warning regarding use in female subjects for in vivo stimulation.

The newly submitted labeling of Ortho Diagnostics, Inc., and Armour Pharmaceutical Co. is acceptable.

6. *Benefit/risk evaluation.* Side effects are so infrequent that despite varying rates of successful stimulation of anti-A or B antibodies, blood group specific substances for this purpose should continue.

7. *Recommendations.* a. The products should be placed in Category I on a generic basis. The product made by Armour should be placed in Category I. Pfizer's product should be placed in Category IIIB because of obsolete labeling and because no current effectiveness data are available.

b. Bureau of Biologics guidelines and manufacturer's labeling should indicate that reimmunization of subjects within less than a year is likely to result in little or no response.

c. Further studies for other uses are recommended. Although Cryoprecipitated Antihemophilic Factor redissolved in saline solution and antihemophilic factor concentrate can be administered, at least in moderate quantities, without regard to the blood group of the recipient, under some circumstances a hemolytic state is induced. This reaction can be managed by administration of group specific cryoprecipitated antihemophilic factor, but at times this is not practical. The use of A and B substance to neutralize the residual anti-A and/or anti-B content of pooled cryoprecipitated antihemophilic factor and antihemophilic factor concentrate should be investigated as an approach to this problem.

**References**

(1) Weiner, A.S., "Advances in Blood Grouping," Volume III, Grune and Stratton, New York, 1970.

(2) Race, R.R. and R. Sanger, *"Blood Groups in Man,"* 5th Edition, Blackwell Scientific Publications, Oxford, 1968.

(3) Watkins, W.M., "Blood Group Substances—Their Nature and Genetics," *in* "The Red Blood Cell," Chapter 7, edited by Bishop, C. and D.M. Surgenor, 2d Edition, Academic Press, New York, pp. 293–362, 1964.

(4) BER Volume 6074.

(5) BER Volume 6092.

(6) BER Volume 6143.

(7) "Unsolved Therapeutic Problems in Hemophilia," Proceedings of a Conference, March 1–2, 1976, DHEW Publication No. (NIH) 77–1089 (Superintendent of Documents, U.S. Government Printing Office Stock No. 017–043–00071–4).

(8) Minimum Requirements: Blood Group Specific Substances A and B, U.S. Department of Health, Education, and Welfare, Public Health Service, National Institutes of Health, Division of Biologics Standards, Bethesda, Maryland, 1st revision, July 14, 1954 (Copy in BER Volume 6145).

### 24. Cobra Venom Products

**Generic Statement**

Cobra venom is obtained from mature cobra snakes (Naja naja). Lyophilized venom is subsequently fractionated, reduced to a powder, and later reconstituted as cobra venom solution. It was marketed by Hynson, Westcott &

Dunning, Inc., Baltimore, MD, as "Cobroxin"™ and in combination with Silicic and Formic Acids as "Nyloxin"™. The beneficial effects claimed from its parenteral administration is the alleviation of intractable pain.

Three main activities of cobra venom fractions are recognized: the hemolytic factor (phosphatidases); the proteolytic factor (proteases); and the neurotoxic factor (neurotoxins). The fractionation procedures for obtaining the cobra venom product were designed to eliminate the hemolytic and proteolytic factors but to retain the neurotoxic factor. Cobra venom solution is reported to have no effect on hepatic and renal function or blood clotting. It has no addictive properties and does not cause gastrointestinal dysfunction.

Most of the published reports on the use of cobra venom appeared during 1930 to 1945 (Refs. 1 through 33). The pain treated was associated mainly with malignant conditions or was secondary to various manifestations of arthritis. Cobra venom has also been suggested for the relief of pain associated with chronic angina, vascular crises, migraine headaches, and neuroses. Relief of pain in malignant diseases has been reported in as high as 60 to 70 percent of patients so treated. Cobra venom has been mentioned in a few subsequent reports (Refs. 34 through 46), but the Panel has found only one published report relative to human use in the last 10 years (Ref. 47).

Cobra venom solution was first marketed in 1952, but has not been advertised to the medical profession following 1957. Only a few thousand ampules were marketed each year.

1. *Evidence of effectiveness.* There have been no placebo-controlled or double-blind studies of pain relief with the cobra venom products; thus there is only anecdotal evidence of effectiveness. In the latest report (Ref. 47) only 5- to 10-percent effectiveness is claimed and then only after a trial period of 4 to 6 weeks.

2. *Evidence of safety.* Occasional severe vomiting or abdominal cramps have been reported (Refs. 21, 34 and 35). Other reactions observed most frequently are hives, diplopia, and dizziness. Cobra venom solution must be administered by deep intramuscular injection to prevent skin and subcutaneous reactions. The only contraindication to the use of cobra venom solution cited in the literature is its use in the presence of acute or chronic respiratory infection (Refs. 25 and 34).

3. *Benefit/risk evaluation.* There appears to be little substantiated benefit and no known serious risk. If any therapeutic effect from cobra venom solution can be demonstrated by appropriate studies then it may be of value in an attempt to reduce narcotic addiction in chronic pain.

4. *Recommendations.* It is recommended that Cobra Venom Solution and Cobra Venom with Silicic and Formic Acids (Cobroxin and Nyloxin) be placed in Category IIIB. During the Panel deliberations, the licenses were voluntarily withdrawn by the manufacturer on May 17, 1978 for Nyloxin and September 30, 1979 for Cobroxin.

**References**


(1) Macht, D.I., "Comparison of Cobra Venom and Morphine as Analgesics," *American Physician*, 116:1–9, 1936.

(2) Macht, D.I., "Experimental and Clinical Study of Cobra Venom as an Analgesic," *Proceedings of the National Academy of Sciences*, 22:61–71, 1936.

(3) Macht, D.I., "Therapeutic Uses of Snake Venom," *Medical Record*, 116:537–539, 1936.

(4) Macht, D.I., "Therapeutic Experiences with Cobra Venom," *Annals of Internal Medicine*, 11:1824–1833, 1938.

(5) Gayle, R.F., Jr. and J.N. Williams, "The Symptomatic Treatment of the Parkinsonian Syndrome with Cobra Venom," *Southern Medical Journal*, 31:188–192, 1938.

(6) Macht, D.I., "Comparative Effect of Cobra Venom and Morphine on Some Psychological Reactions," *The Medical Press and Circular*, 201:254–257, 1939.

(7) "Glutathione—Antitoxic Action of," *Pharmaceutical Abstracts*, American Pharmaceutical Association, Vol. 5, July 1939.

(8) Rutherford, R.N., "The Use of Cobra Venom in the Relief of Intractable Pain," *New England Journal of Medicine*, 221:408–413, 1939.

(9) Macht, D.I. and D.J. Brooks, "Prolonged Administration of Cobra Venom in Relation to Kidney and Liver Function," *Proceedings of the Society for Experimental Biology & Medicine*, 41:418–421, 1939.

(10) Macht, D.I., "New Developments in the Pharmacology and Therapeutics of Cobra Venom," *Transactions of the American Therapeutic Society*, 40:1–8, 1940.

(11) Steinbrocker, O., G.C. McEachern, E.P. LaMotta and F. Brooks, "Experience with Cobra Venom in the Arthralgias and Related Conditions," *Journal of the American Medical Association*, 114:318–322, 1940.

(12) Black, W.T., Jr., "Cobra Venom for the Relief of Pain," *Southern Medical Journal*, 33:432–437, 1940.

(13) Draper, P.A., "The Therapy of the Parkinsonian Syndrome," *Rocky Mountain Medical Journal*, 37:272–277, 1940.

(14) Treves, N., "Recent Therapeutic Measures to Control Pain in Cases of Incurable Cancer," *Medical Clinics of North America*, 24:595–602, 1940.

(15) Macht, D.I. and M.B. Macht, "Quantitative Studies on Pain Threshold After Administration of Various Drugs," *Journal of the American Pharmaceutical Association*, 29:193–199, 1940.

(16) Hayman, M. and D.I. Macht, "Clinical and Biochemical Studies in Cobra Venom Therapy," *Medical Record*, 152:67–69, 1940.

(17) Thomas, L., "A Clinical Experience with Cobra Venom in Migraine Headaches," *Medical Record*, pp. 109–110, August 7, 1940.

(18) Parsonnet, A.E. and A. Bernstein, "Cobra Venom—Its Use in Stenocardia," *American Journal of the Medical Sciences*, 200:581–586, 1940.

(19) Behan, R.J., "The Treatment of Intractable Pain," *American Journal of Surgery*, 50:450–473, 1940.

(20) Greenhill, J.P., "Control of Pain in Cases of Cancer," *Medical Clinics of North America*, 25:117–128, 1941.

(21) Drueck, C.J., "Cobra Venom and Opiates in the Pain of Cancer of the Rectum," *The Medical World*, 59:20–22, 1941.

(22) Lee, L.E., Jr., "Medication in the Control of Pain in Terminal Cancer," *Journal of the American Medical Association*, 116:216–220, 1941.

(23) McDowell, M.M., "The Use of Cobra Venom for the Relief in Herpes Zoster," *Medical Record*, pp. 173–174, March 5, 1941.

(24) Poole, W.B., "The Use of Cobra Venom for the Relief of Intractable Pain," *Medical Record*, 153:287–292, 1941.

(25) Craig, P.E. "The Cobra Strikes at Pain (Analgesia with Cobra Venom)," *Clinical Medicine*, 48:184–186, 1941.

(26) Macht, D.I., "Recent Developments in the Pharmacology and Therapeutics of Cobra Venom," *Medical Record*, 153:369–379, 1941.

(27) Craig, P.E., "Cobra Venom Analgesia in Surgery," *Journal of the Kansas Medical Society*, 42:289–292, 1941.

(28) Hanson, K., "The Use of Cobra Venom and Oxygen in the Control of Cardiac Pain," *Journal of the Florida Medical Association*, 28:381–383, 1942.

(29) Taylor, F.R., "The Use of Cobra Venom in the Treatment of Osteitis Deformans," *North Carolina Medical Journal*, pp. 244–245, May 1942.

(30) Talkov, R.H., and W. Bauer, "The Failure of Cobra Venom to Relieve Pain in Rheumatoid Arthritis," *New England Journal of Medicine*, 228:152–154, 1943.

(31) Albee, F.H. and E. Maier, "A Preliminary Report on the Use of Venom in Arthritis," *Medical Record*, pp. 217–221, April 1943.

(32) Wright, H.P., "Rheumatoid Arthritis," *Current Medical Dialog*, March 1945.

(33) Freedberg, A.S. and J.E.F. Riseman, "Cobra Venom in the Treatment of Angina Pectoris," *New England Journal of Medicine*, 233:462–466, 1945.

(34) Comfort, D.M., "Cobra Venom in the Relief of Pain," *Bulletin of the Norwood Clinic*, 7:89–93, 1952.

(35) Hills, R.G. and W.M. Firor, "The Use of More Potent Cobra Venom for Intractable Pain," *American Surgeon*, 18:875–879, 1952.

(36) Porges, N., "Snake Venoms, Their Biochemistry and Mode of Action," *Science*, 117:47–51, 1953.

(37) Taren, J.A., "A Clinical Evaluation of Cobra Venom Extracts for Control of Pain," *University of Michigan Medical Bulletin*, 19:206–211, 1953.

(38) Wylie, P., "Will Snake Venoms Stop Polio"? *This Week Magazine*, November 29, 1953.

(39) Jackman, A.L., "Cobra Venom Therapy with Neuroses," *Diseases of the Nervous System*, 15:99–102, 1954.

(40) Bryson, K.D., "The Treatment of Chronic Arthritis with a Combination of Cobra Venom, Formic Acid, and Silicic Acid," *American Surgeon*, 20:751–755, 1954.

(41) Lumpkin, W.R. and W.M. Firor, "Evaluation of the Bryson Treatment of Arthritis," *American Surgeon*, 200:756–759, 1954."

(42) Balfour-Lynn, S., "Treatment of Chronic Osteo-Arthritis with Cobra Venom, Formic Acid and Silicic Acid (Letter to the Editor)," *Lancet*, 1266–1267, December 15, 1956.

(43) Meiselas, L.E. and A.A. Schlecker, *New Effect of Nyloxin on the Pain of Arthritis," New York State Journal of Medicine*, 2067–2068, June 15, 1957.

(44) Singh, I. and M.C. Srivastava, "Anti-Asthmatic Effects of Immunization with Cobra Venom," *British Journal of Diseases of the Chest*, 62:107–109, 1968.

(45) Bartels, E. and P. Rosenberg, "Correlation Between Electrical Activity and Splitting of Phospholipids, *Neurochemistry*, 19:1251–1265, 1972.

(46) Panel Report "Lick Granuloma," Dr. N.K. Adams, "Has Used Cobra Venom," *Modern Veterinary Practice*, 55:139 and 145, 1974.

(47) Beckner, T.F. and P. Idsvoog, "Drug Use and Distribution in a Pain Rehabilitation Center," *American Journal of Hospital Pharmacy*, 32:285–289, 1975.

### 25. Human Plasma as a Source for Fractionation Products

1. *Plasma as a source for fractionation products.* Human plasma is the source material for albumin, plasma protein fraction, immunoglobulins, factor VIII concentrate, factor IX complex, and blood grouping reagents. The major clinically useful plasma fractions that were prepared when human blood was collected in glass bottles were albumin and gamma globulin (Ref. 1). Since these products are relatively stable on storage, it was possible to salvage plasma from whole blood stored at refrigerator temperatures for 21 days. Although the red cells are no longer suitable for use, the recovered plasma can be used as a source of derivatives such as albumin and gamma globulin.

When blood is collected in glass bottles, the container must be entered to remove the plasma following centrifugation of the bottle or sedimentation of the blood. Because of the potential danger of bacterial contamination, the remaining red cells must be used within 24 hours or discarded. The basic criteria for donor selection when collecting blood in glass bottles are the same as for whole blood to be used for transfusion purposes. The limiting factor for frequency of donation by this procedure is the donor's ability to regenerate red blood cells and maintain iron stores.

As methods were developed for preparation of the labile coagulation product, factor VIII (antihemophilic factor, AHF), it became necessary to freeze the plasma within a few hours after collection of blood from the donor (Refs. 2 and 3). Plasma salvaged from whole blood stored at refrigerator temperatures for more than 4 to 6 hours is not suitable as a starting material for preparation of factor VIII because of the attendant loss of activity (Ref. 4). If AHF concentrates are to be prepared, it is now the usual practice to use only plasma frozen while fresh and stored at −20° C or lower.

2. *Plasmapheresis.* Plasmapheresis is a procedure whereby plasma is removed from whole blood and the cells are returned to the donor as an autotransfusion. The technique had been known for many years (Ref. 5), but with the supplies and equipment available earlier it was a cumbersome and inefficient procedure to obtain plasma. With the availability of plastic transfusion equipment it became possible to separate plasma from cells in a closed system. Thus, with little danger of contamination, it was possible to separate the plasma from whole blood and return the cells to the donor (Ref. 6).

When plasmapheresis is carried out, the donor's ability to regenerate cells and to maintain iron stores are no longer limitations on the frequency of donation of plasma. With the technique of plasmapheresis, the limitations are the volume of blood that can be removed safety from the circulation acutely and the donor's subsequent ability to restore the protein which has been removed. The amount of blood that can be removed acutely depends on the donor's blood volume, which is proportional to body size. On the basis of considerable experience with collection of whole blood, it was established that at least 450 mL of blood can be removed without jeopardizing the health of the donor. This is now the standard transfusion unit. It became general practice in plasmapheresis to collect a unit of whole blood, separate the plasma, and return the cells to the donor and then collect a second unit of blood and repeat the process. In this manner, two units of about 250 mL each of plasma can be obtained at one time. The deficit in the donor's circulating blood volume is promptly restored by a shift of fluid from the interstitial space as well as by fluids administered during the blood collection and the autotransfusion of the cells. Since there are approximately 6 g/dL of plasma proteins, the collection of 500 mL of plasma represents a loss of approximately 30 g of protein with each such procedure.

3. *Donor safety considerations.* The frequency with which plasmapheresis donations can be made without jeopardizing the donor's health depends on the rate at which the lost proteins can be resynthesized. During intensive plasmapheresis over a short period of time in which 5 liters of plasma were removed in 5 days, normal donors replaced up to 49 grams of protein per day (Ref. 7). Protein loss in excess of this amount was reflected in a decrease in the total serum protein (Ref. 7). Two to 4 weeks were required for total serum protein and albumin to return to normal levels after this procedure, but 1 to 3 months were required for the gamma globulins to return to normal levels (Ref. 7).

Of the several different plasma proteins, albumin has been studied more extensively. Even for albumin, there are many unanswered questions regarding its homeostasis in health and disease (Ref. 8). It is apparent that the amount of albumin in the plasma represents only about half of the total body albumin pool. The remainder is in interstitial fluids. Following loss of plasma there is a shift of this albumin into the circulating plasma. The plasma protein level is promptly restored toward normal following the completion of a plasmapheresis procedure even though there is a net loss of protein (Ref. 6). On the basis of studies done in patients that lose plasma proteins over a period of time as a result of burns, renal disease or certain gastrointestinal disorders, it is apparent that there is a limit to the body's ability to compensate for protein loss (Ref. 9). The ability to compensate depends on a number of factors including the general health of the individual and his/her nutritional status (Ref. 9). Although the clinical manifestations of overt deficiency of albumin are well recognized, the possible effects of a borderline deficiency are as yet poorly defined. The procedure to determine total serum protein is relatively simple and rapid. The procedure to determine the amounts of specific plasma proteins is more complex. It is generally considered that, as long as the plasmapheresis donor is able to maintain total plasma proteins at established normal levels, the protein loss being incurred is not detrimental to the individual. However, there is no simple and direct way to determine the protein content of extravascular spaces so that protein reserves cannot be evaluated (Ref. 10).

There have been several retrospective studies in which accumulated data obtained from individuals participating in less intensive plasmapheresis programs have been evaluated (Refs. 11 through 13). Although these studies provide valuable information on the effects of long-term plasmapheresis on selected individuals, the primary objective was to obtain plasma and not to test the safety of the procedure. Because of the nature of the studies, it is inevitable that those who tolerate the procedure best will elect to continue, while those who do not tolerate the procedure may elect to withdraw from the program voluntarily. In those individuals who participate as plasmapheresis donors for only a short while, it is not clear whether they withdraw because of adverse changes in their health or for some other reason. However, the studies do indicate that as a selected group, plasmapheresis donors can maintain normal plasma protein levels while losing up to 1,000 mL of plasma, about 60 grams of protein, per week (Refs. 11 through 13).

It is of significance that even in a group of plasmapheresis donors selected because of obvious good health and robust nutritional status, changes in plasma proteins occurred (Ref. 13). During the first 4 months an increase in alpha globulins occurred, with a decrease in immunoglobulins. Thus the total protein concentration may remain constant since the decrease in immunoglobulins will be masked by the increase in alpha globulins. In individuals continuing on plasmapheresis for more than 6 months there was a trend toward levels, but the IgM level continued to decrease in those donors studied for up to 3 years.

These changes occurred in individuals that were able to maintain a total protein above 6 g/dL; and when, if there was a trend toward a significant decrease in the measured proteins, the intensity of the plasma withdrawal from these donors were decreased. Although the clinical significance of decreased immunoglobulins is not entirely clear, it is apparent that individuals participating in an intensive plasmapheresis program can become partially deficient in immunoglobulins. For the present it appears that there should be careful monitoring of each patient's immunoglobulins, particularly during the first 6 months, and if total protein, albumin, or immunoglobulin levels fall below the established normal range, the procedure should be discontinued at least until normal protein levels are reestablished.

In some studies it has been noted that enzymes such as serum glutamic oxaloacetic transaminase (SGOT) and glutamic pyruvic transaminase (SGPT) become elevated in individuals undergoing intensive plasmapheresis. These enzymes are associated with cellular activity of the liver and when present in the serum in increased amounts are considered to be an indication of hepatic dysfunction. It is not clear if this represents a physiologic response to increased demands for the synthesis of proteins or represents clinically significant impairment of hepatic function. It may be that a change in these enzymes might be an early indication of excessive protein loss. Currently available data are inconclusive on this point.

Other risks of plasmapheresis to the donor include the possibility that the wrong red cells will be returned to the donor. Thus the technique used must include a system for positive identification of the donor and donor's cells.

4. *Safety of plasma obtained by plasmapheresis.* As with all blood products there is a risk that the plasma obtained by plasmapheresis may be responsible for the transmission of hepatitis. Although the risk has been reduced by the requirement that all donors be tested for HBsAg, there is still a risk of both hepatitis B and so-called "non-A" and "non-B" hepatitis which is not detected by present tests. This risk is minimal in products that can be inactivated by heating such as albumin and plasma protein fraction. Products such as factor VIII concentrate and prothrombin complex concentrates which cannot be heated carry a major risk of transmitting hepatitis.

5. *Evaluation of plasmapheresis regulations*—a. *Medical review before repeated donations.* The protein loss resulting from removal of approximately 500 mL of plasma as currently allowed in a plasmapheresis procedure is equivalent to that occurring from the collection of a unit of whole blood. With whole blood donation there is a loss of protein in red cell hemoglobin in addition to the plasma proteins. However, the protein loss due to the donation of whole blood is not apt to be a problem because of the limitations on frequency of donation. Provided that plasmapheresis is done no more frequently than is being recommended by the Panel for donation of whole blood (four times per year) the protein loss would be of no greater consequence than that in whole blood donors. However, if plasmapheresis is done more frequently, protein abnormalities may result. To evaluate this possibility, specific plasma protein determinations must be done periodically in the more intensely plasmapheresed donors. It appears more appropriate for a qualified physician to review all the accumulated information periodically in order to evaluate whether or not an individual should continue in an intensive serial plasmapheresis program than to perform a physical examination prior to the initial plasmapheresis procedure.

b. *Total serum protein determinations.* Although there are differences of opinion regarding the clinical significance, there is adequate information to indicate that individuals undergoing plasmapheresis as allowed by the current regulations do experience changes in plasma proteins. The Panel believes that plasmapheresis should not be done unless the total serum protein determined prior to donation is within the established normal range.

c. *Specific plasma protein determinations.* A blood sample must now be obtained prior to the first plasmapheresis for determinations of specific plasma proteins. Currently, the results of such tests must be available and be found to be within normal limits within 21 days after the sample is drawn. This would allow collection of the plasma from 6,000 mL of blood prior to evaluating the specific plasma proteins. The results of these tests should be evaluated sooner to protect the donor that may have preexisting protein abnormalities.

d. *Physical examinations.* The panel considered on several occasions the requirement that each donor shall be examined by a qualified licensed physician on the day of the first donation or no more than 1 week before the first donation and at subsequent intervals of no longer than 1 year. It was noted that prior to the donation of whole blood and at subsequent plasmapheresis donations, the examination is permitted to be done by someone under the physician's direction. There are informed opinions that this requirement and the requirement for determination of specific plasma proteins will limit the participation of volunteer donors in plasmaphereses programs (Ref. 14).

e. *Donation frequency.* Current regulations allow the collection of 2,000 mL of whole blood per week. Thus it would be possible to retain approximately 52 liters of plasma per year. On the basis of anecdotal information, relatively few individuals are actually plasmapheresed for a long period of time or at the maximal rate. It appears that most individuals are plasmapheresed at the maximum

allowable rate for only a few months and then discontinue. Although some drop out because they are unable to continue to meet the requirements, there is little or no information concerning why most individuals discontinue donation.

Current regulations allow plasmapheresis to be done at the maximal rate provided that the donor maintains total serum proteins above 6 g/dL. The ability of the donor to maintain plasma protein concentrations appears to be a more important criterion for safety than the amount of plasma retained during a specific time period.

Currently, it is required that tests for specific plasma proteins be done at least every 4 months in individuals in serial plasmapheresis programs. During this period approximately 16,000 mL of plasma may be collected. Since reductions in immunoglobulins appear early, this volume appears to be excessive. It appears appropriate to base the frequency of determination of specific plasma protein levels on both time and volume of plasma collected. There is a lack of firm data on which to base a recommendation concerning the degree of donor safety provided by the current regulations for frequency of plasmapheresis and the volume of plasma that may be retained.

In order to resolve these questions, a prospective and retrospective study is needed. The objective of such a study would be to: (1) Evaluate the utility of the total serum protein measurement as an indicator of protein reserves, (2) evaluate the significance of elevations in liver enzymes such as SGOT as a reflection of developing serum protein abnormalities, and (3) determine whether or not individuals discontinuing their participation in plasmapheresis programs do so because of health reasons that are not detected by currently required tests.

f. *Serological test for syphilis.* There is no indication that the current requirement for serologic testing for syphilis protects either the plasma donor or the recipient of the products prepared from source plasma. Most of the considerations of the serological test for syphilis discussed for whole blood donors apply to plasma donors. There are no data to support the value of the serological test for syphilis in protecting the quality of the donated plasma.

g. *Plasma obtained by techniques other than plasmapheresis.* It is recognized that plasma separated from single unit donations of whole blood is also an important source of material for plasma derivatives. The requirements for donor selection, collection, and initial processing of this source of plasma are covered in the Code of Federal Regulations sections on Whole Blood and Single Donor Plasma (21 CFR Part 640). There are currently no regulations defining conditions of transportation and storage of single units of plasma intended for preparation of plasma derivatives. Some units of plasma will be separated from whole blood and frozen immediately after collection. These units are essentially the same as plasma collected by plasmapheresis. The regulations should be modified to include these recovered units of plasma to encourage their use.

Plasma separated from single units of whole blood more than 6 hours after collection are not a good source of factor VIII. However, such plasma is a useful source of other plasma derivatives and its use should be encouraged.

6. *Recommendations.* a. The requirement for serologic testing for syphilis should be discontinued.

b. Regulations should be modified to require that no more plasma than can be obtained from approximately 2,000 mL of whole blood be retained within 21 days of the first plasmapheresis procedure unless a qualified physician has evaluated all of the accumulated information, including resuts of tests for specific plasma proteins.

c. The requirement for a physician to conduct an examination prior to a donor participating in a serial plasmapheresis program should be discontinued providing adequate safeguards for the donor are developed to allow other trained personnel to screen the donor for acceptability.

d. Regulations should be modified to require the testing for specific plasma proteins at least every 4 months or following the collection of 12,000 mL of whole blood (approximately 6,000 mL of plasma), whichever comes first. In order for an individual to continue as a plasmapheresis donor, the results must be evaluated by a qualified licensed physician and be determined to be within the established normal range.

e. Regulations should be promulgated to permit an individual donor to participate in a single plasmapheresis procedure in lieu of a single donation of whole blood, abiding by the rules governing donor qualification and the frequency of whole blood donations and providing that the total plasma protein level is determined as is presently done for each plasmapheresis procedure. Such donors should be excluded from participation in any plasmapherisis program in which more frequent plasmaphereses are permitted unless physical examination, specific protein determinations, and other donor requirements of 21 CFR Part 640, Subpart G, are met upon the second visit in any 3-month period. Furthermore, all donors engaged in plasmapheresis more frequent than 4 times per year (every 3 months) shall be excluded as donors of whole blood unless at the time of blood donation the person is examined and certified by a physician to be in good health. Written informed consent should be required from each plasmapherisis donor after the hazards of the procedure are explained to the prospective donor by a qualified person.

f. A prospective and retrosspective study should be done to determine the health effects on the donor participating in serial plasmapheresis as it is currently permitted. Such a study is necessary to determine whether or not existing requirements in regard to amount and frequency are appropriate.

g. Regulations should be promulgated to encourage the utilization of single donor plasma recovered from whole blood collections as a source of plasma for fractionation.

**References**

(1) Palmer, J.W., "The Evaluation of Large Scale Human Plasma Fractionation in the United States," *in* "Proceedings of the Workshop of Albumin," DHEW Publication No. (HIH) 76-925, pp. 255-269, 1975.

(2) Pool, J.G. and A.E. Shannon, "Production of High Potency Concentrates of Antihemophilic Globulin in a Closed-Bag System," *The New England Journal of Medicine*, 273:1443-1447, 1965.

(3) Webster W.P., H.R. Roberts, G.M. Thelin, R.H. Wagner and K.M. Brinkhous, "Clinical Use of a New Glycine-Precipitated Antihemophilic Fraction," *American Journal of the Midical Sciences*, 250:643-651, 1965.

(4) Slichter, S.J., R.B. Counts, R. Henderson and L.A. Harker, "Preparation of Cryoprecipitated Factor VIII Concentrates," *Transfusion*, 16:616-626, 1976.

(5) Abel, J.J., L.G. Rowntree and B.B. Turner, "Plasma Removal with Return of Corpuscles," *Journal of Pharmacology and Experimental Therapeutics*, 5:625-641, 1914.

(6) Kliman, A. and M.F. Lesses, "Plasmapheresis as a Form of Blood Donation," *Transfusion*, 4:469-472, 1964.

(7) Kliman, A., P.P. Carbone, L.A. Gaydos and E.J. Freireich, "Effects of Intensive Plasmapheresis on Normal Blood Donors," *Blood*, 23:647-656, 1964.

(8) Rosenoer, V.M., "Albumin Distribution," *in* "Proceedings of the Workshop on Albumin," DHEW Publication No. (NIH) 76-925, pp. 75-90, 1975.

(9) Rothschild, M.A., M. Oratz and S.S. Schreiber, "Albumin Synthesis and Albumin Degradation," *in* "Proceedings of the Workshop on Albumin," DHEW Publication No. (NIH) 76-925, pp. 57-74, 1975.

(10) Granger, H.J., J. Dhar and H.I. Chen, "Structure and Function of the Interstitium," *in* "Proceedings of the Workshop on

Albumin," DHEW Publication No. (NIH) 76-925, pp. 114-125, 1975.
(11) Cohen, M.A. and H.A. Oberman, "Safety and Long-Term Effects of Plasmapheresis," *Transfusion*, 10:58-66, 1970.
(12) Shanbrom, E., R. Lundak and R.L. Walford, "Long-term Plasmapheresis Effects on Specific Plasma Proteins," *Transfusion*, 12:162-167, 1972.
(13) Friedman, B.A., M.A. Schork, J.L. Mocniak and H.A. Oberman, "Short-Term and Long-Term Effects of Plasmapheresis on Serum Proteins and Immunoglobulins," *Transfusion*, 15:467-472, 1975.
(14) Bayer, W.L., Correspondence, BER Volume 6144.

**26. Donor Immunization and Hyperimmunization**

Human donors of blood components serve as the resource for several materials used to prepare products reviewed by the Panel. Many of these donors are subjected to immunization or hyperimmunization procedures to produce materials with higher antibody levels. Therefore, the Panel reviewed these techniques which are similar for several products.

1. *Immunization with blood group antigens.* The initial studies which demonstrated the red blood cell antigens of the ABO system were done with sera from humans. Since that time human serum has been the primary source of reagents to identify human red blood cell antigens. As a result of blood transfusion or pregnancy, individuals are exposed to antigens not present on their own red cells and may produce alloantibodies active against the foreign antigens. Although a blood transfusion will introduce a number of foreign red cell antigens, the antibody response is not alway predictable. The antigens may be poor immunogens and produce no detectable antibody response. One of the antigens may be particularly immunogenic, and the only detectable response will be an antibody that is specific for that antigen. More than one of the antigens may be immunogenic and result in formation of multiple antibodies that react with more than one type of antigen. Sera containing antibodies which are reactive with more than one antigen may not be suitable for processing into reagents. The desired immune response in respect to an antiserum for reagent purposes is to elicit a potent antibody which is reactive with a single antigen.

The initially available blood-grouping reagents were obtained from the plasma of individuals that had developed antibodies as a result of pregnancy of the transfusion of blood. In general the amount of antibody available from an individual donor decreases with time following exposure to the antigenic material. It was found that more potent antisera could be obtained by reexposing these antibody-producing individuals to the antigenic stimulus. Red blood cells of known antigenic composition are used for these immunizations. Red blood cells are not ideal antigens since they contain a number of different antigens, each of which may be immunogenic and may elicit an antibody response. Thus in an attempt to increase the amount of one antibody, a second antibody may be produced. To minimize this possibility it is necessary to identify the antigens of both the red cells to be injected and the individual being immunized.

Current guidelines indicate that all donors and recipients shall be phenotyped for C, D, E, c, e, Kell and $Fy^a$. Except for the specific blood group antigen intended to stimulate antibody response, the donor and recipient phenotypes for the above listed blood group antigens should be identical. Since these factors are relatively highly antigenic, matching for all but the desired antigen will reduce the incidence of second antibody responses which make the plasma donor useless. Although more extensive phenotyping and matching is desirable, it is not presently required.

a. *Blood Group A and B antigens.* The ABO system must be considered separately form the point of view of donor immunization since immunogenic materials with A and B specificities are widely present in the environment; thus antibodies develop "naturally" because immunization followed by antibody response occurs spontaneously without deliberate exposure to antigenic materials by blood transfusion. Thus, with rear exceptions, individuals lacking the A antigen on their red blood cells have anti-A antibodies in their plasma and individuals lacking the B antigen on their red blood cells have anti-B. Substances which function like the red blood cell antigens A and B also can be obtained from varous nonhuman sources (see the section on Blood Group Substances A and B). These A and B substances are used to stimulate the production of anti-A or anti-B antibodies in selected individuals. Most of the problems related to the use of human red blood cells as antigens are thus avoided.

b. *$Rh_o$*(D) antigen. When it was found that Rh immune globulin was effective in prevention of sensitization of Rh-negative women by the $Rh_o$(D) antigen, the need for human plasma containing anti-D antibody increased. In order to obtain this antibody in sufficient quantities to meet the apparent need for prophylaxis, it became common practice to immunize selected Rh-negative individuals intentionally with red blood cells containing the D antigen. It was rationalized that the presence of a blood group specific antibody such an anti-D is of no immediate harm to a male. The potential danger to a male is that if the individual requires a blood transfusion, it would be essential that only Rh-negative blood be used. It is assumed that there would be no problem in locating the required blood since donor blood is routinely tested for the presence of $Rh_o$ (D), and approximately 15 percent of the population are Rh-negative. The donor-recipient cross match test for compatibility provides another safeguard. For obvious reasons it is not appropriate to stimulate anti-D antibody formation in women who are potentially childbearing.

Current guidelines allow immunization of Rh-negative men with $Rh_o$(D) cells provided the protocol is filed with the Director, Bureau of Biologics. The maximum volume of red blood cells used shall not exceed 50 mL within any 4-month period. Subjects not responding after receiving a total of 150 mL of red blood cells shall be dropped from the program. Smaller volumes of red blood cells have been shown to elicit an antibody response in some individuals. However, these volumes may be too low to elicit the desired antibody response in those now being exposed. The dosage schedule should be based on the minimal red cell exposure that will produce the maximum results most often in the exposed individuals. The Panel feels that since intentional immunization to produce anti-D has been done for a number of years, the most effective dose schedule could be derived from the existing records of the manufacturers. This supposedly proprietary information was not submitted by the various manufacturers.

C. *Donor/recipient selection and safety.* It is required that all donor blood be tested for A, B, and D antigens. Thus there is a great demand for reagents to test for those antigens. The use of reagents for other red blood cell antigens is more limited. However, there is a need for reagents to identify other red blood cell antigens in order to provide compatible blood in certain problem situations. To obtain these reagents, it is common practice to obtain plasma from individuals that already have a demonstrable antibody. It is rationalized that once an antibody has developed there is little additional danger in stimulating that individual with an appropriate antigen.

Since production of antibody of more than one specificity is undesirable,

identification of the antigenic characteristics of the red blood cells of both the recipient and the donor is essential. In spite of careful selection of the cells to be injected, there remains a possibility that additional antibodies may be produced. It is not practical to remove the unwanted antibodies and thus modify the specificity of the sera. Therefore, when multiple antibodies are produced by a donor of antibody, the recipient individual is exposed to all the risks of immunization but would receive none of the monetary benefits contingent upon becoming a donor. In essence, the immunization procedure is a series of blood transfusions of variable, usually small size. The risks to the recipient are the same as those of a blood transfusion given for therapeutic purposes.

Since red blood cells are used for the immunogenic material, the recipient is exposed to the risk of hepatitis. At the present time it is not possible to eliminate this risk. However, by carefully monitoring the donors and recipients and limiting the number of individuals used as red cell donors, the risk can be minimized. In some programs of immunization of donors, the red cells from some donors have been used to immunize a number of different individuals. As no evidence of hepatitis has been detected in the recipients, this would indicate that it is unlikely that the donor bloods have been transmitting hepatitis. However, the fact that the donor blood was not responsible for transmission of hepatitis in the past cannot be taken to mean that the donor cannot transmit hepatitis in the future if he unknowingly acquires an infection. Thus both the donors of cells used for immunization and the recipients of these cells must be continually monitored for evidence of hepatitis. If it were possible to freeze-preserve sufficient amounts of cells to be used for immunization, failure of transmission of the disease with the first portion of the cells would be strong evidence that the remaining frozen cells were "hepatitis free." However, under existing practices, freeze-preserved cells are rapidly used and new cells must be obtained frequently.

2. *Immunization with other antigens.* Antibodies with specificity for antigens outside the red blood cell systems are also needed. These are antibodies against various infectious agents. Individuals found to have these antibodies may be plasmapheresed sometimes following hyperimmunization with the microbial antigen. The indications for effectiveness and safety of these other immune globulin products are outside the purview of this Panel. However, to the extent that source plasma is used in the preparation of the immune globulins, these immunization procedures will be considered briefly in the recommendations.

3. *Recommendations*—a. *Immunizations for production of anti-A and anti-B.* There appears to be no need to use red blood cells for the purpose of stimulating the formation of anti-A and anti-B antibodies. Immunization for this purpose should be conducted with blood group substances A and B, used according to their licensed use (see the section on Blood Group Substances A and B).

b. *Immunization with red blood cells.* Much of what has been done in the past was done empirically and the Panel was unable to obtain complete data about these practices from the collectors of Source Plasma (Human). Until such information is available, the Panel is limited in what it can recommend that will not jeopardize the availability of essential reagents on one hand and yet provide reasonable safeguards to the individual being immunized on the other. The Panel recognizes that such things as the amount of antigenic red cells used as a primary immunizing dose, the amount of red cells and frequency of administration of the stimulating doses, and the antigenic composition of the cells of the donor and the recipient are critical variables in producing the desired immune response. At the same time the Panel cannot condone indiscriminately exposing individuals to what is essentially the risk of a blood transfusion not for therapeutic purposes.

(1) Although the risk of transmitting hepatitis can be minimized, it cannot be eliminated. The Panel concurs with current guidelines which indicate that cells from a new donor should be given to no more than three recipients during the initial 6 months of his/her use as a donor.

If no evidence of hepatitis occurs in the three recipients or in the donor during the 6-month period, the donor's cells may be used in routine stimulation. The Panel feels that no donor can be considered permanently safe and that all donors and recipients must be continually monitored for evidence of hepatitis. Recipients should be exposed to blood products from as few different donors as is practical.

(2) Although the Panel feels that freeze-preserved red cells of known low risk of hepatitis should be used where possible, more data are needed before making an unqualified recommendation. The immunogenicity of frozen red cells should be established.

(3) The Panel recommends that more extensive phenotyping and matching of donors and recipients of red cell antigens should be required and should include $JK^a$ of the Kidd system, $Lu^a$ and $Lu^b$ of the Lutheran system, k (Cellano) of the Kell system and both S and s of the MNSs system. The rational of this extended typing is mentoned above.

(4) The Panel recommends that women who are potentially child-bearing should not be immunized for either the purpose of increasing titers of existing antibodies or for de novo immunization. This recommendation does not exclude plasmapheresis of women with existing antibody. However, because of the danger of producing antibodies with another specificity, women should not be given red blood cells to maintain the titer of antibody.

(5) In the absence of information about dosage schedules commonly employed by industry for the stimulation of anti-$Rh_0$ (D) antibody, the Panel recommends that the current FDA guidelines be retained until such time as there are sufficient data to indicate how or if they should be modified.

(6) De novo immunization for specificities other Rh0 (D) should only be performed under investigational new drug procedures. Such immunization protocols should be considered on an individual basis. The Panel was not provided with sufficient information to justify these de novo immunizations. Although it would be ideal to have available potent reagent antisera for all known red blood cell antigens, the risks of routine de novo immunization appear to be too great to justify the benefits.

(7) Current guidelines allow for injection of red blood cells into individuals with preexisting antibodies. Up to 4.0 mL red blood cells can be given as a single injection. This volume may be administered up to five times in a single month, but not more than 40 mL can be given within any 6-month period. the Panel feels that these guidelines are arbitrary and based on a "best guess" logic. However, in the absence of adequate data, it is recommended that these guidelines be retained until such time as more data indicate how and if they should be modified.

(8) Only licensed products should be used for stimulating antibody formation. If no licensed products are available, nonlicensed materials may be used with specific approval from the Director of the Bureau of Biologics.

**27. FDA's Response to the Panel's Recommendations**

FDA is responding to the Panel's recommendations as follows:

1. The Panel reviewed many blood products only on a generic basis, and the Panel's recommendations are intended to apply to all products in that generic category. In other cases, the Panel identified and made recommendations concerning certain individual licensed products in addition to recommendations concerning that generic category of products. FDA considers the recommendations concerning the individual product, where differing, to supersede that applied to the generic category.

The Panel recommended that blood and blood derivatives be grouped into regulatory categories as follows:

1. Category I, *biological products determined to be safe, effective, and not misbranded* [and may continue in interstate commerce]: Whole Blood (Human) ACD; Whole Blood (Human) CPD; Whole Blood (Human) Modified-Platelets Removed; Whole Blood (Human) Modified-Antihemophilic Factor Removed; Red Blood Cells (Human) Frozen; Red Blood Cells (Human) Deglycerolized; Cryoprecipitated Antihemophilic Factor (Human); Single Donor Plasma (Human); Single Donor Plasma (Human), Fresh Frozen; Normal Serum Albumin (Human); Plasma Protein Fraction (Human); Antihemophilic Factor (Human); Factor IX Complex (Human); Factor IX Complex (Human) (Konyne), Miles Laboratories, Inc. (formerly Cutter Laboratories, Inc.), License No. 8; Factor IX Complex (Human) (Proplex), for the treatment of congenital factor IX deficiency, Travenol Laboratories, Inc., Hyland Therapeutics Division, License No. 140; $Rh_o$ (D) Immune Globulin (Human); Thrombin (for in vitro use), Ortho Diagnostics, Inc., License No. 156; Thrombin, Topical (Bovine), Parke-Davis, Division of Warner-Lambert Co., License No. 1; Blood Grouping Serum (all products); Reagent Red Blood Cells (Human) (all products); anti-Human Serum (all products); licensed third generation hepatitis testing reagents; Antivenin (*Crotalidae*) Polyvalent; Antivenin (*Micrurus fulvius*); Antivenin (*Latrodectus mactans*); Blood Group Substance A, B, AB, Armour Pharmaceutical Co., License No. 149; Normal Horse Serum.

The Panel found Normal Serum Albumin (Human) (NSA) to be safe and effective and not misbranded, and recommended that the product be placed in Category I. This recommendation applied to NSA derived from venous blood sources and that derived, all or in part, from placental sources. At the time of the Panel's review, one manufacturer, Parke, Davis & Co. (since April 15, 1980, named Parke-Davis, Division of Warner-Lambert Co.), License No. 1, was using a venous plasma and placental mixture as the source material for NSA. Subsequently, the Parke-Davis product license was amended at the manufacturer's request to exclude the use of placental materials. Another manufacturer, Michigan Department of Public Health (formerly, Bureau of Laboratories, Michigan Department of Public Health), License No. 99, has discontinued the fractionation of placental source materials for several years, but its product license still provides for the optional use of placental materials in the manufacture of NSA.

In its discussions, the Panel noted the potential existence of several hazardous substances in the placental NSA product for which there were inadequate data to determine the extent of the hazard or the impact of these substances upon the users of the product. The findings of the Panel related to the safety and effectiveness of NSA from placental sources are discussed below.

(i) The Panel observed that, unlike units of venous blood or plasma, placentas are not individually tested for hepatitis B surface antigen (HBsAg). As a result, it is possible that sufficient amounts of HBsAg may be carried over from placental source material to act as an immunogen for recipients of the final product. Accordingly, the Panel suggested that NSA from placental sources be tested for its immunizing potential.

Section 610.40(a) of the biologics regulations requires that each donation of blood or plasma used in preparing a biological product be tested for the presence of HBsAg by a method having a defined sensitivity (a third generation test). (Note: unless otherwise identified, all existing regulations referenced in this Response are in Title 21 of the Code of Federal Regulations.) Although FDA has not in the past required the testing of each placental unit for HBsAg, potential placenta donor populations have been screened for HBsAg, periodically. This testing was not, however, done in a manner which made it possible to link the results with individual placental units, nor was the sensitivity established for the test used.

(ii) The Panel observed that women in labor are more likely to have received a variety of drugs than are blood donors from the general population. Therefore, placental source materials may contain significant amounts of potentially dangerous drugs which are absent, or may be present in lesser quantities, in venous plasma. The extent to which these drugs are carried through to the final product is not known. The possibility that penicillin may be carried over into the final product was of particular concern to the Panel. In a closed Panel session, Parke-Davis representatives presented assay results which showed that there was no detectable penicillin in two lots of their final product. The Panel was, however, unable to determine the sensitivity of the microbiological assay method used. Accordingly, the Panel recommended that a significant number of lots be tested by a sensitive assay for the presence of penicillin allergen.

(iii) The Panel expressed concern that a variety of biological substances, present in placental source material but absent in venous plasma, may be bound by albumin and carried over into the final product. Several biological substances were identified which in fact are carried over to the product. The Panel recommended that the labeling of albumin prepared from placental sources inform users that a variety of biological materials may be present in small amounts.

(iv) During Panel discussions it was noted that although minimal data were available concerning the osmotic effectiveness of albumin prepared from venous plasma, no data concerning this subject were available for albumin from placental sources. Although the Panel did not mention this absence of data in its Final Report, the agency now considers this information necessary to demonstrate the effectiveness of the product in providing the intended osmotic activity in the blood of the recipient.

FDA agrees with the Panels' findings. The agency has carefully considered the findings of the Panel and has determined that the available data are insufficient to classify Normal Serum Albumin (Human) derived wholly or partially from placental sources as being safe, effective, and not misbranded for its intended uses. In addition, the agency finds that, because there remain signficant questions concerning the product's safety, the potential risks from use of this product outweigh its potential benefits. Accordingly, FDA proposes that Normal Serum Albumin (Human), when manufactured wholly or partially from placental source materials, be placed in Category IIIB, rather than Category I as recommended by the Panel.

Under § 601.25(f), FDA proposes to revoke the product license for Normal Serum Albumin (Human) held by the Michigan Department of Public Health. In the near future, FDA intends to publish a Notice of Opportunity for Hearing (NOH) to revoke the license for the product, unless the licensee applies to amend its license to exclude placentas as an optional source material.

Based upon the available evidence, FDA Agrees that Plasma Protein Fraction (Human) (PPF) should be considered safe and effective for its indicated uses. The agency notes, however, that several significant unresolved questions about PPF remain which are relevant to a complete assessment of the safety and effectiveness of this product. See paragraphs 17, 21, and 22 of FDA's response to the Panel's recommendations. Laboratories at FDA's Center for Drugs and Biologics (CDB) are investigating some of these questions related to the safety and effectiveness of PPF. Upon completion of these studies, FDA intends to reassess the safety and effectiviness of PPF and, if necessary, propose appropriate administrative or regulatory action. (Note: FDA's Bureau of Biologics and Bureau of Drugs have been merged to form the Center for Drugs and Biologics (see 49 FR 14931; April 16, 1984).) The regulatory and scientific functions concerning biological products, formerly performed by the Bureau of Biologics, are now performed by the Office of Biologics Research and Review, Center for Drugs and Biologics (see 49 FR March 19, 1984).

FDA agrees with the Panel's findings and recommedations for the remaining Category I products and hereby proposes to adopt its conclusions, including recommended labeling revisions. Comments and additional data on these classifications are invited.

b. Category II. *Biological products determined to be unsafe or ineffective or to be misbranded and which should not continue in interstate commerce:* Fibrinogen (Human).

As noted by the Panel, all product licenses for Fibrinogen (Human) were revoked as of December 7, 1977, and no further action is necessary.

c. Category IIIA. *Biological Products for which available data are insufficient to classify their safety and effectivenes but which may remain licensed and in interstate commerce for a limited period of time pending completion of further study:* Whole Blood (Human) Heparin: Factor IX Complex (Human) (Proplex ™), for use in congenital and acquired deficiencies of factors II, VII, and X, Travenol Laboratories, Inc., Hyland Therapeutics Division, License No. 140; Fibrinolysin (Human) (Thrombolysin ™), Merck Sharp & Dohme, Division of Merck & Co., Inc., License No. 2; Fibrinolysin and Desoxyribonuclease, Combined (Bovine), and Fibrinolysin and Desoxyribonuclease, Combined (Bovine), with Chloramphenicol (Elase ™ powder for solution, Elase ™ ointment), Parke-Davis, Division of Warner-Lambert Co., License No. 1.

The Category IIIA designation reflects a determination by the Panel that there are doubts about whether data are sufficient to support an action by the agency to reaffirm or revoke a product license and that, based on an assessment of the present evidence of safety and effectiveness of a product, the potential benefits outweigh the potential risks likely to result from continued use of a product for a limited period of time (see § 601.25(f)(3)).

Under procedures by which the review of biological products was established, FDA would permit the continued interim marketing of products classified in Category IIIA, provided the manufacturer undertook the necessary additional studies to fully determine the safety and effectiveness of the product. The agency has reconsidered this policy and has determined that it is in the best interest of the public health to reclassify those biologics previously classified in Category IIIA and to proceed to either reaffirm or initiate proceedings to revoke the license for each Category IIIA product. The procedures for implementing this policy were codified under § 601.26 by final rulemaking of October 5, 1982 (47 FR 44062). Under the new procedures, the data for each product classified in Category IIIA will be reviewed by a second expert panel to recommend whether:

a. The product is safe, effective, and not misbranded (Category I) and may remain licensed;

b. The product is unsafe, ineffective, or misbranded (Category II) due to the lack of sufficient supportive evidence and for which the product license shall be revoked; or

c. The product lacks sufficient supportive evidence of effectiveness (also administratively identified as Category II) but should remain on the market pending the completion of further testing. Such a recommendation may be made only when there is a compelling medical need and no suitable alternative therapeutic, prophylactic, or diagnostic agent is available in sufficient quantity to meet current needs.

FDA is submitting for review by the Blood Products Advisory Committee the available data for those products recommended for Category IIIA by the Panel. Upon completion of its review, the Advisory Committee will submit a report to FDA containing its conclusions and recommendations for reclassification of the affected products. Then FDA will publish a proposal to either implement or reject the Advisory Committee's recommendations and at that time will provide an opportunity for public comment.

d. Category IIIB. *Biological products for which available data are insufficient to classify their safety and effectiveness and which should not continue in interstate commerce:* Blood Group Substance A and Blood Group Substance B, Pfizer Inc., License No. 164; Cobra Venom Solution and Cobra Venom with Silicic and Formic Acids (Cobroxin ™ and Nyloxin™), Hynson, Westcott & Dunning, License No. 125.

The product licenses for Blood Group Substance A and Blood Group Substance B, manufactured by Pfizer, Inc., were revoked at the request of the licensee on June 24, 1980. Accordingly, no further regulatory action is necessary.

As noted by the Panel, FDA has revoked the licenses for the remaining Category IIIB products, Cobra Venom Solution and Cobra Venom with Silicic and Formic Acids, at the manufacturer's request and further action is unnecessary.

2. The Panel recommended a number of labeling changes for Category I and IIIA products, including in some cases revisions of the indications for which the product is recommended. The agency agrees with the majority of the Panel's recommendations for labeling changes. Those recommendations involving labeling with which FDA disagrees, or which require further elaboration and clarification, are discussed elsewhere in this response. The public is invited to comment on the Panel's recommendations affecting product labeling and use. In the preamble to the final rule, FDA will advise licensed manufacturers to submit appropriately revised draft labeling to OBRR, Center for Drugs and Biologics for review and approval. FDA proposes to require that approved labeling, revised in accordance with the final rule, be available for distribution with blood products initially introduced or initially delivered for introduction into interstate commerce 12 months after the date of publication of the final rule.

On May 16, 1980 (45 FR 32550), FDA published final regulations codifying

under § 201.59 the effective dates for the regulations under §§ 201.56 and 201.57, concerning the content and format for labeling human prescription drugs. The codified effective dates for biologics were further clarified on January 23, 1981 (46 FR 7272). For the blood products reviewed in this report, the effective date for the reformatting of labeling was set at 30 months after the date of publication of the final rule based on this proposal. Draft reformatted labeling was to be submitted to FDA 6 months after publication of the final rule. Consistent with § 201.59, FDA proposes to require that approved labeling, revised in accordance with §§ 201.56 and 201.57, be distributed with products that have been reviewed by the Panel and that are initially introduced or initially delivered for introduction into interstate commerce 30 months after the date of publication of the final rule.

Although FDA is proposing two effective dates for the various required labeling changes, i.e., 12 months for labeling changes specifically required by this rulemaking and 30 months for labeling changes in conformance with §§ 201.56 and 201.57, FDA will promptly review labeling changes proposed by manufacturers who wish to make all of the necessary changes within 12 months, thus avoiding the need to revise and reprint their product labeling twice. Since late 1979 when §§ 201.56 and 201.57 were codified, FDA has reviewed biological product labeling that was submitted for other purposes for consistency with §§ 201.56 and 201.57 and has offered suggestions as to how the labeling could be revised to comply. Thus, many manufacturers of blood products already have voluntarily revised their product labeling to comply with §§ 201.56 and 201.57, and only revisions in accordance with this rulemaking remain necessary. FDA will continue to review labeling submitted at any other time for conformance with §§ 201.56 and 201.57. By this means, FDA believes that manufacturers can readily avoid repetitive revision and reprinting of labeling by having final labeling that complies with this rulemaking and §§ 201.56 and 201.57 available by 12 months after date of publication of the final rule. If a manufacturer so wishes, compliance with §§ 201.56 and 201.57 could be delayed until the proposed effective date, 30 months after date of publication of the final rule.

3. For most of the blood products reviewed, the Panel recommended a new, generally simplified, proper name for each product. Based in part upon the Panel's recommendations, FDA proposed in the **Federal Register** of October 31, 1980 (45 FR 72404) new proper names for biological products, including blood products. FDA published a final rule establishing new proper names for biological products in the **Federal Register** of January 29, 1985 (50 FR 4128). This final rule becomes effective on January 29, 1986. In most cases, the name for a product suggested by the Panel is the same as the one established by FDA. In each case, a simple name was sought that would adequately identify the product. For convenience, FDA is using the former proper names for products in the preamble to this proposed rule, however FDA is using the correct revised proper names in the proposed codified portion of this rule.

4. The Panel stated that the production of blood bags and transfusion tubing needs to be standardized to minimize lot-to-lot variations.

FDA believes that the current regulatory procedures and manufacturing practices achieve this goal. Before a new blood container anticoagulant combination can be marketed, the manufacturer must submit a new drug application (NDA) to FDA for approval. The NDA must include specifications showing the maximum and minimum tolerance limits for each parameter affecting the safety and effectiveness of the product for its intended uses. Extensive clinical data must also be submitted to show that the new product, manufactured in accordance with these specifications, is safe and effective for the uses intended by the manufacturer. After approval of the NDA, it is the manufacturer's responsibility under the current good manufacturing practice (CGMP) regulations for human drugs in Parts 210 and 211 (21 CFR Parts 210 and 211) to ensure that such products continue to meet the specifications in the NDA. Although lot-to-lot variations may occur, the specification limits set in the NDA or approved by FDA as a supplement to the NDA and the manufacturing controls required by the CGMP regulations for human drugs and for blood and blood components in Part 606 (21 CFR Part 606) ensure that the blood products within the containers remain safe and effective throughout their dating periods. Therefore, FDA believes it is unnecessary at this time to require, through issuance of regulations, additional production procedures for blood bags and transfusion tubing. Voluntary performance standards are desirable for such products, however, and the agency is cooperating with the subcommittee of the National Committee for Clinical Laboratory Standards (NCCLS) in their design.

5. The Panel made the following recommendations concerning additional standards for Whole Blood (Human) in Part 640:

a. The maximum number of whole blood donations for an individual should be reduced from 6 to 4 times per year and no more frequently than every 8 weeks. Procedures to bleed donors more frequently could be established with the concurrence of CDB if adequate means are employed to protect donors from the development of iron deficiency.

b. The acceptable minimum hemoglobin level for male donors of whole blood should be increased from 12.5 to 13.5 grams per 100 milliliters of blood. The blood sample used for determining the donor's hemoglobin level should be obtained by finger-stick or by venipuncture.

c. Both cell grouping and serum (reverse) grouping should be required in donor ABO blood grouping. Any discrepancy in the results of these tests should be resolved before the blood is labeled. Licensed reagents or their equivalent should be required for cell grouping tests.

d. The blood should be tested for the $D^u$ variant if the test using Anti-D serum is negative. Routine testing for C and E and other Rh antigens should not be required.

Based in part on these Panel recommendations, in the **Federal Register** of October 31, 1980 (45 FR 72422), FDA proposed to revise the additional standards for Whole Blood (Human). Subsequently, FDA withdrew for reconsideration that proposed rule (July 22, 1983; 48 FR 33494). FDA herein is reproposing to revise additional standards for Whole Blood (Human) consistent with the Panel recommendations. However, several of the reproposed revisions are significantly different from those proposed in October 1980. FDA advises interested persons to resubmit any comments on the October 1980 proposed rule that remain relevant, referencing the docket number found in the heading of this document.

The Panel's recommendation that the maximum permissible donation frequency should be reduced from six to four times per year reflects its concern, based on published data from a number of clinical studies, that under the current donor suitability requirements some individuals may develop an iron deficiency when donating at or near the current maximum rate. The Panel's recommendations concerning the

determination of a donor's hemoglobin level (item b. above) are also related to the protection of individuals with low iron stores.

FDA shares the Panel's concern that the present donation schedule may result in a significant depletion of iron reserves in blood donors, which may not be detectable by the currently required donor-screening procedures. Data made available to FDA since the Panel's review and the October 31, 1980 proposal further substantiate the relationship of frequent blood donation and the development of an iron deficiency, especially for female blood donors (Simon, T.L., "Iron Stores in Blood Donors," *Journal of the American Medical Association*, 246:2035, May 22, 1981). Accordingly, FDA agrees that the present standards concerning donation frequency and donor suitability should be modified to protect individuals with low iron stores. Although FDA agrees that the specific measures recommended by the Panel would ensure the health of all donors, the agency believes that alternative modifications to the standards would be equally effective in protecting the health of blood donors. FDA believes that, in some localities, a fixed reduction in donation frequency could have a significant adverse effect on a community's blood supply and alternative procedures, such as establishing more stringent donor suitability requirements, would be preferable. In other localities, the effect of reducing the donation frequency would be negligible. Consequently, the agency believes that each facility should be allowed maximum flexibility for selecting appropriate standards for adequately protecting the health of its donor population.

Accordingly, for those establishments that elect to operate under routine donor suitability requirements, FDA is proposing to amend § 640.3 to reduce the routine maximum donation frequency to five times per year for male blood donors and four times per year for female blood donors. The lower rate proposed for female donors is consistent with data showing that iron levels are more critical for females. FDA is proposing to retain the requirement that individuals donate no more frequently than once every 8 weeks.

Under the proposed regulation, blood establishments will be offered several alternatives by which an individual may donate blood more frequently than allowed by the proposed routine limits. First, as is provided in the current regulations, an individual may donate more frequently if examined by a licensed physician at the time of donation and the physician certifies in writing that the donor meets all donor requirements described under § 640.3. Second, a licensed blood establishment may submit to OBRR, a protocol describing the procedures the establishment intends to use to protect the health of individuals donating more frequently than allowed by the proposed routine limits, particularly procedures to prevent the development of an iron deficiency by the donor. Upon approval by OBRR, the procedures would be incorporated into the establishment's written standard operating procedures (SOP) and used to protect those individuals donating more frequently than allowed by the proposed routine limits. Finally, FDA invites the submission by any of the organizations representing the blood-banking industry of protocols for procedures to protect donors contributing blood more frequently than allowed by the proposed routine limits. Upon approval by OBRR, the procedures could be published in a procedural manual sponsored by the organization or otherwise distributed to individual blood establishments. Individual establishments could then incorporate the procedures into their SOP and begin implementation without the direct approval of OBRR. By the use of these alternatives, the agency believes that the health of the donors will be protected without any adverse effect on the Nation's blood supply. OBRR will begin the review of submitted protocols immediately upon receipt so that such alternative procedures for protecting donors may be put into effect in a timely manner.

The Panel's recommendation that the blood sample used for determining a donor's hemoglobin level be obtained by fingerstick or venipuncture is based upon data demonstrating that the alternative technique, earlobe puncture, gives less consistent and generally higher hemoglobin values. FDA agrees that the earlobe puncture technique produces results that do not correlate consistently with the hemoglobin level of venous blood; however, FDA believes that the use of this sample technique does not necessarily invalidate the test results. There are some donors who, for reason of comfort, prefer the earlobe puncture technique and in fact may not donate if alternative techniques were used. Many establishments use the earlobe puncture technique only upon the request of the donor. At some of these establishments, a higher minimum acceptable hemoglobin level is used when the blood sample is collected by earlobe puncture. Because of the insensitivity of the method routinely used to determine the hemoglobin level, the copper sulfate method, FDA does not believe that the technique for obtaining the blood sample will significantly alter the health protection characteristics of this screening procedure. Accordingly, although FDA considers venipuncture and finger puncture the preferred techniques, the agency intends to continue to permit the use of the earlobe puncture technique, with each blood establishment establishing appropriate minimum hemoglobin levels as discussed below.

FDA agrees that in most cases the acceptable minimum hemoglobin level for male donors should be 13.5 grams per 100 milliliters (1 deciliter) of blood. Many blood banks have already adopted this level as a voluntary standard. The agency recognizes, however, that the average hemoglobin level of a population varies according to the geographic location. Specifically, individuals residing in a high-altitude location tend to have a higher hemoglobin level. As a result, a specific minimum hemoglobin level may be reasonable for some locations while resulting in the rejection of healthy donors at other locations.

Accordingly, FDA is proposing to amend the regulations in § 640.3(b)(3) by no longer prescribing specific acceptable minimum hemoglobin levels, and placing the responsibility on each blood establishment for determining what minimum hemoglobin levels should be set for the adequate protection of its donors. The hemoglobin levels selected should be based on the geographic location of the establishment and shall be consistent with current scientific knowledge and good blood-banking practices. The minimum acceptable hemoglobin levels and the method of blood sample collection shall be documented in the establishment's SOP. Major organizations representing the blood-banking industry, as part of the protocols for the protection of iron-deficient donors, may recommend appropriate methods and criteria for the screening of donors on the basis of hemoglobin levels. A licensed establishment intending to modify its hemoglobin testing procedures and criteria in a manner other than that established by a major blood-banking organization must notify the Director, OBRR, of the prospective change and have its establishment license amended accordingly.

Currently, the regulations concerning ABO blood grouping under § 640.5(b) require that at least two blood group tests be made on each unit of blood and that these tests must agree before the

unit is issued. Serum grouping (testing the donor's serum against known group A and group B cells) is not specifically required. FDA agrees with the Panel that serum grouping is the most reliable means of confirming the results obtained by cell grouping. Indeed, most blood establishments already perform both of these tests in determining a donor's ABO group. Accordingly, FDA is proposing to revise § 640.5(b) to require that both cell grouping and serum grouping be performed in determining the ABO group of a donor's blood and that any discrepancy in the results of these tests shall be resolved before the blood is labeled. The current regulations already permit the use of unlicensed blood grouping sera if the sera are shown to meet the same regulatory standards as the licensed reagents. This provision is revised only for clarity and to identify the requirements that unlicensed sera must meet.

Under current § 640.5(c), the testing of blood for the D antigen variant known as $D^u$ is optional, provided that blood otherwise tested as Rh negative is labeled to show when testing for $D^u$ was not done. The testing of Rh negative blood for other Rh antigens, such as C and E, is optional. Most blood banks routinely test blood negative for the D antigen for $D^u$, while tests for the other antigens in the Rh system generally are not done. FDA agrees that D negative blood should always be tested for $D^u$ to ensure the accurate characterization of the blood and to prevent the possible immunization of blood recipients who are Rh negative. Accordingly, FDA is proposing to revise § 640.5(c) to require that blood tested as negative using Anti-D Blood Grouping Serum be tested for $D^u$. FDA is proposing to clarify the provision in § 640.5(c) concerning the use of unlicensed reagents and to identify the requirements that unlicensed reagents must meet. Provisions for the appropriate labeling of blood according to Rh group were included in the Uniform Blood Labeling proposal of October 31, 1980 (45 FR 72416) and final rule of August 30, 1985 (50 FR 35458).

6. The Panel recommended that: (1) Each unit of blood from selected donors should be tested for clinically significant unexpected antibodies unless the unit of blood will be issued without significant amounts of plasma, in which case antibody screening should not be required; (2) blood found to contain significant antibodies should not be transfused unless the plasma is first removed; and (3) a preliminary donor screening based on the donor's medical history could be allowable as an alternative procedure to testing for clinically significant unexpected antibodies.

FDA agrees that blood from a donor whose medical history indicates that significant unexpected antibodies maybe present should be tested for significant antibodies. The proposal to revise the additional standards for Whole Blood (Human) published on October 31, 1980, included a requirement that blood from previously transfused or previously pregnant donors be screened for significant alloantibodies—antibodies in blood plasma that could react with antigens on a recipient's red blood cells. Although that proposal was subsequently withdrawn for further consideration (July 22, 1983; 48 FR 33494), FDA remains convinced that such a requirement should be promulgated. Accordingly, FDA is reproposing in § 640.5(d) to require the screening of blood from previously transfused or previously pregnant blood donors for the presence of significant alloantibodies. FDA is proposing a cross-reference to this provision in § 640.33(a) of the additional standards for Single Donor Plasma (Human). As discussed in FDA's response to the Panel recommendation that follows, FDA also is proposing to require that the procedures for screening for significant donor alloantibodies be described in each establishment's standard operating procedures manual.

In its Uniform Blood Labeling regulations (August 30, 1985; 50 FR 35458), FDA included a requirement that significant unexpected antibodies be identified on the label of blood and blood components containing significant amounts of plasma. Because the donor blood sample is taken at the time of collection of the unit, the intended use of the unit is usually unclear and plasma may subsequently be used for transfusion. Consequently, FDA is proposing to require that all units of blood from the selected donor be screened for the presence of significant alloantibodies. FDA notes, however, that the screening procedure may be omitted if the plasma is immediately separated from the unit and labeled in a manner to prevent the plasma's use for transfusion. The agency believes that donor blood containing significant alloantibodies does not constitute a hazard to the recipient if the plasma is removed or if it is properly crossmatched with the recipient's cells. The proposed rules would continue to permit the use of such blood for transfusion, provided that the unit is labeled adequately to inform the clinician.

7. The Panel recommended that the major crossmatch (testing the compatibility of donor erythrocytes against recipient serum) should employ methods that demonstrate significant hemolyzing, agglutinating, and coating antibodies which are active at 37° C and should include the antiglobulin test or its equivalent. The Panel also recommended that a minor crossmatch (donor serum tested against recipient cells) should not be required as part of the pretransfusion testing.

FDA agrees with the Panel's recommendations. Section 606.151 of the biologics regulations describes the procedures for compatibility testing of donor and recipient blood which must be included in each blood establishment's written SOP. FDA is proposing to revise this section in response to the above recommendations and other related Panel recommendations, and to update and clarify the section consistent with current medical knowledge and existing regulations. The proposed amendments to each paragraph of § 606.151 are described below:

a. Proposed § 606.151(a) would require that the SOP describe a method to ensure the positive identification of blood samples of donors, as well as the blood samples of recipients, as is currently required. This proposed requirement is consistent with current § 640.4 (e) and (g) which require appropriate handling and positive identification of a donor's blood samples.

b. Current § 606.151(b) would be deleted. Through practical experience it has been determined that the normal length of storage of serum samples does not affect the accuracy of pretransfusion test results. Accordingly, FDA is proposing to delete the requirement to use only recipient serum less than 48 hours old.

c. Proposed § 606.151(b) would require a description in the SOP of the procedures for determining the ABO and Rh groups of donors and recipients using licensed blood grouping sera or their equivalent. The proposed requirement is consistent with the requirements of § 640.5 (b) and (c) concerning the testing of donor blood samples.

(d) Proposed § 606.151(c) would replace current § 606.151(d) concerning the minor crossmatch of each donor's serum with the recipient's cells for the detection of significant antibodies. As noted by the Panel, it is now considered unnecessary to crossmatch a donor's serum with the recipient's red blood cells for the detection of significant antibodies. Proposed § 606.151(c) would

require a description in the SOP of the procedures for the detection of significant alloantibodies in the plasma of those donors who are most likely to have significant alloantibodies, namely, previously transfused or previously pregnant donors. The more general term, "significant alloantibodies," antobodies produced by an individual that react with antigens of another individual of the same species, is substituted for "agglutinating, coating and hemolytic antibodies." Proposed § 606.151(d) is worded consistently.

e. Based on current § 606.151(c), FDA is proposing to revise § 606.151(d) concerning the major crossmatch. Consistent with the Panel's recommendation, FDA is proposing to require that the SOP specify a method that will demonstrate significant alloantibodies which are active at 37° C. Proposed § 606.151(d) would permit the use of alternative methods to the antiglobulin technique, which are equally sensitive for the detection of unexpected alloantibodies. This less restrictive requirement will allow new antibody detection methods to be used as technology develops.

f. FDA is proposing to delete the recordkeeping provisions now included in § 606.151(e). Such recordkeeping requirements already are included in current § 606.160 *Records* under paragraph (b)(3)(v). FDA is proposing to add to § 606.151(e) a requirement to descrive in the SOP the procedures for neonatal and autologous transfusions, two other situations, where the full regimen of pretransfusion testing might not be appropriate.

8. The Panel recommended that the requirements for the serological test for syphilis (STS) be removed from the regulations for determining the suitability of whole blood donors and plasma donors. The Panel's conclusions follows:

a. *STS is a nonspecific and inaccurate test.* The majority of positive test results are "biological false positive" (BFP), due to various acute or chronic conditions and illnesses unrelated to syphilis that are nonspecifically detected by the STS test. In addition, early in the onset of the disease, the STS is often nonreactive, even though the causative agent of syphilis, *Treponema Pallidum*, is circulating in the person's blood stream.

b. *Syphilis is not transmitted by blood transfusion.* Because of modern blood banking and transfusion practices, syphilis is not known to be transmitted by blood transfusion. As described above, blood containing the causative agent of syphilis may be nonreactive by the STS and may be transfused; however, not one case of transfusion-transmitted syphilis has been reported in the past 20 years.

FDA agrees with the Panel's findings; the STS is no longer useful for is original intended purpose, namely, the prevention of the transmission of syphilis through either blood transfusion or the use of other injectable blood products. However, because of considerations evolving subsequent to the Panel's review, FDA intends to publish separately rulemaking to remove the requirements for performing the STS for syphilis.

9. The Panel presented a list of information that should be exclusively included on Whole Blood (Human) and Red Blood Cell (Human) container labels. Of particular note, the Panel suggested that only paid donors and not volunteer donors need to be identified on the blood label. The Panel also suggested that, in the event machine-readable codes are included on the container label, the codes should not detract from the eye-readable aspects of the label.

FDA agrees in part and disagrees in part with the Panel's recommendations. In the **Federal Register** of August 30, 1985 (50 FR 35458), FDA promulgated revised requirements for the uniform labeling of blood and blood components. With several exceptions, the final rule agrees with the Panel's recommendations regarding labeling. FDA will require that the instructions, "transfuse through a filter" and "do not add medication other than 0.9% NaCl solution," be placed in the instruction circular, rather than on the container label as suggested by the Panel. Also, FDA wil retain unchanged the requirement in §606.120(b)(2) regarding the donor classification, "volunteer donor".

In the **Federal Register** of January 13, 1978 (43 FR 2142), FDA promulgated the requirement that a donor classification statement be included on the label to protect public health. FDA based its regulation on data showing that blood from paid donors generally presents a higher risk of transmitting hepatitis than blood from volunteer donors. At a June 1982 meeting, FDA's Blood Products Advisory Committee was asked to consider, among other things, FDA's donor classification requirements. The Blood Products Advisory Committee recommended that the current donor classification requirements be retained without change. A number of States have enacted legislation that requires donor classification on blood labels, with specific labeling requirements varying from State to State. FDA intends to require a uniform label for blood products shipped in interstate commerce and will protect public health by continuing to require a statement of donor classification on the label of each unit of blood.

In its uniform blood labeling final rule of August 30, 1985, FDA recommended that machine-readable (bar-code) information be included on each blood container label. FDA is also recommending that each blood label have all information in a standard position and format. FDA believes that the additional bar coding should not detract from the eye-readable accuracy of the label.

10. The Panel determined that there is limited evidence supporting a 48-hour dating period for Whole Blood (Human) Heparin and recommended that the dating period be reduced to 8 hours.

FDA agrees that the available data are inadequate to support a 48-hour dating period for the product. There is a lack of data to show that adequate red blood cell viability is maintained for 48 hours or data to identify any molecular and cellular changes that may occur in heparinized blood during storage. Accordingly, the agency is proposing to amend § 610.53 *Dating periods for specific products* by prescribing an 8-hour dating period for Whole Blood (Human) Heparin, pending the submission of satisfactory data in support of a longer dating period for this product.

11. The Panel noted that some institutions add ACD or CPD anticoagulant to heparinized blood and use it up to 12 days thereafter. The Panel advised that, if there is a need for such a modification, additional studies would be appropriate to demonstrate the safety and effectiveness of the product.

FDA believes that such a modified product is not safe and effective and its use clearly is not permitted under the regulations. (See §§ 601.12(b), 610.52, 610.53, 640.2(c), and 640.4(d) of the biologics regulations.)

12. The Panel recommended that frozen and deglycerolized red blood cell products should meet the following criteria.

a. Red Blood Cells (Human) Deglycerolized should be prepared by a method resulting in a minimum in vitro yield of 80 percent of the original red blood cell mass.

b. At least 70 percent of the red blood cells should survive in the recipient 24 hours after transfusion.

c. The effective yield (mean in vitro yield multiplied by the mean percent of survival at 24 hours post-transfusion) should be at least 65 percent.

d. The final suspending solution for deglycerolized red blood cells should be isotonic and contain between 130 and 160 milliequivalents of sodium per liter.

e. The final product should contain no more than 0.5 gram of glycerol and 175 milligrams of supernatant hemoglobin per deciliter.

Three methods, the low- and high-glycerol methods and cytoagglomeration, currently may be used by licensed establishments for the freezing of Red Blood Cells (Human). Each of these methods has been shown by manufacturers' data, scientific literature, and practical experience to produce an isotonic final product that meets the cell viability criteria specified above. New product license applications for Red Blood Cells (Human) Frozen must be accompanied by data demonstrating adherence to one of the established acceptable methods, or, if approval is sought for a significantly modified or new method of freezing and/or thawing, appropriate supportive data must be submitted to demonstrate that the final product is safe and effective. FDA considers the current policy adequate for determining the safety and effectiveness of these products, and no changes to the criteria are proposed at this time.

13. The Panel suggested that the dating period for Red Blood Cells (Human) Frozen may be extended beyond the currently codified 3-year period (§ 610.53(b)), provided the product is shown to meet specified viability and recovery criteria. The Panel also recommended that the shelf-life for Red Blood Cells (Human) Deglycerolized (the period between removal of the product from storage at −65 °C to the time of transfusion) should be extended beyond the currently permitted 24 hours, if specified viability and recovery criteria are met and no increased risk of bacterial contamination is shown when compared with the product stored in a liquid state.

FDA agrees with these recommendations. The agency is aware that on many occasions frozen red blood cells of rare phenotypes have been transfused without apparent adverse effect after storage for significantly longer periods than 3 years. FDA requests that interested persons submit any data available to support a longer dating period for Red Blood Cells (Human) Frozen. The supporting information should be submitted for each of the currently approved cryopreservation methods and should include recovery, survival, and effective yield data at the end of the extended storage period.

FDA also will consider amending the 24-hour post-thaw shelf life period in the current regulatory standards for Red Blood Cells (Human) Deglycerolized upon receipt by FDA of data demonstrating that neither the risk of bacterial contamination nor the level of free hemoglobin is greater with the extended shelf life period than that associated with currently licensed deglycerolized red blood cell products with shelf life limited to 24 hours, and that acceptable viability and recovery criteria are met.

14. The Panel recommended that each registered establishment (blood bank or laboratory) processing Cryoprecipitated Antihemophilic Factor (Human) should standardize its factor VIII assay and correlate the in vitro test results with in vivo recovery and survival testing, and reestablish the correlation each time a significant change in the production process occurs.

FDA agrees that a standardized factor VIII assay should be used by all registered blood establishments and testing laboratories involved in the processing of cryoprecipitate. A dried plasma standard with an assigned potency based on comparison with the World Health Organization (WHO) standard is availale from the Office of Biologics Research and Review, FDA (see § 640.55 (21 CFR 640.55)). Manufacturers should obtain such a standard from FDA to be used to calibrate their house standard for the factor VIII assay.

FDA agrees that in vitro factor VIII assay results should be correlated with the clinical effects of the product. The agency recognizes that there are technical difficulties in obtaining reliable in vivo recovery data known to correlate with in vitro test results. Until an appropriate standard method of in vivo testing can be developed, the agency will consider the in vitro test validated when the assayed product is found to achieve the expected clinical results, as determined by careful patient monitoring. FDA advises that this form of validation is necessary at the time of the initial manufacture of the product and when the production process is significantly changed.

15. In the text of their review of Cryoprecipitated AHF, the Panel made several technical suggestions pertinent to the preparation of cryoprecipitate. The Panel also recommended several changes in the labeling for Cryoprecipitated AHF. The recommendations are summarized below.

a. If the unit is frozen in a liquid medium, an overwrap should be used to prevent interaction of the freezing liquid with the plastic bag and its contents. (All licensed blood banks already follow this procedure.)

b. Cryoprecipitate containers should be thawed at 30° to 37° C for at least 15 minutes to ensure maximum Factor VIII recovery.

c. Saline is the preferred diluent if cryoprecipitates are provided on a non-blood-group-specific basis.

d. Pooling should be performed by experienced personnel to ensure complete removal of all concentrated material from each container.

e. The labeling should indicate that cryoprecipitate usually contains at least 150 milligrams of fibrinogen per unit.

f. The labeling should indicate that good patient management requires monitoring treatment responses to cryoprecipitate transfusions with periodic plasma Factor VIII or fibrinogen assays in hemophilia A and hypofibrinogenemic recipients, respectively.

FDA finds that many of these suggestions are appropriate for inclusion in the SOP manual required for each establishment by § 606.100(b). Accordingly, FDA proposes to require that the above procedures (a) through (d) be added to the SOP manuals for cryoprecipitate production upon the effective date of the final rule. Because the technical suggestions are directed toward the user of the product, FDA finds the information (b) through (d), as well as the specific labeling recommendations listed in (e) and (f), appropriate for inclusion in the instruction circular made available with the product. Accordingly, as provided in the Uniform Blood Labeling final rule of [date pending], FDA will require that the information described in items (b) through (f) be included in the instruction circular.

In regard to suggestion (d) concerning pooling, FDA advises that the final pooled product, except when specifically provided for in the product license, may not be transported in interstate commerce. As a result, it is usually more practical to pool the product at the hospital or at the home of the patient immediately prior to use rather than at the processing facility. Accordingly, the information has been proposed for inclusion in the instruction circular. OBRR has information on the safety of the procedures for pooling cryoprecipitate at the time of manufacture. FDA currently is reviewing license amendments to permit this procedure.

16. The agency has determined that the following biologics regulations

respond fully to specific Panel recommendations, or to suggestions contained in the text of their review concerning Cryoprecipitated Antihemophilic Factor (Human). The regulations are summarized below only to the extent that they relate to a Panel recommendation:

*Section 640.56 (a) and (d)*—Each blood bank must test at least four units of cryoprecipitate in each month of preparation to assure an average potency of no less than 80 units of antihemophilic factor per container.

*Section 606.122(n)(1)*—The instruction circular shall bear a statement that the average potency is 80 or more units of antihemophilic factor.

*Section 606.122(n)(5)*—The instruction circular shall bear instruction to store at room temperature after thawing and to use as soon as possible, but no later than 4 hours after entering or pooling and within 6 hours after thawing.

17. The Panel noted that research is needed to establish the fate and function of monomeric, dimeric, and polymeric forms of Normal Serum Albumin (Human) (NSA). As an interim measure, the Panel recommended that the production process for NSA be designed to assure that the maximum amount of albumin is in the monomeric form. The Panel also noted that if minimum limits are set for the monomeric content of NSA, the expiration times (dating periods) may need to be revised.

The agency agrees and has carried out research to develop suitable methods for measuring the amount of monomeric, dimeric, and polymeric forms of albumin in both NSA and Plasma Protein Fraction (Human) (PPF). Furthermore, FDA has carried out laboratory measurements that show that nonmonomeric albumin is less effective osmotically than the native (monomeric) form. During an open meeting of FDA's Blood Products Advisory Committee on February 8, 1983, FDA discussed with manufacturers of plasma derivatives a number of possible changes in the regulations for NSA, PPF, and immune globulins. FDA discussed determining the monomeric, dimeric, and polymeric albumin content of NSA and PPF by measuring the molecular distribution of each lot of final product. Through separate rulemaking, FDA intends to propose revised additional standards for NSA and PPF. The proposed rule would add new requirements, such as a requirement for a test for molecular distribution, while deleting or relaxing some existing requirements, as indicated by recent advances in technology. FDA will continue to examine stability data and, if appropriate, will propose revised dating periods or storage conditions for NSA and PPF in § 610.53(a).

18. In their review of Normal Serum Albumin (Human), the Panel recommended that:

a. The sodium content of NSA should be limited to 130 to 160 milliequivalents per liter (mEq/L);

b. CDB should be informed by the manufacturer of the amount of "reworking" in the production of each lot released;

c. The term "salt poor" should be discontinued on the product labeling;

d. The approximate concentration of chloride and potassium ions should be given in the package insert.

FDA agrees with the Panel's recommendations. Regulations in accordance with items a. and b. above are already codified under §§ 640.82(d) and 640.85(b)(1) and (3) of the biologics regulations.

FDA advises that the Panel's recommendation concerning the term "salt poor" was implemented in the **Federal Register** of May 31, 1977 (42 FR 27577), and the term is no longer used in product labeling.

FDA agrees that the approximate concentrations of chloride and potassium ions should be included in the product labeling. The potassium ion concentration is of particular significance because high potassium concentrations in a patient's plasma (hyperkalemia) caused, for example, by large volume transfusions, are known to affect cardiac function adversely.

FDA is proposing to amend the additional standards for Normal Serum Albumin (Human) in § 640.82 to require that the potassium concentration of the final product not exceed 2 milliequivalents per liter (2 mEq/L). Laboratories at OBRR have tested a number of recently released lots of NSA at various protein concentrations to determine their potassium content. All lots tested, regardless of the protein concentration, contained less than 1 mEq/L potassium. Under § 640.82(d), manufacturers of NSA are required to determine the sodium content of the final product. The test used by nearly all manufacturers for determining the sodium content of the product (flame photometry) may simultaneously be used for determining the potassium concentration; therefore, the proposed requirement does not impose any additional testing burden upon the manufacturer. An identical requirement is already in effect for a similar licensed product, Plasma Protein Fraction (Human) (§ 640.92(d)).

Consistent with the Panel's recommendations, FDA also intends to require that the package insert note under the "Description" section of the labeling that the product contains less than 2 mEq/L of potassium. Alternatively, the labeling may note the approximate potassium concentration of the product as determined by the assay of a representative number of lots.

The package insert should also include the approximate chloride ion content of the final product. The approximate concentration may be established by determining the range of chloride ion concentrations of an adequate number of representative lots and be expressed in the package insert either as a range of values or by other means which note the possible variation in concentration. For certain patients, the clinician must know the approximate chloride concentration of a product used for replacing lost plasma to ensure that the proper acid-base relationship of electrolytes in the patient is being maintained (Rahilly, G.T., and T. Berl, "Severe Metabolic Alkalosis Caused by Administration of Plasma Protein Fraction in End-Stage Renal Failure," *The New England Journal of Medicine*, 301:824–826, 1979).

The chloride ion concentration is equally relevant for the proper administration of Plasma Protein Fraction (Human). With the exception of the product labeling for two licensees, this information is already included in the package circular. FDA intends to require that all package circulars for Plasma Protein Fraction (Human) include this information.

19. In accordance with FDA's finding that placental plasma is unsuitable as a source material for the manufacture of Normal Serum Albumin (Human), the agency proposes to amend § 640.80(b) of the biologics regulations to delete reference to placentas as an acceptable source material. In addition, because FDA believes that placental plasma should no longer be used for manufacture of NSA, FDA proposes to delete § 640.84(b) which requires that the labeling of the final product identify whether the product was derived from venous plasma, placental plasma, or both.

In a related matter not specifically addressed by the Panel, FDA is proposing to delete reference to serum and blood as allowable source materials for the manufacture or Normal Serum Albumin (Human), Plasma Protein Fraction (Human), Immune Serum Globulin (Human), and Measles Immune Globulin (Human).

Serum has not been used as a source material for blood derivatives since the advent of the modern anticoagulants, more than two decades ago. Since that

time, serum has not been available to derivative manufacturers. In recent years, the blood clotting mechanism has become more completely understood. It is known that a variety of blood enzyme systems are activated during clotting and that many of these activated enzymes have vasoactive properties. Before FDA would again permit the use of serum as a derivative source material, it would be necessary to demonstrate that these extraneous activated enzymes have been removed, either before or during the fractionation process. Accordingly, FDA is proposing to amend §§ 640.80, 640.90, 640.100, and 640.110, to delete the references to serum as an allowable source material for blood derivatives. Furthermore, licensed manufacturers of plasma derivatives no longer receive whole blood and remove the red blood cells at the fractionation facility. Accordingly, FDA proposes to amend the sections above by deleting the word "blood."

20. The Panel stated that manufacturers of Plasma Protein Fraction (Human) should have a control testing program for measuring prekallikrein activator (PKA) in the product and that the acceptable level of PKA should be no more than 25 percent of the then-current Bureau of Biologics (now CDB) reference standard (Reference Lot No. 1). The panel also recommended that, as technology permits, limits for bradykinin content in PPF should also be established.

FDA accepts these recommendations. Both of these issues were discussed at FDA's Workshop, "Roundtable Discussion of PKA and Bradykinin Measurements in PPF and Albumin," held March 16, 1978. At this meeting, it was found that test methods used by manufacturers for determining the enzyme activity yielded values for the PKA concentration in the product which agreed well with those values determined by the agency. Although FDA does not at this time propose limits for PKA levels, all manufacturers of PPF have instituted control testing programs for measuring PKA and a maximum PKA level equal to 25 percent of that in the 1978 reference preparation (Reference Lot No. 1) is now a product-release criterion with which the manufacturers voluntarily comply. FDA also believes it would be appropriate for manufacturers to establish voluntarily a maximum permissible PKA level for Normal Serum Albumin (Human).

Although PPF has caused hypotensive adverse reactions that cannot be related to its PKA content, at present few, if any, of the reported reactions can be ascribed to the bradykinin content of the product; nor are data currently available to establish the magnitude of a safe and appropriate required limit of bradykinin content. The agency has invited the submission of such data (42 FR 27581; May 31, 1977), but none has been received. Some manufacturers have set voluntarily an in-house bradykinin limit for their products.

21. In its review of Plasma Protein Fraction (Human) (PPF), the Panel noted in several instances that there were inadequate data available for accurately determining the benefit-to-risk ratio for the product. In particular, the Panel found that PPF is effective in maintenance of a normal circulating blood volume, but PPF has not been proven to be effective in the maintenance of oncotic pressure and that the degree of effectiveness of this product may be related to the method of preparation. The Panel recommended that more sophisticated in vivo studies be sponsored within the medical community to evaluate the effectiveness of PPF in elevating oncotic pressure and that, in the absence of such data, the package insert should indicate that no evidence exists that PPF appreciably increases the oncotic pressure of the patient's plasma.

FDA agrees that there are inadequate data to support the oncotic effectiveness of PPF and that the recommended study should be performed. Because the recommended study is directly related to demonstrating the effectiveness of the product for its labeled indications, FDA believes that it is primarily the responsibility of the manufacturers of this product to ensure that such studies are done. Consistent with the Panel's Category I recommendation and because adequate methods to measure oncotic effectiveness may not yet be available, FDA is not proposing to require manufacturers of PPF to undertake these studies at this time. FDA agrees that until adequate data are available the labeling should note that there is no evidence that PPF appreciably elevates oncotic pressure. Accordingly, FDA proposes that this revision in PPF labeling be made in accordance with the Panel's recommendations.

22. In its review of Antihemophilic Factor (Human) (AHF), the Panel recommended that:

a. The labeling should include information about the content of anti-A and anti-B antibodies which may cause hemolytic anemia when given in large amounts.

b. Manufacturers should test each lot of the product to determine its anti-A and anti-B levels.

c. When applicable, the final product should be tested to demonstrate that it contains no more than 0.1 microgram of aluminum per unit of antihemophilic factor.

d. When applicable, the final product should be demonstrated to be free of heparin activity, or the amount of heparin activity remaining should appear in the labeling.

e. The labeling should contain information about the fibrinogen content of the final product.

FDA agrees with these recommendations. All current instruction circulars for AHF include a statement that the product contains anti-A and anti-B isoagglutinins which may cause hemolytic anemia when given in large amounts. In addition, each manufacturer of this product has voluntarily set specification limits for these antibodies, which are included in the product license and are subject to approval by OBRR. All manufacturers now test each lot of final product to ensure that the anti-A and anti-B antibody levels are within the specification limits set in their product license.

All manufacturers using aluminum hydroxide in the processing of AHF have submitted data to FDA demonstrating that all recent lots contain aluminum levels below the maximum limit recommended by the Panel. In addition, the majority of manufacturers routinely test each lot of final product for aluminum. FDA proposes to require that any manufacturer using aluminum hydroxide to process AHF amend its product license to provide for the testing of each lot to ensure that the aluminum content falls below 0.1 microgram per unit of antihemophilic factor.

FDA is aware that there are technical difficulties in measuring low levels of heparin in an accurate and reproducible manner. In addition, because the small amount of heparin used in processing this product is not considered to be clinically significant, there is little value in providing to the consumer a precise measurement of the amount of heparin present. Therefore, FDA advises those manufacturers using heparin to revise their labeling to note the maximum amount of heparin which may be present in the final product, as calculated from the amount introduced during processing. Alternatively, the labeling may state the average amount of heparin found in the final product, as determined by a validated assay of a representative number of lots.

Although AHF is not indicated for the treatment of any form of fibrinogen

deficiency (Cryoprecipitated AHF is the indicated product), the approximate fibrinogen content remains relevant to inform the clinician of the composition of the product. Accordingly, FDA proposes that manufacturers revise their product labeling (package insert) to state the fibrinogen content in terms of an average percentage of the total protein.

23. The Panel made the following recommendations concerning the labeling for Factor IX Complex (Human):

a. Because of the potential side effects associated with Factor IX Complex (Human), the product should be administered only when the patient cannot be managed appropriately with single-donor plasma.

FDA agrees with this recommendation. Because of the product's unavoidable potential for inducing thrombosis and transmitting hepatitis, the physician should be informed that use of single-donor plasma may be more appropriate. Therefore, FDA is proposing to require that the statement "Factor IX Complex (Human) should be used only when the patient cannot be managed adequately with plasma" be included under the "Indications" section of the labeling.

b. The Panel recommended that certain additional information be included on the container label for Factor IX Complex (Human).

FDA agrees in part and disagrees in part with the recommendations. FDA recognizes the necessity of limiting the information on the container label to that absolutely necessary for the product's proper handling and use. As additional information is added to the label, the label becomes crowded and overall clarity is reduced substantially. FDA believes that the assayed quantity of each clotting factor used for the treatment of an indicated deficiency should be stated on the container label. FDA also believes that a warning concerning hepatitis should be included on the container label, such as the hepatitis warning that now is required for other blood products capable of transmitting hepatitis.

However, FDA believes that information concerning the sodium and potassium content of the final product should be included in the package insert, rather than on the container label as recommended by the Panel. Similarly, FDA believes that a warning concerning thrombosis should be included in the "Warnings" section of the package insert. Although thrombosis from use of this product is a significant hazard, because of the infrequency of the occurrence of thrombosis this warning need not be highlighted on the container label.

c. The Panel recommended that the quantity of anticoagulant in the product should be included in the labeling.

FDA interprets the term "anticoagulant" to mean heparin or a calcium-binding ion (specifically, citrate or phosphate). Because of the difficulty of reliably assaying low levels of heparin, either the maximum possible heparin level or the amount determined to be in the final product by a reliable and validated assay should be noted in the labeling. The amount of citrate or phosphate may be determined by assaying a representative number of lots. Such assays must be repeated each time a significant change in the manufacturing process occurs, and the quantities shown in the labeling revised if necessary.

d. The Panel recommended that the labeling include more detailed information regarding the dosage and frequency of administration of the product and information about how to monitor effectiveness of treatment for each indicated clotting deficiency.

FDA agrees with this recommendation. FDA recommends that the dosage information include a data summary on in vivo recovery, biologic turnover rates, and hemostatic levels of the appropriate clotting factors. To keep the labeling as concise as possible, readily available references may be provided for the laboratory measurement of the appropriate clotting factors.

24. In the text of their review of Fibrinolysin (Human) (a combination product containing plasminogen and streptokinase (SK)), the Panel summarized the factors that a clinician should consider before initiating repeated parenteral administration of a product containing SK. The Panel also recommended that all fibrinolytic agents (Fibrinolysin (Human), Streptokinase, and urokinase) should be reviewed again at a later date by a single panel of experts.

FDA advises that, at the present time, there are no plans for these products to be reviewed again by an advisory group from outside FDA; however, if the need should arise, FDA intends that this family of products be reviewed as a group. For the present, these fibrinolytic agents are the regulatory responsibility of OBRR and every effort will be made to assure that FDA's regulatory policies for these products are enforced equitably and consistently. As an example, on April 10 and 11, 1980, a public workshop was held in which the current labeling for these fibrinolytic agents was discussed. One of the objectives of this meeting was to develop consistent labeling for these products. In addition, the considerations for SK therapy summarized by the Panel, their other labeling recommendations, and recent scientific information were reviewed with the intent of updating the product labeling in light of current medical knowledge.

25. The Panel recommended that all lots of $RH_o$(D) Immune Globulin should be assayed by an approved method and that there should be consistency in assay standardization and expression of potency.

For the present, the agency does not consider it necessary to require a specific standardized test method for determining the potency of this product. Although all manufacturers do not use the same potency assay method, each lot must be tested against a U.S. Reference $RH_o$(D) Immune Globulin obtained from OBRR. Each dose of the final product is contained in a volume between 0.5 and 2.0 mL of immunoglobulin and, as specified in each manufacturer's product license, each dose has a potency equal to or greater than that of 1 mL of the reference material. Consistency in dosage is assured by the above requirements, although the antibody concentration may vary according to the lot being tested. Lot-to-lot consistency is further assured by means of the following procedures:

a. The U.S. Reference $RH_o$(D) Immune Globulin is tested in parallel with the product on the same day.

b. Several red blood cell phenotypes are used.

c. Potency assays are performed at both the bulk and final container stage during manufacture.

d. Frequently, the potency is confirmed by assays at FDA.

26. The Panel noted three current uses of $RH_o$(D) Immune Globulin (i.e., postpartum administration to Rh-negative mothers after delivery of an Rh-positive child, post-abortion administration to Rh-negative women, and after transfusion of Rh-positive blood to Rh-negative recipients). Six possible uses of the product were also reviewed. The Panel recommended that the requirement for an $RH_o$(D) Immune Globulin crossmatch prior to administration be eliminated and the labeling revised accordingly.

FDA agrees that an $RH_o$(D) Immune Globulin crossmatch prior to administration is no longer necessary and has approved amendments to product licenses to eliminate this requirement.

With regard to the current uses, two manufacturers have submitted appropriate data to FDA supporting low-dose $RH_o$(D) Immune Globulin prophylaxis of Rh-negative women following abortion up to 12 weeks gestation. Product license amendment for this dosage have been approved, and the labeling has been revised accordingly.

In addition to the currently approved indications, the Panel recommended that the product be approved for use after transfusion of any blood product containing Rh-positive red cells to an Rh-negative recipient in whom it is desirable to suppress primary immunization. FDA agrees with this recommendation and advises that manufacturers may revise their product labeling accordingly. In relation to this indication, the Panel mentioned that some preparations of platelets or granulocytes may contain substantial numbers of Rh-positive red cells. FDA advises that the uniform labeling requirements for blood and blood components provide for the inclusion of the Rh group on the container label so that the clinician may determine when primary Rh immunization may occur.

The Panel also suggested that administration of $RH_o$(D) Immune Globulin should be permitted for a period longer than the present labeling limitation of 72 hours postpartum. The Panel recommended that, although administration within 72 hours after exposure to Rh-negative red cells is highly preferable, administration up to 2 weeks after such exposure should be permitted, provided the labeling warns that efficacy may be reduced. FDA agrees with this recommendation. Because the supporting evidence is very limited, the labeling should continue to emphasize the importance of administering the product within 72 hours after exposure. However, the labeling may be revised to provide, with suitable warnings, for administration up to 2 weeks after exposure.

The Panel also recommended that $RH_o$(D) Immune Globulin be administered after significant abdominal trauma, including amniocentesis, to a pregnant, non-sensitized, Rh-negative woman. In principle, FDA agrees with this recommendation, but advises that no clinical data are available to support a specific dosage for the product when used in this manner. Therefore, for this indication, any license amendment submitted to FDA requesting approval of a dose which is lower than the usual postpartum dose must be accompanied by adequate, supportive clinical information. For the remaining three suggested uses—routine intrapartum administration, administration to Rh-negative infants of Rh-positive mothers, and administration to $D^u$-positive women after delivery—FDA agrees with the Panel's finding that further study is needed before recommendations for these uses can be made.

27. In their review of Blood Grouping Serum, the Panel presented the following recommendations:

a. The regulations should be reviewed to reduce, if possible, the number of antigens for which testing must be accomplished in the specificity test.

b. Certain information specified by the Panel should be included on the container label.

c. Manufacturers should provide an Rh control serum for use with anti-D Serum when testing a patient's (but not a normal donor's) blood.

d. Bulk packaging should be permitted for some Blood Grouping Sera.

FDA agrees with the Panel's intent that the regulations not impose unnecessary restrictions which would limit the availability of these products or increase their cost. FDA believes, however, that the present policy meets the Panel's intent, while providing necessary information to the users of this product. Under § 660.26(c), Blood Grouping Serum must be tested with red blood cells having, as a group, the 42 antigens listed in subparagraph (c)(1) of that section. These specificity tests determine whether any contaminating or undesirable antibodies are present in the candidate serum. Under § 660.26(c)(2) and (d)(2), a manufacturer may readily be exempted from testing for any of the less significant antigens when appropriate cells are not available, provided the package insert identifies those antigens for which no specificity test has been performed. In this manner, a user who suspects that the reagent serum is giving nonspecific results may consult the package insert for a list of those factors not tested. If the number of antigens listed for specificity testing were simply reduced, most consumers would have a difficult time in determining what tests the manufacturer was required to perform, and what untested antigens might be suspected.

FDA agrees that because of the vial's small size, the container label should be reserved for only critical information. The container label requirements under § 660.28(a)(2) were promulgated by FDA with the intent of limiting the amount of required information to a minimum. As an additional consideration, this product is often separated from the package insert and package label during use; therefore, it is essential that the vial label include all information necessary for the product's proper use by a knowledgeable consumer, e.g., a trained technician. Accordingly, information in addition to that recommended by the Panel, such as the expiration date, recommended test method, antibody specificity, and the source material used if other than human, is required on the vial label. The volume of the product is also required on the label because it would be a greater burden for manufacturers to print separate package inserts for each volume of product marketed. Accordingly, FDA proposes no changes in the current container label requirements.

As noted by the Panel, an Rh control is not necessary with Anti-D Serum when testing the blood of a normal donor. Current anti-D labeling of high-protein reagents recommends the use of either bovine albumin or an Rh control serum for patient testing. Because Anti-D Serum functions adequately in many situations without a control, FDA does not consider an Rh control serum to be a necessary and integral part of the licensed product. Accordingly, FDA does not require that manufacturers of Anti-D Serum provide an Rh control serum.

FDA agrees that bulk packaging should be permitted for some Blood Grouping Sera. In a proposed rule published in the **Federal Register** of March 5, 1985 (50 FR 8743), FDA proposed to amend § 660.21(e) to remove all specific volume restrictions for the final product.

28. The Panel recommends that the labeling for Reagent Red Blood Cells be revised to include the following information:

a. A caution against use after the end of the dating period.

b. Specific instructions about how to obtain additional information concerning the test cells.

c. Information about how to dilute test cells and the useful life of the cells so diluted.

d. More specific information about the loss of reactivity with storage.

The Panel also recommended that the data supporting the dating periods for these products be reviewed to determine their adequacy.

FDA agrees that more specific information is needed in the labeling about the loss of antigen reactivity with storage of Reagent Red Blood Cells. In the **Federal Register** of June 11, 1985 (50 FR 24546), FDA proposed to amend the labeling regulations in § 660.35 to require that, for Reagent Red Blood Cell products recommended for the detection

or identification of unexpected antibodies, the package insert identify the specific antigens which are most likely to decrease in reactivity during storage. FDA also proposed to require that the labeling include a statement that the rate at which antigen reactivity is lost is partially dependent upon characteristics of the red blood cell donor, characteristics which are neither controlled nor predicted by the manufacturer.

Although some manufacturers' inserts already warn that Reagent Red Blood Cells are not to be used beyond the expiration date, FDA does not agree that this statement should be required. FDA believes that the technicians using this product are clearly aware of the meaning and implications of the expiration date given on the label and recognize that the performance of the reagent cannot be warranted beyond that date. FDA does not permit use of outdated reagents for required tests in the manufacture of licensed biological products. In some other settings, such as under carefully controlled conditions in a consultant reference laboratory, highly experienced personnel may occasionally use outdated cells successfully for other purposes without endangering the accuracy of the test results.

FDA believes that the current labeling provides appropriate information for the proper use of Reagent Red Blood Cells in normal situations. In addition, manufacturers routinely provide additional information or test results to individual consumers upon request. FDA does not believe, however, that the manufacturer should be required to provide regularly a burdensome compilation of highly technical information and test results. Therefore, FDA believes that at the present time the current system of providing specific information upon individual request functions adequately.

FDA agrees that the data supporting the dating periods for Reagent Red Blood Cells should be reviewed. Currently, in § 610.53(a), a dating period of 35 days is established; however, through the amendment of individual product licenses, a number of manufacturers have been granted dating periods longer than 35 days under the authority of § 610.53(b). The data supporting these dating periods have been reviewed by CDB and confirming data are being sought. FDA will, as appropriate, propose to amend the codified dating period for Reagent Red Blood Cells or advise individual manufacturers to amend their product licenses consistent with the available supportive stability data.

The agency believes that a manufacturer should not provide instructions on how to modify their product by means other than those recommended in the product labeling. Because the current labeling does not recommend dilution of the test cells, consumers who do dilute the cells assume responsibility for the reactivity and stability of the product. Before a manufacturer would be permitted to recommend diluting the test cells, an amendment to the product license accompanied by appropriate supportive data would be necessary.

29. The Panel presented a number of recommendations, further described below, concerning the labeling of Anti-Human Serum. The Panel also identified the antibody specificities that the product should contain when used for each of the reviewed indications.

FDA agrees with the majority of the Panel's recommendations, many of which are already in practice. A guideline concerning the labeling and lot-release requirements for this product was made available and was sent to licensed manufacturers in 1977. The guideline is on file with FDA's Dockets Management Branch (Docket No. 770–0219). FDA believes that the guideline and the current product labeling adequately respond to the Panel's recommendations with few exceptions. The remainder of the recommendations with which FDA agrees are addressed in a proposed rule concerning additional standards for Anti-Human Serum, published in the **Federal Register** of April 30, 1982 (47 FR 18623). FDA advises that the agency published in the **Federal Register** of February 11, 1985 (50 FR 5574) a final rule based on the proposal of April 30, 1982. Elsewhere in that same issue of the **Federal Register**, FDA revoked the guideline on the product.

The Panel recommended that the specific antibodies present in each lot be identified on the vial label. Currently, in conformance with FDA's guideline, the package insert should specify each of the antibody reactivities present. The product is identified on the vial label by a proper name reflecting only the significant antibodies present. For example, a product labeled as "polyspecific" must contain anti-IgG and anti-C3d activity but may or may not also include anti-IgA, anti-IgM, Anti-C3d, anti-C4b and anti-C4d. To require the inclusion on the vial label of each antibody reactivity present could confuse the consumer, who might not be aware of its limited significance, and might be burdensome to the manufacturer by necessitating the printing of customs labels for each lot product. Therefore, FDA intends to continue the current labeling policy for Anti-Human Serum.

For the evaluation of suspected incompatible transfusions, the Panel states that Anti-Human Serum should contain anti-IgG activity, either alone or with anti-complement. FDA requires that both anti-IgG and anti-C3d activity be present in reagents recommended for this use. There is evidence that particular antibody transfusion reactions sometimes are detected best by anti-C3d reagents. Because of the possible serious consequences of an incompatible blood transfusion and because it is not always possible to obtain ideal clinical samples at the optimum time following a suspected transfusion reaction, FDA permits only the polyspecific reagent to be labeled for use in evaluating suspected incompatible transfusions, thereby providing maximum assurance of correct test results.

The Panel recommended that, if anti-C4 activity is present in Anti-Human Serum, the amount should be such that the product is not reactive with normal, clotted, refrigerated red cells. The current guidelines specifies that the product should not agglutinate clotted, normal red cells stored at 2 to 8° C for at least 24 hours. FDA believes that "false positive" reactions may not always be due to anti-C4 activity; high levels of anti-C3d may also agglutinate "normal" cells. In relation to this question, the agency sponsored a study to evaluate the frequency and nature of the "false positive" reactions which are associated with reagents containing anticomplement. The results of the study offer further support for the belief that false positive reactions are not always due to anti-C4 activity. (Nasongkla, M., J. Hummert, and H. Chaplin, Jr., "False positive direct antiglobulin test reactions with polyspecific antiglobulin reagents." *Transfusion*, 22:273–275, 1982).

30. Although all currently available licensed third generation tests for the detection of Hepatitis B Surface Antigen (HBsAg) were found to meet the standards for safety and effectiveness, the Panel urged that a workshop be held for the purpose of redefining "third generation test" sensitivity on the basis of an absolute minimum standard amount of HBsAg that must be detected by an acceptable method, without an inordinate number of false-positive results.

FDA agrees that the development of an appropriate absolute HBsAg standard could improve the

standardization of the third generation test. The FDA Reference Hepatitis B Surface Antigen Panel currently in use is prepared from the sera of known HBsAg positive and negative donors. The quantitation of the HBsAg is not always exactly reproducible as a new reference panel is made; however, licensed manufacturers are given an opportunity to test each panel in order to resolve any disparities before the new panel becomes the standard reference panel.

FDA believes that considerable technical problems remain to be resolved before developing an absolute standard, and that a workshop on this issue is premature. Specifically, FDA considers the available evidence insufficient for establishing the absolute amounts of antigen HBsAg subtypes to be incorporated into such a standard. In addition, present technology cannot assure the preparation of a standard that is suitable for use in determining the sensitivity of licensed third generation tests. Therefore, FDA believes that the use of a reference panel—a procedure which admittedly is somewhat arbitrary, but which is equitable to all test methods—is the best option at present. FDA continues to pursue the development of an absolute standard for HBsAg and, as technology advances, will seek the adoption of a well-defined, absolute minimum reference standard.

31. The Panel recommended that antivenins from sources other than horses should be made available in the United States to treat patients having severe horse serum hypersensitivity.

FDA agrees that antivenins from other animal sources are sometimes needed as alternative drugs to the currently licensed antivenins prepared from horse serum. No such drug presently is licensed in the United States. If antivenins from alternative animal sources are produced in a foreign country, the agency will consider in appropriate circumstances permitting the importation of the product under individual investigational new drug exemptions solely for emergency use for individuals severely hypersensitive to horse serum. FDA expects that new hybridoma technology, now under development, may result in the manufacture of highly purified antivenin products to which recipients would not be severely hypersensitive.

32. The Panel noted that with the presently marketed 10-milliliter size of reconstituted antivenin, 2 to 4 vial doses are recommended for mild envenomation, while 10 to 20 vials may be necessary for treatment of a severe *Crotalidae* envenomation. The Panel stated that a problem with the effective use of these products appears to be undertreatment, partially related to the relatively small amount of material per vial. The small dosage size might encourage an unwarranted over-cautious attitude on the part of the treating physician and result in undertreatment of a patient. Accordingly, the Panel recommended that the container size be doubled.

FDA will consider any application to amend the license for an antivenin product to provide for larger container volumes; however, FDA believes that such a change is unlikely at this time. FDA considers the likelihood of undertreatment due to the small vial size to be minimal. Antivenins have been manufactured in 10 mL volumes for nearly 50 years and many medical texts provide adequate information for aiding the physician in determining an appropriate dosage. Further decreasing the likelihood of undertreatment is the trend toward the designation of regional centers for the treatment of venomous bites, where the personnel are familiar with the proper use of antivenin products.

FDA is also aware that there are technical problems that may outweigh any benefits accured from an increase in container volume. The lyophilization (freeze-drying) of larger product volumes may affect adversely the stability of the product, thereby shortening the dating period of the product. Because emergencies requiring the administration of antivenins rarely occur, a venin product often is held until its expiration date and then discarded. Thus, any decrease in the dating period for antivenins would result in a proportional increase in product wastage through outdating.

33. The Panel recommended that the use of Single Donor Plasma (Human) and of plasma recovered from single unit donations of whole blood should be encouraged for use in fractionation. To this end, the Panel recommended that the regulations be revised to define the appropriate storage and shipping conditions for recovered units of plasma.

Recovered human plasma is an unlicensed source material to be used for further manufacturing only. Blood establishments commonly recover this plasma from units of blood or Single Donor Plasma (Human). The recovered human plasma is then shipped to a manufacturer for fractionation or for preparing in vitro reagents. The agency is reviewing all aspects of the handling, storage, and use of recovered human plasma. Upon completion of this review, the agency intends to take any necessary action to encourage the efficient use of recovered human plasma, while ensuring that the products derived from the plasma are safe and effective.

The agency advises that the current additional standards for Whole Blood (Human) and the plasma derivatives do not prohibit the use of Single Donor Plasma (Human) as a source for blood derivatives. Indeed, Single Donor Plasma (Human), Fresh Frozen, is routinely used by manufacturers as a source of Antihemophilic Factor (Human).

FDA encourages the preparation of as many individual components from a unit of blood as is safely possible, thereby allowing the use of this valuable national resource with the maximum efficiency. As part of this effort, FDA is proposing to amend the regulations in §§ 640.24(b) and 640.34(d) to increase from 4 to 6 hours the time period within which platelet products must be separated from whole blood. With the increased trend toward regionalization of blood-banking centers, there are many instances in which a collection facility is remote from the locations where the components are separated and processed. The proposal would allow such facilities more time to collect and transport blood for the separation of platelet products, thus freeing the remaining components for other uses, including plasma for fractionation. A licensed manufacturer has submitted data to OBRR demonstrating that blood may be held for up to 6 hours at 20° to 24° C before the separation of platelet rich plasma without jeopardizing the safety and effectiveness of the products involved. These data are on file with FDA's Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville MD 20857.

FDA also proposes to clarify § 640.24(b) to apply the proposed 6-hour limit only to the period between the collection of the blood and the separation of the plasma and platelets (platelet rich plasma) from the red blood cells. Previously, if Platelet Concentrate (Human) was the desired product, the regulations were ambiguous as to whether the platelet concentrate had to be separated from the red blood cells and excess plasma within the specified time period. Recently, a representative of a licensed blood bank requested clarification of this provision, noting that there is no scientific basis for prohibiting the separation of platelet concentrate from platelet rich plasma at any time during the 72-hour dating period. Furthermore, it was noted that keeping the full volume of plasma with

the platelets during the storage period would aid in maintaining a proper pH balance, an important element for preserving platelet function. Upon review, FDA agrees that there is no scientific evidence to indicate that the safety and effectiveness of the product would be adversely affected if it were stored initially as platelet rich plasma and subsequently centrifuged to produce platelet concentrate. Accordingly, FDA is proposing to clarify the regulations to provide greater flexibility for maintaining platelet products.

34. Consistent with a proposed amendment to § 640.3(b)(3) in the additional standards for Whole Blood (Human), FDA is proposing to revise the donor suitability requirements in § 640.63(c)(1) to require that donors of Source Plasma (Human) have a blood hemoglobin level within normal limits as prescribed in the written SOP of the establishment. Occasionally a plasma donor's red blood cells cannot be returned to the plasma donor, for example, because of a clot in the collected blood or a leak in the blood container. Accordingly, a plasmapheresis center should determine that a donor's blood has a normal hemoglobin level to assure that the donor can tolerate the loss of up to a unit of whole blood. As recommended by the Panel, FDA believes that the acceptable minimum hemoglobin level generally should be 13.5 grams per deciliter (g/dL) of blood for males and 12.5 g/dL for females. However, the appropriate limits for hemoglobin level at each establishment is dependent on factors such as the establishment's location and the method of collecting the blood sample. Under proposed § 640.63(c)(1), FDA would permit each plasmapheresis establishment to select appropriate normal limits for the hemoglobin level of its donors, based on sound scientific principles. The establishment would be required to include in its written SOP the selected limits and the method of collecting the sample of blood used in determining a donor's hemoglobin level. As provided under § 601.12, establishments should submit the SOP above to the Director, OBRR, for approval as an establishment license amendment. Establishments not submitting an SOP to FDA would be presumed to have adopted the normal limits for hemoglobin level recommended by the Panel, i.e., 13.5 g/dL for males and 12.5 g/dL for females.

35. The Panel recommended that the frequency of testing a plasmapheresis donor's blood for specific plasma proteins should be based upon the cumulative volume of plasma collected, as well as on the time elapsed since the last tests were conducted, as is currently required. The Panel also recommended that, while the blood sample is being tested and the accumulated laboratory data are being reviewed, the amount of plasma collected from the donor should be limited to that obtained from 2 liters of whole blood.

Currently, under § 640.65(b)(1)(i), a blood sample must be taken on or before the day of the first donation and each 4 months thereafter. A variety of tests, including measurement of specific plasma proteins, are performed on the sample. The results of these tests, along with other laboratory data, must then be reviewed to determine whether the donor may continue in the plasmapheresis program. Under § 640.65(b)(2)(i), this review must be completed within 21 days after the sample is drawn. The 4-month period was initially based on data submitted in support of product licenses and has since been supported by additional information gathered by licensees and by the review of records during FDA inspections. These data show that, although the levels of individual plasma components may fluctuate, the total protein remains relatively constant during a 4-month period. Under § 640.65(b)(2)(i), if the 4-month blood sample is found to have a total protein value of less than 6.0 grams per deciliter or a protein composition not within the normal limits established by the testing laboratory, the donor must be removed from the plasmapheresis program until the values return to normal. These provisions are intended to ensure that a donor is removed from an extended plasmapheresis program before his or her health may be clinically impaired. The agency is not aware of any data that suggest that the safety of a donor, having previously been determined to be in good health, may be adversely affected by plasmapheresis during the 4-month interval between blood tests, nor is FDA aware of evidence to support the required retesting of a donor's blood after the donation of a given volume of plasma, e.g., that obtained from 12,000 mL of whole blood as was suggested by the Panel. Lacking such data, FDA rejects the Panel's recommendation and proposes to retain the present 4-month interval for the required testing of a donor's blood.

As stated previously, a donor's serum protein levels and other accumulated laboratory data must be reviewed every 4 months to determine whether long-term plasmapheresis is adversely affecting the donor's plasma protein composition or general health and whether the donor should at least temporarily be removed from the plasmapheresis program. The initial test of a new donor's protein composition primarily serves to establish the normal baseline levels of that donor's plasma components, with which future determinations of the donor's plasma components may be compared. FDA considers the initial medical examination, which includes a urinalysis, and the tests and observations performed on each visit (e.g., weight, blood pressure and pulse, hemoglobin level, and total protein) adequate to ensure that the donor is healthy and has no pre-existing abnormalities which might be significantly aggravated by plasmapheresis during a 4-month interval. Because the protein composition test performed every 4 months is primarily a long-term assessment tool, the agency does not consider it imperative that the results be reviewed immendiately to ensure the safety of the donor.

The 21-day interval currently permitted for the completion of the review process allows for possible delays which may occur when the samples and reports are exchanged between a collection facility and a remotely located testing laboratory. For establishments testing their own samples, this process is routinely handled much more expeditiously. During this maximum 21-day interval, as much as 4.4 liters of plasma may be contributed before the donor's plasma protein profile is examined. FDA does not believe that donation of plasma during the 21-day interval will jeopardize the health of a donor who has previously undergone a medical examination and has, on each day of donation, been determined to be suitable as a donor through a regimen of tests and observations. Accordingly, FDA proposes to retain the 21-day interval currently permitted for reviewing a donor's laboratory data, without imposing any additional volume restrictions on the amount of plasma donated during the interval.

36. The Panel recommended that the donor suitability requirements for plasma donors who are plasmapheresed at the frequency recommended for donations of whole blood or less should be revised to be equivalent to the suitability requirements for whole blood donors, except that the total plasma protein should be determined at each donation as is currently required.

FDA agrees that less stringent donor suitability requirements should be provided for plasma donors contributing

at no greater frequency than that proposed for whole blood donors, i.e., those donors not donating more often than once every 8 weeks, nor more frequently than 4 times a year for females, or 5 times a year for males. The existing regulations related to donor suitability in §§ 640.63 and 640.65 are designed to protect donors who may be the subject of a rigorous plasmapheresis schedule, donating up to 50 to 60 liters of plasma per year. For discussion, the existing donor suitability requirements may be divided into three parts:

a. A medical examination is required on or before the first day of donation and once a year thereafter (§§ 640.61 and 640.63(b));

b. Before the initial donation, the hazards of the procedure are explained and written informed consent obtained from the donor. On each day of donation, the donor's medical history is reviewed, the total serum (or plasma) protein is determined, and other tests and observations are made (§ 640.63 (c) and (d));

c. A blood sample is taken to determine the donor's plasma or serum protein composition on or before the day of the initial donation and every 4 months thereafter; the test results, and other accumulated laboratory data, are then reviewed to determine the donor's suitability (§ 640.65(b)).

The initial medical examination and plasma protein tests are intended to provide the necessary information for determining whether the donor may safely engage, or continue, in a long-term serial plasmapheresis program. The medical history review and the other donor suitability requirements determined on each day of donation are intended to ensure that the donor may be plasmapheresed on that day without jeopardizing the safety of the donor or adversely affecting the quality of the product. Except for the required test for total serum protein, requirements under § 640.63(c) are basically the same as those required on the day of a whole blood donation under § 640.3.

The primary limiting factor for the frequency of donating whole blood is the donor's ability to regenerate red blood cells and maintain iron stores. Because the protein portion of the blood is replaced quite rapidly, protein loss has not been shown to be a significant limiting factor when whole blood is donated every 8 weeks. Similarly, plasma donors donating on an 8-week schedule are not subject to the potential long-term effects which might result from the loss of large volumes of protein during intensive plasmapheresis.

Accordingly, FDA is proposing to add new paragraph (f) to § 640.63 to provide for less stringent donor suitability requirements for those donors contributing plasma (and whole blood) at no greater frequency than that proposed for whole blood donors, i.e., once every 8 weeks and no more frequently than 5 times a year for males and 4 times a year for females. Under the proposed rules, establishments plasmapheresing such a donor would not be required to perform a physical examination, nor would a total serum protein test and specific plasma protein determinations be required.

A significant effect of the proposed exemption is that for many new donors a medical examination and a blood sample for protein component analysis will not be required on the initial visit of the donor. New donors meeting the specified criteria, including those donors who intend to contribute plasma on a regular basis, would be considered exempt under proposed § 640.63(f). Accordingly, the blood sample would be taken and medical examination performed on the second or later visit, whenever the donor fails to meet the criteria specified in proposed § 640.63(f).

The proposed exemption would not apply to donors being immunized for the production of high-titer plasma, although previously immunized donors may qualify for exemption. The exemption also would not apply to donors who require careful monitoring for health-related reasons, such as donors being plasmapheresed for therapeutic purposes, hemophilic donors, and hepatitis B surface antigen reactive donors. FDA also proposes to amend the regulations prescribing the initial donor screening (medical examination), plasma protein tests, and periodic laboratory review by referencing the proposed exemption.

Under proposed § 640.63(f), the suitability requirements for plasma donors meeting the specified criteria would be essentially the same as those applied to whole blood donors, except that informed consent as provided under § 640.61 would still be required. A qualified licensed physician or, as provided under proposed § 640.62(b), another adequately trained and qualified person identified to the Director, OBRR, would be required to explain the hazards of the procedure to the prospective donor before the initial donation.

FDA recognizes that the proposed exemption from a total serum protein determination is inconsistent with the Panel's recommendation that it be retained. FDA is not aware of any data in support of the recommendation to retain this test for individuals donating at a frequency no greater than that permitted for donation of whole blood. To require this test would be inconsistent with the requirements for whole blood donors who, if hemoglobin loss is included, experience loss in protein nearly identical to that experienced by plasma donors on each donation. Past experience has shown that the total protein level of even the most extensively plasmapheresed donor rarely falls below the minimum acceptable level, 6 grams per deciliter, established under § 640.65(b)(2)(i). An 8-week interval between donations will be ample time for the resynthesis of plasma components and for the total protein to return to previous levels. Accordingly, the agency finds that the total protein level is not a limiting factor in determining the suitability of donors being plasmapheresed according to the criteria in proposed § 640.63(f).

FDA is also proposing to amend § 640.65(b)(1)(i) by removing a gender-specific pronoun. In the future, the agency will remove other gender-specific pronouns in Subpart G of Part 640.

37. The Panel suggested that trained personnel other than a licensed physician be permitted to screen donors for acceptability providing there are adequate safeguards for the donor.

FDA agrees that adequately qualified and trained persons other than a licensed physician may safely screen normal healthy donors. In addition, the agency has reviewed the routine duties which currently either require the presence or the active participation of a licensed physician. The agency has determined that these routine duties, related to the assessment and plasmapheresis of normal healthy donors, may be performed by an adequately qualified and trained individual other than a licensed physician without jeopardizing the health of the donor or resulting in adverse effects on the quality of the final products. Specifically, these duties includes the following: (1) Explanation of the hazards of the plasmapheresis procedure to a potential donor (§ 640.61); (2) determination of donor suitability, collection of whole blood and return of red blood cells, during which a licensed physician must be on the premises (§ 640.62); (3) the initial medical examination and certification of good health (§ 640.63(b)); and (4) the periodic review of laboratory data (§ 640.65(b)(2)(i)).

Accordingly, FDA is proposing to amend § 640.62 to permit an adequately trained and qualified person other than a licensed physician to perform routine duties specified above, as they relate to

the assessment and plasmapheresis of normal healthy donors, provided the Director, OBRR, is notified at least 30 days in advance of the assumption of such duties by the individual. Before such a person could assume these additional duties, FDA believes there should be a brief training period during which a licensed physician acquaints the person with the procedures and problems particular to the plasma center. Thereafter, the person would be under the direction of a licensed physician, but the presence of the physician during any of the specified duties would not be required.

The proposed provisions would not apply to the assessment to donors with a previously diagnosed disease who are being plasmapheresed for the further manufacturing of in vitro diagnostic reagents, or who are being immunized for the production of high-titer plasma. A licensed physician responsible to the establishment shall continue to determine that the donor remains in generally good health, as judged by the applicable criteria for medical history and laboratory measurements defined under § 640.3. Exceptions to these general health standards, including laboratory measurements, may be made on application to the Director, OBRR. Examples of donors with a previously diagnosed disease who may be in generally good health and, therefore, plasmapheresed for special purposes, but for whom the proposed exemption would not apply, include donors with a coagulation factor deficiency, rheumatoid arthritis, systemic lupus erythematosis, syphilis, or a variety of autoimmune type syndromes.

FDA advises that the term "on the premises" as used in § 640.62 has consistently been interpreted by FDA to include when a physician is available within 15 minutes of the facility to respond to medical emergencies. Although under the proposed provisions a specific licensed physician would no longer need to be available, adequate emergency medical care must continue to be available with 15 minutes. For example, a plasmapheresis establishment could arrange with an ambulance service to provide emergency transport service, when needed, to a nearby hospital.

The extent and elements of the initial medical examination required by § 640.63(b) vary according to the standard operating procedure of the individual plasmapheresis location. However, FDA has established as basic requirements those elements of a medical examination necessary to determine whether the donor has a condition which might jeopardize the safety of the donor during plasmapheresis or affect the quality of the plasma. The basic elements include a blood pressure determination, ausculation of heart and lungs, abdominal palpitation, a brief neurological examination, and a urinalysis. These basic donor screening procedures are not comparable to the more comprehensive physical examination that a person would receive from the person's personal physician. In addition, a medical or physical examination is often construed to involve the direct participation or close supervision of a licensed physician. Accordingly, the agency considers the term "initial medical examination" no longer appropriate in § 640.63(b) and is proposing to revise this paragraph by substituting the term "initial donor screening" for the term "initial medical examination," where appropriate. The basic required elements of the initial donor screening, as established under each establishment's license application, remain unchanged.

The agency recognizes that the provision to permit adequately qualified and trained individuals other than a licensed physician to perform the periodic review of laboratory data is additional to the Panel's recommendation. Currently, the acceptable limits by which the various laboratory data are assessed must be set in the establishment's standard operating procedures and license application. Although considerable expertise is required initially to determine appropriate acceptable limits, the agency believes that an adquately qualified and trained individual other than a licensed physician may readily interpret laboratory data to determine whether they fall within the specified acceptable limits.

A significant effect of the proposed regulations would be that the presence of a licensed physician would no longer be required at many plasmapheresis establishments which only collect plasma from normal healthy donors. A licensed physician shall, however, remain responsible for setting appropriate standard operating procedures and reviewing and assessing all donor reactions, and he/she must be available to offer guidance, as necessary, to the plasmapheresis establishment. FDA advises that State and local laws may place additional restrictions upon the qualifications and degree of supervision required to perform certain medically related duties. Each plasmapheresis establishment is responsible for ensuring that its assignment of duties is in conformance with State and local laws.

Upon initial review, the agency had determined that a physician assistant who has undergone training in a plasmapheresis center is an example of an individual appropriately qualified to perform the duties specified under proposed § 640.62(b). In recent years there has been increased use of professional physician assistants who are trained to perform, under a physician's supervision, some of the more routine duties previously reserved for a licensed physician, such as routine medical examinations and the assessment of laboratory data. These physician assistants, also variously known as Medix, health practitioners, or physician associates, are certified by the National Commission on Certification of Physician Assistants (NCCPA).

FDA recognizes that there may be other para-medical professionals, such as certain specialists within the nursing profession, who are as qualified as a physician assistant for performing routine medical examinations and reviewing laboratory data at a plasmapheresis establishment. FDA invites the submission of information concerning training programs which should be considered adequate in providing the appropriate qualifications. Upon review of the submitted information, FDA will prepare a list of those training programs determined to be acceptable. Thereafter, the list will be updated, as necessary, as additional training programs are determined to be acceptable. At the time of the final rule and thereafter, this list will be made available, through the Director, Office of Biologics Research and Review, to plasmapheresis centers as an aid for selecting individuals whom FDA considers qualified for performing the duties specified in proposed § 640.62(b).

Licensed plasmapheresis establishments intending to employ an individual for the purposes specified in § 640.62(b) will be required to notify the Director, OBRR, at least 30 days in advance of the assumption of duties by the individual. The notification should include the individual's name, information demonstrating that the individual meets appropriate qualification requirements established by FDA, certification that the individual has successfully completed an introductory training period at a plasmapheresis center that was conducted by a licensed physician, and certification that emergency medical care is suitably available.

38. The Panel presented a number of recommendations regarding the procedures for the immunization or hyperimmunization of plasma donors for the production of high-titer plasma.

Many of these recommendations have already been implemented by FDA in "Guidelines for Immunization of Source Plasma (Human) Donors with Blood Substances," last revised and made available on October 21, 1980 (45 FR 69561). The FDA guideline, is used by blood establishments as a guide for the safe and effective immunization of donors with Blood Group Substances or red blood cells for the production of high-titer plasma. Provisions of the guideline which are consistent with specific Panel recommendations are:

a. Women should not be immunized except when documented to be incapable of childbearing;

b. Protocols for de novo immunization (immunization with an antigen to which the individual has no preexisting antibodies) with red blood cells for elicitation of antibodies other than anti-$Rh_o$ (D) will be considered by FDA only on an individual basis under IND protocol.

c. At each donation, the red blood cell donor should be found nonreactive by a third generation HBsAg test. During the first 6 months that a new donor's red blood cells are used, each recipient should have a monthly HBsAg test. (Thereafter, the recipient's blood is tested for HBsAg reactivity upon each donation of Source Plasma (Human), under § 640.67.)

d. The guideline provides for the extensive characterization of new red blood cell donors, including phenotyping of the red cells, and, as described above, a preliminary 6-month trial period for new donors during which the donor's blood is documented not to have transmitted hepatitis or other blood-transmissible diseases to the recipient. Because adequate donor characterization is time-consuming and expensive, the guideline promotes continued use of well-characterized donors. Thus, the agency believes there is adequate incentive for establishments to limit to a minimum the number of donors used as the source for the immunizing red blood cells.

39. In its review of procedures for immunizing plasma donors with red blood cell antigens, the Panel found that a more complete phenotyping and matching of donors and recipients should be required. The Panel recommended that donors and recipients of red blood cells be phenotyped for the following additional antigens: $Jk^a$ of the Kidd system, $Lu^b$ of the Lutheran system, S and s of the MNSs system, and k (Cellano) of the Kell system.

The current guideline for the red blood cell immunization of Source Plasma (Human) donors, last revised and made available May 5, 1978 (43 FR 19461), calls for the phenotyping of donors and recipients for C, D, E, c, e, $Fy^a$ and K (Kell), and phenotyping for other specificities is recommended. FDA agrees that further characterization is desirable; but, except as described below, it may not be practicable at this time.

In May 1979, FDA surveyed all manufacturers of Source Plasma (Human) who had been approved to immunize donors with red blood cells. The manufacturers reported that a total of 2,219 donors were immunized during the year preceding the survey and that 122 (5.5 percent) of these donors produced an unwanted antibody. The unwanted antibodies were of 24 different specificities, including anti-$Jk^a$, -$Lu^a$, -S and -s. No examples of anti-k of anti-$Lu^b$ were found.

Each of the over 2,000 donors immunized yearly must be phenotyped and suitable immunizing red blood cells identified using specific antisera (Blood Grouping Sera). The same reagents are used to select safe blood for transfusing patients sensitized to specific red blood cell antigens, an essential function necessary to prevent a hemolytic transfusion reaction. Currently, no establishment is licensed for the manufacture of anti-$Lu^a$ or anti-$Lu^b$ Blood Grouping Serum; the remainder of those antisera necessary to meet the Panel's recommendation are in short supply. If the Panel's recommendations were implemented, the availability of the reagent antisera for the more important function of selecting safe blood for sensitized patients would be jeopardized.

The agency recognizes that it is especially important to avoid immunization of persons with rare phenotypes. These phenotypes include k (Cellano)-negative (0.2 percent of population) and $Lu^b$ negative (0.15 percent), but there is a long list of such high-incidence antigens which could be considered of equal importance.

In the case of the Cellano antigen, however, persons with the k-negative phenotype may be readily identified with minimal additional testing. Tests for the antithetical antigen, K (Kell), are already required. With rate exceptions, persons who are Cellano-negative are Kell-positive. Therefore, it is reasonable to test only candidate recipients of red blood cells who are Kell-positive (10 percent of the population) for Cellano. The Cellano status of the immunizing cells is irrelevant when the recipient is Cellano-positive. By testing only those recipients who are K (Kell)-positive and not testing the immunizing cells for Cellano, the potential antiserum requirement is reduced by more than 90 percent while adequately protecting the k (Cellano)-negative population.

Accordingly, FDA intends to revise the guideline for the red blood cell immunization of Source Plasma (Human) donors to provide for the testing of Kell-positive recipients of red blood cells for the Cellano antigen. Consistent with the existing guideline, persons found to be k (Cellano)-negative should not be injected with k-positive cells unless they have preexisting anti-k antibody. Pending the consideration of comments, FDA is announcing that the revised guideline will be made available at the time of publication of any final rule based on this proposal.

40. The Panel noted that there is a lack of supportive data for the dosage schedules recommended in the guideline for de novo immunization for anti-$Rh_o$ (D) and for injection of red blood cells into donors with preexisting antibody titers. The Panel recommended the retention of the guideline schedules until such time as more data are available to provide a basis for the modification of the dosage schedules.

FDA recognizes the desirability of gathering data which either support the present schedules or provide the basis for their modification. Source Plasma (Human) manufacturers licensed for the immunization of donors with red blood cells completed a questionnaire in June 1979, which provided some preliminary data regarding the success of the current dosage schedules. Another survey is planned to further define the effectiveness of the current dosage schedules.

Through the continued cooperation of the plasma establishments and the review and analysis of data on file in license applications, FDA will continue to investigate this question. When supportive data are obtained, the agency will revise the dosage schedules recommended in the guideline appropriately.

41. Throughout its Final Report, the Panel identified many areas in which there should be further investigation beyond that immediately required of a manufacturer for a safe, effective, and properly labeled product. In many cases, the Panel identified the appropriate sector of the medical research community and possible sources of support for carrying out the recommended investigations.

FDA believes that these recommendations provide an outline of what may be, through the cooperative efforts of public, private, and governmental research organizations, the major advances in improving the safety and efficacy of blood and blood derivatives throughout the next decade. In several instances in this response to the Panel's recommendations, the agency has identified areas of research recommended by the Panel in which FDA has been, or is now, actively engaged. Furthermore, FDA will continue to use the Panel's recommendations as a basis for initiating or supporting investigative studies in the future. Because FDA is primarily a regulatory agency, the areas and extent of research in which it may justifiably engage are limited to areas supportive of product regulation; therefore, many of the suggested investigations are beyond the scope of FDA's research authority of capabilities. The agency strongly urges the cooperation of all interested research organizations in meeting the objectives defined by the Panel for improving the safety and effectiveness of blood and blood derivatives.

Additional background data, information, and references concerning this proposal may be seen in the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday.

The agency has determined under 21 CFR 25.24(c)(10) (April 26, 1985; 50 FR 16636) that this proposed action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor environmental impact statement is required.

FDA has examined the regulatory impact and regulatory flexibility implications of the proposed regulation in accordance with Executive Order 12291 and the Regulatory Flexibility Act. The agency concludes that the requirements would affect four groups of establishments in the blood products industry.

*Blood Banks*

The economic impact is expected to be neutral on 3,000 blood banks, of which 1,500 are small businesses, because some minor burdens would be imposed while others would be removed.

*Plasma Centers*

An average yearly savings of about 6,600 dollars is expected to result for each of 350 plasma centers, of which 100 are small businesses, because several significant regulatory burdens would be removed.

*Plasma Derivative Manufacturers*

An expense increase of about 100 dollars annually is expected to result for each of 18 plasma derivative manufacturers, none of which are small businesses, because some additional product testing burdens would be imposed.

*Diagnostic Reagent Manufacturers*

A one-time expense of $560 is expected to result for each of seven diagnostic reagent manufacturers, of which three are small businesses, because of additional product labeling burdens for Reagent Red Blood Cells.

The expected economic impact of the proposal on small businesses or on consumers of the affected products are insufficient to warrant designation of the proposal as a major rule under any of the criteria specified under section 1(b) of Executive Order 12291 or to require a regulatory flexibility analysis. Accordingly, under section 605(b) of the Regulatory Flexibility Act, the Commissioner of Food and Drugs certifies that this rulemaking, if promulgated, will not have a significant economic impact on a substantial number of small entities. A copy of the threshold assessment supporting this determination is on file with the Dockets Management Branch.

Section 606.151 of this proposed rule contains collection of information requirements already reviewed and approved by the Office of Management and Budget (OMB) under section 3507 of the Paperwork Reduction Act of 1980. OMB assigned these collection of information requirements approval number 0910–0116. In this proposal, FDA is continuing these collection of information requirements. Organizations and individuals desiring to submit comments on these requirements are directed to submit them to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, and to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., Rm. 3208, Washington, DC 20503, Attention: Bruce Artim.

**List of Subjects**

*21 CFR Part 606*

Blood, Laboratories.

*21 CFR Part 610*

Biologics, Labeling.

*21 CFR Part 640*

Blood, Reporting requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, the Public Health Service Act, and the Administrative Procedure Act, it is proposed that Parts 606, 610, and 640 be amended as follows:

## PART 606—CURRENT GOOD MANUFACTURING PRACTICE FOR BLOOD AND BLOOD COMPONENTS

1. The authority citation for 21 CFR Part 606 continues to read as follows:

**Authority:** Secs. 201, 502, 505, 701, 52 Stat. 1040–1042 as amended, 1050–1053 as amended, 1055–5056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371) and the Public Health Service Act (sec. 351, 58 Stat. 702 as amended (42 U.S.C. 262)) and the Administrative Procedure Act (secs. 4, 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 701–706)); 21 CFR 5.10.

2. By revising § 606.151, to read as follows:

**§ 606.151 Compatibility testing.**

Standard operating procedures for routine compatibility testing of Whole Blood or Red Blood Cells shall include the following:

(a) A method of collecting and identifying the blood samples of recipients and donors to ensure positive identification.

(b) The determination of the ABO and Rh groups of the donors and recipient using licensed blood grouping sera of their equivalent.

(c) Antibody detection tests that will demonstrate significant alloantibodies active at 37° C in the serum or plasma of a previously transfused or previously pregnant donor.

(d) The testing of the recipient's serum for unexpected alloantibodies, by the antiglobulin technique or an equally sensitive method that will demonstrate significant antibodies reactive with the donor's cells at 37° C.

(e) Procedures to expedite transfusions in life-threatening emergencies and, if applicable, procedures for testing blood for neonatal transfusions and autologous transfusions.

(Collection of information requirements approved by the Office of Management and Budget under approval number 9010–0116.)

## PART 610—GENERAL BIOLOGICAL PRODUCTS STANDARDS

3. The authority citation for 21 CFR Part 610 continues to read as follows:

**Authority:** Secs. 215, 351, 58 Stat. 690 as amended, 702 as amended (42 U.S.C. 216, 262); 21 CFR 5.10.

4. In § 610.53(a), by revising the item "Whole Blood" to read as follows:

**§ 610.53 Dating Periods for specific products.**

(a) * * *

| | |
|---|---|
| Whole blood collected in: | (a) ACD solution—21 days, provided labeling recommends storage between 1° and 6° C. Sec. 610.51 does not apply.<br>(b) Heparin solution—8 hours, provided labeling recommends storage between 1° and 6° C. Sec. 610.51 does not apply.<br>(c) CPD solution—21 days, provided labeling recommends storage between 1° and 6° C. Sec. 610.51 does not apply.<br>(d) CPDA-1 solution—21 days, provided labeling recommends storage between 1° and 6° C. Sec. 610.51 does not apply. |

* * * * *

## PART 640—ADDITIONAL STANDARDS FOR HUMAN BLOOD AND BLOOD PRODUCTS

5. The authority citation for 21 CFR Part 640 continues to read as follows:

**Authority:** Secs. 215, 351, 58 Stat. 690 as amended, 702 as amended (42 U.S.C. 216, 262); 21 CFR 5.10.

6. In § 640.3, by revising the introductory text of paragraph (b) and by revising paragraphs (b) (3) and (f), to read as follows:

**§ 640.3 Suitability of donor.**

* * * * *

(b) *Qualifications of donor; general.* Donors shall be in good health, as indicated in part by:

* * * * *

(3) A determination that the hemoglobin level is within normal limits. The technique for obtaining the blood sample and the acceptable normal limits for the hemoglobin level shall be prescribed in the written standard operating procedures of the establishment.

* * * * *

(f) *Frequency of donation.* A donor may not serve as a source of Whole Blood more than once in 8 weeks; female donors of Whole Blood shall donate no more frequently than 4 times per year; and male donors of Whole Blood shall donate no more frequently than 5 times per year; *except*, an individual may donate more frequently if:

(1) The donor is examined by a licensed physician at the time of donation and certified in writing to meet all other donor qualifications of this section; or,

(2) Adequate procedures are employed to protect the health of the donor, including procedures to prevent the development of an iron deficiency. The procedures shall be described in the written standard operating procedures of the establishment and shall have been approved by the Director, Office of Biologics Research and Review, Center for Drugs and Biologics.

7. In § 640.5, by revising the introductory text and paragraphs (b) and (c), by redesignating existing paragraphs (d) and (e) as (e) and (f), respectively, and by adding a new paragraph (d), to read as follows:

**§ 640.5 Testing the blood.**

All laboratory tests shall be performed on a pilot or processing sample of blood, and these tests shall include the following:

* * * * *

(b) *Determination of the ABO blood group.* Whole Blood shall be classified according to ABO blood group by testing the red blood cells with licensed Anti-A and Anti-B Blood Grouping Sera and by testing the serum or plasma with known group A and B cells. The unit of Whole Blood shall not be labeled unless any discrepancy in the results of the two tests is resolved. The testing facility may use unlicensed blood grouping sera prepared at such facilities, if the blood grouping sera meet the requirements of Part 660 of this subchapter.

(c) *Determination of the Rh group.* Whole Blood shall be classified according to Rh blood group by testing the red blood cells with licensed Anti-D Blood Grouping Serum. If the test using Anti-D Blood Grouping Serum is positive, no further testing is required. If the test using Anti-D Blood Grouping Serum is negative, the results shall be confirmed by further testing for the D antigen variant $D^u$, using the antiglobulin technique or a technique of equivalent sensitivity. The testing facility may use unlicensed Anti-D Blood Grouping Serum and unlicensed Anti-Human Globulin prepared at such facility, if the sera meet the requirements of Part 660 of this chapter.

(d) *Test for unexpected antibodies.* Whole blood from previously pregnant or transfused donors shall be tested for unexpected antibodies by a method that demonstrates significant alloantibodies.

* * * * *

8. By revising § 640.24(b) to read as follows:

**§ 640.24 Processing.**

* * * * *

(b) Immediately after collection, the whole blood or plasma shall be held in storage between 20° to 24°C, unless it must be transported from the donor clinic to the processing laboratory. During such transport, all reasonable methods shall be used to maintain the temperature as close as possible to a range between 20° and 24°C until it arrives at the processing laboratory where it shall be held between 20° and 24°C until the platelet rich plasma is separated. The platelet rich plasma shall be separated within 6 hours after the collection of the unit of whole blood.

* * * * *

9. By revising § 640.33(a) to read as follows:

**§ 640.33 Testing the blood.**

(a) Blood from which plasma is separated shall be tested as prescribed in § 640.5 (a), (b), (c), and (d).

* * * * *

10. By revising § 640.34(d), to read as follows:

**§ 640.34 Processing.**

* * * * *

(d) *Plasma Platelet Rich.* Plasma Platelet Rich shall be prepared from blood collected by a single uninterrupted venipuncture with minimal damage to and manipulation of the donor's tissue. The plasma shall be separated from the red blood cells by centrifugation within 6 hours after phlebotomy. The time and speed of centrifugation shall have been shown to produce a product with at least 250,000 platelets per microliter. The plasma shall be stored at a temperature between 20° and 24°C, or between 1° and 6°C, immediately after filling the final container. A gentle and continuous agitation of the product shall be maintained throughout the storage period, if stored at a temperature of 20° to 24°C.

11. Section 640.62 is revised to read as follows:

**§ 640.62 Medical supervision.**

(a) *Supervision by a licensed physician.* Except as provided in paragraph (b) of this section, a qualified licensed physician shall be on the premises when donor suitability is being determined, immunizations are being made, whole blood is being collected, or red blood cells are being returned to the donor.

(b) *Alternative supervision.* An adequately trained and qualified person other than a licensed physician, under the direction of a qualified licensed physician, may assume the functions and responsibilities, otherwise reserved

for such physician by the requirements of this subpart with respect to normal donors contributing plasma by plasmapheresis; *provided*, the Director, Office of Biologics Research and Review, Center for Drugs and Biologics, is notified at least 30 days in advance of an assignment of duties in conformance with this paragraph and raises no objection. The provisions of this paragraph shall not apply to functions and responsibilities pertaining to donors with known diseases, such as hemophilic donors, or when donors are being immunized for the production of high-titer plasma.

12. In § 640.63, by revising the heading of paragraph (b), by revising paragraphs (b)(2)(i) and (c)(3), and by adding new paragraph (f), to read as follows:

**§ 640.63 Suitability of donor.**

* * * * *

(b) *Initial donor screening.* (1) * * *

(2)(i) If a donor is to be immunized for the production of high-titer plasma, the initial donor screening for immunization shall be performed by a qualified licensed physician within no more than 1 week before the first immunization injection. The initial donor screening for plasmapheresis need not be repeated if the first donation occurs within 3 weeks after the first injection.

* * * * *

(c) * * *

(3) A determination that the hemoglobin level is within normal limits. The technique for obtaining the blood sample and the acceptable normal limits for the hemoglobin level shall be prescribed in the written standard operating procedures of the establishment.

* * * * *

(f) *Exemptions from donor suitability requirements.* An establishment is not required to perform the initial donor screening, total protein test, tests to determine the immunoglobulin composition of the plasma, and review of laboratory data, as prescribed in paragraphs (b) and (c)(5) of this section and § 640.65(b) (1) and (2), provided the donor meets the following criteria:

(1) The donor has neither donated whole blood nor been plasmapheresed in the preceding 8 weeks;

(2) The donor is not donating plasma (and blood) for more than the fourth time, if female, or fifth time, if male, in a year; and

(3) The donor is healthy and is not being immunized for the production of high-titer plasma.

13. In § 640.65, by revising paragraph (b) (1)(i) and (2)(i), to read as follows:

**§ 640.65 Plasmaphereses.**

* * * * *

(b) * * *

(1)(i) Except as provided under paragraph (f) of § 640.63, a sample of blood shall be drawn from each donor on the day of the initial donor screening or plasmapheresis, whichever comes first, and at least every 4 months thereafter by a qualified licensed physician or by persons under the physician's supervision and trained in such procedure. A serological test for syphilis, a total plasma or serum protein determination, and a plasma or serum protein electropheresis or quantitative immuno-diffusion test or an equivalent test to determine immunoglobulin composition of the plasma or serum shall be performed on the sample.

* * * * *

(2)(i) Expect as provided under paragraph (f) of § 640.63, the accumulated laboratory data, including tracings, if any, of the plasma or serum protein electropheresis pattern, the calculated values of each component, and the collection records shall be reviewed by a qualified licensed physician within 21 days after the sample is drawn to determine whether or not the donor may continue in the program. The review shall be signed by the reviewing physician. If the protein composition is not within normal limits established by the testing laboratory, or if the total protein is less than 6.0 grams per deciliter of sample, the donor shall be removed from the program until these values return to normal.

* * * * *

14. In § 640.80, by revising paragraph (b), to read as follows:

**§ 640.80 Albumin (Human).**

* * * * *

(b) *Source material.* The source material Albumin (Human) shall be plasma from human donors determined at the time of donation to have been free from disease-causative agents that are not destroyed or removed by the processing method, as determined by the medical history of the donor and from such physical examination and clinical tests as may appear necessary for each donor at the time the blood was obtained. Where the source material is a product for which additional standards are effective, the requirements of those additional standards shall determine the propriety of the source material for use in the production of Albumin (Human). Where no additional standards are effective with respect to the source material for the production of Albumin (Human), such source material shall:

* * * * *

15. In § 640.82, by redesignating existing paragraphs (e) and (f) as (f) and (g), respectively, and adding new paragraph (e), to read as follows:

**§ 640.82 Tests on final product.**

* * * * *

(e) *Potassium content.* The potassium content of the final product shall not exceed 2 milliequivalents per liter.

* * * * *

16. By revising § 640.84, to read as follows:

**§ 640.84 Labeling.**

In addition to the labeling requirements of §§ 610.60, 610.61, and 610.62 of this chapter, the container and package labels shall contain the following information:

(a) The osmotic equivalent in terms of plasma and the sodium content in terms of a value or a range in millieqivalents per liter.

(b) The caution "DO NOT USE IF TURBID. NO NOT BEGIN ADMINISTRATION MORE THAN 4 HOURS AFTER THE CONTAINER HAS BEEN ENTERED" placed in a prominent position on the label;

(c) The need for additional fluids when 20 percent of 25 percent albumin is administered to a patient with marked dehydration;

(d) The protein content, expressed as a 4-percent, 5-percent, 20-percent, or 25-percent solution.

17. In § 640.90 by revising the introductory text of paragraph (b), to read as follows:

**§ 640.90 Plasma Protein Fraction (Human).**

* * * * *

(b) *Source material.* The source material of Plasma Protein Fraction (Human) shall be plasma from human donors determined at the time of donation to have been free from disease-causative agents that are not destroyed or removed by the processing method, as determined by the medical history of the donor and from such physical examination and clinical tests as may appear necessary for each donor at the time the blood was obtained. Where the source material is a product for which additional standards are effective, the requirements of those additional standards shall be the criteria for determining the propriety of the material for use in the production of Plasma Protein Fraction (Human). When no additional standards are effective with respect to source material for the production of Plasma Protein Fraction (Human), such source material shall:

* * * * *

18. In § 640.100, by revising paragraphs (b) and (c), to read as follows:

**§ 640.100 Immune Globulin (Human).**

* * * * *

(b) *Source material.* The source of Immune Globulin (Human) shall be plasma from human donors determined at the time of donation to have been free of disease-causative agents that are not destroyed or removed by the processing methods, as determined by the donor's history and from such physical examination and clinical tests as appear necessary for each donor at the time the blood was obtained. The source plasma shall not contain a preservative and shall be stored in a manner that will prevent contamination by microorganisms, pyrogens, or other impurities.

(c) *Additives in source material.* Source plasma shall not contain an additive unless it is shown that the processing method yields a product free of the additive to such an extent that the safety, purity, and potency of the product will not be affected adversely.

19. In § 640.110, by revising paragraphs (b) and (c) to read as follows:

**§ 640.110 Measles Immune Globulin (Human).**

* * * * *

(b) *Source material.* The source of Measles Immune Globulin (Human) shall be plasma from human donors determined at the time of donation to have been free of disease-causative agents that are not destroyed or removed by the processing method, as determined by the donor's history and from such physical examination and clinical tests as appear necessary for each donor at the time the blood was obtained. The source plasma shall not contain a preservative and shall be stored in a manner that will prevent contamination by microorganisms, pyrogens, or other impurities.

(c) *Additives in source material.* Source blood or plasma shall not contain an additive unless it is shown that the processing method yields a product free of the additive to such an extent that the safety, purity, and potency of the product will not be affected adversely.

Interested persons may, on or before March 24, 1986, submit to the Dockets Management Branch (address above), written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: December 13, 1985.

**Frank E. Young,**

*Commissioner of Food and Drugs.*

[FR Doc. 85-30007 Filed 12-23-85; 8:45 am]

BILLING CODE 4160-01-M

Federal Register

Tuesday
December 24, 1985

# Part III

# Department of Defense

# General Services Administration

# National Aeronautics and Space Administration

48 CFR Part 31
Federal Acquisition Regulation (FAR); Selling Costs; Proposed Rule

DEPARTMENT OF DEFENSE

GENERAL SERVICES ADMINISTRATION

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

48 CFR Part 31

Federal Acquisition Regulation (FAR); Selling Costs

AGENCIES: Department of Defense (DOD), General Services Administration (GSA), and National Aeronautics and Space Administration (NASA).

ACTION: Proposed rule.

SUMMARY: The Civilian Agency Acquisition Council and the Defense Acquisition Regulatory Council are considering changes to Federal Acquisition Regulation (FAR) 31.205–38, Selling costs, that are intended to clarify the definition and allowability policy for the cost.

Comments: Comments should be submitted to the FAR Secretariat at the address shown below on or before January 23, 1986 to be considered in the formulation of a final rule.

ADDRESS: Interested parties should submit written comments to: General Services Administration, FAR Secretariat (VRS), 18th & F Street NW., Room 4041, Washington, DC 20405.

Please cite FAR Case 85–71 in all correspondence related to this issue.

FOR FURTHER INFORMATION CONTACT: Ms. Margaret A. Willis, FAR Secretariat, Telephone (202) 523–4755.

SUPPLEMENTARY INFORMATION:

A. Background

The proposed rule is, in part a response to the requirements of Pub. L. 99–145, the Defense Procurement Improvement Act of 1986. The proposed definition of selling includes all aspects of marketing the contractor's products. Included are those aspects which are more specifically addressed in other subsections of the contract cost regulations. Those other relevant subsections, such as advertising and public relations, are cross-referenced in the proposed selling rule and remain controlling as to allowability policy. The proposed rule essentially limits allowable selling costs to market planning costs and direct selling, which is defined as those acts or actions to induce particular customers to purchase particular products or services of the contractor. This revised allowability policy was necessitated by the need to achieve compatibility with revisions currently pending to the subsection on advertising and public relations, and to reduce the negotiable range in a cost area in which the Congress and GAO had noted substantial reinstatements of questioned costs.

B. Regulatory Flexibility Act

The proposed changes to FAR 31.205–38 are not expected to have a significant economic impact on a substantial number of small entities under the Regulatory Flexibility Act (5 U.S.C. 601 et seq.) because most contracts awarded to small entities are awarded on a competitive fixed-price basis and cost principles do not apply.

C. Paperwork Reduction Act

The Paperwork Reduction Act (Pub. L. 96–511) does not apply because this proposed change to FAR 31.205–28 provides clarifications as to the allowability of selling costs, and does not impose any additional reporting or recordkeeping requirements or collection of information from offerors, contractors, or members of the public which require the approval of OMB under 44 U.S.C. 3501 et. seq.

List of Subjects in 48 CFR Part 31

Government procurement.

Dated: December 18, 1985.

Lawrence J. Rizzi,

*Director, Office of Federal Acquisition and Regulatory Policy.*

Therefore, it is proposed that 48 CFR Part 31 be amended as follows:

## PART 31—CONTRACT COST PRINCIPLES AND PROCEDURES

1. The authority citation for Part 31 continues to read as follows:

Authority: 40 U.S.C. 486(c); 10 U.S.C. Chapter 137; and 42 U.S.C. 2453(c).

2. Section 31.205–38 is revised to read as follows:

**31.205–38 Selling costs.**

(a) "Selling" is a generic term encompassing all efforts to market the contractor's products, some of which are covered specifically in other subsections of 31.205. Selling activity includes the following broad categories.

(1) Advertising;

(2) Corporate image enhancement including broadly-targeted sales efforts, other than advertising;

(3) Bid and proposal costs;

(4) Market planning; and

(5) Direct selling.

(b) Advertising costs are defined at 31.205–1(b) and are subject to the allowability provisions of 31.205–1 (d) and (f). Corporate image enhancement activities are included within the definitions of public relations at 31.205–1(a) and entertainment at 31.205–14 and are subject to the allowability provisions at 31.205–1 (e) and (f) and 31.205–14, respectively. Bid and proposal costs are defined at 31.205–18 and have their allowability controlled by that subsection. The allowability of market planning cost is controlled by the provisions of 31.205–12. Costs of activities which are disallowed under cost principles referenced in this paragraph (b) are not to be reconsidered for reimbursement under any other provision of this subsection.

(c) Direct selling efforts are those acts or actions to induce particular customers to purchase particular products or services of the contractor. Direct selling is characterized by person-to-person contact and includes such activities as familiarizing a potential customer with the contractor's products, conditions of sale, service capabilities, etc. It also includes negotation, liasion between customer and contractor personnel, technical and consulting activities, individual demonstrations, and any other activities having as their purpose the application or adaptation of the contractor's products for a particular customer's use. The cost of direct selling efforts is allowable if reasonable in amount.

(d) The costs of any selling efforts other than those addressed in paragraphs (b) or (c) of this subsection are unallowable.

(e) Costs of the type identified in paragraphs (b), (c), and (d) of this subsection are often commingled on the contractor's books in the selling expense account because these activities are performed by the sales departments. However, identification and segregation of unallowable costs is required under the provisions of 31.201–6 and CAS 405, and such costs are not allowable merely because they are incurred in connection with allowable selling activities.

(f) Notwithstanding any other provision of this subsection, selling costs incurred in connection with potential and actual Foreign Military Sales as defined by the Arms Export Control Act, or foreign sales of military products are unallowable on U.S. Government contracts for U.S. Government requirements.

(g) Notwithstanding any other provision of this subsection, sellers' or agents' compensation, fees, commissions, percentages, retainer or brokerage fees, whether or not contingent upon the award of contracts, are allowable only when paid to bona fide employees or established commercial or selling agencies maintained by the contractor for the purpose of securing business (see 3.408–2).

[FR Doc. 85–30310 Filed 12–23–85; 8:45 am]

BILLING CODE 6820–61–M

federal register

Tuesday
December 24, 1985

Part IV

# Office of Management and Budget

**Management of Federal Information Resources; Final Publication of OMB Circular No. A-130**

## OFFICE OF MANAGEMENT AND BUDGET

### Management of Federal Information Resources

December 12, 1985.

**AGENCY:** Office of Management and Budget, Executive Office of the President.

**ACTION:** OMB Circular No. A-130; final publication.

**SUMMARY:** This Circular provides a general policy framework for management of Federal information resources. The Circular implements provisions of the Paperwork Reduction Act of 1980 as well as other statutes, Executive Orders, and policies concerning general information policy, information technology, privacy, and maintenance of Federal records. The Office of Management and Budget (OMB) published a draft Circular for public comment on March 15, 1985, and received comments and suggestions from the public. This Circular supersedes OMB Circular Nos. A-71, A-90, A-108, and A-121.

**DATE:** This Circular is effective December 12, 1985.

**FOR FURTHER INFORMATION CONTACT:** J. Timothy Sprehe, Office of Information and Regulatory Affairs, Room 3235 New Executive Office Building, Office of Management and Budget, Washington, D.C. 20503. Telephone: (202) 395-4814.

**SUPPLEMENTARY INFORMATION:** The Paperwork Reduction Act of 1980, Pub. L. 96-511, 94 Stat 2812, codified at Chapter 35 of Title 44 of the United States Code, establishes a broad mandate for agencies to perform their information activities in an efficient, effective, and economical manner. Section 3504 of the Act provides authority to the Director, Office of Management and Budget (OMB), to develop and implement uniform and consistent information resources management policies; oversee the development and promote the use of information management principles, standards, and guidelines; evaluate agency information management practices in order to determine their adequacy and efficiency; and determine compliance of such practices with the policies, principles, standards, and guidelines promulgated by the Director.

This Circular implements OMB authority under the Paperwork Reduction Act with respect to section 3504(b), general information policy, section 3504(e), records management, section 3504(f), privacy, and section 3504(g), Federal automatic data processing and telecommunications; the Privacy Act of 1974 (5 U.S.C. 552a); sections 111 and 254 of the Federal Property and Administrative Services Act of 1949, as amended (40 U.S.C. 759); the Budget and Accounting Act of 1921 (31 U.S.C. 1 et seq.); and Executive Order No. 12046 of March 27, 1978. The Circular complements 5 CFR Part 1320, Controlling Paperwork Burden on the Public, which implements other sections of the Paperwork Reduction Act dealing with controlling the reporting and recordkeeping burden placed on the public.

In addition, the Circular revises and consolidates policy and procedures in five existing OMB directives and rescinds these directives.

A-71—Responsibilities for the Administration and Management of Automatic Data Processing Activities
Transmittal Memorandum No. 1 to Circular No. A-71—Security of Federal Automated Information Systems
A-90—Cooperating with State and Local Governments to Coordinate and Improve Information Systems
A-108—Responsibilities for the Maintenance of Records about Individuals by Federal Agencies
A-121—Cost Accounting, Cost Recovery, and Interagency Sharing of Data Processing Facilities

### Development of the Circular

On September 12, 1983, OMB published a Notice in the **Federal Register**, 48 FR 40964, announcing development of the OMB Circular on Federal information resources management and soliciting public comment. In response to this notice, OMB received comments from 14 Federal agencies and 39 members of the public. On March 15, 1985, OMB published its draft Circular on the Management of Federal Information Resources (50 FR 10734-10747), inviting the public to comment by May 14, 1985. OMB informally extended the public comment period in order to allow Federal agencies and the public more time to submit their views. By August 1985, OMB had received about 350 letters of comment; 52 percent of these were from the library and academic community, 28 percent were from other members of the public, and 20 percent from Federal agencies and Members of Congress.

### Form of the Circular and Addition of Appendix IV

The draft Circular followed the form of a notice of proposed rulemaking, which is to say that the text of the proposed Circular was accompanied by Supplementary Information containing a lengthy analysis of key sections. The analysis explained the management context and philosophy behind the language of the draft Circular.

The Circular also follows the form of a notice of proposed rulemaking. Many who commented on the draft Circular requested that the explanatory contextual materials not be lost when the Circular was published in final form. OMB accepted this recommendation. Accordingly, in addition to the three appendices included in the draft Circular, OMB has added *Appendix IV, Analysis of Key Sections.* Appendix IV contains a revision and expansion of the analysis of key sections that accompanied the March 15 draft Circular.

This Supplementary Information section focuses on comments received to the March 15 draft Circular and the disposition OMB has made of the comments.

### Additional Comment

Because of the perceived seriousness of deficiencies in the draft Circular of March 15, 1985, several commentators urged that OMB revise the draft, and issue the revision for another round of public comment. With the public notices of September 12, 1983, and March 15, 1985, OMB has twice sought public comment. After analyzing public comment on the March 15 draft and revising the Circular, OMB decided not to accept this recommendation. OMB believes that the Circular as now revised accommodates valid criticisms and objections, that adequate public comment has been sought, and sees little benefit and much delay in a third round of public comment.

### Section-by-Section Analysis

*Section 1. Purpose*

OMB rejected a recommendation that the phrase "management of Federal information resources" be changed to "management and dissemination of Federal information resources" because the definitions of information resources management and government information already include dissemination within management.

*Section 3. Authorities*

OMB expanded the citation of the Federal Property and Administrative Services Act to include section 206 in order to reflect Federal telecommunication standards authorities. Executive Order No. 12472, Assignment of National Security and Emergency Preparedness

Telecommunications Functions, has been added to this section.

*Section 4. Applicability and Scope*

OMB revised this section to include a reference to national security and emergency preparedness telecommunications activities subject to Executive Order No. 12472. One commentator suggested that a general disclaimer be added here stating that the policies apply only where feasible, cost effective, and appropriate in the context of a particular activity. OMB rejected this suggestion because specific disclaimers are included in specific policies and because section 9a(1) assumes that heads of Federal agencies are responsible for managing their information resources in the context of particular activities and agency missions.

Another commentator suggested that the Circular address which guidance will be controlling in the event of inconsistency: the Circular on national security directives. OMB does not believe such inconsistencies exist until shown in specific instances; if they should exist, they should be resolved on an individual basis. Another commentator recommended that this section should make exception for the exclusions identified in the Warner Amendment in the Department of Defense Authorization Act of 1982. OMB believes these exclusions are appropriately treated in the contexts to which they apply, and notes that statute always takes precedence over policy guidance. For clarity, OMB added an explicit reference to this Department of Defense exclusion in the definition of information technology (Section 6h).

*Section 6. Definitions*

*a. Agency.* Although no one commented on the definition of "agency," OMB changed the definition because the previous wording was confusing and did not adequately convey that independent regulatory agencies are included within the meaning of the term.

*b. Information.* One commentator noted that the definition is broader than the definition of the same term in OMB's regulation, 5 CFR 1320. The breadth of the definition is due to the fact that the scope of the Circular is broader than the scope of the regulation. Another commentator believed there were major omissions in the definition, e.g., micrographics, printing and publishing, mail and distribution, libraries, voice communications, reprographics, audiovisual, and manual information systems. OMB believes these are information media, processes, or institutions, rather than information as such, and that the definition as formulated covers them.

*c. Government Information.* One commentator noted that the definition of "government information" does not include information that may be required to be maintained by a Federal agency, presumably as in Federal recordkeeping requirements imposed upon members of the public (e.g., individuals' tax records). OMB does not intend that such information should be considered government information, nor does the Circular extend to such information except as specifically provided (e.g., Appendix I, Section 3a(1)). Another commentator pointed out that the definition would include information maintained by the legislative and judicial branches of government. While it is true that the definition encompasses information held by the legislative and judicial branches, the Circular applies only to agencies of the executive branch as defined in Section 6a. Another recommended that the definition of government information be restricted only to information created or collected by the Federal Government, and not be extended to information processed, transmitted, disseminated, used, stored, and disposed of by the Federal Government. OMB rejected this recommendation because 44 U.S.C. 3504 clearly applies, for example, to information processing and records management.

Several commentators recommended that the definition should pertain to information "created . . . or disposed of by, *or on behalf of*, the Federal Government." (emphasis added) The intent of the recommendation was to make clear that the Circular's policies applied to all information under government control or sponsorship, irrespective of the information processing agent; that is, to include all information created, collected, processed, transmitted, disseminated, used, stored, or disposed of by government contractors or grantees.

OMB rejected the recommendation for several reasons. First, while agencies doubtless have the choice to treat information created or collected on their behalf as government information, OMB does not intend, except where explicitly stated, that policies in the Circular extend to persons or entities that create, collect, process, transmit, disseminate, use, store, or dispose of information on behalf of the government. Section 4 of the Circular states that the policies apply to executive agencies; Section 3a(1) of Appendix I is an explicit statement of application to Federal contracts. Second, existing and longstanding policy embodied in OMB Circular No. A-110, Uniform Administrative Requirements for Grants and Agreements with Institutions of Higher Education, Hospitals, and Other Nonprofit Organizations, permits grantees in such institutions to copyright information created or collected under Federal grants. The fact that such information may be copyrighted implies that the information is not government information, because the government may not copyright government information (17 U.S.C. 101 and 105). Third, the courts have held that requests to Federal agencies for release of information under the Freedom of Information Act do not always extend to those performing information activities under grant or contract to a Federal agency; hence, such information is not government information.

Several commentators recommended that government information be subdistinguished, with special definitions being formulated for, and special policy treatment given to, scientific and technical information, statistical information, or printed information. OMB did not accept the recommendation because the Circular is intended to implement the Paperwork Reduction Act, and the Act itself does not distinguish among various kinds of information.

*f. and g. Access to Information and Dissemination of Information.* The definitions of "access to information" and "dissemination of information," particularly when considered together with Section 8a on information management, drew more comment than any other definitions. Twenty-three persons commented on the definitions. Commentators specially objected to the phrase "upon their request" in the definition of access. They noted that the public may gain access to government information through Freedom of Information Act requests but argued that the Circular makes no provisions to ensure the public knows what information is available or how to obtain the information. They suggested that the tone of the definitions was narrow, negative, and restrictive, and the implications ran contrary to the proper role of government in providing information in a democratic society.

OMB believes that the definitions of access and dissemination, as found in the draft Circular, are sound. In OMB's view, the commentators' objections arose not out of the definitions themselves but out of the uses to which they were put in the draft Circular's policies and their explanation. Accordingly, OMB has made revisions

to the policies and to the Analysis of Key Sections (Appendix IV), but has retained the definitions.

*i. Information Technology Facility.* Several persons pointed out the desirability of standardizing the definition of "information technology facility," as found in the Circular and Appendix II, with "information technology installation," as found in Appendix III. The two terms are retained because they apply to different contexts, and the relationship between the terms is explained in Appendix II, Section 2b.

*k. Government Publication.* A new term, "government publication," has been defined because a new policy statement pertains to government publications. The definition of the term is taken directly from statute (44 U.S.C. 1901).

*Section 7. Basic Considerations and Assumptions*

*7a and 7b.* These statements have been amended and broadened to reflect points raised in comments, namely, that the statements were too narrowly conceived.

*Deleted statement.* The draft Circular contained the statement: The value of government information to the government is solely a function of the degree to which the information contributes to achieving agencies' missions. Comments concerning this statement alleged that the statement underestimated the value of government information to the government, and failed to take account of other public needs, including those of State and local government, that are included in the value of information to the Federal Government. Because of other revisions to Section 7, OMB determined the statement was superfluous and deleted it.

*7c.* A new statement has been inserted in response to many comments that the draft Circular failed to address the positive aspects of government information. The statement incorporates three of the purposes of the Paperwork Reduction Act (44 U.S.C. 3501).

*7d.* Commentators on this statement objected to the application of cost-benefit analysis to government information activities. Many stated that the benefits of government information cannot be easily calculated and that such information holds more benefits than simply economic. Recalling that the statement is an assumption underlying policy, not itself a policy prescription, OMB notes that the statement does not preclude the existence of benefits other than economic (some of which are enumerated in statement 7b) nor does it necessarily presuppose that benefits can be easily calculated. The statement has been revised to incorporate by reference the purposes of the Paperwork Reduction Act cited in the preceding statement. Ensuring that benefits exceed costs, insofar as these are calculable, is a means to minimizing burden and costs and maximizing usefulness.

*7e.* Because many commentators misperceived the role accorded the private sector in the draft Circular, a new statement has been added that summarizes the existing policy found in OMB Circular No. A-76, Performance of Commercial Activities. The import of the new statement is simply that policy stated in Circular No. A-76 is and consistently has been assumed to apply to the management of Federal information resources.

*7g.* Several commentators believed that this statement (formerly statement 7f) did not sufficiently recognize the importance of public disclosure of government information. The statement has been revised to strengthen this point.

One commentary focused on the fact that this statement pertained to the management of Federal agency records rather than management of Federal information resources. Although the Freedom of Information Act and the Privacy Act pertain only to information in agency records, the statement has been broadened, as a basic assumption, to extend to all information resources. The statement is not limited, either by intention or implication, to paper documents, but may also include electronic records.

*7h.* The comments on this statement (formerly statement 7g) offered suggestions already provided for in statute or policy; for example, a distinction involving statistical uses of personal information. No changes were made to the statement.

*7j and 7k.* These statements (formerly statements 7h and 7j) were revised to incorporate language suggested by commentators.

*Section 8. Policies*

*a. Information Management.*

*(1) and (2). Information Collection and Sharing.* Many commentators believed that the formulation of 8a(1) in the draft Circular was too narrow and restrictive, that in fact the Circular would limit the collection of information by Federal agencies more than was intended by the Paperwork Reduction Act. Revised policy statement 8a(1) uses the expression "necessary for the proper performance of the functions of the agency," which is taken directly from the language of the Act (44 U.S.C. 3504 (c)(2)), and introduces a requirement for practical utility, also taken from same section of the Act. Some commentators believed the language should be couched in even broader terms, such as information needed by society or the general public. The intent of the Act, however, was to circumscribe, not to broaden, agency discretion to impose information collection and recordkeeping burdens on the public.

Commentators pointed out that many statutes condition the interagency or intergovernmental sharing of information by Federal agencies. Revised policy statement 8a(2) reflects the existence of such conditions. Many also commented on the phrase "or through commercial sources" in this statement. The revision qualifies this phrase and Appendix IV provides further explanatory analysis of the policy.

*(3) through (6). Privacy Act and Freedom of Information Act.* OMB revised statement 8a(3) to be consistent with statement 8a(1). Statements 8a(4)(b) and 8a(5) have been amended to eliminate ambiguity identified by commentators.

*(8) through (12). Information Dissemination.* Statements 8a(8) and 8a(9) in the draft Circular received more comments than any other sections. First, as regards the policy that dissemination be either required by law or essential to agency missions, commentators believed these criteria were too negative and restrictive, and failed to emphasize the positive value of government information dissemination and the obligation of the government to inform the citizenry. OMB reformulated both the Circular and the analysis in Appendix IV to emphasize the government's obligations to disseminate information, and to conform more closely to the language and intent of the Paperwork Reduction Act.

Second, commentators challenged the policy that agency information products or services should not duplicate similar products or services "that could reasonably be expected to be provided" by other agencies or the private sector "in the absence of agency dissemination." This policy was believed to be vague and impossible to apply. OMB acknowledges that "could reasonably be expected" is an inadequate formulation and has accordingly revised the policy. However, the general stricture against duplicating products or services that are or would otherwise be provided by other government or private sector organizations has been retained because the criterion of non-duplication for

government information resources is clearly stated in the Act; if it is clear that an agency's dissemination would duplicate that of a private organization, the same considerations apply. The analysis in Appendix IV has been expanded to clarify the meaning of this policy.

Third, many commentators suggested that agencies provide adequate notice and opportunity for public comment before terminating information products and services. OMB believes this suggestion has merit as applied to any significant termination, and has incorporated the idea in the revised policy and Appendix IV. With respect to the non-duplication criterion, OMB added the provision that adequate notice should be provided before *initiating* new information products and services. This provision will allow other agencies and private sector interests to inform the initiating agency if a new product or service will duplicate their product or service, and hence satisfies the intent of the draft Circular's language. Further explanation of this policy is also found in Appendix IV.

Fourth, commentators, questioned the language in the draft Circular's statement 8a(9)(a) requiring that agencies disseminate information products and services "in a manner that reasonably ensures the information will reach the members of the public the agency is responsible for reaching." OMB has slightly altered the language while providing a fuller explanation in Appendix IV.

Fifth, commentators challenged the language in the draft Circular's statement 8a(9)(b) that dissemination should be accomplished "in the manner most cost effective for the government, including placing maximum feasible reliance on the private sector . . ." OMB has retained this language, but added a reference to OMB Circular No. A–76 which provides the context for the policy and conditions that address most points raised by commentators. For example, OMB Circular No. A–76 distinguishes between functions that are inherently governmental in nature, and hence should be performed by government employees, and functions that are commercial in nature and may be performed by the private sector. Again, Appendix IV contains additional discussion of the role of the private sector in disseminating government information products and services.

Sixth, commentators criticized the reference to user charges in the draft Circular's statement 8a(9)(c). OMB has retained the draft Circular's language, because OMB Circular No. A–25 already takes account of objections raised. For example, some pointed out that the costs of assessing user charges can be greater than the revenues yielded from the charges; Circular No. A–25 provides for this contingency. Also, commentators failed to note that this policy statement requires user charges only for costs of dissemination of government information, not for creation, collection, processing, and transmission of the information. User charges also are more fully discussed in Appendix IV.

Seventh, in response to comments OMB added new language requiring that agencies establish procedures for ensuring compliance with 44 U.S.C. 1902 concerning Federal depository libraries. Many commentators referenced the Federal depository library program as an existing institutional mechanism for ensuring that much government information is disseminated to and actually reaches the general public. They believed the Circular should strengthen the depository library system. Because OMB agreed with the comments, and since the law provides that government publications be made available to the depository libraries, OMB accepted this recommendation; the Circular requires agencies to make government publications available to the depository library system, and Appendix IV elaborates this point.

*b. Information Systems and Information Technology Management.*

*(1) through (3).* One commentator recommended that these policies be expanded to include a requirement that agencies document a 10 percent return on information technology investments. OMB rejected this recommendation as being too specific for inclusion in a general policy statement.

*(4) and (5).* Several commentators recommended that these statements also include provision for cost effectiveness and meeting specific agency needs. OMB revised the policy to reflect this recommendation and also expanded on the point in Appendix IV.

*(6) and (7).* Commentators noted that the desirability of competition is sometimes conditioned by the fact that competitive processes unnecessarily slow down procurement of information technology, and that other requirements, such as the need for compatibility, may legitimately limit competitive processes. OMB recognizes the validity of these points but believes they may be taken into account without altering the policy statements.

*(8).* Commentators pointed out that agencies have some legitimate needs for customized software, and that acquisition of off-the-shelf software carries its own risks, such as uncertainty over continued maintenance. OMB believes that these quite meritorious considerations do not invalidate the policy statement as it stands.

*(9).* Several commentators said that the term "interconnectivity" has specific and limited meaning in telecommunications, and that "necessary compatibility" would better convey the meaning intended. OMB revised the policy to reflect these comments and expanded on the point in Appendix IV.

*(14).* Commentators recommended that the background materials for this policy statement be strengthened to stress the positive values of standards and that national security directives be referenced. OMB revised Appendix IV to reflect this recommendation and the fact that the General Services Administration issues Federal Telecommunications Standards.

*(15).* Several agencies commented that what may be cost effective for individual program managers may not be cost effective for the agency as a whole and that the policy as drafted places the burden of proof on the agency rather than the program manager. OMB recognizes the potential conflict between agency and program cost effectiveness but believes the burden of proof belongs with the agency to demonstrate that its arrangements for information technology facilities and services are the most cost effective for agency programs.

One commentator recommended that agency information technology facilities be permitted to charge users market rates rather than cost recovery, because cost recovery will not be competitive with market rates. OMB's view is that, if cost recovery is not competitive with market rates, this is prima facie evidence that agency information technology facility arrangements are not cost effective, and that program managers should be freed from mandatory use of such arrangements.

*(16).* Agencies commented that cost recovery systems may be expensive and should not be required where there is no clear benefit to such systems. OMB recognizes this problem and has revised Appendix II, but not the policy statement, to cover this contingency.

*Section 9. Assignment of Responsibilities*

Some commentators on this section objected to a perceived concentration in OMB of decisionmaking power over Federal information resources, believing that the Circular places program decisions in OMB's hands. OMB notes first that the Paperwork Reduction Act

requires the director of OMB to develop and implement Federal information policies, principles, standards, and guidelines (44 U.S.C. 3504). Second, the Circular states, and Appendix IV emphasizes, that program decisionmaking for Federal information resources belongs with the heads of agencies, operating within the policy framework set forth by OMB.

Several commentators recommended that this section include a statement concerning the Federal depository libraries. OMB believes the addition of statement 8a(12)(b) regarding the depository libraries covers this recommendation. Also, OMB did not accept a commentator's recommendation that certain responsibilities be assigned to Federal libraries; such libraries are subunits of agencies and the Circular assigns responsibilities only at the agency level.

Several commentators recommended that OMB assign responsibility for the Office of Personnel Management to develop and implement occupational and position standards for information resources managers. OMB does not believe management of Federal information resources requires establishing new job titles and series. Furthermore, such establishment would require legislation and could not be legally accomplished through an OMB Circular.

Several Federal agencies requested that various statements assigning responsibilities be revised to include reference to their statutory or regulatory responsibilities. OMB reviewed these requests and determined that revisions were unnecessary. The Circular presupposes the existence of, and compliance with, other applicable laws and regulations.

*a(6).* In response to comments OMB revised this statement more accurately to reflect agency responsibilities for Federal records management.

*a(9).* OMB inserted a reference to convey that the "senior official" is identical to the provision of 44 U.S.C. 3506(b).

*b(1).* At the suggestion of a commentator, OMB substituted "information resources management policy" for "information policy" because the latter term is not defined or used elsewhere in the Circular.

*e(4).* One commentator noted that assigning GSA responsibility for providing guidelines and regulations on the *use* of information technology contravenes the Brooks Act (40 U.S.C. 759(g)). OMB revised the statement to reflect this point.

*h(12).* OMB revised the statement in the same manner as statement 9b(1).

*Appendix I*

Several commentators expressed concern that promulgation of the appendix would rescind the OMB "Guidelines on Implementing the Privacy Act," and other suggested combining the appendix with all guidance OMB has issued on the Act. OMB did not intend to replace existing guidance with the appendix. The appendix replaces only the procedural requirements contained in OMB Circular No. A-108. All other guidance remains in force, and OMB has revised the appendix to make that clear. OMB declined to follow the suggestion that the appendix and other guidance be combined, because the purposes of each issuance are different.

Other commentators pointed out inconsistencies in the timing of various reviews required by the Circular's different appendices; suggested clarifying by examples what constitutes a "minor change to a system of records"; suggested changing the timing of the review of section (m) contracts to more frequently than every five years, since review is conducted on a random sample basis and should not prove overly burdensome; and suggested that the first triennial review of routine uses be commenced immediately upon issuance of the Circular. OMB revised the appendix to reflect these comments. OMB revised the appendix to reflect these comments. OMB added a requirement for an annual review of all systems notices; added certain data collection requirements for the annual report pursuant to section (p); and dropped a requirement for the Office of the Federal Register to provide OMB with a consolidated list of changes to agencies' systems of records.

*Appendix II*

Several commentators expressed concern about the cost effectiveness of requiring detailed accounting and chargeback for use of relatively small information technology facilities. OMB agreed with these comments. The intent of Appendix II is to encourage cost effective behavior in the management of Federal information technology resources. In revising the Appendix OMB raised the threshold so that the Appendix applies only to facilities having obligations in excess of $3 million per year.

A number of commentators pointed out that the Appendix does not allow facilities to justify resource requests based upon sharing, except in unusual circumstances. OMB revised the Appendix to clarify that this restriction is included because the normal practice is for users of a facility to include resource requests for the amount of technology use in their budget and appropriation requests.

Several commentators believed that requiring full costs to be recovered from all users within an agency would not be cost effective. OMB disagreed with this viewpoint and retained the draft Circular's formulation. Viable management of a large information technology facility requires that managers know the amount of resources devoted to each user when providing services. Furthermore, effective management of the use of information technology requires that the user have responsibility for and control over the resources consumed by use of the facility.

Finally, a number of commentators questioned the advisability of giving users of significant new applications primary responsibility for selecting which facility will support the applications. OMB disagreed and retained the draft Circular's formulation. When users are dependent on effective technology support to perform their function, control over selection of facility is essential and consistent with holding users responsible for producing their government information products.

*Appendix III*

Several commentators asked for clarification of the relationship between Appendix III and OMB Circular No. A-123. The Appendix itself relates certain of its requirements to requirements in Circular No. A-123 (e.g., annual reporting of security weaknesses as material weaknesses, and a separate assurance of the security of agency automated information systems in the annual internal control report required by Circular No. A-123). Beyond these specific requirements, application controls specified in the Appendix should be verified in vulnerability assessments and internal control reviews of the functional area supported by the application. Installation controls specified in the Appendix should be reviewed as one of the generic controls of an information technology unit itself.

Several commentators asked how the Circular relates to OMB Circular No. A-127, Financial Management Systems. The evaluation and reporting requirements for the systems integrity objective contained in OMB Circular No. A-127 may be met by fulfilling the evaluation and reporting requirements contained in Appendix III to this Circular and in OMB Circular No. A-123.

Several commentators also expressed confusion about the relation between Appendix III and security of national security information. OMB revised Appendix III to clarify that the Appendix provides a minimal set of requirements for the security of Federal automated information systems; required agencies to also incorporate additional requirements for security of information classified for national security purposes; and clarified central agency responsibilities related to national security information.

Several commentators suggested that Appendix III use the term "information technology facility" for consistency with the Circular and Appendix II. The term "information technology installation," as used in Appendix III, includes information technology facilities as well as small localized processing capabilities. OMB retained the term "information technology installation" in order to emphasize the importance of assuring adequate security of such smaller systems as well as of larger facilities. OMB expects that management processes for assuring a proper level of security at small installations will be less detailed and resource intensive than at larger facilities.

Several commentators expressed concern that personnel security responsibilities in the Appendix focused only on screening employees. They pointed out that other personnel activities, such as separation of duties and actions relating to employees leaving an agency, may be more cost effective security measures. OMB agreed with these comments and clarified the language concerning agency personnel programs so as not to limit agency personnel programs to employment screening of personnel, while still requiring employment screening as one tool in agency security programs.

**Circular No. A–130**

*To the Heads of Executive Departments and Establishments*

December 12, 1985.

Subject: Management of Federal Information Resources

1. *Purpose:* This Circular establishes policy for the management of Federal information resources. Procedural and analytic guidelines for implementing specific aspects of these policies are included as appendices.

2. *Rescissions:* This Circular rescinds OMB Circulars No. A–71, A–90, A–108, and A–121, and all Transmittal Memoranda to those circulars.

3. *Authorities:* This Circular is issued pursuant to the Paperwork Reduction Act of 1980 (44 U.S.C. 35); the Privacy Act of 1974 (5 U.S.C. 552a), sections 111 and 206 of the Federal Property and Administrative Services Act of 1949 as amended (40 U.S.C. 759 and 487, respectively), the Budget and Accounting Act of 1921 as amended (31 U.S.C. 11), Executive Order No. 12046 of March 27, 1978, and Executive Order No. 12472 of April 3, 1984.

4. *Applicability and Scope:*

a. The policies in this Circular apply to the information activities of all agencies of the executive branch of the Federal Government.

b. Information classified for national security purposes should also be handled in accordance with the appropriate national security directives. National security emergency preparedness activities should be conducted in accordance with Executive Order No. 12472.

5. *Background:* The Paperwork Reduction Act establishes a broad mandate for agencies to perform their information management activities in an efficient, effective, and economical manner. To assist agencies in an integrated approach to information resources management, the Act requires that the Director of the Office of Management and Budget (OMB) develop and implement uniform and consistent information resources management policies; oversee the development and promote the use of information management principles, standards, and guidelines; evaluate agency information management practices in order to determine their adequacy and efficiency; and determine compliance of such practices with the policies, principles, standards, and guidelines promulgated by the Director.

6. *Definitions:* As used in this Circular—

a. The term "agency" means any executive department, military department, government corporation, government controlled corporation, or other establishment in the executive branch of the government, or any independent regulatory agency. Within the Executive Office of the President, the term includes only the Office of Management and Budget and the Office of Administration.

b. The term "information" means any communication or reception of knowledge such as facts, data, or opinions, including numerical, graphic, or narrative forms, whether, oral or maintained in any medium, including computerized data bases, paper, microform, or magnetic tape.

c. The term "government information" means information created, collected, processed, transmitted, disseminated, used, stored, or disposed of by the Federal Government.

d. The term "information system" means the organized collection, processing, transmission, and dissemination of information in accordance with defined procedures, whether automated or manual.

e. The term "major information system" means an information system that requires special continuing management attention because of its importance to an agency mission; its high development, operating or maintenance costs; or its significant impact on the administration of agency programs, finances, property, or other resources.

f. The term "access to information" refers to the function of providing to members of the public, upon their request, the government information to which they are entitled under law.

g. The term "dissemination of information" refers to the function of distributing government information to the public, whether through printed documents, or electronic or other media. "Dissemination of information" does not include intra-agency use of information, interagency sharing of information, or responding to requests for "access to information."

h. The term "information technology" means the hardware and software used in connection with government information, regardless of the technology involved, whether computers, telecommunications, micrographics, or others. For the purposes of this Circular, automatic data processing and telecommunications activities related to certain critical national security missions, as defined in 44 U.S.C. 3502(2) and 10 U.S.C. 2315, are excluded.

i. The term "information technology facility" means an organizationally defined set of personnel, hardware, software, and physical facilities, a primary function of which is the operation of information technology.

j. The term "information resources management" means the planning, budget, organizing, directing, training, and control associated with government information. The term encompasses both information itself and the related resources, such as personnel, equipment, funds, and technology.

k. The term "government publication" means informational matter which is published as an individual document at government expense, or as required by law.

Other definitions specific to the subjects of the appendices appear in the appendices.

*7. Basic Considerations and Assumptions:*

a. The Federal Government is the largest single producer, consumer, and disseminator of information in the United States. Because of the size of the government's information activities, the dependence of government information activities upon the public's cooperation, and the value of government information to the entire Nation, the management of Federal information resources is an issue of continuing importance to the public and to the government itself.

b. Government information is a valuable national resource. It provides citizens with knowledge of their government, society, and economy—past, present, and future; is a means to ensure the accountability of government; is vital to the healthy performance of the economy; is an essential tool for managing the government's operations; and is itself a commodity often with economic value in the marketplace.

c. The free flow of information from the government to its citizens and vice versa is essential to a democratic society. It is also essential that the government minimize the Federal paperwork burden on the public, minimize the cost of its information activities, the maximize the usefulness of government information.

d. In order to minimize the cost and maximize the usefulness of government information activities, the expected public and private benefits derived from government information, insofar as they are calculable, should exceed the public and private costs of the information.

e. Although certain functions are inherently governmental in nature, being so intimately related to the public interest as to mandate performance by Federal employees, the government should look first to private sources, where available, to provide the commercial goods and services needed by the government to act on the public's behalf, particularly when cost comparisons indicate that private performance will be the most economical.

f. The use of up-to-date information technology offers opportunities to improve the management of government programs, and access to, and dissemination of, government information.

g. Because the public disclosure of government information is essential to the operation of a democracy, the public's right to access to government information must be protected in the management of Federal information resources.

h. The individual's right to privacy must be protected in Federal Government information activities involving personal information.

i. The open and efficient exchange of government scientific and technical information, subject to applicable national security controls and proprietary rights others may have in such information, fosters excellence in scientific research and the effective use of Federal research and development funds.

j. The value of preserving government records is a function of the degree to which preservation protects the legal and financial rights of the government or its citizens, and provides an official record of Federal agency activities for agency management, public accountability, and historical purposes.

k. Federal Government information resources management policies and activities can affect, and be affected by, the information policies and activities of other nations.

*8. Policies:*

a. *Information Management.* Agencies shall:

(1) Create or collect only that informtion necessary for the proper performance of agency functions and that has practical utility, and only after planning for its processing, transmission, dissemination, use, storage, and disposition;

(2) Seek to satisfy new information needs through legally authorized interagency or intergovernmental sharing of information, or through commercial sources, where appropriate, before creating or collecting new information;

(3) Limit the collection of individually indentifiable information and proprietary information to that which is legally authorized and necessary for the proper performance of agency functions;

(4) Maintain and protect individually identifiable information and proprietary information in a manner that precludes:

(a) Unwarranted intrusion upon personal privacy (see Appendix I); and

(b) Violation of confidentiality;

(5) Provide individuals with access to, and the ability to amend errors in, systems of records, consistent with the Privacy Act;

(6) Provide public access to government information, consistent with the Freedom of Information Act;

(7) Ensure that agency personnel are trained to safeguard information resources;

(8) Disseminate information, as required by law, describing agency organization, activities, programs, meetings, systems of records, and other information holdings, and how the public may gain access to agency information resources;

(9) Disseminate such information products and services as are:

(a) Specifically required by law; or

(b) Necessary for the proper performance of agency functions, provided that the latter do not duplicate similar products or services that are or would otherwise be provided by other government or private sector organizations;

(10) Disseminate significant new, or terminate significant existing, information products and services only after providing adequate notice to the public;

(11) Disseminate such government information products and services:

(a) In a manner that ensures that members of the public whom the agency has an obligation to reach have a reasonable ability to acquire the information;

(b) In the manner most cost effective for the government, including placing maximum feasible reliance on the private sector for the dissemination of the products or services in accordance with OMB Circular No. A-76; and

(c) So as to recover costs of disseminating the products or services through user charges, where appropriate, in accordance with OMB Circular No. A-25;

(12) Establish procedures for:

(a) Reviewing periodically the continued need for and manner of dissemination of the agency's information products or services; and

(b) Ensuring that government publications are made available to depository libraries as required by law.

b. *Information Systems and Information Technology Management.* Agencies shall:

(1) Establish multiyear strategic planning processes for acquiring and operating information technology that meet program and mission needs, reflect budget constraints, and form the bases for their budget requests;

(2) Establish systems of management control that document the requirements that each major information system is intended to serve; and provide for periodic review of those requirements over the life of the system in order to determine whether the requirements continue to exist and the system continues to meet the purposes for which it was developed;

(3) Make the official whose program an information system supports responsible and accountable for the products of that system;

(4) Meeting information processing needs through interagency sharing and from commercial sources, when it is cost effective, before acquiring new information processing capacity;

(5) Share available information processing capacity with other agencies to the extent practicable and legally permissible;

(6) Acquire information technology in a competitive manner that minimizes total life cycle costs;

(7) Ensure that existing and planned major information systems do not unnecessarily duplicate information systems available from other agencies or from the private sector;

(8) Acquire off-the-shelf software from commercial sources, unless the cost effectiveness of developing custom software is clear and has been documented;

(9) Acquire or develop information systems in a manner that facilitates necessary compatibility;

(10) Assure that information systems operate effectively and accurately;

(11) Establish a level of security for all agency information systems commensurate with the sensitivity of the information and the risk and magnitude of loss or harm that could result from improper operation of the information systems (See Appendix III);

(12) Assure that only authorized personnel have access to information systems;

(13) Plan to provide information systems with reasonable continuity of support should their normal operations be disrupted in an emergency;

(14) Use Federal Information Processing and Telecommunications Standards except where it can be demonstrated that the costs of using a standard exceed the benefits or the standard will impede the agency in accomplishing its mission;

(15) Not require program managers to use specific information technology facilities or services unless it is clear and is convincingly documented, subject to periodic review, that such use is the most cost effective method for meeting program requirements;

(16) Account for the full costs of operating information technology facilities and recover such costs from government users as provided in Appendix II;

(17) Not prescribe Federal information system requirements that unduly restrict the prerogatives of heads of State and local government units;

(18) Seek opportunities to improve the operation of government programs or to realize savings for the government and the public through the application of up-to-date information technology to government information activities.

9. *Assignment of Responsibilities:*

a. *All Federal Agencies.* The head of each agency shall:

(1) Have primary responsibility for managing agency information resources;

(2) Ensure that the information policies, principles, standards, guidelines, rules, and regulations prescribed by OMB are implemented appropriately within the agency;

(3) Develop internal agency information policies and procedures and oversee, evaluate, and otherwise periodically review agency information resources management activities for conformity with the policies set forth in this Circular;

(4) Develop agency policies and procedures that provide for timely acquisition of required information technology;

(5) Maintain an inventory of the agencies' major information systems and information dissemination programs;

(6) Create, maintain, and dispose of a record of agency activities in accordance with the Federal Records Act of 1950, as amended;

(7) Identify to the Director, OMB statutory, regulatory, and other impediments to efficient management of Federal information resources and recommend to the Director legislation, policies, procedures, and other guidance to improve such management;

(8) Assist OMB in the performance of its functions under the Paperwork Reduction Act, including making services, personnel, and facilities available to OMB for this purpose to the extent practicable;

(9) Appoint a senior official, as required by 44 U.S.C. 3506(b), who shall report directly to the agency head, to carry out the responsibilities of the agency under the Paperwork Reduction Act. The head of the agency shall keep the Director, OMB, advised as to the name, title, authority, responsibilities, and organizational resources of the senior official. For purposes of this paragraph military departments and the Office of the Secretary of Defense may each appoint one official.

b. *Department of State.* The Secretary of State shall:

(1) Advise the Director, OMB, on the development of United States positions and policies on international information policy issues affecting Federal Government information activities and ensure that such positions and policies are consistent with Federal information resources management policy;

(2) Ensure, in consultation with the Secretary of Commerce, that the United States is represented in the development of international information technology standards, and advise the Director, OMB, of such activities.

c. *Department of Commerce.* The Secretary of Commerce shall:

(1) Develop and issue Federal Information Processing Standards and guidelines necessary to ensure the efficient and effective acquisition, management, security, and use of information technology;

(2) Advise the Director, OMB, on the development of policies relating to the procurement and management of Federal telecommunications resources;

(3) Provide OMB and the agencies with scientific and technical advisory services relating to the development and use of information technology;

(4) Conduct studies and evaluations concerning telecommunications technology, and concerning the improvement, expansion, testing, operation, and use of Federal telecommunications systems and advise the Director, OMB, and appropriate agencies of the recommendations that result from such studies;

(5) Develop, in consultation with the Secretary of State and the Director, OMB, plans, policies, and programs relating to international telecommunications issues affecting government information activities;

(6) Identify needs for standardization of telecommunications and information processing technology, and develop standards, in consultation with the Secretary of Defense and the Administrator of General Servcies, to ensure efficient application of such technology;

(7) Ensure that the Federal Government is represented in the development of national and, in consultation with the Secretary of State, international information technology standards, and advise the Director, OMB, of such activities.

d. *Department of Defense.* The Secretary of Defense shall develop, in consultation with the Administrator of General Services, uniform Federal telecommunications standards and guidelines to ensure national security, emergency preparedness, and continuity of government.

e. *General Services Administration.* The Administrator of General Services shall:

(1) Advise the Director, OMB, and agency heads on matters affecting the procurement of information technology;

(2) Coordinate and, when required, provide for the purchase, lease, and

maintenance of information technology required by Federal agencies;

(3) Develop criteria for timely procurement of information technology and delegate procurement authority to agencies that comply with the criteria;

(4) Provide guidelines and regulations for Federal agencies, as authorized by law, on the acquisition, maintenance, and disposition of information technology;

(5) Develop policies and guidelines that facilitate the sharing of information technology among agencies as requried by this Circular;

(6) Review agencies' information resources management activities to meet the objectives of the triennial reviews required by the Paperwork Reduction Act and report the results to the Director, OMB;

(7) Manage the Automatic Data Processing Fund and the Federal Telecommunications Fund in accordance with the Federal Property and Administrative Services Act, as amended;

(8) Establish procedures for approval, implementation, and dissemination of Federal telecommunications standards and guidelines and for implementation of Federal Information Processing Standards.

f. *Office of Personnel Management.* The Director, Office of Personnel Management, shall:

(1) Develop and conduct training programs for Federal personnel on information resources management, including end user computing;

(2) Evaluate periodically future personnel management and staffing requirements for Federal information resources management;

(3) Establish personnel security policies and develop training programs for Federal personnel associated with the disgn, operation, or maintenance of information systems.

g. *National Archives and Records Administration.* The Archivist of the United States shall:

(1) Administer the Federal records management program in accordance with the National Archives and Records Act;

(2) Assist the Director, OMB, in developing standards and guidelines relating to the records management program.

h. *Office of Management and Budget.* The Director of the Office of Management and Budget shall:

(1) Provide overall leadership and coordination of Federal information resources management within the executive branch;

(2) Serve as the President's principal adviser on procurement and management of Federal telecommunications systems, and develop and establish policies for procurement and management of such systems;

(3) Issue policies, procedures, and guidelines to assist agencies in achieving integrated, effective, and efficient information resources management;

(4) Initiate and review proposals for changes in legislation, regulations, and agency procedures to improve Federal information resources management;

(5) Review and approve or disapprove agency proposals for collection of information from the public, as defined in 5 CFR 1320.7;

(6) Develop and publish annually, in consultation with the Administrator of General Services, a five-year plan for meeting the information technology needs of the Federal government;

(7) Evaluate agencies' information resources management and identify cross-cutting information policy issues through the review of agency information programs, information collection budgets, information technology acquisition plans, fiscal budgets, and by other means;

(8) Provide policy oversight for the Federal records management function conducted by the National Archives and Records Administration and coordinate records management policies and programs with other information activities;

(9) Review, with the advice and assistance of the Administrator of General Services, selected agencies' information resources management activities to meet the objectives of the triennial reviews required by the Paperwork Reduction Act;

(10) Review agencies' policies, practices, and programs pertaining to the security, protection, sharing, and disclosure of information, in order to ensure compliance with the Privacy Act and related statutes;

(11) Resolve information technology procurement disputes between agencies and the General Services Administration pursuant to Section 111 of the Federal Property and Administrative Services Act;

(12) Review proposed U.S. government position and policy statements on international issues affecting Federal Government information activities and advise the Secretary of State as to their consistency with Federal information resources management policy.

10. *Oversight.* the Director, OMB, will use information technology planning reviews, fiscal budget reviews, information collection budget reviews, management reviews, GSA reviews of agency information resources management activities, and such other measures as he deems necessary to evaluate the adequacy and efficiency of each agency's information resources management and compliance with this Circular.

11. *Effective Date.* This Circular is effective upon publication [December 12, 1985].

12. *Inquiries.* All questions or inquiries should be addressed to Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, D.C. 20503. Telephone: (202) 395-3287.

13. *Sunset Review Date.* This Circular shall have an independent policy review to ascertain its effectiveness three years from the date of issuance.

**James C. Miller III,**

*Director.*

Appendix I: Federal Agency Responsibilities for Maintaining Records about Individuals
Appendix II: Cost Accounting, Cost Recovery, and Interagency Sharing of Information Technology Facilities
Appendix III: Security of Federal Automated Information Systems
Appendix IV: Analysis of Key Sections

**Darrell A. Johnson,**

*Assistant Director for Administration.*

## Appendix I to OMB Circular No. A-130—Federal Agency Responsibilities for Maintaining Records About Individuals

1. *Purpose and Scope.*

This Appendix describes agency responsibilities for implementing the Privacy Act of 1974, 5 U.S.C. 552a as amended (hereinafter "the Act"). It applies to all agencies subject to the Act. The Appendix constitutes a revision to procedures formerly contained in OMB Circular No. A-108, now rescinded. Note that this Appendix does *not* rescind other guidance OMB has issued to help agencies interpret the Privacy Act's provisions, e.g., Privacy Act Guidelines (40 FR 28949-28978, July 9, 1975), or Guidance for Conducting Matching Programs (47 FR 21656-21658, May 19, 1982).

2. *Definitions.*

a. The terms "agency," "individual," "maintain," "record," "system of records," and "routine use," as used in this Appendix, are defined in the Act (5 U.S.C. 552a(a)). The definition of "agency" in the Act differs somewhat from the definition in the Circular.

b. The term "minor change to a system of records" means a change that does not significantly change the system; that is, does not affect the character or

purpose of the system and does not affect the ability of an individual to gain access to his or her record or to any information pertaining to him or her which is contained in the system; e.g., changing the title of the system manager.

3. *Assignment of Responsibilities.*

a. *All Federal Agencies.* In addition to meeting the agency requirements contained in the Act, and the specific reporting requirements detailed in this Appendix, the head of each agency shall ensure that the following reviews are conducted as often as specified below, and be prepared to report to the Director, OMB, the results of such reviews and the corrective action taken to resolve problems uncovered. The head of each agency shall:

(1) *Section (m) Contracts.* Review every two years a random sample of agency contracts that provide for the maintenance of a system of records on behalf of the agency to accomplish an agency function, in order to ensure that the wording of each contract makes the provisions of the Act apply. [5 U.S.C. 552a(m)(1)]

(2) *Recordkeeping Practices.* Review annually agency recordkeeping and disposal policies and practices in order to assure compliance with the Act.

(3) *Routine Use Disclosures.* Review every three years the routine use disclosures associated with each system of records in order to ensure that the recipient's use of such records continues to be compatible with the purpose for which the disclosing agency originally collected the information. The first such review should commence immediately upon the issuance of this Appendix.

(4) *Exemption of Systems of Records.* Review every three years each system of records for which the agency has promulgated exemption rules pursuant to Section (j) or (k) of the Privacy Act in order to determine whether such exemption is still needed.

(5) *Matching Programs.* Review annually each ongoing matching program in which the agency has participated during the year, either as a source or as a matching agency, in order to ensure that the requirements of the Act, the OMB Matching Guidelines, and the OMB Model Control System and Checklist have been met.

(6) *Privacy Act Training.* Review annually agency training practices in order to ensure that all agency personnel are familiar with the requirements of the Act, with the agency's implementing regulation, and with any special requirements that their specific jobs entail.

(7) *Violations.* Review annually the actions of agency personnel that have resulted either in the agency being found civilly liable under Section (g) of the Act, or an employee being found criminally liable under the provisions of Section (i) of the Act, in order to determine the extent of the problem and to find the most effective way to prevent recurrences of the problem.

(8) *Systems of Records Notices.* Review annually each system of records notice to ensure that it accurately describes the system. Where minor changes are needed, ensure that an amended notice is published in the Federal Register. Agencies may choose to make one annual comprehensive publication consolidating such minor changes. This requirement is distinguished from and in addition to the requirement to report to OMB and the Congress major changes to systems of records and to publish those changes in the Federal Register (see paragraph 4b of this Appendix).

b. *Department of Commerce.* The Secretary of Commerce shall, consistent with guidelines issued by the Director, OMB, develop and issue standards and guidelines for assuring the security of information protected by the Privacy Act in automated information systems.

c. *General Services Administration.* The Administrator of General Services shall, consistent with guidelines issued by the Director, OMB, issue instructions on what agencies must do in order to comply with the requirements of Section (m) of the Act when contracting for the operation of a system of records to accomplish an agency purpose.

d. *Office of Personnel Management.* The Director of the Office of Personnel Management shall, consistent with guidelines issued by the Director, OMB:

(1) Develop and maintain government-wide standards and procedures for civilian personnel information processing and recordkeeping directives to assure conformance with the Act.

(2) Develop and conduct training programs for agency personnel, including both the conduct of courses in various substantive areas (e.g., legal, administrative, information technology) and the development of materials that agencies can use in their own courses. The assignment of this responsibility to OPM does not affect the responsibility of individual agency heads for developing and conducting training programs tailored to the specific needs of their own personnel.

e. *National Archives and Records Administration.* The Archivist of the United States shall, consistent with guidelines issued by the Director, OMB:

(1) Issue instructions on the format of the Agency notices and rules required to be published under the Act.

(2) Compile and publish annually the rules promulgated under 5 U.S.C. 552a(f) and agency notices published under 5 U.S.C. 552a(e)(4) in a form available to the public.

(3) Issue procedures governing the transfer or records to Federal Records Centers for storage, processing, and servicing pursuant to 44 U.S.C. 3103. For purposes of the Act, such records are considered to be maintained by the agency that deposited them. The Archivist may disclose deposited records only according to the access rules established by the agency that deposited them.

f. *Office of Management and Budget.* The Director of the Office of Management and Budget will:

(1) Issue guidelines and directives to the agencies to implement the Act.

(2) Assist the agencies, at their request, in implementing their Privacy Act programs.

(3) Review the new and altered system reports agencies submit pursuant to Section (o) of the Act.

(4) Compile the annual report of the President to the Congress in accordance with Section (p) of the Act.

4. *Reporting Requirements.*

a. *Privacy Act Annual Reports.* To provide the necessary information for the annual report of the President, agencies shall submit a Privacy Act Annual Report to the Director, OMB, covering their Privacy Act activities for the calendar year. The exact format and timing of the report will be established by the Director, OMB. [5 U.S.C. 552a(p)]; but, agencies should, at a minimum collect, and be prepared to report the following data on a calendar year basis:

(1) Total number of active systems of records and changes to that population during the year, e.g., publications of new systems, additions and deletions of routine uses, exemptions, automation of record systems.

(2) Public comments received on agency publications and implementation activities.

(3) Number of requests from individuals for access to records about themselves in systems of records *that cited the Privacy Act in support of their requests.*

(4) Number granted in whole or part, denied in whole, and for which no record was found.

(5) Number of amendment requests from individuals to amend records about them in systems of records *that cited the Privacy Act in support of their requests.*

(6) Number granted in whole or part, denied in whole, and for which no record was found.

(7) Number of appeals of access and amendment denials and the results of such appeals.

(8) Number of instances in which individuals litigated the results of appeals of access or amendment, and the results of such litigation.

(9) Number and description of matching programs participated in either as source or matching agency.

b. *New and Altered System Reports.* The Act requires agencies to publish notices in the **Federal Register** describing new or altered systems of records, and to submit reports on these systems to the Director, OMB, and to the Congress.

(1) *Altered System of Records.* Minor changes to systems of records need not be reported. For example, a change in the designation of the system manager due to a reorganization would not require a report, so long as an individual's ability to gain access to his or her records is not affected. Other examples include changing applicable safeguards as a result of a risk analysis, deleting a routine use when there is no longer a need for the authorized disclosure. These examples are not intended to be all-inclusive.

The following changes are those for which a report is required:

(a) An increase or change in the number or types of individuals on whom records are maintained. For example, a decision to expand a system that originally covered only residents of public housing in major cities to cover such residents nationwide would require a report. Increases attributable to normal growth should not be reported.

(b) A change that expands the types or categories of information maintained. For example, a personnel file that has been expanded to include medical records would require a report.

(c) A change that alters the purpose for which the information is used.

(d) A change to equipment configuration (either hardware or software) that creates substantially greater access to the records in the system. For example, locating interactive terminals at regional offices for accessing a system formerly accessible only at the headquarters would require a report.

(e) The addition of an exemption (pursuant to Section (j) or (k) of the Act). Note that, in submitting a rulemaking for an exemption as part of a report of a new or altered system, agencies will meet the reporting requirements of Executive Order No. 12291 and need not make a separate submission under that order.

When an agency makes a change to an information technology installation, telecommunication network, or any other general changes in information collection, processing, dissemination, or storage that affect multiple systems of records, it may submit a single consolidated new or altered system report, with changes to existing notices and supporting documentation included in the submission.

(2) *Contents of the Report.* The report for a new or altered system has three elements: a transmittal letter, a narrative statement, and supporting documentation that includes a copy of the proposed **Federal Register** notice. There is no prescribed format for either the letter or the narrative statement. The notice must appear in the format prescribed by the Office of the Federal Register's *Document Drafting Handbook.*

(a) *Transmittal Letter.* The transmittal letter shoud be signed by the senior agency official responsible for implementation of the Act within the agency and should contain the name and telephone number of the individual who can best answer questions about the system. The letter should contain the agency's assurance that the proposed system does not duplicate any existing agency systems. It should also state that a copy of the report has been distributed to the Speaker of the House and the President of the Senate as the Act requires. The letter may also include requests for waiver of the reporting time period.

(b) *Narrative Statement.* The narrative statement should be brief. It should make reference, as appropriate, to information in the supporting documentation rather than restating such information. The statement should:

(1) Describe the purpose for which the agency is establishing the system of records.

(2) Identify the authority under which the system is maintained. The agency should avoid citing housekeeping statutes, but rather cite the underlying programmatic authority for collecting, maintaining, and using the information. When the system is being operated to support an agency housekeeping program, e.g., a carpool locator, the agency may, however, cite a general housekeeping statute that authorizes the agency head to keep such records as are necessary.

(3) Provide the agency's evaluation of the probable or potential effects of the proposal on the privacy of individuals.

(4) Describe the relationship of the proposal, if any, to the other branches of the Federal Government and to State and local governments.

(5) Provide a brief description of the steps taken by the agency to minimize the risk of unauthorized access to the system of records. A more detailed assessment of the risks and specific administrative, technical, procedural, and physical safeguards established shall be made available to OMB upon request.

(6) Explain how each proposed routine use satisfies the compatibility requirement of subsection (a)(7) of the Act. For altered systems, this requirement pertains only to any newly proposed routine uses.

(7) Provide OMB control numbers, expiration dates, and titles of any OMB approved information collection requirements contained in the system of records. If the request for OMB clearance of an information collection is pending, the agency may simply state the title of the collection and the date it was submitted for OMB clearance.

(c) *Supporting Documentation.* Attach the following to all new or altered system reports:

(1) An advance copy of the new or altered system notice (consistent with the provisions of 5 U.S.C. 552a(e)(4)) that the agency proposes to publish for the new or altered system. For proposed altered systems the documentation should be in the same form as the agency proposes to publish in the public notice.

(2) An advance copy of any new rules or changes to published rules (consistent with the provision of 5 U.S.C. 552a (f), (j), and (k)) that the agency proposes to issue for the new or altered system. If no changes to existing rules are required, the agency shall so state in the narrative portion of the report. Proposed changes to existing rules shall be provided in the same form as the agency proposes to publish for formal notice and comment.

(3) *Timing and Distribution for Submitting New and Altered System Reports.* Submit reports on new and altered systems of records not later than 60 days prior to establishment of a new system or the implementation of an altered system (5 U.S.C. 552a(o)). Submit three copies of each report to:

President of the Senate, Washington, D.C. 20510

Speaker of the House of Representatives, Washington, D.C. 20515

Administrator, Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, D.C. 20503.

Agencies may assume that OMB concurs in Privacy Act aspects of their proposal if OMB has not commented

within 60 days from the date the transmittal letter was signed. Agencies may publish system and routine use notices as well as exemption rules in the Federal Register at the same time that they send the new or altered system report to OMB and the Congress. The 60-day period for OMB and Congressional review and the 30-day notice and comment period for routine uses and exemptions will then run concurrently.

(4) *Waivers of Report Time Period.* The Director, OMB, may grant a waiver of the 60-day period if the agency asks for the waiver and can demonstrate compelling reasons. Agencies may assume that OMB concurs in their request if OMB has not commented within 30 days of the date the transmittal letter was signed. When a waiver is granted, the agency is not thereby relieved of any other responsibility or liability under the Act. Note that OMB cannot waive time periods specifically established by the Act. Agencies will still have to meet the statutory notice and comment periods required for establishing a routine use or claiming an exemption.

**Appendix II to OMB Circular No. A–130—Cost Accounting, Cost Recovery, and Interagency Sharing of Information Technology Facilities**

1. *Purpose.*

This Appendix establishes procedures for cost accounting, cost recovery, and interagency sharing of Federal information technology facilities. The Appendix revises procedures formerly contained in OMB Circular No. A–121, now rescinded.

2. *Applicability.*

This Appendix applies to all information technology facilities that are operated by or on behalf of a Federal agency; provide information technology service to more than one user; operate one or more general management computers; and have obligations in excess of $3 million per year.

3. *Definitions.*

a. The term "information technology facility" means an organizationally defined set of personnel, hardware, software, and physical facilities, a primary function of which is the operation of information technology. An information technology facility includes:

(1) The personnel who operate computers or telecommunications systems; develop or maintain software; provide user liaison and training; schedule computers, prepare and control input data; control, reproduce, and distribute output data; maintain tape and disk libraries; provide security, maintenance, and custodial services; and directly manage or provide direct administrative support to personnel engaged in these activities.

(2) The owned or leased computer and telecommunications hardware, including central processing units; associated peripheral equipment such as disk drives, tape drives, drum storage, printers, card readers, and consoles; data entry equipment; data reproduction, decollation, booking, and binding equipment; telecommunications equipment including control units, terminals, modems, and dedicated telephone and satellite links provided by the facility to enable data transfer and access to users. Hardware acquired and maintained by users of the facility is excluded.

(3) The software, including operating system software, utilities, sorts, language processors, access methods, data base processors, and other similar multi-user software required by the facility for support of the facility and/or for general use by users of the facility. All software acquired or maintained by users of the facility is excluded.

(4) The physical facilities, including computer rooms; tape and disk libraries; stockrooms and warehouse space; office space; physical fixtures.

b. The term "full costs" means all significant expenses incurred in the operation of an information technology facility. The following elements are included:

(1) Personnel, including salaries, overtime, and fringe benefits of civilian and military personnel; training; and travel.

(2) Equipment, including depreciation for owned, capitalized equipment; equipment rental or lease; and direct expenses for noncapitalized equipment.

(3) Software, including depreciation for capitalized costs of developing, converting, or acquiring software; rental of for software; and direct expenses for noncapitalized acquisition of software.

(4) Supplies, including office supplies; data processing materials; and miscellaneous expenses.

(5) Contracted services, including technical and consulting services; equipment maintenance; data entry support; operations support; facilities management; maintenance of software; and telecommunications network services.

(6) Space occupancy, including rental and lease of buildings, general office furniture, and equipment; building maintenance; heating, air conditioning and other utilities; telephone services; power conditioning and distribution equipment and alternate power sources; and building security and custodial services.

(7) Intra-agency services, including normal agency support services that are paid by the installation.

(8) Interagency services, including services provided by other agencies and departments that are paid by the installation.

c. The term "user" means an organizational or programmatic entity that receives service from an information technology facility. A user may be either internal or external to the agency organization responsible for the facility, but normally does not report either to the manager or director of the facility or to the same immediate supervisor.

d. The term "general management computer" means a digital computer that is used for any purpose other than as a part of a process control system, space system, mobile system, or a system meeting one of the exclusions identified in the Department of Defense Authorization Act of 1982.

4. *Accounting and Reimbursement for Sharing of Information Technology Facilities.*

a. *Interagency Sharing.* Agencies shall:

(1) Share their information technology facilities with users from other agencies to the maximum extent feasible;

(2) Document sharing arrangements, where the total annual reimbursement exceeds $500,000, with individual written agreements that identify:

(a) Services available for sharing;

(b) Service priority procedures and terms (e.g., quality performance standards) to be provided to each user;

(c) Prices to be charged for providing services;

(d) Reimbursement arrangements for services provided; and

(e) Arrangements for terminating the sharing agreement;

(3) Provide standard terms and conditions to users obtaining similar services insofar as possible;

(4) Include such sharing arrangements, when fully documented and part of a formal sharing program, in justifications to OMB for resource requests (see OMB Circular No. A–11, revised) and allocations. Direct funding by a shared facility should be requested only where exceptional circumstances preclude the user agency from using alternative sources.

b. *Cost Accounting.* Agencies shall account for the full cost of the operation of information technology facilities.

c. *User Cost Distribution System.* Agencies shall implement a system to distribute the full cost of providing services to all users. That system will:

(1) Be consistent with guidance provided in the Federal Information Processing Standards Publication No. 96, "Guidelines for Developing and Implementing a Charging System for Data Processing Services" (National Bureau of Standards, Department of Commerce, 1982).

(2) Price each service provided by the facility to the users of that service on an equitable basis commensurate with the amount of resources required to provide that service and the priority of service provided. The price of individual transactions may be estimated provided that they are periodically reconciled to assure that the full costs of operations are equitably distributed among all users.

(3) Directly distribute to the recipient of the services the full costs of dedicated services, including applications developed and maintained; software unique to a single application; and telecommunications equipment, including control units, terminals, modems, and dedicated telephone or satellite links provided by the facility to enable data transfer and computer access to users.

d. *Cost Recovery.* Consistent with statutory authority, agencies shall:

(1) Submit periodic statements to all users of agency information technology facilities specifying the costs of services provided;

(2) Recover full costs from Federal users of the facility; and

(3) Recover costs from nonfederal users of the facilities consistent with OMB Circular No. A–25.

e. *Accounting for Reimbursements Received.* Agencies shall:

(1) Include resource requests for the amount of planned information technology use in user budget and appropriation requests;

(2) Assure that shared facilities reduce budget and appropriation requests by the amount of planned reimbursements from users;

(3) Prepare, at the close of each fiscal year, a report that documents in the agency's official records the full past year cost of operating information technology facilities that recover more than $500,000 per year from sharing reimbursements; and

(4) Use the portion of reimbursements arising from equipment and software depreciation for the replacement of equipment and software capital assets, provided such usage is included in the agency's budget.

5. *Selection of Information Technology Facilities To Support New Applications.*

In selecting information technology facilities to support new applications, agencies shall establish a management control procedure for determining which facility will be used to support each significant application. This procedure shall ensure that:

(a) All alternative facilities are considered, including other Federal agency and nonfederal facilities and services;

(b) Agency rules do not require that priority be given to the use of in-house facilities; and

(c) The user of the application has primary responsibility for selecting the facility.

6. *Assignment of Responsibilities.*

a. *All Federal Agencies.* The head of each agency shall:

(1) Establish policies and procedures and assign responsibilities to implement the requirements of this Appendix; and

(2) Ensure that contracts awarded for the operation of information technology facilities include provisions for compliance with the requirements of this Appendix.

b. *General Services Administration.* The Administration of General Services shall:

(1) Ensure that information technology facilities designated as Federal Data Processing Centers comply with the procedures established by this Appendix;

(2) Ensure that provisions consistent with this Appendix are included in contracts for the operation of information technology facilities when acquiring services on behalf of an agency:

7. *Implementation Requirements.*

Agencies shall implement the provisions of this Appendix effective at the beginning of fiscal year 1987.

**Appendix III to OMB Circular No. A–130—Security of Federal Automated Information Systems**

1. *Purpose.*

This Appendix establishes a minimum set of controls to be included in Federal automated information systems security programs; assigns responsibilities for the security of agency automated information systems; and clarifies the relationship between such agency security programs and internal control systems established in accordance with OMB Circular No. A–123, Internal Control Systems. The Appendix revises procedures formerly contained in Transmittal Memorandum No. 1 to OMB Circular No. A–71, now rescinded, and incorporates responsibilities from applicable national security directives.

2. *Definitions.*

a. The term "automated information system" means an information system (defined in Section 6d of the Circular) that is automated.

b. The term "information technology installation" means one or more computer or office automation systems including related telecommunications, peripheral and storage units, central processing units, and operating and support system software. Information technology installations may range from information technology facilities such as large centralized computer centers to individual stand-alone microprocessors such as personal computers.

c. The term "sensitive data" means data that require protection due to the risk and magnitude of loss or harm that could result from inadvertent or deliberate disclosure, alteration, or destruction of the data. The term includes data whose improper use or disclosure could adversely affect the ability of an agency to accomplish its mission, proprietary data, records about individuals requiring protection under the Privacy Act, and data not releasable under the Freedom of Information Act.

d. The term "sensitive application" means an application of information technology that requires protection because it processes sensitive data, or because of the risk and magnitude of loss or harm that could result from improper operation or deliberate manipulation of the application.

e. The term "security specifications" means a detailed description of the safeguards required to protect a sensitive application.

3. *Automated Information Systems Security Programs.*

Agencies shall assure an adequate level of security for all agency automated information systems, whether maintained in-house or commercially. Specifically, agencies shall:

—Assure that automated information systems operate effectively and accurately;

—Assure that there are appropriate technical, personnel, administrative, environmental, and telecommunications safeguards in automated information systems; and

—Assure the continuity of operation of automated information systems that support critical agency functions.

Agencies shall implement and maintain an automated information systems security program, including the preparation of policies, standards, and procedures. This program will be consistent with government-wide policies, procedures, and standards issued by the Office of Management and Budget, the Department of Commerce,

the Department of Defense, the General Services Administration, and the Office of Personnel Management. Agency programs shall incorporate additional requirements for securing national security information in accordance with appropriate national security directives. Agency programs shall, at a minimum, include four primary elements: applications security, personnel security, information technology installation security, and security awareness and training.

a. *Applications Security.*

(1) *Management Control Process and Sensitivity Evaluation.* Agencies shall establish a management control process to assure that appropriate administrative, physical, and technical safeguards are incorporated into all new applications, and into significant modifications to existing applications. Management officials who are the primary users of applications should evaluate the sensitivity of new or existing applications being substantially modified. For those applications considered sensitive, the management control process shall, at a minimum, include security specifications and design reviews and systems tests.

(a) *Security Specifications.* Agencies shall define and approve security requirements and specifications prior to acquiring or starting formal development of the applications. The results of risk analyses performed at the information technology installation where the applications will be processed should be taken into account when defining and approving security specifications for the applications. Other vulnerabilities of the applications, such as in telecommunications links, shall also be considered in defining security requirements. The views and recommendations of the information technology user organization, the information technology installation, and the individual responsible for security at the installation shall be considered prior to the approval of security specifications for the applications.

(b) *Design Reviews and System Tests.* Agencies shall conduct and approve design reviews and system tests, prior to placing the application into operation, to assure the proposed design meets the approved security specifications. The objective of the system tests should be to verify that required administrative, technical, and physical safeguards are operationally adequate. The results of the design reviews and systems tests shall be fully documented and maintained in the official agency records.

(c) *Certification.* Upon completion of the system tests, an agency official shall certify that the system meets all applicable Federal policies, regulations, and standards, and that the results of the tests demonstrate that the installed security safeguards are adequate for the application.

(2) *Periodic Review and Recertification.* Agencies shall conduct periodic audits or reviews of sensitive applications and recertify the adequacy of security safeguards. Audits or reviews shall evaluate the adequacy of implemented safeguards, assure they are functioning properly, identify vulnerabilities that could heighten threats to sensitive data or valuable resources, and assist with the implementation of new safeguards where required. They are intended to provide a basis for recertification of the security of the application. Recertification shall be fully documented and maintained in the official agency records. Audits or reviews and recertifications shall be performed at least every three years. They should be considered as part of agency vulnerability assessments and internal control reviews conducted in accordance with OMB Circular No. A-123. Security or other control weaknesses identified shall included in the annual internal control assurance letter and report required by Circular No. A-123.

(3) *Contingency Plans.* Agencies shall establish policies and assign responsibilities to assure that appropriate contingency plans are developed and maintained by end users of information technology applications. The intent of such plans is to assure that users can continue to perform essential functions in the event their information technology support is interrupted. Such plans should be consistent with disaster recovery and continuity of operations plans maintained by the installation at which the application is processed.

b. *Personnel Security.* Agencies shall establish and manage personnel security policies and procedures to assure an adequate level of security for Federal automated information systems. Such policies and procedures shall include requirements for screening all individuals participating in the design, development, operation, or maintenance of sensitive applications as well as those having access to sensitive data. The level of screening required by these policies should vary from minimal checks to full background investigations, depending upon the sensitivity of the information to be handled and the risk and magnitude of loss or harm that could be caused by the individual. These policies shall be established for both Federal and contractor personnel. Personnel security policies for Federal employees shall be consistent with policies issued by the Office of Personnel Management.

c. *Information Technology Installation Security.* Agencies shall assure that an appropriate level of security is maintained at all information technology installations operated by or on behalf of the Federal Government (e.g., government-owned, contractor-operated installations).

(1) *Assigning Responsibility.* Agencies shall assign responsibility for the security of each installation to a management official knowledgeable in information technology and security matters.

(2) *Periodic Risk Analysis.* Agencies shall establish and maintain a program for the conduct of periodic risk analyses at each installation to ensure that appropriate, cost effective safeguards are incorporated into existing and new installations. The objective of a risk analysis is to provide a measure of the relative vulnerabilities and threats to an installation so that security resources can be effectively distributed to minimize potential loss. Risk analyses may vary from an informal review of a microcomputer installation to a formal, fully quantified risk analysis of a large scale computer system. The results of these analyses should be documented and taken into consideration by management officials when certifying sensitive applications processed at the installation. Such analyses should also be consulted during the evaluation of general controls over the management of information technology installations conducted in accordance with OMB Circular No. A-123. A risk analysis shall be performed:

(a) Prior to the approval of design specifications for installations;

(b) Whenever a significant change occurs to the installations (e.g., adding a local area network; changing from batch to online processing; adding dial-up capability). Agency criteria for defining significant change shall be commensurate with the sensitivity of the data processed by the installation.

(c) At periodic intervals established by the agency commensurate with the sensitivity of the data processed, but not to exceed every five years if no risk analysis have been performed during that period.

(3) *Disaster and Continuity Plan.* Agencies shall maintain disaster recovery and continuity of operations plans for all information technology installations. The objective of these plans should be to provide reasonable continuity of data processing support

should events occur that prevent normal operations at the installation. For large installations and installations that support essential agency functions, the plans should be fully documented and operationally tested periodically, at a frequency commensurate with the risk and magnitude of loss or harm that could result from disruption of information technology support.

(4) *Acquistion Specifications.* Agencies shall assure that appropriate technical, administrative, physical, and personnel security requirements are included in specifications for the acquisition or operation of information technology installations, equipment, software, and related services, whether procured by the agency or by GSA. These security requirements shall be reviewed and approved by the management official responsible for security at the installation making the acquisition.

d. *Security Awareness and Training Programs.* Agencies shall establish a security awareness and training program to assure that agency and contractor personnel involved in the management, operation, programming, maintenance, or use of information technology are aware of their security responsibilities and know how to fulfill them. Users of information technology systems should be apprised of the vulnerabilities of such systems and trained in techniques to enhance security.

4. *Assignment of Responsibilities.*

a. *Department of Commerce.* The Secretary of Commerce shall:

(1) Develop and issue standards and guidelines for assuring the security of Federal automated information systems;

(2) Establish standards, approved in accordance with applicable national security directives, for systems used to process sensitive information the loss of which could adversely affect the national security interest; and

(3) Provide technical assistance to Federal agencies in implementing Department of Commerce standards and guidelines.

b. *Department of Defense.* The Secretary of Defense shall:

(1) Act, in accordance with applicable national security directives, as executive agent of the government for the security of telecommunications and automated information systems that process information the loss of which could adversely affect the national security interest; and

(2) Provide technical material and assistance ot Federal agencies concerning security of Federal telecommunications and automated information systems.

c. *General Services Administration.* The Administrator of General Services shall:

(1) Issue policies and regulations for the physical and environmental security of computer rooms in Federal buildings consistent with standards issued by the Department of Commerce and the Department of Defense.

(2) Assure, that agency procurement requests for computers, software, telecommunications services, and related services include security requirements. Delegations of procurement authority to agencies by GSA under mandatory programs, dollar threshold delegations, certification programs, or other so-called blanket delegations shall include requirements for agency specification of security requirements.

(3) Assure that information technology equipment, software, computer room construction, guard or custodial services, telecommunications services, and any other related services procured by GSA meet the security requirements established and specified by the user agency and are consistent with other applicable policies and standards issued by OMB, the Department of Commerce, the Department of Defense, and the Office of Personnel Management.

(4) Issue appropriate standards for the security of Federal telecommunications systems. Standards related to systems used to communicate sensitive information, the loss of which could adversely affect the national security interest, shall be developed and issued in accordance with applicable national security directives.

d. *Office of Personnel Management.* The Director, Office of Personnel Management, shall maintain personnel security policies for Federal personnel associated with the design, programming, operation, maintenance, or use of Federal automated information systems. Requirements for personnel checks imposed by these policies should vary commensurate with the risk and magnitude of loss or harm that could be caused by the individual. The checks may range from merely normal reemployment screening procedures to full background investigations.

5. *Reports.* In their annual internal control report to the President and the Congress, required under OMB Circular No. A-123, agencies shall:

a. Describe any security or other control weaknesses identifed during aduits or reviews of sensitive applications or when conducting risk analyses of installations; and

b. Provide assurance that there is adequate security of agency automated information systems.

**Appendix IV to OMB Circular No. A-130—Analysis of Key Sections**

**1. Purpose**

The purpose of this Appendix is to provide a general context and explanation for the contests of the key sections of the Circular.

**2. Background**

The Paperwork Reduction Act of 1980, Pub. L. 96-511, 94 Stat 2812, codified at Chapter 35 of Title 44 of the United States Code, establishes a broad mandate for agencies to perform their information activities in an efficient, effective, and economical manner. Section 3504 of the Act provides authority to the Director, Office of Management and Budget (OMB), to develop and implement uniform and consistent information resources management policies; oversee the development and promote the use of information management principles, standards, and guidelines; evaluate agency information management practices in order to determine their adequacy and efficiency; and determine compliance of such practices with the policies, principles, standards, and guidelines promulgated by the Director.

The Circular implements OMB authority under the Act with respect to Section 3504(b), general information policy, Section 3504(e), records management, Section 3504(f), privacy, and Section 3504(g), Federal automatic data processing and telecommunications; the Privacy Act of 1974 (5 U.S.C. 552a); Sections 111 and 206 of the Federal Property and Administrative Services Act of 1949, as amended (40 U.S.C. 759 and 487, respectively); the Budget and Accounting Act of 1921 (31 U.S.C. 1 et seq.); and Executive Order No. 12046 of March 27, 1978 and Executive Order No. 12472 of April 3, 1984, Assignment of National Security and Emergency Telecommunications Functions. The Circular complements 5 CFR Part 1320, Controlling Paperwork Burden on the Public, which implements other sections of the Paperwork Reduction Act dealing with controlling the reporting and recordkeeping burden placed on the public.

In addition, the Circular revises and consolidated policy and procedures in five existing OMB directives and rescinds those directives, as follows:

A-71—Responsibilities for the Administration and Management of Automatic Data Processing Activities

Transmittal Memorandum No. 1 to Circular No. A-71—Security of

Federal Automated Information Systems

A–90—Cooperating with State and Local Governments to Coordinate and Improve Information Systems

A–108—Responsibilities for the Maintenance of Records about Individuals by Federal Agencies

A–121—Cost Accounting, Cost Recovery, and Interagency Sharing of Data Processing Facilities.

OMB's review of the five existing policy directives led to the conclusion that much, but not all, of their content was procedural in nature, concerned chiefly with how policies were to be carried out. OMB determined that it was important clearly to distinguish the statement of policies from the procedures for implementing those policies. For this reason, the main body of the Circular consists of basic considerations and assumptions, policies, and assignments of responsibility; the appendices to the Circular consist of procedures for implementing various policies and with analysis of key sections.

OMB developed the main body of the Circular relying upon comments on the **Federal Register** notice as well as other forms of Federal agency and public input, principally meetings with interested parties. For the procedural revisions, OMB relied on the assistance of interagency task groups.

The revised contents of OMB Circular No. A–71, dealing with assignments of responsibilities, are in the main body of this Circular. The contents of OMB Circular No. A–90 are rescinded entirely, with the exception of a policy statement at Section 8(b)(17) of this Circular. Revisions of the procedural aspects of the other three policy directives—Transmittal Memorandum No. 1 to A–71, A–108, and A–121—are appendices to this Circular. Appendices I, II, and III have the same prescriptive force as the Circular; Appendix IV is an explanatory document.

On September 17, 1984, the President signed National Security Decision Directive (NSDD) No. 145, National Policy on Telecommunications and Automated Information Systems Security. The NSDD requires that the Director, OMB, review for consistency with NSDD, and amend as appropriate, OMB Circular No. A–71, Transmittal Memorandum No. 1. The Circular and Appendix III satisfy the NSDD requirement.

**3. Analysis**

*Section 6. Definitions.*

*f. Access to information. g. Dissemination of information.* The Circular defines "access to information" as the function of providing to members of the public, upon their request, the government information to which they are entitled under law. Access refers to those situations in which the government agency's role is passive; access is what the government's responsibilities are when the public comes to the government and ask for information the government has and the public is entitled to. "Dissemination," in the Circular's usage, refers to the function of distributing government information; dissemination connotes an active outreach by a government agency. Dissemination refers to those situations in which the government provides the public with information without the public having to come and ask for it.

The distinction between access and dissemination is posed in order to elaborate the responsibilities of Federal agencies for providing information to the public. Two fundamentally different situations exist: one in which the public goes to the agency to ask for information the agency holds and may or may not have disseminated; and one in which the agency chooses to take the information it holds to the public. In the first instance—access—Congress has provided specific statutory policy in the Freedom of Information Act (FOIA) and in the Privacy Act. These laws and policies concerning access to government information are explicit, well known, and now so widely accepted in practice by Federal agencies as not to require policy elaboration in this Circular. Agencies should know that, if members of the public ask for information subject to FOIA or the Privacy Act, the agencies should normally provide the information forthwith, because the public has a formal legal process for forcing the agencies to yield the information.

The relationship between access to the dissemination of information is explained below, in the discussion of 8a(8) through (12).

*Section 7. Basic Considerations and Assumptions*

Basic considerations and assumptions are statements that provide the underpinnings for the prescriptive policies in Section 8; they are not themselves policy statements. They are either derived from statutes or legislative history, or represent executive branch management philosophy as embodied in the Circular.

—Statements 7–a through 7–d provide the general context for management of Federal information resources.

—Statement 7–e summarizes policy found in OMB Circular No. A–76, Performance of Commercial Activities.

—Statement 7–f states a general predisposition to use up-to-date information technology to manage Federal information resources.

—Statements 7-g and 7-h pertain to the Privacy Act and the Freedom of Information Act, respectively.

—Statement 7-i pertains to the National Science and Technology Policy, Organization and Priorities Act.

—Statement 7-j pertains to the Federal Records Act.

—Statement 7-k states a relationship between Federal information policy and international information policy.

*Section 8. Policies*

This section is divided into two subsections that generally correspond to the twofold definition of information resources management in Section 6-b, namely, information itself and the resources associated with information.

*a. Information Management.* The Paperwork Reduction Act acknowledges that information is a valuable resource and should be managed as such. Proceeding from this premise, this subsection states policies concerning the management of Federal information.

*(1) and (2). Information Collection and Sharing.* The Circular's basic considerations and assumptions (Section 7) establish the value of government information activities. Without question, some information created or collected by Federal agencies is so vital that the American form of government, the economy, national security, and citizens' safety and wellbeing could not continue to exist in its absence. Nothing in this Circular is intended to diminish or derogate the creation or collection of such information, nor to serve as a pretext under which a Federal agency could damage the Nation's critical needs by failing to create or collect such information.

At the same time, the Paperwork Reduction Act was designed to remedy deficiencies Congress perceived in Federal information activities. In the words of the report of the House Committee on Government Operations (Report No. 96–835, p. 3):

> The legislation is the result of a growing concern that the way the Government collects, uses, and disseminates information must be improved. Inefficiencies in current Federal information practices drastically reduce the effectiveness of the Government while, at the same time, drowning our

citizens in a sea of forms, questionnaires, and reports.

The Act intends that the creation or collection of information be carried out within the context of efficient, effective, and economical management. When Federal agencies create or collect information—just as when they perform any other vital functions—they consume scarce resources and such activities must be continually scrutinized in light of good management principles. The applicable principles provided in the purposes of the Act are:

—To minimize the Federal paperwork burden for individuals, small businesses, State and local governments, and other persons;
—To minimize the cost to the Federal Government of collecting, maintaining, using and disseminating information; and
—To maximize the usefulness of information collected by the Federal Government. (44 U.S.C. 3501)

Agencies must justify the creation or collection of information in the light of their statutory functions. Policy statement 8a(9) uses the standard, "necessary for the proper performance of agency functions," taken directly from the Paperwork Reduction Act (44 U.S.C. 3504(c)(2)). Further, the policy statement includes the requirement that the information have practical utility, as defined in the Paperwork Reduction Act (44 U.S.C. 3502(15)) and elaborated in Controlling Paperwork Burdens on the Public (5 CFR Part 1320). Note that practical utility includes characteristics pertaining to the quality of information such as accuracy, adequacy, and reliability, and that, in the case of general purpose statistics or recordkeeping, practical utility means that actual uses can be demonstrated (5 CFR 1320.7 (q)).

Good management and the requirement of practical utility dictate that agencies must plan from the outset for the steps in the information life cycle. The Act also stipulates that agencies must "formulate plans for tabulating the information in a manner which will enhance its usefulness to other agencies and to the public" (44 U.S.C. 3507(a)(1)(C)). When creating or collecting information, agencies must plan how they will process and transmit the information, how they will use it, what provisions they will make for access to it, whether and how they will disseminate it, how they will store it, and finally, how the information will ultimately be disposed of. While agencies cannot at the outset achieve absolute certitude in planning for each of these processes, the requirement for information resources planning is clearly contained in the Act (44 U.S.C. 3506(c)(1)), and the absence of adequate planning is sufficient reason not to create or collect information in the first place.

Before creating or collecting new information, agencies should look first to other agencies and the private sector so as not to duplicate existing information sources or services that would satisfy their needs. The Act requires that agencies shall not conduct or sponsor information collections unless they have eliminated collections "which seek to obtain information available from another source within the Federal Government" (44 U.S.C. 3507(a)(1)(A)). Each agency must also "ensure its information systems do not overlap each other or duplicate the systems of other agencies" (44 U.S.C. 3506(c)(2)). The Act also contains provisions governing the sharing of information between agencies (44 U.S.C. 3510). Applying the policy of OMB Circular No. A–76, the Circular also requires agencies to examine the possibility of acquiring the necessary information from private sector sources.

This is not to say that information creation or collection functions should be indiscriminately turned over to other agencies or to the private sector, but rather to say that agencies have an obligation to examine other potential sources of information which may satisfy agency needs. Some information can only be created or collected by Federal agencies themselves in the exercise of the government's sovereign powers. For some information, the government can satisfy its legitimate needs only when a Federal agency is the creation or collection agent. But other information needs can be met, and in many cases are routinely met, through existing services and sources in other agencies or the private sector. In many cases there is no inherently governmental function that is served by having information collected by a Federal agency; agencies should and do consider acquiring information collection services from the private sector. The Circular emphasizes that these sources should always be looked to first in the interests of efficiency and economy.

*(3) through (6). Privacy Act and Freedom of Information Act.* These statements contain policy statements pertaining to the Privacy Act and incorporating the policies of OMB Circular No. A–108, which is rescinded and superseded. Agencies are to ensure that they meet the requirements of the Privacy Act regarding collection of individually identifiable information. Such information is to be maintained and protected so as to preclude intrusion into the privacy of individuals. Individuals must be accorded access and amendment rights to records, as provided in the Privacy Act. Appendix I prescribes procedures for the maintenance of records about individuals in accordance with the Privacy Act.

In addition to Privacy Act considerations, statements (3) and (4) include provisions concerning proprietary information. Agencies are to minimize their collection of proprietary information, consistent with legal requirements and operational necessity and, when such information must be collected, agencies must provide for its protection.

*(7). Training.* Agency personnel must receive proper training to safeguard information resources. Training is particularly important in view of the changing nature of information resources management. The development of end user computing and office automation, for example, place the management of information and information technology in the hands of nearly all agency personnel rather than in the hands of a few employees at centralized facilities such as large computer centers. Policies and procedures for computer security, records management, protection of privacy, and other safeguards need to be incorporated into information resources management training programs.

*(8) through (12). Information Dissemination.*

*(8) and (9). General Policy.* How does the public know what information is available from Federal agencies? That is, given the distinction the Circular makes between access and dissemination, what is the relationship between the two? How does the public know what government information is accessible? The answer is: through the government's dissemination of information on what is available and how to gain to access it.

The Freedom of Information Act requires each agency to publish currently in the **Federal Register**, for the guidance of the public, descriptions of agency organization; where and how the public may obtain information; the general course and methods by which agency functions are determined, including all procedural requirements; rules of procedure; descriptions of forms and how to obtain them; substantive regulations; statements of general policy; and revisions to all the foregoing (5 U.S.C. 552(a)(1)). The Privacy Act also requires publication of information

concerning systems of records (see Appendix I); the Government in the Sunshine Act requires agencies to make public announcement of meetings (5 U.S.C. 552b(e)(1)). The Paperwork Reduction Act (44 U.S.C. 3507(a)(2)) and Controlling Paperwork Burdens on the Public (5 CFR Part 1320) require agencies to publish notices when they submit information collection requests for OMB approval.

In sum, every Federal agency has obligations to disseminate basic information to the public concerning what the agency does, how its programs operate, what the public must do to comply with laws or regulations, how to receive benefits, and how the public can use agency services. These obligations are the basic linkage between access to, and dissemination of, government information.

Beyond generic requirements, specific laws affect agency dissemination of information in two ways. First, for some agencies their basic enabling legislation stipulates that information dissemination is part of their statutory mission. General purpose statistical agencies, for example, have information dissemination as part of their very reason for existence. These agencies conduct substantial information dissemination programs in order to carry out their necessary functions. In contrast, other agencies such as some regulatory agencies have basic information access, but minimal information dissemination, responsibilities; the existence of substantial information dissemination programs in such agencies would be unusual. Second, statutes may sometimes require that agencies produce and disseminate specific information products or services. For example, the law may state that the President or head of an agency shall make reports to the Congress on given subjects; these would be legally required disseminations of information.

Beyond generic and specific statutory requirements, agencies have positive obligations to disseminate information as a necessary part of performing their functions. Each agency head must clarify the nature of these obligations for the agency's particular mission and set appropriate boundaries for dissemination functions. Before deciding to disseminate an information product or service, and periodically therefore, an agency must be able to demonstrate that the dissemination of the product or service passes the test of either being required by law or being necessary for the proper performance of agency functions.

In conformity with the purposes of the Paperwork Reduction Act, the agency's positive obligations to disseminate information must be discharged within a responsible management framework of minimizing costs to the Federal Government while maximizing the usefulness of the information. Efficient, effective, and economical dissemination does not translate into diminishing or limiting the flow of information from the agency to the public. To the contrary, good management of information resources should result in more useful information flowing with greater facility to the public, at less cost to the taxpayer.

Given an adequate basis for dissemination, agencies must also ask themselves whether a proposed or existing information product or service substantially duplicates similar products or services that would otherwise be available, either from another agency or from the private sector. This requirement of non-duplication, originating in the Paperwork Reduction Act, husbands scarce resources and leads to more efficient, effective, and economical information dissemination by the government.

Similarly, the fact that an agency has created or collected information is not itself a valid reason for creating a program, products, or service to disseminate the information to the public. Agencies create and collect much information, often for purely internal governmental purposes, that is not intended for dissemination, for which there is no public demand, and the dissemination of which would serve no public purpose and would not be cost-justified: e.g., compilations of routine time and attendance records for Federal employees, or publication of the thousands of pages of common carrier tariff filings by regulatory agencies. While such information may be subject to access upon request under provisions of agency statutes, the Freedom of Information Act, or the Privacy Act, the agency must demonstrate in each case the need actively to disseminate such information. Over time, changes in laws, economic conditions, or information technology can result in changes in public demand, public purpose, or dissemination costs; for example, an agency's shift to electronic filing of reports, perhaps carried out primarily in order to improve internal information management, might generate a public demand for electronic dissemination that could be satisfied at minimal cost to the government and also improve the performance of the agency's information access function. The decision to disseminate information, however, entails potentially significant costs, must be addressed separately from the decision to create or collect information, and must hinge upon a determination that dissemination is necessary for proper performance of agency functions.

If agencies do contemplate disseminating particular information, they should plan for its dissemination when creating or collecting the information (see 8a(1)). Planning for dissemination should proceed from the Paperwork Reduction Act premises of minimizing the cost to the government while maximizing the usefulness of information. The focus of information dissemination plans should be on elevating to a policy level decisions regarding the agency's positive obligations to disseminate information and ensuring that the agency discharges the obligations in the most efficient, effective, and economical manner.

*(10) Adequate Notice.* Because many government information activities are important to the government and to the public, agencies must exercise care not to act capriciously with respect to information products and services. When agencies intend to commence offering new products or services, they should provide adequate advance notice so that the public may comment as to the need for the product or service. For example, if private sector interests believe they are already offering or are about to offer the same or a similar product or service—in which event the government may potentially be entering into unfair competition—such notice will allow these interests to present their case before the product or service is launched. By the same token, if many members of the public greatly depend on a particular product or service, they should be permitted to voice their views to an agency that is contemplating termination of the product or service.

The Circular refers to "significant" information products and services. It is not the Circular's intent that agencies should follow notice and comment procedures when terminating relatively inconsequential information products and services; examples might be minor brochures or flyers, products and services that were never intended to be continuing, or for which there is now little or no public audience. Agencies should determine for themselves whether information products and services are "significant," and in some cases may wish to establish procedures and thershold criteria for making such determinations. If a product or service is considered significant, as determined ultimately by the agency head, the

agency may be well advised to follow notice and comment procedures prior to initiation or termination.

*(11)(a). Reaching the Public; Avoiding Information Monopolies.* When agencies have justified and made the basic decision to disseminate information, they must also satisfy conditions regarding the manner of dissemination. First, agencies must take steps to ensure that members of the public who the agency has an obligation to reach have a resonable ability to acquire the information. The audiences for information products and services will vary, and agencies should tailor the dissemination methods so as to place the information into the hands of those whom the agency intends to receive it.

Federal agencies are often the sole holders of certain information; hence, when they disseminate, they are sole suppliers and in a position of natural monopoly. When agencies use private sector contractors to accomplish dissemination, they must take care that they do not permit contractors to exercise monopolistic controls in ways that defeat the agencies' information dissemination obligations, for example, by setting unreasonably high prices. In some cases agencies may need to formulate contractual terms with a sole supplier contractor so that the contractor functions as a mere intermediary for the agency in dealing with end users in the public.

*(11)(b). Reliance on the Private Sector.* In disseminating information—as with other activities—agencies must act in the most cost effective manner, which includes maximum feasible reliance on the private sector. This is merely an application to agency information dissemination programs of the policy stated in OMB Circular No. A–76, Performance of Commercial Activities, and summarized in Section 7f of this Circular. It is "the general policy of the government to rely on commercial sources to supply the products and services the government needs," including products and services the government needs in order to disseminate information to the public. For example, before an agency establishes a service for electronic dissemination of government information via an online computer system, the agency should compare the cost of contracting for operation of the service versus in-house performance and determine whether in-house performance is less costly both for the government and for the public who will receive the service.

Policies contained in OMB Circular No. A–76 are applicable to information dissemination, including the policy that inherently governmental functions should be performed by government employees. The general policy of reliance on the private sector is balanced by the "inherent governmental function" policy, and the Circular in no way intends to abrogate the latter. Where agencies determine that information dissemination activities are inherently governmental, the agencies themselves should carry out the activities.

*(11)(c). User Charges.* The Federal Government is the sole possessor and supplier of certain types of information, which is frequently of substantial commerical value. Dissemination of such information, or its dissemination in a specific form or medium, may represent a government service from which identifiable recipients derive special benefits, in which case they may be subject to OMB Circular No. A–25, User Charges. For example, where the information is already substantially available in printed form, agencies may consider dissemination in electronic form to be a service of special benefit, the costs of which should be recovered through user charges. Many agencies do not have consistent, agency-wide policies and procedures for setting user charges for information products and services with a view to cost recovery. Agencies must establish user charges for the costs of information dissemination, and recover such costs, where appropriate. Whether user charges are appropriate depends, in principle, on whether identifiable recipients will receive special benefits from information products and services.

The requirement to establish user charges is not, however, intended to make the ability to pay the sole criterion for determining whether the public receives government information. Agencies must balance the requirement to establish user charges and the level of fees charged against other policies, specifically, the proper performance of agency functions and the need to ensure that information products and services reach the public for whom they are intended (see Section 8a(11)(a)). If an agency has a positive obligation to place a given product or service in the hands of certain specific groups or members of the public and also determines that user charges will constitute a significant barrier to discharging this obligation, the agency may have grounds for reducing or eliminating its user charges for the product or service, or for exempting some recipients from the charge.

*(12). Periodic Review and Depository Libraries.* Agencies must also establish procedures for periodically reviewing their information dissemination programs. Agency information dissemination plans must ask whether the agency should disseminate a given information product or service at all; if the agency is already disseminating the product or service, reviews should ask whether the agency should continue to do so; or whether the manner or medium of dissemination is the most efficient, effective, and economical.

In addition, agencies must establish procedures to ensure compliance with 44 U.S.C. 1902, which requires that government publications (defined in 44 U.S.C. 1901 and repeated in Section 6k of the Circular) be made available to the Federal depository libraries through the Government Printing Office. The depository libraries provide a kind of information "safety net" to the public, an existing institutional mechanism that guarantees a minimum level of availability of government information to all members of the public. Providing publications to the depository library program complies with the law and costs executive agencies virtually nothing.

*b. Information Systems and Information Technology Management.* This subsection states policies concerning the planning, acquisition, operation, and management of Federal information systems and technology. The Federal information systems and technology budget, which was $14 billion in FY 1985, is projected to increase at a rate faster than that of the overall Federal budget. With outlays at these levels and agencies becoming increasingly dependent upon information technology to accomplish their missions, it is essential that planning processes be applied to the acquisition and application of information technology.

*(1). Planning.* The Paperwork Reduction Act mandates a stronger central role in information resources planning. Specifically, the Act requires that OMB: (1) publish a five-year government-wide automatic data processing and telecommunications plan; (2) review and coordinate agency proposals for the acquisition and use of information technology; and (3) promote the use of the technology to improve governmental efficiency and effectiveness. In order to meet these objectives, it is necessary to initiate a government-wide process for developing and institutionalizing information technology planning that is based in agency programs and missions. The planning must also be tied to the budget so that budgetary decisions derive from plans, and conversely, so that budgetary constraints are reflected in the plans.

The process must further ensure that sufficient information is available to the central agencies to enable them to monitor compliance with Federal policies and identify major issues, including cross-cutting issues where more active centralized planning and management may be appropriate. Hence, agencies must institute information planning processes tied to both the conduct of programs and the preparation of the agency's budget.

*(2) and (3). Management Controls and Accountability.* Basic management controls for agency information systems are fundamental to sound information resources management. These controls should ensure the documentation and periodic review of major information systems, as well as periodic cost-benefit evaluation of overall information resources management in light of agency missions. In order to provide greater incentative for management efficiencies, accountability for information systems should be vested in the officials responsible for operating the programs that the systems support.

Program managers depend upon information systems to carry out their programs, and yet frequently they do not have direct control over the technical and operational support for those systems. Program managers often depend upon agency computer centers or contracted service organizations, the heads of which may not be directly accountable to the program managers in a formal organizational sense. Program managers are nonetheless responsible for conducting their programs and, to the extent successful conduct of the programs entails support from information systems, program managers must be held accountable for acquiring that support. The responsibilities of program managers are therefore presumed to include securing information systems support as needed, and planning for contingencies. Technical support organizations have a concomitant responsibility to meet their commitments, contractual or otherwise, to their program clients, but the program official has the ultimate responsibility for delivering a program's product or service.

*(4) and (5). Sharing Information Processing Capacity.* OMB Circular No. A-121, which is rescinded and superseded, required only that the holder of excess automatic data processing capacity share such capacity. Because the holder of excess capacity has little incentive to seek opportunities for sharing, however, the new policy requires both that the holder share capacity and that the agency seeking information processing capacity fulfill its needs from other agencies or the private sector, whenever possible, before acquiring the new capacity itself. The policy establishes an order of preference in meeting needs—look first to existing sources before acquiring new capacity—but is not intended to assert blindly that sharing or commercial sources are the sole considerations. Agencies must also consider whether existing sources are more cost effective and whether they in fact will meet agency specific needs. Procedural aspects of these policy statements are found in Appendix II.

*(6) and (7). Life Cycle Costing; and Avoiding Duplication.* Agencies frequently develop information technology incrementally, through a series of interim upgrades, without regard for longer term considerations such as the information systems' life cycle. As part of their planning, agencies need to consider the full information system life cycle when determining the cost of information technology. While competitive procurement is generally to be valued, its costs should be taken into account, including the cost to program effectiveness of unnecessarily lengthy procurement processes. Other conditions, such as the need for compatibility, may also be legitimate limitations on the competitive process. Similarly, agency planning should ensure that information systems are not unnecessarily duplicative of systems available elsewhere in government or from the private sector.

*(8). Software Management.* The prevailing agency practice of developing customized computer software is a source of inefficiency, as the General Accounting Office and others have noted. While some agency applications can only be satisfied with customized software, the tendency to prefer custom development is excessively costly in terms of initial development, continued maintenance, and eventual conversion to new technology, because it requires the agency to bear the full cost of developing and maintaining the software it uses. While recognizing that off-the-shelf software has pitfalls, such as uncertainty of continued maintenance, managers are generally to prefer acquiring generic, off-the-shelf software available from the private sector instead of developing their own.

*(9). Necessary Compatibility.* Agencies often acquire technology that is incapable of communicating with other systems with which the agencies need to communicate. Compatibility among information systems has consequently emerged as a significant information resources management problem. Agencies must acquire or develop information systems in a manner that enhances necessary compatibility. The qualifier "necessary" is used because compatibility is not an unrestricted goal; information systems need to be compatible with other systems only to the extent that they must communicate with those systems.

*(10) through (13). Security.* Security of information systems means both the protection of information while it is within the systems and also the assurance that the systems do exactly what they are supposed to do and nothing more. Information system security entails management controls to ensure the integrity of operations including such matters as proper access to the information in the systems and proper handling of input and output. In this sense, security of information systems is first and foremost a management issue and only secondly a technical problem of computer security.

The recent introduction of smaller and more powerful computer systems and new communications technology and transmission media, together with the greater involvement of end users in managing information resources, have increased the potential vulnerability of Federal information systems and hence the level of management concern. Protecting personal, proprietary, and other sensitive data from unauthorized access or misuse; detecting and preventing computer related fraud and abuse; and assuring continuity of operations of major information systems in the event of emergency related disruptions are increasingly serious policy issues. Policy previously found in Transmittal Memorandum No. 1 to OMB Circular No. A-71 is here revised; procedural aspects of the policy are in Appendix III to the Circular.

The General Accounting Office reported in its review of the first-year implementation of the Federal Managers Financial Integrity Act (FIA) that internal controls in automatic data processing systems received inadequate coverage in FIA evaluations. GAO noted that some agencies were uncertain of the relationship between (a) OMB Circular No. A-71, Transmittal Memorandum No. 1, Security of Federal Automated Information Systems, and (b) OMB Circular No. A-123, Internal Control Systems. The relationship between security of automated information systems and agency internal control reports is now stated clearly in Appendix III.

Appendix III provides a minimal set of requirements for the security of all

Federal automated information systems. The Appendix also requires agencies to incorporate additional requirements for the security of information classified for national security purposes, in accordance with appropriate national security directives.

*(14) Standards.* The National Bureau of Standards, Department of Commerce, develops and issues Federal Information Processing Standards. The National Communications System develops and the General Services Administration issues Federal Telecommunications Standards. Some standards are mandatory for Federal agencies, while others are voluntary. Agencies may waive the use of Federal standards under certain conditions and pursuant to certain procedures, which vary depending upon the individual standard. In general, OMB strongly recommends use of these standards government-wide. Such standards can contribute to overall government economy and efficiency by increasing compatibility in computer and telecommunications networks, improving the transportability of software, and enabling computer systems to be developed using components of different manufacturers. These advantages can result in reduced procurement costs for equipment and services, improved competition, and better utilization of staff training and skills. While government-wide standards can result in management efficiencies, agencies should be mindful that standards can also have the untoward effects of regulations, as noted in OMB Circular No. A–119. Agencies should continuously assess relative costs and benefits of standards and their effects upon the agency's accomplishment of its mission. Note also that national security directives prescribe standards for computer security.

*(15) Avoiding Information Technology Monopolies.* Many agencies operate one or more central information technology facilities to support agency programs. In these agencies, program managers are often required to use the central facilities. The manager of such a monopoly facility has a lesser incentive to control costs, since he or she has a captive clientele. The program manager has little leverage to ensure that information processing resources are efficiently allocated since he or she cannot seek, or can seek only with great difficulty, alternative sources of supply. When users are dependent on effective technology support to perform their functions, control over selection of facility is essential and consistent with holding users responsible for producing their government information products. To provide incentives conducive to more businesslike procedures in information technology facilities, agencies should avoid monopolistic information processing arrangements and should enter into them only if their cost effectiveness is clear and they are subject to periodic review. Appendix II specifies certain procedures with respect to this policy.

*(16) Cost Recovery.* This policy constitutes a revision to policy stated in OMB Circular No. A–121. Whereas Circular No. A–121 required only that costs for automatic data processing facilities be allocated to users, agencies must now recover the costs of information technology facilities from government users. Viable management of a large information technology facility requires that managers know the amount of resources devoted to each user when providing services. Furthermore, effective management of the use of information technology requires that the user have responsibility for and control over the resources consumed by use of the facility. Experience with Circular No. A–121 showed OMB that allocating costs had little effect on agencies' behavior; recovering costs means that actual transfers of funds will take place between suppliers and users of information technology facilities. Procedural aspects of the policy appear in Appendix II.

*(17) Coordination with State and Local Governments.* This policy reaffirms policy previously found in OMB Circular No. A–90, Transmittal Memorandum No. 1. The interagency group that worked on the revision of Circular No. A–90 recommended, and OMB agreed, that the Circular should be rescinded except for a single policy statement prohibiting Federal agencies from placing unnecessary restrictions on the information systems that State and local governments use to carry out federally financed program activities.

*(18) Application of Up-to-date Information Technology.* Recent availability of low cost, highly efficient and effective electronic information technology can greatly increase worker productivity and facilitate operation of Federal agency programs. The Circular states a predisposition, based in the Paperwork Reduction Act, in favor of applying such technology to the information life cycle within a responsible management context. Two broad areas of information technology merit further discussion: (1) electronic information collection and dissemination, and (2) end user computing.

—*Electronic Collection and Dissemination of Information.* Federal agencies are moving rapidly to provide for collection and dissemination of information through electronic media. In developing this Circular, OMB considered whether it was necessary to provide specific policies concerning electronic collection and dissemination of governmental information. OMB concluded that, except for the general predisposition in favor of applying new technological developments to information resources management, the policies that apply to information collection and dissemination in other media also apply to electronic collection and dissemination. It is important, however, that agencies recognize the necessity of systematically thinking through the application of policies stated elsewhere in this Circular to electronic collection and dissemination of information. For example, when developing electronic collection programs, agencies should give particular attention to issues such as privacy, public access, and records management. When developing electronic dissemination programs, agencies should ensure that access is provided to each class of users upon reasonable terms, avoid problems arising from monopolistic control, ensure maximum reliance upon the private sector, and take necessary steps for cost accounting and cost recovery.

—*End User Computing.* Federal agencies are also moving rapidly to acquire end user computing capabilities. OMB endorses the managed innovation approach to end user computing presented in GSA's publication Managing End User Computing in the Federal Government (June 1983). Because end user computing places management of information in the hands of individual agency personnel rather than in a central automatic data processing organization, the Circular requires that agencies train end users in their responsibilities for safeguarding information; Appendix III deals in part with the security of end user computing.

*Section 9. Assignment of Responsibilities*

This section assigns responsibilities for the management of Federal information resources addressed in this Circular. OMB Circular No. A–71 is

rescinded and its contents are revised and incorporated into this section along with responsibilities assigned under the Paperwork Reduction Act; Section 111 of the Federal Property and Administrative Services Act, as amended; and Executive Order No. 12046. Certain assignments of responsibility from OMB to other agencies, as noted below, are also included. Following are principal noteworthy aspects of this section.

*Responsibility for Managing Information Resources.* Statement 9a(1) is a key element in the Circular because it establishes that the locus of responsibility for actual management of Federal information resources is the head of each agency. This means, for example, that the determination of what is "necessary for the proper performance of agency functions" with respect to information creation or collection (8a(1)) and information dissemination (8a(9)) lies with the head of the agency. In the Circular OMB sets the policy framework within which such determinations are to be made and the standards and provisions for reviewing the determinations, but the management decisions and their implementation belong properly with the agency holding the information resources.

*Triennial Reviews.* The Paperwork Reduction Act provides that the Director of OMB ". . . shall, with the advice and assistance of the Administrator of General Services, selectively review, at least once every three years, the information management activities of each agency to ascertain their adequacy and efficiency." (44 U.S.C. 3513) The Administrator of Information and Regulatory Affairs, OMB, and the Deputy Administrator of the General Services Administration, in an exchange of correspondence dated June 13 and July 22, 1983, concurred that GSA has the necessary statutory authority to conduct reviews of Federal agency information resources management activities. Separate triennial reviews of agency activities by OMB and GSA would be unnecessarily duplicative, which would not be consistent with the Act. Accordingly, the triennial reviews conducted by GSA will be designed to meet OMB's requirements under the Paperwork Reduction Act as well as GSA's own needs.

*Senior Officials for Information Resources Management.* In accordance with 44 U.S.C. 3506(b) and 5 CFR 1320.8, agencies are required to designate a senior official to carry out responsibilities under the Paperwork Reduction Act. The designation of the official is intended to assure clear accountability for setting policy for agency information resources management activities, provide for greater coordination among the agency's information activities, and ensure greater visibility of such activities within the agency. The responsibilities of the senior official for information resources management were identified in OMB Bulletin No. 81-21, which has expired. Those responsibilities are now estabished in this Circular.

*International Information Policy.* The Circular deals with the management of information resources held by the Federal government. While the creation, collection, processing, transmission, dissemination, use, storage, and disposition of information by the Federal government has international ramifications, Federal government information resources management policy is not the same as "U.S. information policy," which refers to U.S. national interests in the information field vis-a-vis the policies and interests of other nations. The Circular formally acknowledges this distinction and assigns responsibilities for international information policy only insofar as it relates to Federal government information resources management policy.

*Timely Technology Procurement.* Inherent in effective management of information technology is the ability of program managers to acquire technology in a timely manner. GSA is assigned the responsibility in Section 9 to develop criteria that will streamline procurement procedures and delegate procurement authority to agencies that comply with those procedures. All Federal agencies are directed in Section 9 to develop internal policies and procedures that further provide for timely acquisition of information technology.

*Records Management.* The Paperwork Reduction Act makes the management of Federal records an integral part of information resources management. While no new policies are embodied in this Circular, responsibilities have been assigned in order to ensure that agency records management programs are considered within the context of Federal information resources management.

*Section 10. Oversight*

The broad scope of the Circular dictates a strategy of focusing oversight on a series of aspects of information resources management rather than on a single comprehensive reporting scheme. OMB intends to use existing mechanisms, such as the fiscal budget, information collection budget, and management reviews, to examine agency compliance with the Circular. For example, during 1984 the management reviews for the FY 1986 budget year concentrated on five cross-cutting information issues: overall information resources management strategy, telecommunications, software management, "electronic filing," and end user computing. OMB issued data call bulletins requesting information specific to these issues, targeted the issues for special attention during the management reviews, and requested individual agencies to submit management improvement plans on specific aspects of the issues. Pursuit of this kind of selective oversight strategy permits OMB and the agencies the flexibility to shift the focus of oversight as information issues and the technological environment change.

[FR Doc. 85-30330 Filed 12-23-85; 8:45 am]
BILLING CODE 3110-01-M

federal register

Tuesday
December 24, 1985

Part V

# The President

**Proclamation 5423—Amending the Generalized System of Preferences**

# Part V

# The President

Federal Register
Vol. 50, No. 247
Tuesday, December 24, 1985

# Presidential Documents

Title 3—

The President

**Proclamation 5423 of December 20, 1985**

## Amending the Generalized System of Preferences

**By the President of the United States of America**

**A Proclamation**

1. Pursuant to section 502(b) of the Trade Act of 1974 (the Trade Act) (19 U.S.C. 2462(b)), as amended, and section 604 of the Trade Act (19 U.S.C. 2483), I have determined that it is appropriate to provide for the termination of preferential treatment under the Generalized System of Preferences (GSP) for articles which are currently eligible for such treatment and which are imported from Portugal. Such termination is the result of the accession of Portugal to the European Economic Community.

2. Section 502(b) of the Trade Act specifies that member states of the European Economic Community are ineligible for such preferential treatment under the GSP.

NOW, THEREFORE, I, RONALD REAGAN, President of the United States of America, acting under the authority vested in me by the Constitution and the statutes of the United States of America, including but not limited to sections 502(b) and 604 of the Trade Act, do proclaim that:

(1) General headnote 3(e)(v)(A) to the Tariff Schedules of the United States (TSUS), listing those countries whose products are eligible for benefits of the GSP, is amended by striking out "Portugal."

(2) No article the product of Portugal and imported into the United States after the effective date of this proclamation shall be eligible for preferential treatment under the GSP.

(3) The modifications to the TSUS made by this proclamation shall be effective with respect to articles both: (1) imported on or after January 1, 1976, and (2) entered, or withdrawn from warehouse for consumption, on or after January 1, 1986.

IN WITNESS WHEREOF, I have hereunto set my hand this 20th day of December, in the year of our Lord nineteen hundred and eighty-five, and of the Independence of the United States of America the two hundred and tenth.

Ronald Reagan

[FR Doc. 85-30006
Filed 12-23-85; 11:08 am]
Billing code 3195-01-M

# Reader Aids

Federal Register

Vol. 50, No. 247

Tuesday, December 24, 1985

## INFORMATION AND ASSISTANCE

### SUBSCRIPTIONS AND ORDERS

| | |
|---|---|
| Subscriptions (public) | 202-783-3238 |
| Problems with subscriptions | 275-3054 |
| Subscriptions (Federal agencies) | 523-5240 |
| Single copies, back copies of FR | 783-3238 |
| Magnetic tapes of FR, CFR volumes | 275-1184 |
| Public laws (Slip laws) | 275-3030 |

### PUBLICATIONS AND SERVICES

**Daily Federal Register**

| | |
|---|---|
| General information, index, and finding aids | 523-5227 |
| Public inspection desk | 523-5215 |
| Corrections | 523-5237 |
| Document drafting information | 523-5237 |
| Legal staff | 523-4534 |
| Machine readable documents, specifications | 523-3408 |

**Code of Federal Regulations**

| | |
|---|---|
| General information, index, and finding aids | 523-5227 |
| Printing schedules and pricing information | 523-3419 |

**Laws** 523-5230

**Presidential Documents**

| | |
|---|---|
| Executive orders and proclamations | 523-5230 |
| Public Papers of the President | 523-5230 |
| Weekly Compilation of Presidential Documents | 523-5230 |

**United States Government Manual** 523-5230

**Other Services**

| | |
|---|---|
| Library | 523-4986 |
| Privacy Act Compilation | 523-4534 |
| TDD for the deaf | 523-5229 |

## FEDERAL REGISTER PAGES AND DATES, DECEMBER

| | |
|---|---|
| 49341-49504 | 2 |
| 49505-49664 | 3 |
| 49665-49824 | 4 |
| 49825-49918 | 5 |
| 49919-50156 | 6 |
| 50157-50268 | 9 |
| 50269-50608 | 10 |
| 50609-50754 | 11 |
| 50755-50890 | 12 |
| 50891-51234 | 13 |
| 51235-51382 | 16 |
| 51383-51510 | 17 |
| 51511-51664 | 18 |
| 51665-51834 | 19 |
| 51835-52206 | 20 |
| 52207-52434 | 23 |
| 52435-52756 | 24 |

## CFR PARTS AFFECTED DURING DECEMBER

At the end of each month, the Office of the Federal Register publishes separately a List of CFR Sections Affected (LSA), which lists parts and sections affected by documents published since the revision date of each title.

**3 CFR**

**Proclamations:**

| | |
|---|---|
| 5414 | 49665 |
| 5415 | 49825 |
| 5416 | 49827 |
| 5417 | 50269 |
| 5418 | 50271 |
| 5419 | 50255 |
| 5420 | 50757 |
| 5421 | 51511 |
| 5422 | 51665 |
| 5423 | 52755 |

**Executive Orders:**

| | |
|---|---|
| 12345 (Amended by EO 12539) | 49829 |
| 12539 | 49829 |

**Administrative Orders:**

**Presidential Determinations:**

| | |
|---|---|
| No. 86-03 November 25, 1985 | 50273 |

**4 CFR**

| | |
|---|---|
| 6 | 49505 |
| 8 | 49505 |
| 9 | 49505 |
| 30 | 49505 |
| 33 | 49505 |
| 51 | 49505 |
| 52 | 49505 |
| 75 | 49505 |
| 82 | 49505 |

**5 CFR**

**Proposed Rules:**

| | |
|---|---|
| 530 | 51397 |

**7 CFR**

| | |
|---|---|
| 6 | 49919 |
| 226 | 49341 |
| 301 | 51228 |
| 402 | 52207 |
| 403 | 50275 |
| 404 | 49505, 50275 |
| 408 | 49505, 50275 |
| 409 | 49505 |
| 411 | 49505 |
| 413 | 49505 |
| 415 | 49506 |
| 416 | 49920 |
| 417 | 49506 |
| 418 | 49506 |
| 419 | 49506 |
| 422 | 51383 |
| 423 | 49507 |
| 427 | 49506 |
| 428 | 49513 |
| 429 | 49506 |
| 430 | 49506, 51383 |
| 431 | 52208 |
| 433 | 49518 |
| 434 | 51383 |
| 436 | 51383 |
| 439 | 49505 |
| 443 | 51383 |
| 450 | 50276 |
| 800 | 49667 |
| 907 | 49343, 50759, 51667, 52213 |
| 908 | 50759 |
| 958 | 50157 |
| 959 | 49831 |
| 971 | 49831 |
| 989 | 49831, 50158 |
| 991 | 49831 |
| 1002 | 49674 |
| 1004 | 49674 |
| 1032 | 52435 |
| 1136 | 50159 |
| 1427 | 52214 |
| 1446 | 50280 |
| 1540 | 49524 |
| 1965 | 49832 |

**Proposed Rules:**

| | |
|---|---|
| 68 | 52469 |
| 70 | 50310 |
| 210 | 49933 |
| 225 | 49933 |
| 226 | 49933 |
| 422 | 51687 |
| 430 | 50794 |
| 440 | 49654 |
| 966 | 51872 |
| 971 | 50171 |
| 980 | 50621 |
| 994 | 51344, 52332 |
| 1032 | 49395 |
| 1136 | 50794 |
| 1137 | 50622 |
| 1140 | 50622 |
| 1941 | 49395 |
| 1943 | 49395 |
| 1980 | 49395 |

**8 CFR**

| | |
|---|---|
| 103 | 51235 |
| 211 | 49921 |
| 238 | 51835 |

**Proposed Rules:**

| | |
|---|---|
| 1 | 51693 |
| 3 | 51693 |
| 103 | 51693 |
| 236 | 51693 |
| 242 | 51693 |
| 292 | 51693 |

**9 CFR**

| | |
|---|---|
| 77 | 49922, 51835 |
| 92 | 49344 |
| 102 | 50761 |
| 108 | 50761 |
| 114 | 50761 |
| 307 | 51513 |
| 318 | 50282 |
| 381 | 50282, 51513 |

**Proposed Rules:**
71 ..... 49937
80 ..... 49937
92 ..... 49702

**10 CFR**
9 ..... 50283
50 ..... 50764
440 ..... 49912
**Proposed Rules:**
19 ..... 51992
20 ..... 51992
30 ..... 51992
31 ..... 51992
32 ..... 51992
34 ..... 51992
40 ..... 51992
50 ..... 51992
60 ..... 51701
70 ..... 51992

**11 CFR**
Ch. I ..... 50778
**Proposed Rules:**
Ch. I ..... 51535

**12 CFR**
Ch. VII ..... 51840
204 ..... 50284, 51508
217 ..... 50160
227 ..... 49524
265 ..... 51836
563 ..... 49345, 51837
564 ..... 49524
**Proposed Rules:**
205 ..... 50623
207 ..... 50606
226 ..... 50794
543 ..... 52482
544 ..... 52482
556 ..... 49937
571 ..... 49940
606 ..... 51540
615 ..... 50798

**13 CFR**
101 ..... 52436
120 ..... 49832
125 ..... 52436

**14 CFR**
11 ..... 51188, 51332, 52180
39 ..... 49349–49351, 49832, 49833, 49923, 50609, 50610, 51235–51237, 51667, 52437, 52438
71 ..... 49353, 49528, 49529, 50254, 50285, 50610, 50778, 51238–51240, 51384, 51513, 51840, 52439
73 ..... 50611, 52439
91 ..... 51188, 51193
93 ..... 50264, 52180
95 ..... 49674
97 ..... 50161, 51668
198 ..... 51332
385 ..... 52439
**Proposed Rules:**
1 ..... 50624
21 ..... 51704
27 ..... 50624
29 ..... 50624
39 ..... 49858, 49944, 49945, 50172, 51259, 51707
71 ..... 49704, 49902, 50173, 50174, 50310, 51259, 51260, 51547, 51548, 51873, 52532
73 ..... 51260
91 ..... 50583
93 ..... 52199
121 ..... 50588
125 ..... 50588
129 ..... 50588
135 ..... 50588

**15 CFR**
**Proposed Rules:**
10 ..... 50177

**16 CFR**
4 ..... 50779
13 ..... 49834, 49835, 50781, 51670
305 ..... 49679
455 ..... 50162
1000 ..... 52440
1010 ..... 51670
1032 ..... 51670
1500 ..... 51514
1510 ..... 51514
1610 ..... 51670
1611 ..... 51670
1700 ..... 51514
**Proposed Rules:**
13 ..... 50800, 51398
444 ..... 50178
1500 ..... 50918

**17 CFR**
1 ..... 51385
16 ..... 51385
33 ..... 51671
200 ..... 50286
210 ..... 49529
211 ..... 51671
229 ..... 49529
239 ..... 49529
240 ..... 52440
250 ..... 50611
259 ..... 50611
270 ..... 51673
276 ..... 49835
**Proposed Rules:**
1 ..... 49859
166 ..... 50805
240 ..... 50624
250 ..... 49354, 49705

**18 CFR**
2 ..... 49679, 51240, 52217
32 ..... 49924
33 ..... 49924
34 ..... 49924
35 ..... 49924
36 ..... 49924
45 ..... 49924
101 ..... 49924
152 ..... 51240
154 ..... 51240
157 ..... 51240, 52217
260 ..... 49534
284 ..... 49359, 49371, 49534, 51240, 51841–51845, 52217
292 ..... 49924
375 ..... 49924, 51240, 52217
381 ..... 49924, 51240

**19 CFR**
162 ..... 50287
171 ..... 50287
**Proposed Rules:**
141 ..... 52532

**20 CFR**
404 ..... 50068, 50118
416 ..... 50118, 51514
601 ..... 51241
**Proposed Rules:**
404 ..... 49397, 49556, 50630, 50920, 51550
416 ..... 50920
655 ..... 50311, 50313, 51551

**21 CFR**
19 ..... 52278
21 ..... 52278
172 ..... 49535
173 ..... 49535, 49684
175 ..... 49535, 49684, 51846
176 ..... 49684
177 ..... 51846
178 ..... 49684, 50611, 51847, 52279
181 ..... 49535
184 ..... 49535
193 ..... 49687
310 ..... 49371
510 ..... 49372, 49537
520 ..... 49372, 49537, 49840, 50291
522 ..... 49372, 49840, 50292
524 ..... 49372, 49840
555 ..... 49372, 49924
558 ..... 49372, 49840, 50292, 50612, 50613, 51518
561 ..... 49687
1020 ..... 50293
**Proposed Rules:**
163 ..... 49398, 49405
201 ..... 49947, 51400
343 ..... 49409
357 ..... 49409
606 ..... 52602
610 ..... 51002, 52602
640 ..... 52602
700 ..... 51551
870 ..... 50179

**22 CFR**
514 ..... 49373
**Proposed Rules:**
41 ..... 49705

**23 CFR**
230 ..... 51242
625 ..... 50784
655 ..... 50784
658 ..... 49688
**Proposed Rules:**
625 ..... 51404, 52534
655 ..... 51404, 52534
1325 ..... 49409

**24 CFR**
20 ..... 52280
107 ..... 52441
203 ..... 51673
232 ..... 49538, 51848
235 ..... 49538, 51848
300 ..... 49842
511 ..... 50594
571 ..... 51675
885 ..... 51677
970 ..... 50891
990 ..... 52280

**25 CFR**
23 ..... 51244

**26 CFR**
1 ..... 52281, 52313, 52443
602 ..... 52281, 52313, 52443
**Proposed Rules:**
1 ..... 51874, 52332–52333
602 ..... 52333

**27 CFR**
4 ..... 51849, 51851
5 ..... 51851
7 ..... 51851
19 ..... 51386
240 ..... 51386
245 ..... 51386
270 ..... 51386
285 ..... 51386
295 ..... 51386
**Proposed Rules:**
5 ..... 51408
19 ..... 51408

**28 CFR**
50 ..... 51677
65 ..... 51340
**Proposed Rules:**
16 ..... 51410, 51411, 51413, 52335
544 ..... 51559

**29 CFR**
1 ..... 49822
14 ..... 51390
1625 ..... 50614
1910 ..... 51120, 51852
2203 ..... 51678
2610 ..... 50896
2619 ..... 50898, 50899
2621 ..... 50900
2622 ..... 50896
2642 ..... 49539
**Proposed Rules:**
20 ..... 51354
102 ..... 51414
1910 ..... 49410, 51412, 50512

**30 CFR**
901 ..... 49541
904 ..... 49374
906 ..... 49924, 50788
915 ..... 49925
917 ..... 50293
936 ..... 49376, 50296
944 ..... 49542, 51519
950 ..... 49544, 50901
**Proposed Rules:**
75 ..... 50925
701 ..... 51559
780 ..... 51559
784 ..... 51559
800 ..... 50631
946 ..... 51885

**31 CFR**
357 ..... 51394
358 ..... 51394
361 ..... 51394
362 ..... 51394
**Proposed Rules:**
357 ..... 49412

**32 CFR**
54 ..... 49927
78 ..... 49930
166 ..... 52443

199 ..... 52315
584 ..... 52447
828 ..... 49688
880 ..... 49688
2003 ..... 51826

**Proposed Rules:**
553 ..... 50315

**33 CFR**

72 ..... 50903
110 ..... 49643
117 ..... 49550, 50163, 51246
165 ..... 49844, 50164, 52327
334 ..... 50297

**Proposed Rules:**
66 ..... 50179
110 ..... 51708
117 ..... 50808
161 ..... 51709
166 ..... 49861, 50808, 52534
167 ..... 49861, 50925, 52534
209 ..... 50316
402 ..... 51710

**36 CFR**

7 ..... 51855
1258 ..... 50904

**Proposed Rules:**
1 ..... 51782
2 ..... 51782
3 ..... 51782
4 ..... 51782
5 ..... 51782
7 ..... 51782, 51886
50 ..... 51782
800 ..... 51437
1254 ..... 51414

**37 CFR**

201 ..... 52458
304 ..... 49551

**38 CFR**

3 ..... 50615
36 ..... 51681

**Proposed Rules:**
19 ..... 50632
21 ..... 50632-50642

**39 CFR**

10 ..... 49387, 49689, 50905
111 ..... 49689

**Proposed Rules:**
111 ..... 52534

**40 CFR**

2 ..... 51654
52 ..... 49389, 50906, 50908, 51250, 51521, 52327-52328
52 ..... 52460, 52461
81 ..... 51251
180 ..... 49690, 51856
261 ..... 50789
305 ..... 51196
306 ..... 51205
712 ..... 50910
716 ..... 50910
799 ..... 51683, 51857

**Proposed Rules:**
51 ..... 52418
52 ..... 51262, 51887, 52336
60 ..... 49442
61 ..... 52422
81 ..... 51416, 51887
86 ..... 51559
122 ..... 49904
124 ..... 49904
125 ..... 49904
131 ..... 52540
141 ..... 49423
166 ..... 50643
180 ..... 49705, 50643
261 ..... 51264
264 ..... 51264
265 ..... 51264
271 ..... 49561, 49947, 49949
766 ..... 51794
798 ..... 52338
799 ..... 49863, 51888, 52338

**41 CFR**

101-40 ..... 49551, 49845

**42 CFR**

52a ..... 49692
75 ..... 50710
405 ..... 50165
412 ..... 49930
432 ..... 49389
433 ..... 49389

**Proposed Rules:**
405 ..... 51418

**43 CFR**

2740 ..... 50298
2910 ..... 50298
4100 ..... 51522

**Public Land Orders:**
6610 (Corrected by 6611) ..... 50165
6611 ..... 50165

**Proposed Rules:**
4 ..... 51711
11 ..... 52126
431 ..... 49563

**44 CFR**

64 ..... 49390, 50617
65 ..... 50789, 50790
67 ..... 50791
205 ..... 50618

**Proposed Rules:**
67 ..... 49951, 50810
205 ..... 49959

**45 CFR**

96 ..... 49552
305 ..... 49392

**46 CFR**

10 ..... 52329
308 ..... 50165
309 ..... 50165

**Proposed Rules:**
38 ..... 49563
151 ..... 49563
252 ..... 52338
572 ..... 51418

**47 CFR**

1 ..... 51522
2 ..... 52330, 52462
22 ..... 50167, 51522
31 ..... 50910
43 ..... 50910
68 ..... 49930
69 ..... 50910
73 ..... 49392, 49553, 50916, 51528, 51685
76 ..... 52462
87 ..... 49554
97 ..... 49555

**Proposed Rules:**
Ch. I ..... 50316, 51893
2 ..... 51420
21 ..... 51420
22 ..... 50181
43 ..... 49423
64 ..... 50182
68 ..... 51893
69 ..... 50183
73 ..... 49426-49428, 49565, 49566, 49707, 49863, 50329, 51265-51269, 51432-51434, 51560-51562, 51564, 51712-51717
74 ..... 51420
78 ..... 51420
94 ..... 51420
100 ..... 52543

**48 CFR**

4 ..... 52428
5 ..... 52428
6 ..... 52428
7 ..... 52428
10 ..... 52428
13 ..... 52428
15 ..... 52428
17 ..... 52428
19 ..... 52428
34 ..... 52428
52 ..... 52428
513 ..... 51394
514 ..... 50169
536 ..... 50170
552 ..... 50170
553 ..... 51394
701 ..... 50301
702 ..... 50301
705 ..... 51395
706 ..... 51395
715 ..... 50301
728 ..... 50301
731 ..... 50301
732 ..... 50301
737 ..... 50301
750 ..... 50301
752 ..... 50301
753 ..... 50301

**Proposed Rules:**
Ch. 5 ..... 50502
31 ..... 49662, 51776, 52727
501 ..... 51435
504 ..... 51435
514 ..... 51435
515 ..... 51435
519 ..... 51435
553 ..... 51435
5242 ..... 49819
5252 ..... 49819
5350 ..... 49708

**49 CFR**

1 ..... 52467
90 ..... 49930
171 ..... 49393
173 ..... 49849
175 ..... 49393
212 ..... 50888
217 ..... 50888
218 ..... 50888
219 ..... 50888
225 ..... 50888
391 ..... 49849

**Proposed Rules:**
Ch. X ..... 51565
171 ..... 49866
173 ..... 49866
177 ..... 49866
178 ..... 49866
180 ..... 49866
192 ..... 49429, 49575
195 ..... 49429
571 ..... 52544
1039 ..... 49576

**50 CFR**

17 ..... 50304, 50726, 50792, 51251, 51867
18 ..... 52348
20 ..... 49695
216 ..... 49696
227 ..... 51252
611 ..... 49852
652 ..... 49852, 49931, 51533, 51870
663 ..... 50309
671 ..... 49853, 50793, 51533
675 ..... 49852

**Proposed Rules:**
14 ..... 49709
17 ..... 49868, 49967, 49970, 50646, 51565, 51718, 51894
18 ..... 49577
20 ..... 49870
80 ..... 50185
651 ..... 49582, 51436
652 ..... 51435
655 ..... 50186
658 ..... 50928
663 ..... 49590, 51436

## LIST OF PUBLIC LAWS

**Last List December 23, 1985**

This is a continuing list of public bills from the current session of Congress which have become Federal laws. The text of laws is not published in the **Federal Register** but may be ordered in individual pamphlet form (referred to as "slip laws") from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402 (phone 202-275-3030).

**H.J. Res. 465/Pub. L. 99-190**

Making further continuing appropriations for the fiscal year 1986, and for other purposes. (Dec. 19, 1985)

**H.R. 1789/Pub. L. 99-191**

Relating to the authorization of appropriations for certain components of the National Wildlife Refuge System. (Dec. 19, 1985; 2 pages) Price: $1.00

**H.R. 3735/Pub. L. 99-192**

To designate the pedestrian walkway crossing the Potomac River at Harpers Ferry National Historical Park as the "Goodloe E. Byron Memorial Pedestrian Walkway". (Dec. 19, 1985; 1 page) Price: $1.00

**H.J. Res. 424/Pub. L. 99-193**

To designate the year of 1986 as the "Year of the Flag". (Dec. 19, 1985; 2 pages) Price: $1.00



# The Federal Register

**Regulations** appear as agency documents which are published daily in the **Federal Register** and codified annually in the **Code of Federal Regulations**




The **Federal Register**, published daily, is the official publication for notifying the public of proposed and final regulations. It is the tool for you to use to participate in the rulemaking process by commenting on the proposed regulations. And it keeps you up to date on the Federal regulations currently in effect.

Mailed monthly as part of a **Federal Register** subscription are: the LSA (List of CFR Sections Affected) which leads users of the **Code of Federal Regulations** to amendatory actions published in the daily **Federal Register**; and the cumulative **Federal Register Index.**

The **Code of Federal Regulations** (CFR) comprising approximately 185 volumes contains the annual codification of the final regulations printed in the **Federal Register.** Each of the 50 titles is updated annually.

**Subscription Prices:**

- **Federal Register**
  - **Paper:**
    - One year as issued: $300 domestic; $375 foreign
    - Six months: $150 domestic; $187.50 foreign
  - **24x Microfiche Format:**
    - One year as issued: $145 domestic; $181.25 foreign
    - Six months: $72.50 domestic; $90.65 foreign
- **Code of Federal Regulations**
  - **Paper:**
    - One year as issued: $550.00 domestic; $687.50 foreign
    - Single volumes: Individually priced.
  - **24x Microfiche Format:**
    - Current year (as issued): $185 domestic; $231.25 foreign
    - Previous year's full set (single shipment): $125 domestic; $156.25 foreign

## Order Form

Mail To: Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402

Enclosed is $_____ ☐ check, ☐ money order, or charge to my Deposit Account No.

☐☐☐☐☐☐–☐

Order No._____

**MasterCard and VISA accepted.**

**Credit Card Orders Only**

Total charges $_____

Fill in the boxes below.

Credit Card No.

Expiration Date Month/Year ☐☐☐☐

Customer's Telephone No.: Area Code Home Area Code Office

Charge orders may be telephoned to the GPO order desk at (202)783-3238 from 8:00 a.m. to 4:00 p.m. eastern time, Monday-Friday (except holidays).

**Please send me**

**PAPER:**

_____ **Federal Register:** ___ $300 per year domestic; $375 foreign ___ $150 per six-month domestic; $187.50 foreign

_____ **Code of Federal Regulations:** ___ $550 per year domestic; $687.50 foreign

**24x MICROFICHE FORMAT:**

_____ **Federal Register:** ___ One year as issued: $145 domestic; $181.25 foreign ___ Six months: $72.50 domestic; $90.65 foreign

_____ **Code of Federal Regulations:** ___ Current year: $185 domestic; $231.25 foreign ___ Previous year's full set (single shipment): $125 domestic; $156.25 foreign

**PLEASE PRINT OR TYPE**

Company or Personal Name

Additional address/attention line

Street address

City State ZIP Code

(or Country)

**For Office Use Only**

| Quantity | Charges |
|---|---|
| ___ Publications | |
| ___ Subscription | |
| Special Shipping Charges | |
| International Handling | |
| Special Charges | |
| OPNR | |
| ___ UPNS | |
| ___ Balance Due | |
| ___ Discount | |
| ___ Refund | |

[Rev 7-1-85]