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Federal Register

Tuesday
January 15, 1985

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Drug Enforcement Administration

Aviation Safety
Federal Aviation Administration

Banks, Banking
Federal Reserve System

Crop Insurance
Federal Crop Insurance Corporation

Fisheries
National Oceanic and Atmospheric Administration

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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.

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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.

OFFICE OF PERSONNEL MANAGEMENT

5 CFR Part 553

Deductions from Civilian Pay for Increases in Uniformed Services Retired or Retained Pay

AGENCY: Office of Personnel Management.

ACTION: Revocation.

SUMMARY: The Office of Personnel Management is revoking regulations that provide for deductions from civilian Federal employee pay to offset any cost-of-living increases such employee receives in uniformed service retired or retainer pay during fiscal years 1983, 1984, and 1985. The revocation is the result of section 2203 of the Deficit Reduction Act of 1984 which repealed section 301(d) of the Omnibus Budget Reconciliation Act of 1982. This statutory amendment is effective with respect to pay periods beginning after July 18, 1984.

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Bobby Williams, (202) 632–4634.

SUPPLEMENTARY INFORMATION: Section 301(d) of Pub. L. 97–253, the Omnibus Budget Reconciliation Act of 1982, as amended by section 3(h) of Pub. L. 97–346, provided that militay retirees (other then those receiving retired pay on the basis of a wartime, service-connected disability) who are employed in civilian positions with the Federal Government, would have the amount of any cost-of-living adjustments they received in their retired pay during fiscal years 1983, 1984, and 1985 deducted from their civilian pay. The amounts deducted would be deposited in the general fund of the U.S. Treasury. On July 18, 1984, the enactment of Pub. L. 98–369, the Deficit Reduction Act of 1984, prospectively repealed section 301(d) of Pub. L. 97–253. Because this administrative action follows directly and necessarily from an Act of Congress, OPM has no discretion in the matter. No pubic interest or legal requirement would be served by a process of notice and comment. Accordingly, this rulemaking—in the nature of the rescision of a rule—is final and effective immediately upon publication.

List of Subjects in 5 CFR Part 553

Adminstrative practice and procedure, Government employees, Wages.

U.S. Office of Personnel Management.
Donald J. Devine,
Director.

PART 553—[REMOVED]

For the reasons set forth in the preamble, the Director of the Office of Personnel Management hereby revokes Part 553 of title 5, Code of Federal Regulations.

Authority: Sec. 2203, Pub. L. 98–369.

[FR Doc. 85–1176 Filed 1–14–85; 8:45 am]
BILLING CODE 6325–01–M

DEPARTMENT OF AGRICULTURE

Federal Crop Insurance Corporation

7 CFR Part 425

[Docket No. 1382S; Amdt. No. 7]

Peanut Crop Insurance Regulations

AGENCY: Federal Crop Insurance Corporation, USDA.

ACTION: Final rule.

SUMMARY: This action makes final a new provision prescribing procedures for a higher price election for non-quota (additional) peanuts, and a new subsection to contain control numbers assigned by the Office of Management and Budget (OMB) to information collection requirements of these regulations. These actions were implemented by the Federal Crop Insurance Corporation (FCIC) on an interim basis to: (1) Provide the insured grower with a higher price election for non-quota peanuts while there was still time to decide on this additional program benefit and before the grower was required to submit an acreage report under the provisions of the Peanut Crop Insurance Regulations (7 CFR Part 425) and (2) comply with OMB directions to codify the information collection requirement control numbers. This rule is promulgated under the authority contained in the Federal Crop Insurance Act, as amended.

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Peter F. Cole, Secretary, Federal Crop Insurance Corporation, U.S. Department of Agriculture, Washington, D.C., 20250, telephone (202) 447–3325.

SUPPLEMENTARY INFORMATION: This action has been reviewed under USDA procedures established in Departmental Regulation No. 1512–1 (December 15, 1983). This action does not constitute a review as to the need, currency, clarity, and effectiveness of these regulations under those procedures. The sunset review date established for these regulations is April 1, 1988.

Merritt W. Sprague, Manager, FCIC, has determined that this action (1) is not a major rule as defined by Executive Order No. 12291 (February 17, 1981), because it will not result in: (a) An annual effect on the economy of $100 million or more; (b) major increases in costs or prices for consumers, individual industries, Federal, State, or local governments, or a geographical region; or (c) significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of U.S.-based enterprises to compete with foreign-based enterprises in domestic or export markets; and (2) will not increase the Federal paperwork burden for individuals, small businesses, and other persons. This action conforms to the Federal Crop Insurance Act, as amended (7 U.S.C. 1501 *et seq.*), and other applicable law.

The title and number of the Federal Assistance Program to which this proposed rule apply are: Title—Crop Insurance; Number 10.450.

This program is not subject to the provisions of Executive Order 12372 which requires intergovernmental consultation with State and local officials. See the Notice related to 7 CFR Part 3015, Subpart V, published at 48 FR 29115 (June 24, 1983).

This action is exempt from the provisions of the Regulatory Flexibility

Act; therefore, no Regulatory Flexibility Analysis was prepared.

This action is not expected to have any significant impact on the quality of the human environment, health, and safety. Therefore, neither an Environmental Assessment nor an Environmental Impact Statement is needed.

On Tuesday, July 26, 1983 FCIC published an interim rule in the **Federal Register** at 48 FR 33845, (Amendment No. 7) amending the Peanut Crop Insurance Regulations (7 CFR Part 425) effective for the 1983 and succeeding crop years by adding a new subsection to provide the insured grower with a higher price election for non-quota (additional) peanuts in response to the growers request for an election that more nearly approximates the higher contract prices available in the market place for non-quota peanuts.

In addition, a new subsection was added to contain the control numbers assigned by OMB to information gathering requirements of these regulations.

In accordance with the regulations, the insured grower is required to submit a price election agreement at least 10 days prior the acreage reporting date for peanuts which establishes a price at which indemnities will be computed for all non-quota peanuts. There would have been insufficient time for the insured to consider these changes and still meet the requirements with regard to submitting a price election timely. Therefore the change was published as an interim rule without the opportunity for prior notice and comment.

Comments on the above actions were solicited for 60 days after publication in the **Federal Register**, but none were received.

List of Subjects in 7 CFR Part 425

Crop insurance, Peanuts.

Final Rule

Accordingly, the Interim Rule, published in the **Federal Register** on July 26, 1983, at 48 FR 33845 (Amendment No. 7), is hereby adopted as final.

Done in Washington, D.C., on July 24, 1984.

Peter F. Cole,

Secretary, Federal Crop Insurance Corporation.

Approved by:

Merritt W. Sprague,

Manager.

Dated: January 7, 1985.

[FR Doc. 85-1146 Filed 1-14-85; 8:45 am]

BILLING CODE 3410-08-M

DEPARTMENT OF JUSTICE

Immigration and Naturalization Service

8 CFR Part 292a

Listing of Free Legal Services Programs; Miscellaneous Amendment

AGENCY: Immigration and Naturalization Service, Justice.

ACTION: Final rule.

SUMMARY: This rule makes a technical amendment to 8 CFR to reflect the transfer of appellate authority formerly held by INS regional commissioners to the Associate Commissioner, Examinations as published in the **Federal Register** of September 22, 1983 (48 FR 43160).

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Loretta J. Shogren, Director, Policy Directives and Instructions, Immigration and Naturalization Service, 425 I Street NW., Washington, D.C. 20536, Telephone: (202) 633-3291.

SUPPLEMENTARY INFORMATION: A final rule amending 8 CFR 103.1(f) published September 22, 1983 (48 FR 43160) transferred to the Associate Commissioner, Examinations the authority to consider all appeals concerning applications by organizations to be listed on the Service listing of free legal services programs and denial of application therefrom under section 292a of this title. This rule amends § 292a.4 to reflect this transfer of authority.

Compliance with 5 U.S.C. 553 as to notice of proposed rulemaking and delayed effective date is unnecessary because this rule relates to agency organization and management.

In accordance with 5 U.S.C. 605(b), the Commissioner of Immigration and Naturalization certifies that this rule does not have a significant impact on a substantial number of small entities. This order is not a rule within the definition of section 1(a) of E.O. 12291.

List of Subjects in 8 CFR Part 292a

Accreditation, Representation of others, Legal service.

Accordingly, Chapter I of Title 8 of the Code of Federal Regulations is amended to read as follows:

PART 292a—LISTING OF FREE LEGAL SERVICES PROGRAMS

Section 292a.4 is revised to read as follows:

§ 292a.4 Approval and denial of applications.

District Directors or officers-in-charge shall have the authority to grant or deny an application submitted by an organization under this part, within their respective jurisdiction. If an application is denied, the applicant shall be notified of the decision in writing giving the grounds of such denial. Denial must be based on the failure of the organization to meet the qualifications specified in § 292a.2. The organization shall be advised of its right to appeal in accordance with §§ 103.1 and 103.3 of this chapter.

(Sec. 103 of the Immigration and Nationality Act, as amended; (8 U.S.C. 1103))

Dated: January 9, 1985.

Andrew J. Carmichael, Jr.,

Associate Commissioner, Examinations, Immigration and Naturalization Service.

[FR Doc. 85-1121 Filed 1-14-85; 8:45 am]

BILLING CODE 4410-10-M

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 39

[Docket No. 83-NM-117-AD; Amdt. 39-4977]

Airworthiness Directives; McDonnell Douglas Model DC-9 and C-9 (Military) Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Final rule.

SUMMARY: This action supersedes an existing airworthiness directive (AD) applicable to McDonnell Douglas Model DC-9 and Military C-9 series airplanes, and requires inspection and replacement, as necessary, of the spoiler drive link and attach fitting assemblies; associated revisions to the FAA approved Airplane Flight Manual (AFM); and the installation of a placard. This amendment is prompted by reports of spoiler drive link and fitting cracks. This action is necessary to detect fatigue cracks, and prevent failures of either the links or fittings which may permit the spoiler to float, thereby degrading the controllability of the aircraft.

DATES: Effective February 14, 1985.

Compliance schedule as prescribed in the body of the AD, unless already accomplished.

ADDRESSES: The applicable service information may be obtained from McDonnell Douglas Corporation, 3855 Lakewood Boulevard, Long Beach,

California 90846, Attention: Director, Publications and Training, C1-750 (54-60). This information also may be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington, or at 4344 Donald Douglas Drive, Long Beach, California.

FOR FURTHER INFORMATION CONTACT: Mr. Michael N. Asahara, Sr., Aerospace Engineer, Airframe Branch, ANM-122L, FAA, Northwest Mountain Region, Los Angeles Aircraft Certification Office, 4344 Donald Douglas Drive, Long Beach, California 90808; telephone (213) 548-2826.

SUPPLEMENTARY INFORMATION: A proposal to amend Part 39 of the Federal Aviation Regulations to include a new airworthiness directive (AD), which would supersede AD 74-16-02, Amendment 39-2213, was published in the **Federal Register**, on September 11, 1984 (49 FR 35649). The proposed amendment would require repetitive inspections of the spoiler drive link and attach fitting assemblies on McDonnell Douglas DC-9 series airplanes. The comment period for the proposal closed on October 29, 1984.

Interested persons have been afforded an opportunity to participate in the making of this amendment. Due consideration has been given to all comments received. Six comments were received. The first commenter felt that the compliance time for the installation of a placard within 48 hours after the effective date of the AD is unrealistic, since it does not allow for sufficient logistical planning and lead time. FAA concurs, and the final rule has been revised to reflect that the placarding of these airplanes must be effective 30 days after the effective date of the AD, to coincide with paragraphs A.2 and A.3 of Part I of the final rule. The second commenter strongly opposed the inclusion of the spoiler actuator housing modification as part of the AD, stating that the purpose of modifying the actuator housing is to extend the life of the spoiler actuator housing. The FAA has determined this to be a valid recommendation, and that the modification of the spoiler actuator housing must be addressed by means other than this AD. The FAA, therefore, has not included modification of the spoiler actuator housing as part of this AD. The third commenter requested that an alternative non-destructive testing method be considered in lieu of the procedures outlined in the McDonnell Douglas Non-Destructive Testing Manual, TR 7-1. The FAA concurs and this AD provides for an alternative means of compliance. The fourth commenter agrees with the intent of the proposed rule, but questioned its applicability to the DC-9-80 series airplanes, since compliance with the intent of this AD is mandated by a Special Inspection Report (Number MDC-J8855) via the type certificate. Reported cases of recent spoiler link/fitting failures on DC-9-80 series airplanes have prompted the FAA to revise AD 74-16-02 to incorporate crucial operational failure information for the crew, should link/fitting failure occur, by amending the existing DC-9-80 series AFM. The fifth commenter has suggested that the NPRM is not required and states that this new rule was an example of excess rulemaking by the FAA. The FAA disagrees, and considers the new rule appropriate in light of several recent spoiler link/fitting failures affecting the DC-9-50/-80 series airplanes. The sixth commenter suggested that the NPRM does not provide for the incorporation of aircraft limitations for the DC-9-80 (MD-80) series airplanes. The FAA concurs, and limitations have been added to the appropriate section of the Airplane Flight Manual.

It is estimated that 647 domestic airplanes (4 units per aircraft) will be affected by this AD. It will require approximately 6 manhours per airplane to accomplish the required repetitive inspections. The average labor charge is $40 per manhour. Based on these figures, the total cost is estimated to be $155,280 per fleet inspection cycle. Replacement cost is not considered.

After careful review of the available data, including the comments noted above, the FAA has determined that air safety and the public interest require the adoption of the rule as proposed, with the changes previously discussed.

For the reasons discussed above, the FAA has determined that this regulation is not considered to be major under Executive Order 12291 or significant under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979) and it is further certified under the criteria of the Regulatory Flexibility Act that this rule will not have a significant economic effect on a substantial number of small entities because few, if any, Model DC-9 airplanes are operated by small entities. A final evaluation has been prepared for this regulation and has been placed in the docket. A copy of it may be obtained by contacting the person identified under the caption "**FOR FURTHER INFORMATION CONTACT.**"

List of Subjects in 14 CFR Part 39

Aviation safety, Aircraft.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, § 39.13 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) is amended by superseding AD 74-14-02, Amendment 39-2213, dated May 27, 1975, with the following new airworthiness directive:

McDonnell Douglas: Applies to McDonnell Douglas Model DC-9 and C-9 (Military) series airplanes, manufacturer's fuselage numbers 1 through 1125, certificated in all categories. Compliance required as indicated, unless previously accomplished.

To prevent failures of the spoiler drive link(s), P/N 3923250-1, -501 and/or -503; and spoiler fitting(s), P/N 3923251-1 and/or -501, accomplish the following:

Part I

A. Applies to McDonnell Douglas DC-9-10 through -50, and C-9 (Military) series airplanes.

1. For operators who have accomplished terminating action in accordance with Airworthiness Directive (AD) AD 74-16-02, Amendment 39-2213, dated May 27, 1975, within the next 3,000 flight hours or 3,000 cycles, whichever occurs first, from the effective date of this AD, and thereafter at intervals not to exceed 3,000 flight hours or 3,000 cycles, whichever occurs first, perform non-destructive inspection (NDI) in accordance with the instructions contained in McDonnell Douglas Non-Destructive Testing (NDT) Manual, TR 7-1 through 7-4, referenced in McDonnell Douglas DC-9 Service Bulletins 27-228 and/or 27-229, both service bulletins dated August 19, 1982, or later NDT Manual or Service Bulletin revisions approved by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region.

Note. McDonnell Douglas Service Bulletins 27-228 and 27-229, both dated August 19, 1982, and 27-240 dated June 30, 1983, are hereinafter referred to as SB 27-228, SB 27-229, and SB 27-240.

2. For operators who have instituted the program of visual/repetitive inspections in accordance with AD 74-16-02, Amendment 39-2213, dated May 27, 1975, at the next scheduled repetitive inspection, comply with the instructions in accordance with this AD, as applicable.

3. For operators who have not implemented AD 74-16-02, Amendment 39-2213, dated May 27, 1975:

a. Within the next 300 flight hours or 300 cycles, whichever occurs first, and thereafter at intervals not to exceed 300 flight hours or 300 cycles from the effective date of this AD:

(1) Visually inspect the exposed surfaces on the forward and aft lugs, including the areas surrounding the grease fittings on the spoiler actuating link, and

(2) Visually inspect the exposed surface and areas surrounding the grease fitting on the spoiler fitting.

b. At or prior to the accumulation of an additional 1,000 flight hours or 1,000 cycles, whichever comes first, from first visual inspection on these parts, and thereafter at intervals not to exceed 3,000 flight hours or 3,000 cycles, whichever comes first, institute the program of NDI inspections as required by Part I, paragraph A.1, above, until terminating action in accordance with Part I, Paragraph A.6., below, is accomplished.

Note. The requirements for visual inspections may be terminated upon instituting the NDI program specified in Part I, paragraph A.1, of this AD.

4. If no cracks are found in the spoiler drive link or fitting assemblies in the areas identified by Figures 1 through 7 of NDT Manual TR 7-1 through TR 7-4 referenced in SB 27-228 and/or SB 27-229, or a FAA approved alternate NDT method in accordance with Part I, paragraph C.3., below, continue repetitive inspections per in accordance with Part I, paragraph A.1., above, until such time terminating action is accomplished in accordance with Part I, paragraph A.6., below.

5. If cracks are found in the spoiler drive links, or fittings in areas identified by Part I, paragraph A.3., above.

a. Replace with new flight spoiler components, in accordance with paragraph 2. of the Accomplishment Instructions, Figure 1, of SB 27-240.

b. Replace with spoiler drive link, or aft attach fitting, and continue repetive inspection per in accordance with Part I, paragraph A.1., above, until terminating action is accomplished in accordance with Part I, paragraph A.6., below.

6. Replacement of the flight spoiler components with new components in accordance with SB 27-240, dated June 30, 1983, or later FAA approved revisions, constitutes terminating action for repetitive inspection requirements of this AD.

Note. Accomplishment of the preventive modification in accordance with SB 27-240 will constitute terminating action for the repetitive inspection requirements of this Ad.

B. Applies to McDonnell Douglas DC-9-80 series airplanes:

1. Airplanes that are not affected by AD 74-16-02, Amendment 39-2213, dated May 27, 1975, but are affected by McDonnell Douglas Report MDC-J8855, Revisions A through G, or later FAA approved revisions, will continue existing inspection program. This program performs NDT inspections of the flight spoiler drive links or fittings, as follows:

a. One time visual inspection prior to exceeding 5000 total airplane flight hours.

b. Initial ultrasonic and/or eddy current inspection within 1000 flight hours after visual inspection.

c. Repetitive ultrasonic and/or eddy current inspections at intervals not to exceed 3000 flight hours or 3000 landings whichever occurs first, until Service Bulletin 27-240 is accomplished.

d. Replacement of flight spoiler drive link with a new P/N 3923250-503 link requires reinstituting the repetitive ultrasonic and/or eddy current inspections within 6000 flight hours or 6000 landings, whichever occurs first.

e. Replacement of flight spoiler drive fitting with new P/N 3923251-1 "G" or -501 fitting assembly requires reinstituting the repetitive ultrasonic and/or eddy current inspections within 6000 flight hours or 6000 landings, whichever comes first.

2. Accomplishment of the preventative modifications in accordance with SB 27-240 will constitute terminating action for the special inspection requirements listed in McDonnell Douglas Report MDC-J8855, Parts, III and IV, Revisions A through G, or later FAA approved revisions.

C. Applies to all McDonnell Douglas DC-9 and Military C-9 series airplanes:

1. Special flight permits may be issued in accordance with Federal Aviation Regulations (FAR) 21.197 and 21.199 to operate airplanes to a base for the accomplishment of modifications required by this AD.

2. Upon the request of an operator, an FAA Maintenance Inspector, subject to approval by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region, may adjust the repetitive inspection intervals specified in this AD to permit compliance at an established inspection period of that operator, if the request contains substantiating data to justify the change for that operator.

3. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region.

Note. For purposes of this AD, if the time-in-service hours of either the spoiler actuating link or the spoiler fitting cannot be established, the part will be considered to have the same number of time-in-service hours as the airplane on which it is installed.

Part II

Applies to all DC-9 series aircraft, fuselage numbers 1 thru 1125, certificated in all categories, as indicated below:

To provide crews with operation information should spoiler float occur, evidenced by abrupt roll, and to provide for a permanent change in the "Emergency Procedures" Section of the FAA approved Airplane Flight Manual (AFM) (and appropriate AFM sections of the operator's manual required by FAR 121.133 and 121.141), accomplish the following:

A. Placard

Within 30 days after effective date of this AD, unless already accomplished, install a placard as close as practicable to the flap position indicator, containing the following wording or an equivalent wording as approved by the Managaer, Los Angeles Aircraft Certificaton Office, FAA, Northwest Mountain Region, reading as follows:

DC-9-10

"Flap selection excess 20 degrees must be made prior to 1000 feet AGL. See Section I, AFM for alternate procedures." (The last sentence may be omitted from the placard if the use of alternate landing flap setting is not desired.)

DC-9-20, -30, -40, -50 and C-9 (Military Series)

"Flap selection excess 25 degrees must be made prior to 1000 feet AGL. See Section I, AFM for alternate procedures." (The last sentence may be omitted from the placard if the use of alternate landing flap setting is not desired.)

DC-9-80 Series

"Flap selection excess 28 degrees must be made prior to 1000 feet AGL. See Section I, AFM for alternate procedures." (The last sentence may be omitted from placard if the use of alternate landing flap setting is not desired).

B. Limitations

1. The limitations set forth below are effective as of June 14, 1974, for the models DC-9-10 through -40 series and C-9A and C-9B airplanes; and effective within 30 days after the effective date for the Models DC-9-50 and -80 series airplanes.

2. Within 30 days after the effective date of this AD, unless already accomplished, incorporate the "Limitations" set forth below into the Airplane Flight Manual (AFM). Operators must initiate actions to notify and ensure that the flight crewmembers are apprised of these limitations.

DC-9-10 Series

Sec. I Limitations: (New Title) "Flaps":

"Flap selection in excess of 20 degrees must be made prior to descending below 1000 feet above ground level except for the following:

Approach and landing may be made with a maximum of 30 degree flap when 15 percent is added to the 50 degree flap landing field length."

Sec. I Limitations: Performance and Operating Limitations.

Add a new paragraph as follows: "When using the 30 degrees flaps for landing, the maximum permissible quick turn around landing weight shown on the plot 'Maximum Permissible Quick Turn Around Landing Weight Flaps Down' in Section IV must be reduced by 15 percent."

DC-9-20, -30, -40, -50, and C-9 (Military Series)

Sec. I Limitations: (New Title) "Flaps"

"Flap selection in excess of 25 degrees must be made prior to descending below 1000 feet above ground level except for the following:

Approach and landing may be made with a maximum of 25 degree flap when 20 percent is added to the 50 degree flap landing field length."

Sec. I Limitations: Performance and Operating Limitations.

Add new paragraph as follows: "When using the 25 degree flap for landing, the maximum permissible quick turn around landing weight shown on the plot 'Maximum Permissible Quick Turn Around Landing Weight Flaps Full Down' in Section IV must be reduced by 20 percent."

DC-9-80 Series

Sec. I Limitations: "Flaps"

"Flap selection in excess of 28 degrees must be made prior to descrending below 1000 feet above ground level."

3. The above "Limitations" may be terminated, and the "Placard" removed when operator(s) have implemented the repetitive inspections required by Part I of this AD.

C. Emergency Procedures

1. The Emergency Procedures set forth below are effective as of June 14, 1974, for the Models DC–9–10 through –40 series and C–9A and C–9B airplanes; and effective within 30 days after the effective date of this AD for the Models DC–9–50 and –80 series airplanes.

2. Within 30 days after the effective date of this AD, unless already accomplished, incorporate the "Emergency Procedures" set forth below into the Airplane Flight Manual. These procedures constitute a permanent change to the manual. Operators must initiate action to notify and ensure that flight crewmembers are apprised of this change.

DC–9–10, –20, –30, –33F, –40, and C–9 (Military Series)

Section II: Emergency Procedure (New Title) "Spoiler Float"; "Should rapid roll develop during extension of flap to 50°, retract immediately to single engine landing flap setting. Adjust speed as required."

DC–9–34, –50 Series

Section II: Emergency Procedure (New Title) "Spoiler Float"; "Should rapid roll develop during extension of flap beyond 25°, retract immediately to single engine landing flap setting. Adjust speed as required."

DC–9–80 Series

Section II: Emergency Procedure (New Title) "Spoiler Float"; "Should rapid roll develop during extension of flap beyond 28°, retract immediately to single engine landing flap setting. Adjust speed as required."

All persons affected by this directive who have not already received these documents from the manufacturer may obtain copies upon request to McDonnell Douglas Corporation, 3855 Lakewood Boulevard, Long Beach, California 90846, Attention: Director, Publications and Training, C1–750 (54–60). These documents also may be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington, or the Los Angeles Aircraft Certification Office, 4344 Donald Douglas Drive, Long Beach, California.

This Amendment becomes effective February 14, 1985.

This supersedes AD 74–16–02, Amendment 39–2213, dated May 27, 1975.

(Secs. 313(a), 314(a), 601 through 610, and 1102 of the Federal Aviation Act of 1958 (49 U.S.C. 1354(a), 1421 through 1430, and 1502); 49 U.S.C. 106(g) (Revised, Pub. L. 97–449, January 12, 1983); and 14 CFR 11.89)

Issued in Seattle, Washington, on December 31, 1984.

Frederick M. Isaac,

Acting Director, Northwest Mountain Region.

[FR Doc. 85–1072 Filed 1–14–85; 8:45 am]

BILLING CODE 4910–13–M

14 CFR Part 39

[Docket No. 84–NM–60–AD; Amdt. 39–4978]

Airworthiness Directives; McDonnell Douglas Model DC–9 and C–9 (Military) Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Final rule.

SUMMARY: This action supersedes an existing airworthiness directive (AD) which requires visual, eddy current, and x-ray inspections of the aft pressure bulkhead on McDonnell Douglas DC–9 series airplanes with an aft passenger entrance door. Cracks, which could result in depressurization, have been reported in several new locations on the aft pressure bulkhead. This amendment would increase the inspection requirements on the bulkhead and provide for preventive modification as a terminating action.

DATES: Effective February 14, 1985.

Compliance schedule as prescribed in the body of the AD, unless already accomplished.

ADDRESSES: The applicable service information may be obtained from McDonnell Douglas Corporation, 3855 Lakewood Boulevard, Long Beach, California 90846, Attention: Director, Publications and Training, C1–750 (54–60). This information may also be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington, or at 4344 Donald Douglas Drive, Long Beach, California.

FOR FURTHER INFORMATION CONTACT: Mr. Michael N. Asahara, Sr., Aerospace Engineer, Airframe Branch, ANM–122L, FAA, Northwest Mountain Region, Los Angeles Aircraft Certification Office, 4344 Donald Douglas Drive, Long Beach, California 90808; telephone (213) 548–2826.

SUPPLEMENTARY INFORMATION: A proposal to amend Part 39 of the Federal Aviation Regulations to include a new airworthiness directive (AD) to require repetitive inspections of the aft pressure bulkhead on McDonnell Douglas DC–9 series airplanes with an aft passenger entrance door was published in the **Federal Register** on August 6, 1984 (49 FR 31295). The comment period for the proposal closed September 28, 1984.

Interested persons have been afforded an opportunity to participate in the making of this amendment. Due consideration has been given to all comments received. Three comments were received. The first commenter felt that the compliance time for the required inspections be 20,000 cycles instead of the 15,000 cycles as proposed in the NRPM. The compliance time was based on a number of factors: results of operators' inspections, number of inspections performed, crack growth data, total time on aircraft at the time crack(s) were first found, size and location of crack(s), and the manufacturer's recommendations. Based on this available data, the FAA considers the 15,000 cycles compliance time appropriate.

The second commenter requested that a repetitive inspection program be established as an alternative to the mandatory modification and compliance schedule of paragraph I. of the proposed rule. The establishment of any repetitive inspection program based on available data would necessitate unusually short repetitive inspection cycles. The FAA considers the modifications and 18-month compliance time appropriate.

The third commenter (the manufacturer) suggested that various paragraphs be revised for clarification and consistency. The FAA concurs and these changes have been incorporated in this AD.

Cost Estimate

It is estimated that 317 domestic airplanes will be affected by this AD. An average of 245 manhours per airplane will be required to accomplish the required rework and modifications; 80 manhours per airplane will be required to accomplish the repetitive inspections. Labor cost will be $40 per hour. Based on these firgures, the total cost impact of this AD is estimated to be $1,014,400.

After careful review of the available data, including the comments noted above, the FAA has determined that air safety and the public interest require the adoption of the proposed rule, with the changes previously noted.

For the reasons discussed above, the FAA has determined that this regulation is not considered to be major under Executive Order 12291 or significant under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979) and it is further certified under the criteria of the Regulatory Flexibility Act that this rule will not have a significant economic effect on a substantial number of small entities because few, if any, Model DC–9 airplanes are operated by

small entities. A final evaluation has been prepared for this regulation and has been placed in the docket. A copy of it may be obtained by contacting the person identified under the caption "FOR FURTHER INFORMATION CONTACT."

List of Subjects in 14 CFR Part 39

Aviation safety, Aircraft.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, § 39.13 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) is amended by superseding AD 80-10-03, Amendment 39-3769 (45 FR 31052) dated May 15, 1980, with the following new airworthiness directive (AD):

McDonnell Douglas: Applies to McDonnell Douglas Model DC-9 and C-9 (Military) series airplanes, certificated in all categories, with ventral aft pressure bulkhead. Compliance required as indicated, unless previously accomplished. To detect fatigue cracks and prevent structural failure of the fuselage cabin aft ventral pressure bulkhead, P/N 5910130 (and rework drawing numbers 5924597 and 5924350), accomplish the following:

A. For airplanes with 15,000 or more landings on or after the effective date of this AD, within the next 700 additional landings or, for airplanes which have been inspected in accordance with AD 80-10-03, at the next inspection scheduled in accordance with AD 80-10-03 after the effective date of this AD, conduct visual and x-ray inspections in accordance with the instructions contained in Service Sketch 2934C, of McDonnell Douglas Service Bulletin 53-137, Revision 3, dated August 4, 1983.

Note.—McDonnell Douglas Service Bulletin 53-137, Revision 3, dated August 4, 1983, is herein referred to as SB 53-137, R3.

B. If no cracks are found in the bulkhead web and doublers, in the areas of the doorjamb upper LH and RH corners, identified in Figure 1 of Service Sketch 2934C of SB 53-137, R3, for those corner areas:

1. At intervals not to exceed 2,000 landings from last inspection, repeat the visual inspections required by paragraph A., above; and

2. At intervals not to exceed 4,000 landings from last inspection, repeat the x-ray inspections required by paragraph A., above.

3. Repetitive inspections must be continued until terminating action in accordance with paragraph K., below, has been accomplished.

C. If cracks are found in the bulkhead web and doublers, for both Group I and II airplanes (as defined in SB 53-137, R) accomplish the following:

1. For cracks found in the upper left and/or right bend radius, with no radial cracks, modify and inspect upper corners of bulkhead in accordance with paragraph 2.C. [Accomplishment Instructions] of SB 53-137, R3.

2. For new cracks found in the upper left bend radius, with no radial cracks and with Condition II modification installed, modify and inspect corners of bulkhead per paragraph 2.D. of SB 53-137, R3.

3. For new cracks found in the upper right bend radius, with no radial cracks and with Condition I modification installed, modify and inspect upper corners of bulkhead in accordance with paragraph 2.E. of SB 53-137, R3.

4. For radial crack(s) found in any or all members of upper right corner, with or without bend radius cracks, modify and inspect corners of bulkhead in accordance with paragraph 2.I. of SB 53-137, R3.

5. For radial and/or bend radius crack(s), found in upper left and/or right corner(s) or portion of upper left and/or right bulkhead skin which exceeds the repairable limits of Conditions I through XVII, XX, or XXII through XXXIV (any noted conditions), or at operator's option for replacement of cracked parts that are within repairable limits, in lieu of repair modification, replace cracked parts in accordance with paragraph 2.J. of SB 53-137, R3. Reinstate repetitive inspections of the upper corners within 15,000 landings and at intervals noted in paragraphs B.1., B.2., and B.3., above.

6. For radial crack(s) found in any or all members of lower left and/or right corner radius (except P/N 5910130-9/-11 side channel), with or without cracks in the lower inboard tab portion of the P/N 5910130-3/-5 bulkhead skin, modify and inspect corners of bulkhead in accordance with paragraph 2.I. of SB 53-137, R3.

7. For crack(s) found in any or all members which extends below the lower edge of the P/N 5910130-37 channel forward vertical leg: replace cracked parts, and inspect corners in accordance with paragraph 2.N. of SB 53-137, R3. Reinstate repetitive inspections within 15,000 landings and at intervals noted in paragraphs B.1., B.2., and B.3., above.

8. For radial crack(s) found in P/N 5910130-3/-5 side bulkhead skin at one or more of the five lower inboard fasteners through the P/N 5910130-9/-11 side channel, install doublers and inspect lower corners in accordance with paragraph 2.O. of SB 53-137, R3.

9. For new radial crack(s) found in P/N 5910130-3/-5 side bulkhead skin at one or more of the five inboard fasteners through the P/N 5910130-9/-11 side channel, and preventive corner repair modification in accordance with Condition XIII has been installed, modify and inspect in accordance with paragraph 2.P. of SB 53-137, R3.

10. For new radial crack(s) found in any or all members of upper right corner, with or without bend radius cracks in P/N 5910130-13 doubler, and with Condition I modification installed, modify and inspect upper corners in accordance with paragraph 2.Y. of SB 53-137, R3.

D. If no crack(s) are found in the lower corners of the bulkhead web and doublers, for both Groups I and II airplanes (as defined in SB 53-137, R3); install preventive repair modification and repetitively inspect lower corners at 15,000 landing intervals in accordance with paragraph 2.M. of SB 53-137, R3. If preventive repair is not installed, repetitively inspect at intervals in accordance with paragraph B., above.

E. If cracks are found in the bulkhead web and doublers in Group I airplanes, accomplish the following:

1. For radial crack(s) found in any or all members of upper left or both upper left/right corners, with or without bend radius cracks, modify and inspect corners of bulkhead in accordance with paragraph 2.F. of SB 53-137, R3.

2. For new radial crack(s) found in any or all members of upper right corners, with or without bend radius cracks, and with Condition XXII modification installed, modify and inspect corners of bulkhead in accordance with paragraph 2.Q. of SB 53-137, R3.

3. For radial crack(s) found in P/N 5910130-13 doubler at upper left and/or right corner running along heel line of P/N 5910130-95 left and/or -96 right door stop angle, with or without radial cracks in any or all member of upper left and/or right corners, and with or without crack(s) in upper left and/or right bend radius of the forward flange of P/N 5910130-13 doubler, modify and inspect upper corners of bulkhead in accordance with paragraph 2.T. of SB 53-137, R3.

4. For new radial crack(s) found in any or all members of upper left corner, with or without bend radius cracks, and with Condition V modification installed, modify and inspect upper corners of bulkhead in accordance with paragraph 2.V. of SB 53-137, R3.

5. For new radial crack(s) found in any or all members of upper left corner, with or without bend radius cracks in P/N 5910130-13 doubler, and with Condition II modification installed, modify and inspect upper corners in accordance with paragraph 2.W. of SB 53-137, R3.

F. If no crack(s) are found in the bulkhead web and doublers in Group I airplanes, the interim crack preventative repair modification may be installed and the upper corners repetitively inspected at 15,000 landing intervals in accordance with paragraph 2.G. of SB 53-137, R3. If preventive repair modification is not installed, repetitively inspect at intervals specified in accordance with paragraph B., above.

G. If cracks are found in the bulkhead web and doublers for Group II airplanes, accomplish the following:

1. For radial crack(s) found in any or all members of upper left or both upper left/right corners, with or without bend radius cracks, modify and inspect corners of bulkhead in accordance with paragraph 2.H. of SB 53-137, R3.

2. For new radial crack(s) found in any or all members of upper right corner, with or without bend radius cracks, and with Condition IV modification installed, accomplish paragraph 2.R. of SB 53-137, R3.

3. For new radial crack(s) found in any or all members of upper left corner, with or without bend radius cracks, and with Condition V modification installed, accomplish paragraph 2.S. of SB 53-137, R3.

4. For radial crack(s) found in P/N 5910130-13 doubler, at upper left and/or right corner running along heel line of P/N 5910130-95/-96, side door stop angle, with or without radial cracks in any or all members of upper left and/or right corners, and with or without crack(s) in upper left and/or right bend radius of forward flange of P/N 5910130-13,

doubler, modify and inspect corners of bulkhead in accordance with paragraph 2.U. of SB 53-137, R3.

5. For radial crack(s) found in any or all members of upper left corner, with or without bend radius cracks in 5910130-13 doubler, and with Condition II modification installed, modify and inspect upper corners in accordance with paragraph 2.X. of SB 53-137, R3.

H. If no crack(s) are found in the bulkhead web and doublers in Group II airplanes, the interim crack preventive modification may be installed and the upper corners repetitively inspected at 15,000 landing interval in accordance with paragraph 2.K. of SB 53-137, R3. If preventive repair modification is not installed, repetitively inspect at intervals specified in accordance with paragraph B., above.

I. McDonnell Douglas DC-9 Service Bulletin A53-144, or later FAA approved revisions, must be accomplished within 18 months after the effective date of this AD.

J. For aircraft modified per DC-9 Service Bulletin 53-139 (basic), or production equivalent, accomplish McDonnell Douglas DC-9 Service Bulletin 53-157 within 18 months after effective date of this AD.

K. The following constitutes terminating action compliance for this AD:

1. For aircraft previously modified in accordance with DC-9 Service Bulletin 53-139 (basic and Revision 1), or production equivalent, rework the aft pressure bulkhead in accordance with Part 2 of the Accomplishment Instructions in McDonnell Douglas DC-9 Service Bulletin 53-165, dated January 31, 1983, or later FAA approved revisions.

2. For aircraft not previously modified in accordance with DC-9 Service Bulletin 53-139 (basic and Revision 1), or production equivalent; modify in accordance with DC-9 Service Bulletin 53-166, R1, or later FAA approved revisions.

L. Previous accomplishment of any rework or inspection(s), or portion(s) thereof, which is outlined in McDonnell Douglas DC-9 Service Bulletin 53-137, Revision 1, dated December 6, 1979, required by AD 80-10-03 Amendment 39-3769, effective May 15, 1980, which is also outlined in McDonnell Douglas DC-9 Service Bulletin 53-137, Revision 2, or SB 53-137, R3, provided for in AD 80-10-03, may be considered an equivalent to that requirement of this AD.

M. The inspections and modifications required by this AD need not be accomplished if, after the effective date of this AD, the aircraft is operated without cabin pressurization and a placard is installed in the cockpit, in full view of the pilots, stating:

"Operation With Cabin Pressurization is Prohibited"

N. Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate airplanes to base for the accomplishment of modifications required by this AD.

O. Upon the request of an operator, an FAA Maintenance Inspector, subject to prior approval by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region, may adjust the repetitive inspection intervals of the operator if the request contains substantiating data to justify the increase for that operator.

P. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, Los Angeles Aircraft Certification Office, FAA, Northwest Mountain Region.

All persons affected by this proposal who have not already received these documents from the manufacturer may obtain copies upon request to the McDonnell Douglas Corporation, 3855 Lakewood Boulevard, Long Beach, California 90846, Attention: Director, Publications and Training, C1-750 (54-60). These documents also may be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington, the Los Angeles Aircraft Certification Office, or 4344 Donald Douglas Drive, Long Beach, California.

This Amendment becomes effective February 14, 1985.

This supersedes AD 80-10-03, Amendment 39-3769 (45 FR 31052; May 15, 1980).

Secs. 313(a), 314(a), 601 through 610, and 1102 of the Federal Aviation Act of 1958 (49 U.S.C. 1354(a), 1421 through 1430, and 1502); 49 U.S.C. 106(g) (Revised, Pub. L. 97-449, January 12, 1983); and 14 CFR 11.89)

Issued in Seattle, Washington, on December 31, 1985.

Wayne J. Barlow,

Acting Director, Northwest Mountain Region.

[FR Doc. 85-1071 Filed 1-15-85; 8:45 am]

BILLING CODE 4910-13-M

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14 CFR Part 39

[Docket No. 84-CE-37-AD; Amdt. 39-4980]

Airworthiness Directives; Pitts Model S-2A Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Final rule.

SUMMARY: This amendment adopts a new Airworthiness Directive (AD), applicable to Pitts Model S-2A airplanes which requires visual inspection and installation of gussets on the P/N 2-5100 cockpit control tube assembly. A recent inflight failure of this assembly occurred. This action will reinforce the cockpit control tube and preclude a failure which could result in loss of normal aileron and elevator control.

DATES: Effective date: January 21, 1985.

Compliance: Required within 25 hours time-in-service after the effective date of this AD.

ADDRESSES: Pitts Service Letter No. 5, dated May 1, 1975, Revision B, applicable to this AD may be obtained from Pitts Aerobatics, Post Office Box 547, Afton, Wyoming 83110. A copy of this information is also contained in the Rules Docket, FAA, Office of the Regional Counsel, Room 1558, 601 East 12th Street, Kansas City, Missouri 64106.

FOR FURTHER INFORMATION CONTACT: Roman T. Gabrys, Aerospace Engineer, FAA, Denver Aircraft Certification Office, Northwest Mountain Region, 10455 East 25th Avenue, Suite 307, Aurora, Colorado 80010; Telephone (303) 340-5594.

SUPPLEMENTARY INFORMATION: As a result of service reports, Pitts Aviation Enterprises issued Pitts Service Letter No. 5, dated May 1, 1975, Revision B, which recommended inspection of the P/N 2-5100 cockpit control tube assembly for cracks in the area of the welds which attaches the P/N 2-5100-12 stick housings to the P/N 2-5100-11 tubes. A P/N 2-5100-20 gusset (erroneously designated as P/N 2-5100-19 in Revision A of the service letter) is also described in this service bulletin. The FAA understood that all airplanes had been modified by installation of these gussets. However, a failure of a cockpit control tube assembly on which the gussets had not been installed was recently reported. Consequently, the FAA is concerned that the gussets may not have been installed on all other control tube assemblies which require them and that failures may occur on these assemblies. Separation of the P/N 2-5100-12 control stick housing from the cockpit control tube assembly will result in loss of normal aileron and elevator control. Since this condition is likely to exist on other airplanes of the same type design, an AD is being issued requiring inspection of the cockpit control tube assembly on Pitts Model S-2A airplanes for cracks, repair of any cracks found and installation of the P/N 2-5100-20 gussets per Pitts Service Letter No. 5, Revision A or B.

Since an emergency condition exists that requires the immediate adoption of this regulation, it is found that notice and public procedure hereon are impractical and contrary to the public interest, 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 major under section 8 of 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 document 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 regulation, a final regulatory evaluation or analysis, as appropriate, will be prepared and placed in the regulatory docket (otherwise, an evaluation is not required). A copy of it, when filed, may be obtained by contacting the Rules Docket under the caption "**ADDRESSES**" at the location identified.

List of Subjects in 14 CFR Part 39

Air transportation, Aviation safety, Aircraft, Safety.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, § 39.13 of the Federal Aviation Regulations (14 CFR 39.13) is amended by adding the following new AD.

Pitts: Applies to Model S-2A (S/N's 2001 through 2105) airplanes certificated in any category.

Compliance: Required within the next 25 hours time-in-service after the effective date of this AD, unless already accomplished.

To prevent loss of normal aileron and elevator control:

(a) Visually inspect the cockpit control tube assembly using a 10 power glass for cracks in the area of the welds attaching the P/N 2-5100-12 stick housings to the P/N 2-5100-11 tube.

(1) If cracks are detected weld shut the cracks and install a P/N 2-5100-20 gusset at both the fore and aft stick housing locations in accordance with Pitts Service Letter No. 5, Revision B.

(2) If cracks are not present, install P/N 2-5100-20 gussets in accordance with Pitts Service Letter No. 5, Revision B.

(b) The aircraft may be flown in accordance with Federal Aviation Regulation 21.197 to a location where this AD can be accomplished.

(c) Installation of P/N 2-5100-19 gussets in accordance with Pitts Service Letter No. 5, Revision A, satisfies the requirements of this AD.

(d) An equivalent means of compliance with this AD may be used if approved by the Manager, Denver Aircraft Certification Office, Federal Aviation Administration, Northwest Mountain Region, 10455 East 25th Avenue, Suite 307, Aurora, Colorado 80010; Telephone (303) 340-5594.

(Secs. 313(a), 601 and 603 of the Federal Aviation Act of 1958, as amended (49 U.S.C. 1354(a), 1421 and 1423); 49 U.S.C. 106(g) (Revised, Pub. L. 97-449, January 12, 1983); § 11.89 of the Federal Aviation Regulations (14 CFR 11.89))

This amendment becomes effective on January 21, 1985.

Issued in Kansas City, Missouri, on January 4, 1985.

Murray E. Smith,

Director, Central Region.

[FR Doc. 85-1070 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1316

Amended Rules of Administrative Procedure

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Final rule.

SUMMARY: This final rule amends the administrative procedures of the Drug Enforcement Administration by deleting the requirement that the Hearing Clerk provide copies of hearing transcripts and exhibits to any person requesting such material.

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Stephen E. Stone, Associate Chief Counsel, Drug Enforcement Administration, U.S. Department of Justice, Washington, D.C. 20537, Telephone: (202) 633-1106.

SUPPLEMENTARY INFORMATION: 21 CFR 1316.63(a) provides, in pertinent part, that any person desiring a copy of the transcript of the testimony and exhibits taken at a hearing or any part thereof shall be entitled to the same upon application to the Hearing Clerk of the Administration and upon payment of the costs thereof. In recent years, hearings before this Administration have become voluminous. The requirement that the Hearing Clerk provide copies of such records imposes an undue burden upon the limited resources of the Office of the Administrative Law Judge. All parties to DEA proceedings are provided with copies of exhibits and other papers as they are filed, and any party or other interested person may purchase a copy of the transcript from the court reporting service at the time of the hearing or subsequent thereto. After the hearing, the entire record, with the exception of such portions as are received as proprietary information or are subject to a protective order, becomes public information which can be reviewed by any person who gives adequate notice to the Hearing Clerk. Persons desiring copies of the record, or any part thereof, may request the same under the provisions of the Freedom of Information Act. Accordingly, this rule amends 21 CFR 1316.63(a) by deleting the requirement that the Hearing Clerk provide copies of the transcript and exhibits to any requestor.

It has been determined that this is an internal management matter not requiring consultation with the Office of Management and Budget under Executive Order 12291. Moreover, I hereby certify that this action will have no impact upon small entities within the meaning and intent of the Regulatory Flexibility Act, 5 U.S.C. 601, et seq.

By virtue of the authority vested in the Attorney General by 21 U.S.C. 871(b), and redelegated to the Administrator of the Drug Enforcement Administration by 28 CFR 0.100 and 0.104, the following amendment is made to 21 CFR 1316.63(a).

List of Subjects in 21 CFR Part 1316

Administrative practice and procedure, Drug traffic control and research.

PART 1316—ADMINISTRATIVE FUNCTIONS, PRACTICES AND PROCEDURES

Subpart D—Administrative Hearings

§ 1316.63 [Amended]

Section 1316.63, Official transcript; index; corrections, is amended by removing the third sentence of paragraph (a) in its entirety.

Dated: January 9, 1985.

Francis M. Mullen, Jr.,

Administrator.

[FR Doc. 85-1114 Filed 1-14-85; 8:45 am]

BILLING CODE 4410-09-M

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 704

[OPTS-82018, TSH FRL-2756-8]

Toxic Substances Control Act; Reporting and Recordkeeping Requirements; Editorial Amendment

AGENCY: Environmental Protection Agency (EPA).

ACTION: Editorial amendment.

SUMMARY: This rule alphabetizes the existing definitions in 40 CFR 704.3 and removes their paragraph designations. This action is taken for the convenience of the user and to allow for orderly additions to the definitions in the future.

DATE: This final rule is effective January 15, 1985.

FOR FURTHER INFORMATION CONTACT: John A. Richards, Federal Register Staff, Office of Pesticides and Toxic

Substances, Rm. E-125, Environmental Protection Agency, 401 M Street, SW., Washington, D.C. 20460, (202-382-3826).

SUPPLEMENTARY INFORMATION: In the interest of making the Code of Federal Regulations easier for people to use and reference, the definitions under 40 CFR 704.3 are being put into alphabetical order and their lettered paragraph designations are being removed.

This regulation is a nonsubstantive editorial amendment and as such no opportunity for comment or public participation is required.

List of Subjects in 40 CFR Part 704

Hazardous materials, Chemicals recordkeeping and reporting requirements, Environmental Protection.

(15 U.S.C. 2605)

Dated: January 7, 1985.

John A. Moore,

Assistant Administrator for Pesticides and Toxic Substances.

PART 704—[AMENDED]

Therefore, 40 CFR Part 704 is amended by revising § 704.3 to read as follows:

§ 704.3 Definitions.

All definitions as set forth in the Toxic Substances Control Act (TSCA) section 3 apply for this Part. In addition, the following definitions are provided for the purposes of this Part.

"Annual" means the corporate fiscal year.

"Article" means a manufactured item (1) which is formed to a specific shape or design during manufacture, (2) which has end use function(s) dependent in whole or in part upon its shape or design during end use, and (3) which has either no change of chemical composition during its end use or only those changes of composition which have no commercial purpose separate from that of the article, and that result from a chemical reaction that occurs upon end use of other chemical substances, mixtures, or articles; except that fluids and particles are not considered articles regardless of shape or design.

"Byproduct" means a chemical substance produced without a separate commercial intent during the manufacture, processing, use, or disposal of another chemical substance(s) or mixture(s).

"Domestic" means within the geographic boundaries of the 50 United States, including the District of Columbia, the Commonwealth of Puerto Rico, the Virgin Islands, Guam, the Canal Zone, American Samoa, the Northern Mariana Islands, and any other territory or possession of the United States.

"EPA" means the United States Environmental Protection Agency.

"Import in bulk form" means to import a chemical substance (other than as part of a mixture or article) in any quantity, in cans, bottles, drums, barrels, packages, tanks, bags, or other containers, if the chemical substance is intended to be removed from the container and the substance has an end use or commercial purpose separate from the container.

"Importer" means (1) any person who imports any chemical substance or any chemical substance as part of a mixture or article into the customs territory of the United States, and includes:

(i) The person primarily liable for the payment of any duties on the merchandise, or

(ii) An authorized agent acting on his behalf (as defined in 19 CFR 1.11).

(2) Importer also includes, as appropriate:

(i) The consignee.

(ii) The importer of record.

(iii) The actual owner if an actual owner's declaration and superseding bond has been filed in accordance with 19 CFR 141.20.

(iv) The transferee, if the right to draw merchandise in a bonded warehouse has been transferred in accordance with Subpart C of 19 CFR Part 144. For the purpose of this definition, the customs territory of the United States consists of the 50 States, Puerto Rico, and the District of Columbia.

"Impurity" means a chemical substance which is unintentionally present with another chemical substance.

"Manufacture" means to manufacture for commercial purposes.

"Manufacture for commercial purposes" means (1) to import, produce, or manufacture with the purpose of obtaining an immediate or eventual commercial advantage for the manufacturer, and includes among other things, such "manufacture" of any amount of a chemical substance or mixture:

(i) For commercial distribution, including for test marketing, and

(ii) For use by the manufacturer, including use for product research and development, or as an intermediate.

(2) Manufacture for commercial purposes also applies to substances that are produced coincidentally during the manufacture, processing, use, or disposal of another substance or mixture, including both byproducts that are separated from that other substance or mixture and impurities that remain in that substance or mixture. Such byproducts and impurities may, or may not, in themselves have commercial value. They are nonetheless produced for the purpose of obtaining a commercial advantage since they are part of the manufacture of a chemical product for a commercial purpose.

"Manufacturer" means a person who imports, produces, or manufactures a chemical substance. A person who extracts a component chemical substance from a previously existing chemical substance or a complex combination of substances is a manufacturer of that component chemical substance.

"Own or control" means ownership of 50 percent or more of a company's voting stock or other equity rights, or the power to control the management and policies of that company. A company may own or control one or more plant sites. A company may be owned or controlled by a foreign or domestic parent company.

"Parent company" is a company that owns or controls another company.

"Person" includes any individual, firm, company, corporation, joint venture, partnership, sole proprietorship, association, or any other business entity; any State or political subdivision thereof; any municipality; any interstate body; any department, agency, or instrumentality of the Federal Government.

"Production volume" means the quantity of a chemical substance which is produced by a manufacturer, as measured in kilograms or pounds.

"Propose to manufacture or import" means that a person has made a firm management decision to commit financial resources for the manufacture or import of the specified chemical.

"Site" means a contiguous property unit. Property divided only by a public right-of-way shall be considered one site. There may be more than one plant on a single site.

"Small manufacturer" means a manufacturer (or importer) that meets either of the standards set forth below. Small manufacturers should read the introductory paragraph of § 704.5 and paragraph (d) of § 704.5 to obtain complete information on the TSCA section 8(a) small manufacturer exemption.

(1) *First standard.* A manufacturer of a chemical substance is small if its total annual sales, when combined with those of its parent company (if any), are less than $40 million. However, if the annual production volume of a particular chemical substance at any individual site owned or controlled by the manufacturer is greater than 45,400

kilograms (100,000 pounds), the manufacturer shall not qualify as small for purposes of reporting on the production of that chemical substance at that site, unless the manufacturer qualifies as small under "small manufacturer" (2) of this section.

(2) *Second standard.* A manufacturer of a chemical substance is small if its total annual sales, when combined with those of its parent company (if any), are less than $4 million, regardless of the quantity of chemicals produced by that manufacturer.

(3) *Inflation index.* EPA shall makes use of the Producer Price Index for Chemicals and Allied Products, as compiled by the U.S. Bureau of Labor Statistics, for purposes of determining the need to adjust the total annual sales values and for determining new sales values when adjustments are made. EPA may adjust the total annual sales values whenever the Agency deems it necessary to do so, provided that the Producer Price Index for Chemicals and Allied Products has changed more than 20 percent since either the most recent previous change in sales values or the date of promulgation of this rule, whichever is later. EPA shall provide **Federal Register** notification when changing the total annual sales values.

"Total annual sales" means the total annual revenue (in dollars) generated by the sale of all products of a company. Total annual sales must include the total annual sales revenue of all sites owned or controlled by that company, and the total annual sales revenue of that company's foreign or domestic parent company, if any.

"TSCA" means the Toxic Substances Control Act, 15 U.S.C. 2601 *et seq.*

§ 704.85 [Amended]

2. By amending § 704.85(d) by changing the cross reference to "§ 704.85(p)" to read "§ 704.3 'Proposed to manufacture or import'."

[FR Doc. 85-1091 Filed 1-14-85; 8:45 am]
BILLING CODE 6560-50-M

DEPARTMENT OF THE INTERIOR

Bureau of Land Management

43 CFR Part 3110

[Circular No. 2558]

Noncompetitive Leases; Amendment Clarifying Minimum Noncompetitive Lease Size

AGENCY: Bureau of Land Management, Interior.

ACTION: Final rulemaking.

SUMMARY: This final rulemaking amends the existing regulations to clarify that the minimum size for a noncompetitive oil and gas lease offer in the coterminous States is 640 acres or an entire surveyed or protracted section, whichever is larger. The final rulemaking also changes the minimum size for a noncompetitive lease in Alaska to 2,650 acres or 4 entire contiguous surveyed or protracted sections, whichever is larger. It also adds a new section clarifying that parcels offered under the simultaneous oil and gas leasing program are not controlled by the new limit imposed by this amendment on the size of lease offers. This change should promote more efficient economic exploration and development of the mineral resources on the public lands.

EFFECTIVE DATE: February 14, 1985.

ADDRESS: Any suggestions or inquiries should be sent to: Director (620), Bureau of Land Management, 1800 C Street, NW., Washington, D.C. 20240.

FOR FURTHER INFORMATION CONTACT: Valliere Cacy, (202) 653-2190;

or

Robert C. Bruce, (202) 343-8735.

SUPPLEMENTARY INFORMATION: A proposed rulemaking to change the minimum lease offer size for a noncompetitive over-the-counter oil and gas lease was published in the **Federal Register** on August 15, 1984 (49 FR 32609), with a 60-day comment period. During the comment period, comments were received from 3 sources, all corporations.

One comment endorsed the changes made by the proposed rulemaking, while another comment objected to any change because there are too many situations in the Western States where sections contain less than 640 acres and a status check of adjoining lands would be required to meet the minimum requirement of 640 acres. This opposing comment also recommended that the Department of the Interior determine the regulations it wishes to impose and leave those regulations unchanged for extended periods of time, suggesting that changes should not be made more than twice a year. The third comment asserted that if an entire section or 640 acres is available to lease, the entire acreage should issue under one lease.

The establishment of a minimum acreage size serves to promote expeditious development of oil and gas resources by prospective producers. Allowing issuance of leases smaller than the minimum provided in the proposed rulemaking in those instances where adjoining lands are available would be counterproductive to a meaningful oil and gas leasing program. Reviewing adjoining lands to determine their availability for leasing is an action that would be undertaken by any serious individual filing an over-the-counter offer for lands for oil and gas leasing. After carefully reviewing the issues raised in the comments, the final rulemaking adopts the language of the proposed rulemaking without change.

The principal author of this final rulemaking is Valliere Cacy, Division of Fluid Mineral Leasing, assisted by the staff of the Office of Legislation and Regulatory Management, all of the Bureau of Land Management.

The Department of the Interior has determined that this document is not a major rule under Executive Order 12291 and it will not have a significant economic effect on a substantial number of small entities under the Regulatory Flexibility Act (5 U.S.C. 601 et seq.).

The changes made by the final rulemaking are applicable to anyone offering to lease public lands for oil and gas. For the most part, the changes are designed to clarify the minimum size that a noncompetitive oil and gas lease must encompass. While this will increase the amount of the rental that must be deposited with some offers, the amount will be insignificant and should have little or no effect on those making such offers.

The final rulemaking contains no additional information collection requirements requiring approval of the Office of Management and Budget under 44 U.S.C. 3507.

List of Subjects in 43 CFR Part 3100

Administrative practice and procedure, Environmental protection, Mineral royalties, Oil and gas reserves, Public lands—classifications, Public lands—mineral resources, Surety bonds.

Under the authority of the Mineral Leasing Act, as amended and supplemented (30 U.S.C. 181 et seq.), the Mineral Leasing Act for Acquired Lands, as amended (30 U.S.C. 351-359), the Alaska National Interest Lands Conservation Act (16 U.S.C. 3101 et seq.), the Federal Land Policy and Management Act of 1976 (43 U.S.C. 1701 et seq.), the Federal Property and Administrative Services Act of 1949 (40 U.S.C. 760 et seq.), the Act of May 21, 1930 (30 U.S.C. 301-306), the Omnibus Budget Reconciliation Act of 1981 (Pub. L. 97-35), the Independent Offices Appropriation Act of 1952 (31 U.S.C. 9701), the Department of the Interior Appropriations Act, Fiscal Year 1981 (Pub. L. 96-514) and the Attorney General's Opinion of April 2, 1941 (40

Op. Att. Gen. 41), Subpart 3110, Part 3110, Group 3100, Subchapter C of Title 43 of the Code of Federal Regulations is amended as set forth below.

J. Steven Griles,

Acting Assistant Secretary of the Interior.

December 21, 1984.

PART 3100—[AMENDED]

§3110.1-3 [Amended]

1. Section 3110.1–3 is amended by:

A. Amending paragraph (a) by removing the word "section", where it first appears, and replacing it with the phrase "section, whichever is larger," and by adding at the end of the paragraph the sentence "Public domain lease offers in Alaska shall not be made for less than 2,560 acres or 4 full contiguous sections, whichever is larger, where the lands have been surveyed under the rectangular survey system or are within an approved protracted survey, except where the offer or parcel includes all available lands within the subject sections and there are no continguous lands available for lease."; and

B. Adding a new paragraph (d) to read:

* * * * *

(d) The restrictions set forth in paragraph (a) of this section regarding the minimum size of noncompetitive oil and gas lease offers do not apply to the development of parcels for leasing under subpart 3112 of this title.

[FR Doc. 85–1126 Filed 1–14–85; 8:45 am]

BILLING CODE 4310-84-M

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

48 CFR Part 1833

[NASA FAR Supplement Directive 85–1]

NASA Implementation of the Federal Acquisition Regulation (FAR); NASA Federal Acquisition Regulation Supplement (NASA/FAR Supplement)

AGENCY: Office of Procurement, Procurement Policy Division, NASA.

ACTION: Final rule.

SUMMARY: This notice publishes NASA FAR Supplement Directive (NFSD) 85–1 which amends the NASA Federal Acquisition Regulation Supplement, Chapter 18 of the Federal Acquisition Regulations System (See 40 FR 6388). This NFSD supplements FAR Part 33, Protests, Disputes and Appeals, by adding guidance for internal NASA handling of protests. Although this is promulgated as a final rule, comments will be considered.

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: W. A. Greene, Procurement Policy Division (Code HP), Office of Procurement, NASA Headquarters, Washington, DC 20546, or call (202) 453–2119.

SUPPLEMENTARY INFORMATION:

Impact

The Director, Office of Management and Budget (OMB), by memorandum dated December 14, 1984, exempted certain agency procurement regulations from Executive Order 12291. NASA certifies that this document will not have a significant economic effect on a substantial number of small entities under the Regulatory Flexibility Act (5 U.S.C. 601 et seq.). This rule provides uniformity with other Federal agencies and reduces the administrative impact on bidders as set forth in OFPP Policy Letter 83–2.

List of Subjects in 48 CFR Ch. 18

Government procurement.

Dated: January 15, 1985.

S.J. Evans,

Assistant Administrator for Procurement.

Accordingly Part 1833 of Title 48 of the Code of Federal Regulations is amended as set forth below.

PART 1833—PROTESTS, DISPUTES, AND APPEALS

1833.009, 1833.011 and 1833.014 [Redesignated as 1833.209, 1833.211 and 1833.214]

1. The existing sections 1833.009, 1833.011 and 1833.014 are redesignated as sections 1833.209, 1833.211 and 1833.214 respectively. These sections are further designated as Subpart 1833.2. The subpart heading reads:

Subpart 1833.2—Disputes and Appeals

2. Subpart 1833.1 is added to read as follows:

Subpart 1833.1—Protests

Sec.

1833.103 Protests to the agency.
1833.104 Protests to GAO.
1833.105 Protests to GSBCA.

Subpart 1833.1—Protests

1833.103 Protests to the agency.

(a) Immediately upon notice of the filing of a protest, the contracting officer shall notify the Headquarters Procurement Policy Division, Code HP. When a protest is filed directly with an installation, the determination required by FAR 33.103(a), i.e., whether to award the contract prior to resolution of the protest, will be made by the contracting officer. When a protest is filed with NASA Headquarters, the Assistant Administrator for Procurement will make the required determination.

(b) When a protest is filed directly with an installation or with NASA Headquarters, the notice required by FAR 33.103(b)(1) to other offerors whose offers might become eligible for award will be made by the contracting officer.

(c) For protests filed with NASA Headquarters, the contracting officer shall forward to the Procurement Policy Division, Code HP, a report essentially the same as that required under FAR 33.104(a)(2).

1833.104 Protests to GAO.

(a) *General.* (1) No action shall be taken by NASA personnel to respond to or resolve any protest filed with the GAO other than in accordance with this regulation.

(2) The cognizant Procurement Officer shall immediately contact Code HP for guidance upon receipt of any communication from GAO regarding a protest. Conversely, upon Headquarters receipt of a notice from the GAO of the filing of a protest, Code HP shall immediately notify the cognizant Center Procurement Officer. Within three work days of the notice, the contracting officer shall forward to Headquarters Code HP a copy of the procurement file including all documents referred to in FAR 33.104(a)(2) (i) thru (v) as well as any others requested by Code HP. The contracting officer's statement (FAR 33.104(a)(2)(vi)) shall be forwarded no later than ten work days from receipt of the notice. If more time is needed, requests for extension may be made by telephone to Headquarters, Code HP. When the GAO elects to use its express option procedure, the contracting officer's statement shall be forwarded to Code HP within six work days from receipt of notice. If that is not possible, a report to Code HP shall be made by telephone.

(3) The notices required by FAR 33.104(a)(3) shall be made by the contracting officer.

(4) The report required by FAR 33.104(a)(4) shall be filed by Headquarters Code HP.

(5) Headquarters Code HP will furnish copies of the report as required by FAR 33.104(a)(5) and, in consultation with the Office of General Counsel, decide which documents are relevant.

(6) Headquarters Code HP will provide the information required by FAR 33.104(a)(6) to the GAO.

(b) *Protests before award.* (1) The contracting officer shall provide Headquarters Code HP with information

and recommendations relevant to a determination under FAR 33.104(b)(1). The determination required by FAR 33.104(b)(1) to award a contract prior to resolution of a protest shall be made by the Assistant Administrator for Procurement.

(2) The notices and requests required by FAR 33.104(b)(2) will be made by the contracting officer.

(c) *Protests after award.* (1) Protests filed after award shall be handled in accordance with FAR 33.104(c). A file containing the documents required by FAR 33.104(a)(2) (i) thru (v) shall be forwarded by the contracting officer to Headquarters Code HP within three work days of receipt of notice of filing of the protest. The contracting officer's statement (FAR 33.104(A)(2)(vi)) shall be forwarded to Code HP within ten work days.

(2) The notice of protest to the contractor required by FAR 33.104(c)) shall be made by the contracting officer. If the contracting officer considers it likely that the award may be invalidated and a delay in receiving the supplies or services would not prejudice the Government's interest, the contracting officer shall consult with Headquarters Code HP prior to suspending or terminating the contract.

1833.105 Protests to GSBCA.

(a) The Office of Chief Counsel at the cognizant center shall, in consultation with the Assistant General Counsel for Procurement Matters, and the Assistant Administrator for Procurement, represent the agency in protests filed with the GSBCA. The cognizant Chief Counsel shall be responsible for taking or otherwise ensuring the taking of all actions required by FAR 33.105 and the GSBCA Rules of Procedure.

(b) Upon receiving notice from a non-NASA source of a protest filed with the GSBCA, the receiving office shall immediately notify cognizant Center Counsel who shall further notify the Assistant Administrator for Procurement (Code H), the Assistant General Counsel for Procurement Matters (Code GK), and the Procurement Officer.

(c) The contracting officer shall be responsible for preparing the protest file required by FAR 33.105(b) and otherwise assisting counsel.

(d) The determination and finding required by FAR 33.105(d)(2) shall be prepared and executed by the Director or Assistant Director of the cognizant technical directorate, cognizant Program/Project Manager, or cognizant staff official who reports directly to the Head of the installation, and forwarded to the Assistant Administrator for Procurement (Code H) for concurrence.

(42 U.S.C. 2473(c)(1))

[FR Doc. 85-1138 Filed 1-14-85; 8:45 am]

BILLING CODE 7501-01-M

DEPARTMENT OF COMMERCE

National Oceanic and Atmospheric Administration

50 CFR Part 655

[Docket No. 31220-244]

Atlantic Mackerel, Squid, and Butterfish Fisheries

AGENCY: National Marine Fisheries Service (NMFS), NOAA, Commerce.

ACTION: Final determination of squid specification.

SUMMARY: NOAA issues this notice to provide the final determination of the specification increase for the *Loligo* squid fishery during fishing year 1984–1985, ending March 31, 1984. This action is required by procedures established in the regulations implementing the Fishery Management Plan for the Atlantic Mackerel, Squid, and Butterfish Fisheries (FMP).

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Salvatore A. Testaverde, NMFS, 617–281–3600, extension 273.

SUPPLEMENTARY INFORMATION: The final initial specifications for the FMP for the fishing year 1984–1985 (49 FR 17512, April 24, 1984) established an initial optimum yield (IOY) for *Loligo* squid of 21,125 metric tons (mt). Regulations at 50 CFR Part 655 require that any adjustments to the IOY will be published in the **Federal Register**, giving the reasons for such adjustments. Paragraph 655.22(f) of the regulations directs the Secretary of Commerce (Secretary) to issue a notice of adjustment and to provide a public comment period. A notice was published (49 FR 47269, December 3, 1984) which increased the *Loligo* squid IOY by 3,800 mt. This amount represents an increase in the total allowable level of foreign fishing (TALFF) for Italy in exchange for promises to make shoreside purchases. No comments were received during the comment period, which ended December 17, 1984. Therefore, the Secretary allocates the additional 3,800 mt of *Loligo* squid to the IOY. In addition, TALFFs of bycatch species increase by regulation as follows:

Illex Squid, 10 percent, 380 mt, § 655.21(b)(1) (iv) and (v)

Atlantic mackerel, 1 percent, 38 mt, § 655.21(b)(2) (i) (A)

Butterfish, 6 percent, 228 mt, § 655.21(b)(3)(iii)

Because some confusion has recently occurred due to three adjustments to the initial annual specifications in the last 30 days, NOAA publishes a table of all initial and total adjusted specifications showing the current total adjustments for the fisheries.

REVISED SPECIFICATIONS FOR FISHING YEAR—APR. 1, 1984 THROUGH MAR. 31, 1985

[In metric tons (mt)]

	Loligo squid		*Illex* squid		Butterfish		Atlantic mackeral	
	Initial specifications	Adjusted specifications	Initial specifications	Adjusted specifications	Initial specifications	Adjusted specifications	Initial specifications	Adjusted specifications
MAX OY [a]	44,000		30,000		[b] 16,000			
ABC	44,000		30,000		16,000			
AC							87,000	
IOY	21,125	30,125	15,750	16,650	[b] 16,000		[c] 83,500	
DAH	17,875		13,500		11,000		[d] 26,500	
DAP	13,000		5,000		11,000		7,300	
JVP [b]	4,875		8,500				13,400	
Reserve	0	0	0	0	0	0	28,500	[e] 14,559
TALFF	3,250	12,250	2,250	3,150	[c] 571	1,111	28,500	[f] 42,441

[a] Up to figure given.
[b] These are maximum OYs (as stated in the FMP) to which the IOYs may rise.
[b] Total sum of the initial over-the-side amount. Does not include 3,625 mt *Loligo* or 9,700 mt *Illex* which will be available depending upon performance of joint ventures.
[c] May be increased by 3,500 mt based upon domestic performance.
[d] Includes 5,800 mt for the recreational fishery.
[e] This amount is increased as unallocated amounts of squid are allocated of squid are allocated to TALFF and reserves of hakes and mackerel are allocated to TALFF.
[f] Amounts reflects the proposed January 1985 reallocations of reserves to TALFF.

Other matters

This action is authorized by 50 CFR Part 655, and complies with Executive Order 12291.

(16 U.S.C. 1801 *et seq.*)

Dated: January 10, 1985.

William G. Gordon,

Assistant Administrator for Fisheries.

[FR Doc. 85-1173 Filed 1-10-85; 4:52 pm]

BILLING CODE 3510-22-M

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50 CFR Part 663

[Docket No. 41155-4175]

Pacific Coast Groundfish Fishery

AGENCY: National Marine Fisheries Services (NMFS), NOAA, Commerce.

ACTION: Notice of fishing restrictions and request for comments.

SUMMARY: NOAA issues this notice establishing restrictions to reduce the levels of fishing in 1985 for widow rockfish, the *Sebastes* complex of rockfish, Pacific ocean perch, and sablefish taken off the coasts of Washington, Oregon, and California, and seeks public comment on these actions. These actions are authorized under regulations implementing the Pacific Coast Groundfish Fishery Management Plan and are necessary because biological stress to these stocks has been identified or is projected to occur before the end of 1985. These actions are intended to lower fishing rates, reduce biological stress, and avoid or reduce the probability of a fishery closure before the end of the year. This action supersedes fishing restrictions imposed in 1984 for these species.

EFFECTIVE DATE: 0001 hours (Pacific Standard Time) January 10, 1985 until modified, superseded, or rescinded. Comments will be accepted through January 30, 1985.

ADDRESSES: Submit comments on these actions to Dr. T.E. Kruse, Acting Director, Northwest Region, National Marine Fisheries Service, 7600 Sand Point Way NE, Bin C15700, Seattle, WA 98115; or Mr. E. C. Fullerton, Director, Southwest Region, 300 South Ferry Street, Terminal Island, CA 90731.

FOR FURTHER INFORMATION CONTACT: T.E. Kruse at 206-526-6150, E.C. Fullerton at 213-548-2575, or the Pacific Fishery Management Council at 503-221-6352.

SUPPLEMENTARY INFORMATION: The Pacific Coast Groundfish Fishery Management Plan (FMP) was approved on January 4, 1982, and final implementing regulations were published October 5, 1982 (47 FR 43964). This action supersedes the **Federal Register** notices closing the widow rockfish fishery (49 FR 47005, November 30, 1984), modifying trip limits for the *Sebastes* complex and Pacific ocean perch (49 FR 30949, August 2, 1984), and setting the trip limit for the *Sebates* complex and for sablefish smaller than 22 inches in length (49 FR 597, January 5, 1984). This notice supplements the **Federal Register** notice announcing the final specifications for 1985 harvest levels of Pacific groundfish species (50 FR 471, January 4, 1985).

The FMP differentiates between species with numerical and with non-numerical optimum yields (OYs). A species which may be harvested fairly selectively has a numerical OY, which is the maximum amount of that species that may be landed in a year; landings in excess of OY are prohibited. Widow rockfish *(Sebastes entomelas)*, Pacific ocean perch (*S. alutus*), and sablefish (*Anoplopoma fimbria*) have numerical OYs. When landing rates became too high, trip limits were imposed to extend the fishery as long as possible throughout the year and to avoid complete closure. Nonetheless, in 1984 the Pacific ocean perch fishery in the Columbia subarea and the coastwide widow rockfish fishery were closed before the end of the year because their OY quotas were reached.

Species which are not harvested selectively, or which are of very little commercial interest, or about which there is little scientific data, are part of the non-numerical OY group and are managed most commonly by gear, area, and landing restrictions. An estimate of the acceptable biological catch (ABC), the annual catch that could be taken without jeopardizing the resource's productively, has been made for most species in this group. Some species in the non-numerical OY group may be fished above the ABC. However, when a species in the group is biologically stressed, or will be before the end of the year, the Secretary of Commerce (Secetary) may determine that harvest of the group as a whole should be reduced even though some species in the group may not be stressed. The *Sebastes* complex (all species of rockfish managed under the FMP except Pacific ocean perch and shortbelly, widow, and *Sebastolobus* rockfishes) is included in this non-numerical OY group. For species in this group which need further protection, a "harvest guideline" is established, an annual goal which is not necessarily but may become a quota.

The regulations implementing the FMP allow the Secretary to reduce fishing levels if it is determined that continued fishing at current levels would cause biological stress to any species. Throughout 1982, 1983, and 1984, the Pacific Fishery Management Council (Council) documented biological stress on widow rockfish and at least one species within the multi-species *Sebastes* complex. Pacific ocean perch, which is managed under a 20-year rebuilding schedule set forth in the FMP, is considered to be under long-term stress. The Council also acknowledged the increased likelihood of biological stress occurring in sablefish if fishing levels were not reduced. Management regimes were implemented for widow rockfish, Pacific ocean perch, and sablefish, all regulated by quotas in 1984, with the intent of avoiding the closure of these fisheries which will occur if the quota is exceeded before the end of the year. Limits also were placed on the *Sebastes*-complex fishery in an attempt to keep landings close to the harvest guideline.

In its deliberations for 1985 management, the Council considered advice from its Groundfish Management Team (State and Federal fishery and social scientists), Groundfish Advisory Subpanel (fishing industry and consumer representatives), Scientific and Statistical Committee (State, Federal, and university scientists), the concerned public, and an *ad hoc* Task Force created by the Council for the purpose of recommending methods of reducing fishing levels with minimal disruption to the fishing industry. The Task Force included representatives from the Council, Groundfish Management Team, fishing industry, and State fishery agencies.

At its November 28-29, 1984, meeting in Seattle, Washington, the Council reviewed the latest data and developed management measures intended to limit landings of grounfish in 1985, thereby minimizing the likelihood or intensity of biological stress on groundfish stocks, and reducing the chances of having to close a fishery before the end of the year. In each case, the Council recommended some kind of trip limit. The Council's recommendations for 1985 and actions taken by the Secretary on those recommendations are presented below. Because the vast majority of groundfish landed off Washington, Oregon, and California is taken from the fishery conservation zone (FCZ) 3-200 nautical miles offshore, all groundfish taken and retained or landed in violation of these restrictions will be treated as though they were taken in the FCZ, the same as in 1984.

Widow Rockfish

Council Recommendation: The Council recommended a trip limit of 30,000 pounds on widow rockfish, with only one landing above 3,000 pounds per vessel per week. The Council also agreed that fishermen could choose biweekly limits, that is: 60,000 pounds could be landed in a two-week period, with only one landing above 3,000 pounds, if proper notification is given. (A similar biweekly provision was established in 1984 for the *Sebastes* complex, but not for widow rockfish.) These limits will be applied coastwide and are subject to inseason adjustment so that the OY is not exceeded before the end of 1985.

Rationale: Widow rockfish are biologically stressed and trip limits to reduce landings have been implemented since 1982. Evidence of stress persisted through 1984 and is expected to continue in 1985. Acknowledging the lack of alternate fisheries and the severe impact on the fishing industry if OY were further reduced, OY was maintained at 9,300 metric tons (mt), 1,900 mt above the 7,400-mt ABC for 1985. Nonetheless, landings will need to be restricted in 1985.

In 1984, weekly trip limits of 50,000 pounds and 40,000 pounds were in effect the first eight months of the year. The 9,300-mt OY for widow rockfish was reached in October and the fishery was closed in November. Accordingly the Council recommended more restrictive trip limits for 1985 to help forestall closure of the fishery. The Council also agreed that fishermen should have the choice of using a biweekly trip limit which would double the amount that could be landed while reducing the trip frequency by half in order to minimize hardship on vessels capable of landings larger than 30,000 pounds.

Secretarial Action: The Secretary concurs with the Council's recommendation and hereby announces:

(1) Except for the biweekly trip limit provided in paragraph (2) below, no more than 30,000 pounds (round weight) of widow rockfish may be taken and retained, or landed, per vessel per fishing trip in a one-week period. Only one landing of widow rockfish above 3,000 pounds (round weight) may be made per vessel in that one-week period. "One-week period" means seven consecutive days beginning 0001 hours Sunday and ending 2400 hours Saturday, local time.

(2) *Biweekly trip limit.* (a) If the appropriate agency is notified as required by paragraph (2)(b), up to 60,000 pounds (round weight) of widow rockfish may be taken and retained, or landed, per vessel per fishing trip in a two-week period. Only one landing of widow rockfish above 3,000 pounds (round weight) may be made per vessel in that two-week period, and only if compliance with paragraph (2)(b) can be demonstrated. "Two-week period" means 14 consecutive days beginning at 0001 hours Sunday and ending 2400 hours Saturday, local time.

(b) The vessel owner or operator must notify the fishery agency of the State where the fish will be landed of his choice to make one landing of window rockfish above 3,000 pounds every two weeks. This notification must be received in writing prior to the first day of the first two-week period in which such landings are to occur and is binding until rescinded in writing.

(c) Notifications must be submitted to the Oregon Department of Fish and Wildlife, Marine Regional Office, Marine Science Drive, Building No. 3, Newport, OR 97365, telephone 503–867–4741; or P.O. Box 5430, Charleston, OR 97420, telephone 503–888–5515, between 8:00 a.m. and 4:30 p.m., and other times at 503–269–5000 or 503–269–5999; 53 Portway Street, Astoria, OR 97103, telephone 503–325–2462; or to the Washington Department of Fisheries, 115 General Administration Building, Olympia, WA 98504; or to the California Department of Fish and Game, Branch Office, 619 Second Street, Eureka, CA 95501.

(3) These restrictions apply to all widow rockfish taken and retained in ocean waters offshore of, or landed in, Washington, Oregon, and California, regardless of where they are caught.

Sebastes Complex

Council Recommendation: The Council recommended that the harvest guideline for the *Sebastes* complex (all rockfish managed under the FMP except Pacific ocean perch and shortbelly, widow, and *Sebastolobus* species of rockfish) should equal the sum of the ABCs for those species taken north of Cape Blanco, Oregon (42°50' N. latitude), which equals 10,100 mt. To achieve this, the Council recommended a trip limit of 30,000 pounds on the *Sebastes* complex taken north of Cape Blanco (of which no more than 10,000 pounds could be yellowtail rockfish), with only one landing above 3,000 pounds allowed per vessel per week. It also provided fishermen with the option of landing up to 60,000 pounds in one trip (of which no more than 20,000 pounds could be yellowtail rockfish) in a two-week period if proper notification is made: this biweekly option has been allowed since May 1984. The Council also recommended maintaining the 40,000-pound trip limit for landings of the *Sebastes* complex caught south of Cape Blanco, with no limit on the number of landings allowed per week. The 10,100-mt harvest guideline established for the *Sebastes* complex caught north of Cape Blanco is not now, but may become, a quota during 1985.

Rationale: The harvest guideline for the *Sebastes* complex of rockfish is the same in 1985 as in 1984, 10,100 mt. Weekly trip limits in 1984 were adjusted to reduce landings from 30,000 pounds in January to 15,000 pounds in May and 7,500 pounds in August. Landings of the *Sebastes* complex are projected to exceed slightly the harvest guideline in 1984.

Yellowtail rockfish, which contributed about half of the landings of the *Sebastes* complex caught north of Cape Blanco in 1984, were documented as biologically stressed in 1983. Other species in the *Sebastes* complex are not believed to be stressed. Some fisherman complain that landings of unstressed species in the *Sebastes* complex are unnecessarily limited in the attempt to protect yellowtail rockfish. Moreover, trip limits applied to the complex as a whole have not kept landings of yellowtail from exceeding its ABC. Yellowtail landings for 1984 are projected at almost twice ABC. The Council decided to recommend a weekly trip limit of 30,000 pounds, the same as initially imposed in 1984, but also adopted a weekly limit on yellowtail rockfish to try to reduce landings of that species without severely inhibiting landings of other species in the complex.

Other provisions remaining the same as in 1984 include the option to declare biweekly trips (60,000 pounds once every two weeks, of which no more than 20,000 pounds may be yellowtail rockfish), the 40,000-pounds trip limit (with no frequency restriction) on the *Sebastes* complex caught south of Cape Blanco, and the necessity of making a prior written declaration to the appropriate State agency if fishing south and landing north of Cape Blanco.

Although the Council recommended maintaining the same reporting requirements as in 1984 with respect to fishing north or south of Cape Blanco, subsequent discussion revealed that the States of Oregon and Washington had adopted reporting requirements slightly different than those established in the Federal regulations. Accordingly, these regulations for 1985 have been modified to accommodate the notification procedures adopted by the States in 1984. These revisions maintain the Council's intent to establish continuity

in the regulations between 1984 and 1985 and among State and Federal fishery agencies, and are no more restrictive on fisherman than the reporting requirements in effect in 1984. The major change is deletion of the declaration required to fish both north and south of Cape Blanco on a single trip and its replacement by a declaration required to fish north and land more than 3,000 pounds of the *Sebastes* complex south of Cape Blanco. This latter notification was imposed by the State of Oregon in 1984. Also, the Oregon addresses for receiving notifications have been changed, and declarations for biweekly limits must be made before the first applicable two-week period and will be binding until rescinded in writing rather than requiring renewal each month.

Secretarial Action: The Secretary concurs with the Council's recommendations and hereby announces the following conditions and restrictions:

(1) *Definitions.* (a) *Sebastes* complex means all rockfish managed by the Pacific Coast Groundfish Fishery Management Plan except Pacific ocean perch (*Sebastes alutus*), widow rockfish (*S. entomelas*), shortbelly rockfish (*S. jordani*), and *Sebastolobus* species of rockfish (which includes idiot rockfish). The *Sebastes* complex includes yellowtail rockfish (*Sebastes flavidus*).

(b) "One week period" means seven consecutive days beginning 0001 hours Sunday and ending 2400 hours Saturday, Local time.

(c) "Two-week period" means 14 consecutive days beginning at 0001 hours Sunday and ending 2400 hours Saturday, local time.

(d) All weights are round weights, the weight of the whole fish.

(2) *General.* (a) These restrictions apply to all fish of the *Sebastes* complex taken and retained in ocean waters (0–200 nautical miles) offshore of, or landed in, Washington, Oregon, and California regardless of the place of taking.

(b) There is not limit on the number of landings under 3,000 pounds of the *Sebastes* complex allowed per week.

(c) It will be presumed that all fish of the *Sebastes* complex which are possessed or landed north of Cape Blanco (42°50' N. latitude) were caught north of Cape Blanco unless compliance with paragraph (2)(d) can be demonstrated.

(d) Unless compliance with this paragraph can be demonstrated, fishing for any groundfish species during a single fishing trip must occur either north or south, but not on both sides, of Cape Blanco if more than 3,000 pounds of the *Sebastes* complex is landed from that trip. Fishing may occur both north and south of Cape Blanco, so long as all other trip limit restrictions imposed by this notice are observed, if the vessel owner or operator notifies the State of Oregon before leaving port on a fishing trip of intent to fish in one area and possess or land in the other. This notification, submitted by telephone or in writing, should be made to the Oregon Department of Fish and Wildlife, Marine Regional Office, Marine Science Drive, Building No. 3, Newport, OR 97365, telephone 503–867–4741; or P.O. Box 5430, Charleston, OR 97420, telephone 503–888–5515, between 8:00 a.m. and 4:30 p.m., and other times at 503–269–5000 or 503–269–5999; or 53 Portway Street, Astoria, OR 97103, telephone 503–325–2462. If fishing occurs both north and south of Cape Blanco, during a single fishing trip, then the restrictions on the *Sebastes* complex caught north of Cape Blanco apply.

(3) *Restrictions on the Sebastes* complex caught north of Cape Blanco. (a) Except for the biweekly trip limit provided in paragraph (3)(b), no more than 30,000 pounds of the *Sebastes* complex, including no more than 10,000 pounds of yellowtail rockfish, may be taken and retained, possessed, or landed, per vessel per fishing trip in a one-week period north of Cape Blanco. Only one landing of the *Sebastes* complex above 3,000 pounds may be made per vessel in that one-week period.

(b) *Biweekly trip limit.* If the appropriate agency is notified as required by this paragraph, up to 60,000 pounds of the *Sebastes* complex, including no more than 20,000 pounds of yellowtail rockfish, may be taken and retained, possessed, or landed, per vessel per fishing trip in a two-week period north of Cape Blanco. Only one landing of the *Sebastes* complex above 3,000 pounds may be made per vessel in that two-week period, and only if compliance with this paragraph can be demonstrated. The vessel owner or operator must notify the fishery agency of the State where the fish will be landed of his choice to make one landing of the *Sebastes* complex above 3,000 pounds every *two* weeks. This notification must be received in writing prior to the first day of the first two-week period in which such landings are to occur and is binding until rescinded in writing.

Notifications must be submitted to the Oregon Department of Fish and Wildlife, Marine Regional Office, Marine Science Drive, Building No. 3, Newport, OR 97365, telephone 503–867–4741; P.O. Box 5430, Charleston, OR 97420, telephone 503–888–5515, between 8:00 a.m. and 4:30 p.m., and other times at 503–269–5000 or 503–269–5999; 53 Portway Street, Astoria, OR 97103, telephone 503–325–2462; or to the

Washington Department of Fisheries, 115 General Administration Building, Olympia, WA 98504; or to the

California Department of Fish and Game, Branch Office, 619 Second Street, Eureka, CA 95501

(4) *Restrictions on Sebastes complex caught south of Cape Blanco.* (a) No more than 40,000 pounds of the *Sebastes* complex may be taken and retained, possessed, or landed, per vessel per fishing trip south of Cape Blanco. There is no limit on the number of landings allowed per week of the *Sebastes* complex caught south of Cape Blanco.

Pacific Ocean Perch

Council Recommendation: The Council recommended a trip limit of 20 percent, by round weight, of all fish on board, to be reviewed inseason for possible refinement. For purposes of this limit, the southern border of the Columbia area is shifted south to Cape Blanco (42°50' N. latitude), the same as for the *Sebastes* complex.

Rationale: Pacific ocean perch is managed under a 20-year rebuilding schedule designed to rebuild the stressed stock to levels that will produce the maximum sustainable yield. Pacific ocean perch is considered to be under long-term stress and has been managed by trip limits since the FMP became effective in 1982. In August 1984, a trip limit of 20 percent (by weight) of all fish on board, not to exceed 5,000 pounds, was imposed to further reduce landings. However, it occurred too late in the year to avoid closure of the Pacific ocean perch fishery in the Columbia area. (Earlier implementation of the trip limit was not possible because an amendment to the FMP authorizing this change was not effective until late July 1984.)

The Council agreed to drop the 5,000-pound limit on Pacific ocean perch landed per tirp in 1985 as the 1985 trip limits on the *Sebastes* complex and widow rockfish are much lower than in 1984, and 20 percent of these limits in 1985 will be smaller than in 1984. The Council will review the number of landings of Pacific ocean perch above 5,000 pounds when this limit is reconsidered in April 1985.

The Council also recommended that the trip limit should apply 10 nautical miles farther south than in 1984, to Cape Blanco, for consistency with statistical reporting areas and regulations on the *Sebastes* complex.

Secretarial Action: The Secretary concurs and hereby announces:

(1) Pacific ocean perch may be no more than 20 percent (by round weight) of all fish on board taken and retained, or landed, per vessel per fishing trip.

(2) This restriction applies to all Pacific ocean perch taken and retained north of Cape Blanco (42°50' N. lattitude) in ocean waters offshore of Washington or Oregon, including the territorial seas of the States.

Sablefish

Council Recommendation: The Council recommended that the 1984 management measures for sablefish should be continued in 1985, with one exception: The Monterey Bay area between 37°00' and 36°30' N. latitude would no longer be excluded from the size and trip limits. Accordingly, in 1985 the trip limit allowing retention of only 5,000 pounds of sablefish smaller than 22 inches applies to all ocean waters north of Point Conception (34°27' N. latitude). As in 1984, no size or trip limit for sablefish is imposed south of Point Conception.

Rationale: A 5,000-pound trip limit on sablefish smaller than 22 inches was imposed in 1983 for the area north of Point Conception except Monterey Bay. This limit was imposed to reduce the likelihood of biological stress which was expected if landings of juvenile sablefish were not curtailed. Recognizing enforcement and compliance difficulties resulting from the "window" at Monterey Bay, and for lack of evidence that Monterey Bay should be managed separately, this trip limit will be applied to all ocean waters north of Point Conception. Although there was discussion that the size limit was no longer necessary because the small, juvenile fish which were abundant in 1982 have now grown, the Council decided that there were compelling reasons to continue the size and trip limits in 1985. These reasons include the presence of a strong year class of small fish, the higher price per pound of larger fish, and the prudence of minimizing landings of juvenile fish which become the future brood stock.

Secretarial Action: The Secretary concurs with the Council's recommendation and hereby announces:

(1) No more than 5,000 pounds (round weight) of sablefish smaller than 22 inches (total length) may be taken and retained, or landed, per vessel per fishing trip in the area north of Point Conception (34°27' N. latitude) to the U.S.-Canada border.

(2) Total length is measured from the tip of the snout (mouth closed) to the tip of the tail (pinched together) without resort to mutilation of the fish or the use of additional force to extend the length of the fish.

(3) For sablefish which have been "headed," the minimum size limit is 16 inches measured from the origin of the first dorsal fin (where the front dorsal fin meets the dorsal surface of the body closest to the head) to the tip of the upper lobe of the tail; the dorsal fin and tail must be left intact.

(4) No sablefish may be retained which is in such condition that its length has been extended or cannot be detemined by the methods stated above.

(5) The above restrictions apply to all sablefish taken and retained in ocean waters (0–200 nautical miles) offshore of, or landed in, Washington, Oregon, and California, regardless of the place of taking, except that no trip or size limits are imposed on sablefish caught south of Point Conception.

Inseason Adjustments

At its April 1985 meeting, the Council will review the data available through March, 1985, and recommend modifications to these management measures if appropiate. The Council intends to examine the progress of these fisheries at least twice during the year in order to avoid overfishing and to extend the fisheries as long as possible throughout the year.

Other Fisheries

These limits for sablefish, widow rockfish, Pacific ocean perch and the *Sebastes* complex apply to vessels of the United States, including those vessels delivering groundfish to foreign processors. Retention of these species by foreign processors is further limited by separate incidental retention allowable limits established under 50 CFR 611.79.

U.S. vessels operating under an experimental fishing permit issued under 50 CFR 663.10 also are subject to these restrictions.

Landings of groundfish in the pink shrimp and spot and ridgeback prawn fisheries are governed by regulations at 50 CFR 663.28.

Classification

The determination to impose these fishing restrictions is based on the most recent data available. The aggregate data upon which the determination is based are available for public inspection at the Office of the Director, Northwest Region (see ADDRESSES) during business hours until the end of the comment period.

These actions are taken under the authority of 50 CFR 663.22 and 663.23, and are in compliance with Executive Order 12291. The actions are covered by the Regulatory Flexibility Analysis prepared for the authorizing regulations.

Section 663.23 of the groundfish regulations states that the Secretary will publish a notice of action reducing fishing levels in proposed form unless he determines that prior notice and public review are impractable, unnecessary, or contrary to the public interest. Anticipated fishing rates at the high levels experienced in 1984 will unquestionably result in several ABCs being exceeded in 1985. Prompt action to reduce those fishing rates is necessary to protect the widow rockfish, *Sebastes* complex, Pacific ocean perch, and sablefish stocks and alleviate the necessity for year-end closures in 1985. Consequently, further delay of these actions is impracticable and contrary to the public interest, and these actions are taken in final form effective January 10, 1985.

The public has had opportunity to comment on these management measures. The public participated in the Task Force, Groundfish Management Team, Groundfish Advisory Subpanel, and Council meetings in October and November 1984 that generated the management actions endorsed by the Council and the Secretary. Further public comments will be accepted for 15 days after publication of this notice in the **Federal Register.**

List of Subjects in 50 CFR Part 663

(16 U.S.C. 1801 *et seq*).

Administrative practice and procedure, Fish, Fisheries, Fishing.

Dated: January 10, 1985.

Carmen J. Blondin,

Deputy Assistant Administrator for Fisheries Resource Management.

[FR Doc. 85–1171 Filed 1–10–85; 4:52 pm]

BILLING CODE 3510-22-M

Proposed Rules

Federal Register
Vol. 50, No. 10
Tuesday, January 15, 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

Agricultural Marketing Service

7 CFR Parts 53 and 54

Standards for Grades of Carcass Beef and Standards for Grades of Slaughter Cattle

AGENCY: Agricultural Marketing Service (AMS), USDA.

ACTION: Proposed rule; extension of comment period.

SUMMARY: On November 8, 1984, the Agricultural Marketing Service (AMS) published a proposal to amend the official U.S. standards for grades of beef carcasses and the related standards for grades of slaughter cattle by eliminating the consideration of kidney, pelvic, and heart (KPH) fact in the determination of yield grade. The AMS is extending the comment period to March 15, 1985, because a trade organization requested additional time to file comments.

DATE: Comments must be received on or before March 15, 1985.

ADDRESSES: Written comments to: Standardization and Reveiw Branch, Livestock Division, Agricultural Marketing Service, U.S. Department of Agriculture, Room 2649, South Building, Washington, D.C. 20250.

FOR FURTHER INFORMATION CONTACT: Dr. Michael L. May, Chief, Standardization and Review Branch, Livestock Division, Agricultural Marketing Service, U.S. Department of Agriculture, Washington, D.C. 20250, (202) 447-4486.

SUPPLEMENTARY INFORMATION: On November 8, 1984, the Agricultural Marketing Service published a proposed rule in the **Federal Register** (49 FR 44724) to amend the beef carcass (7 CFR Part 54) and slaughter cattle (7 CFR Part 53) standards by eliminating the consideration of kidney, pelvic, and heart (KPH) fat in the determination of yield grade. The comment period was originally scheduled to end on February 1, 1985. However, an industry trade organization requested additional time to study the proposal to develop more meaningful comments. The AMS has determined that there is sufficient justification for extending the comment period until March 15, 1985.

Done at Washington, D.C., on January 9, 1985.

William T. Manley,
Deputy Administrator, Marketing Programs.

[FR Doc. 85-1082 Filed 1-14-85; 8:45 am]
BILLING CODE 3410-02-M

Federal Crop Insurance Corporation

7 CFR Part 403

[Doc. No. 1189S Amdt. No. 2]

Peach Crop Insurance Regulations

AGENCY: Federal Crop Insurance Corporation, USDA.

ACTION: Proposed rule.

SUMMARY: The Federal Crop Insurance Corporation (FCIC) proposes to amend the Peach Crop Insurance Regulations (7 CFR Part 403), effective for the 1985 and succeeding crop years, to: (1) Clarify the establishment of the dollar amount of insurance applicable when the crop is damaged by hail; (2) clarify production to count when peaches are not harvested before the general harvest of peaches in the county; and (3) provide for the payment of interest when idemnities are not paid timely. FCIC also proposes to delete Appendix B concerning counties where Peach Crop Insurance is offered from the Code of Federal Regulations. The intended effect of this rule is to clarify the policy, and delete Appendix B. The authority for the promulgation of this rule is contained in the Federal Crop Insurance Act, as amended.

DATE: Written comments, data, and opinions on this proposed rule must be submitted not later than March 18, 1985, to be sure of consideration.

ADDRESS: Written comments on this proposed rule should be sent to the Office of the Manager, Federal Crop Insurance Corporation, Room 4096, South Building, U.S. Department of Agriculture, Washington, D.C. 20250.

FOR FURTHER INFORMATION CONTACT: Peter F. Cole, Secretary, Federal Crop Insurance Corporation, U.S. Department of Agriculture, Washington, D.C., 20250, telephone (202) 447-3325.

SUPPLEMENTARY INFORMATION: This action has been reviewed under USDA procedures established by Departmental Regulation No. 1512-1 (December 15, 1983). This action does not constitute a review as to the need, currency, clarity, and effectiveness of these regulations under those procedures. The sunset review date established for these regulations is April 1, 1988.

Merritt W. Sprague, Manager, FCIC, has determined that this action (1) is not a major rule as defined by Executive Order No. 12291 (February 17, 1981), because it will not result in: (a) An annual effect on the economy of $100 million or more; (b) major increases in costs or prices for consumers, individual industries, Federal, State, or local governments, or a geographical region; or (c) significant adverse effects on competition, employment, investment, productivity, innovation, or the ability of U.S.-abased enterprises to compete with foreign-based enterprises in domestic or export markets; and (2) will not increase the Federal paperwork burden for individuals, small businesses, and other persons.

This action is not expected to have any significant impact on the quality of the human environment, health, and safety. Therefore, neither an Environmental Assesment nor an Environmental Impact Statement is needed.

The title and number of the Federal Assistance Program to which this proposed rule applies are: Title—Crop Insurance; Number 10.450.

This program is not subject to the provisions of Executive Order 12372 which requires intergovernmental consultation with State and local officials. See the Notice related to 7 CFR Part 3015, Subpart V, published at 48 FR 29115 (June 24, 1983).

This action is exempt from the provisions of the Regulatory Flexibility Act; therefore, no Regulatory Flexibility Analysis was prepared.

On December 14, 1983, FCIC published a final rule in the **Federal Register** amending 7 CFR Part 403. The rule was incorrectly listed as Amendment No. 3, and should have read Amendment No. 1. That error is

proposed to be corrected hereby. This is Amendment No. 2.

The changes herein proposed for the Peach Crop Insurance Regulations, effective for the 1985 and succeeding crop years, involve the clarification of the heading of the Amount of Insurance Table illustrating the dollar amount of insurance per acre based on the amount of fruit remaining on the trees. The amended language now defines when the amount is applicable as being the earlier of (a) the time of harvest, or (b) the date of inspection when damage is due to hail. This change allows FCIC sufficient time to inspect for hail damage. These changes also define production to count, for purposes of appraisal, when the crop is not harvested before the harvesting of peaches becomes general in the county; and delete Appendix B.

FCIC is soliciting comments on this proposed rule for 60 days after publication in the **Federal Register.** All written comments made pursuant to this action will be available for public inspection in the Office of the Manager, Federal Crop Insurance Corporation, Room 4096, U.S. Department of Agriculture, Washington, D.C., 20250, during regular business hours, Monday through Friday.

List of Subjects in 7 CFR Part 403

Crop insurance, Peach.

PART 403—AMENDED

Accordingly, pursuant to the authority contained in the Federal Crop Insurance Act, as amended (7 U.S.C. 1501 *et seq.*), the Federal Crop Insurance Corporation proposes to amend the Peach Crop Insurance Regulations (7 CFR Part 403), effective for the 1985 and succeeding crop years, in the following instances:

1. The Authority citation for 7 CFR Part 403 is:

Authority: Secs. 506, 516, Pub. L. 75–430, 52 Stat. 73, 77, as amended (7 U.S.C. 1506, 1516).

2. 7 CFR 403.7 is amended by revising the introductory test of paragraph (d), and revising the following parts of the Peach Crop Insurance Policy; the table in 4.(b); 9.(e)(3)(a); and 9.h. to read:

§ 403.7 The application and policy.

* * * * *

(d) The application for the 1985 and succeeding crop years is found at Subpart D of Part 400—General Administrative Regulations (7 CFR 400.37, 400.38) and may be amended from time to time for subsequent crop years. The provisions of the Peach Insurance Policy for the 1985 and succeeding crop years are as follows:

* * * * *

4. * * *

b. The dollar amount of insurance per acre for each crop year is determined by reference to the following table:

AMOUNT OF INSURANCE TABLE

Dollar amount of insurance per acre

At the time insurance attaches		Fruit remaining on trees at the earlier of (1) harvest, or (2) inspection [1]					
Col. A—expected production reported (bushels)	Col. B—level elected	Col. C—200 or more bushels	Col. D.—150 to 199 bushels	Col. E.—100 to 149 bushels	Col. F.—50 to 99 bushels	Col. G.—10 to 49 bushels	Col. H.—0 to 9 bushels
300 or more:							
High	$800	$800	$720	$640	$560	$480	$400
Medium	600	600	540	480	420	360	300
Low	400	400	360	320	280	240	200
250 to 299:							
High	700	700	630	560	490	420	350
Medium	525	525	475	420	370	315	265
Low	350	350	315	280	245	210	175
200 to 249:							
High	600	600	540	480	420	360	300
Medium	450	450	405	360	315	270	225
Low	300	300	270	240	210	180	150
150 to 199:							
High	500	500	500	440	375	315	250
Medium	375	375	375	330	280	235	190
Low	250	250	250	220	190	155	125
100 to 149:							
High	400	400	400	400	335	265	200
Medium	300	300	300	300	250	200	150
Low	200	200	200	200	165	135	100

[1] Inspection only applicable when damage due to hail.

* * * * *

9. * * *

(e). * * *

(3) * * *

(a) is not harvested before the harvest of peaches becomes general in the country; or

* * * * *

h. We have a policy for paying your indemnity within 30 days of our approval of your claim, or entry of a final judgment against us. We will, in no instance, be liable for the payment of damages, attorney's fee, or other charges in connection with any claim for indemnity, whether we approve or disapprove such claim. We will pay simple interest, however, computed on the net indemnity ultimately found to be due to you by us or by a final judgment from and including the 61st day after the date the insured signs, dates and submits to us the properly completed claim for indemnity form, if the reason for non-payment is not due to your failure to provide information or other material necessary for the computation or payment of the indemnity. The interest rate will be that established by the Secretary of the Treasury under section 12 of the Contract Disputes Act (41 U.S.C. 611) and published in the **Federal Register.** This rate is referred to as the "Renegotiation Board Interest Rate" and is published semi-annually on or about January 1 and July 1. The interest rate to be paid on any indemnity will vary with the rate announced by the Secretary of the Treasury. Interest will be paid in accordance with this section beginning with the 1985 crop year.

* * * * *

3. Appendix B to the policy contained in 7 CFR 403.7(d) is removed.

Done in Washington D.C., on November 1, 1984.

Peter F. Cole,

Secretary, Federal Crop Insurance Corporation.

Approved by:

Merritt W. Sprague,

Manager.

Dated: January 7, 1985.

[FR Doc. 85–1147 Filed 1–14–85; 8:45 am]

BILLING CODE 3410-08-M

NUCLEAR REGULATORY COMMISSION

10 CFR Part 50

Availability of NRC Fire Protection Policy Steering Committee Report For Comment

AGENCY: Nuclear Regulatory Commission.

ACTION: Notice of availability of and request for comments on fire protection policy recommendations.

SUMMARY: The staff of the Nuclear Regulatory Commission is requesting public comment on the recommendations made by the Fire Protection Policy Steering Committee for expediting compliance with fire protection requirements.

DATE: Comment period expires February 14, 1985. Comments received after this date will be considered if it is practicable to do so but assurance for consideration cannot given except as to comments received before this date.

ADDRESS: Mail comments to: Harold R. Denton, Director, Office of Nuclear Reactor Regulation, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, ATTN: Document Control Desk.

FOR FURTHER INFORMATION CONTACT: Thomas V. Wambach, Lead Project Manager, Fire Protection, Nuclear Regulatory Commission, Washington, D.C. 20555. Phone: (301) 492-7072.

SUPPLEMENTARY INFORMATION: The Nuclear Regulatory Commission is intending to review and approve a policy for expediting completion of compliance with the fire protection requirements for nuclear power plants including Appendix R to 10 CFR Part 50. A Steering Committee was appointed by the Executive Director for Operations and the Steering Committee issued recommendations for the policy to be adopted by the Commission in a report dated October 26, 1984. The Office of Nuclear Reactor Regulation (ONRR) is seeking comments on the proposed policy. Copies of the Steering Committee Report are available for inspection and copying at the NRC Public Document Room, 1717 H Street NW., Washington, D.C., and at each of the Local Public Document Rooms located in the vicinity of each nuclear power plant licensed or under construction. (The Steering Committee Report is an enclosure to Generic Letter 85-01, dated January 9, 1985.) Information regarding the location of Local Public Document Rooms can be obtained by calling the Local Public Document Room Branch's toll free number: 800-638-8081.

Dated at Bethesda, Maryland, this 9th day of January 1985.

For the Nuclear Regulatory Commission.

Harold R. Denton,

Director, Office of Nuclear Reactor Regulation.

[FR Doc. 85-1157 Filed 1-14-85; 8:45 am]

BILLING CODE 7590-01-M

FEDERAL RESERVE SYSTEM

12 CFR Part 225

[Docket No. R-0536]

Regulation Y; Permissible Transactions Between Bank Holding Companies and Their Nonbank Bank Subsidiaries

AGENCY: Board of Governors of the Federal Reserve System (FRB).

ACTION: Solicitation of public comments.

SUMMARY: The Federal Reserve Board is soliciting comment on whether the Board should permit bank holding companies that own nonbank banks (institutions that are chartered as banks but which either do not accept demand deposits or do not make commercial loans) to engage in certain transactions or establish or continue certain arrangements with their nonbank bank subsidiaries. Specifically, such transactions or arrangements would include:

1. The provision of certain internal administrative services to a nonbank bank subsidiary;

2. Continuation of trust service and investment arrangements that existed between a bank holding company and its trust company subsidiary prior to the trust company's conversion to a nonbank bank; and

3. Officer and director interlocks.

DATE: All comments should be received by the Board by February 14, 1985.

ADDRESS: All comments, which should refer to Docket No. R-0536, should be mailed to William W. Wiles, Secretary, Board of Governors of the Federal Reserve System, Washington, D.C. 20551, or delivered to Room B-2223, 20th & Consititution Avenue, NW., Washington, D.C., between 8:45 a.m. and 5:15 p.m. weekdays. Comments may be inspected in Room B-1122 between 8:45 a.m. and 5:15 p.m. weekdays.

FOR FURTHER INFORMATION CONTACT: J. Virgil Mattingly, Associate General Counsel (202/452-3430), Carl Howard, Senior Counsel (202/452-3786), or Melanie L. Fein, Senior Attorney (202/452-3594), Legal Division.

SUPPLEMENTARY INFORMATION: On March 23, 1984, the Board approved the application by U.S. Trust Corporation to convert its state chartered Florida trust company into a nationally chartered "nonbank bank" that would accept demand deposits and make consumer, but not commercial, loans as defined by the Board. *U.S. Trust Corporation*, 70 Federal Reserve Bulletin 371 (1984). In its order approving the *U.S. Trust* application, the Board stated that it was constrained to approve the application based on the literal definition of the term "bank" in the Bank Holding Company Act. The Board expressed its concern that the use of these limited purpose banks to avoid the objectives of the Bank Holding Company Act is inconsistent with the intention of Congress and that the proliferation of similar transactions would seriously undermine the policies of the Bank Holding Company Act. The Board found that use of this device presents the potential for a significant, haphazard, and possibly dangerous alteration of the nation's banking structure without Congressional action on the underlying policy issues. In view of these concerns, the Board approved the application subject to the following conditions:

(1) Applicant would not operate the nonbank bank's demand deposit taking activities in tandem with any other subsidiary or other financial institutions;

(2) Applicant would not link in any way the demand deposit and commercial lending services that define a bank under the Act; and

(3) The nonbank bank would not engage in any transactions with affiliates, other than the payment of dividends to Applicant or the infusion of capital by Applicant into the nonbank bank, without the Board's approval.

These conditions were established to ensure that a nonbank bank would be independent of its affiliates and that its banking activities would not be integrated with those of its affiliates such that the institution would be a "bank" under the Act. These conditions were intended to prevent evasion of the basic policy of the Act to separate banking and commerce and to maintain compliance with the Act's limitations on interstate banking. Thus, the framework was intended to establish a set of requirements applicable to the acquisition and operation of nonbank banks by both banking and nonbanking organizations that would assure that these institutions would remain independent and not integrated into the parent's operations in such a manner as to effect a combination of banking and commerce or otherwise prohibited interstate deposit taking and commercial lending.

Following the Board's approval of the *U.S. Trust* application, a number of bank holding companies applied to acquire similar nonbank banks. The Board has approved several of these applications to date, subject to the same conditions it established in its *U.S. Trust* order.[1]

[1] *Bankers Trust New York Corporation*, 71 Federal Reserve Bulletin 51 (1985); *Bank of Boston*

Continued

Several of the bank holding companies that have received Board approval to acquire nonbank banks, as well as a number of bank holding companies with applications to acquire nonbank banks pending before the Board, have requested the Board's approval for certain limited transactions or arrangements between their nonbank bank subsidiaries and other affiliates. These requests have been made pursuant to the third *U.S. Trust* condition, which prohibits transactions with affiliates but contemplates that the Board would consider requests for exceptions to this prohibition. The types of proposed transactions and arrangements for which approval is requested include the provision by a parent bank holding company to its nonbank bank subsidiary of internal data processing and bookkeeping support services, check clearing services, and certain trust services, and the establishment of management interlocks.

Internal administrative support services. The internal administrative support services that bank holding companies have requested to provide to their nonbank bank affiliates include: Loan and deposit account data processing, including the preparation of customer account statement's check clearing; account maintenance and review services; payroll and expense processing services; financial controls and accounting services; audit, compliance, and general legal support services; management information services; credit policy services; loan document preparation services; personnel services; purchasing services; and facilities support services.

The bank holding companies have stated that a complete ban on these internal transactions with their nonbank bank affiliates would create practical difficulties and entail substantial additional cost in the operation of nonbank banks; and that the parent is merely providing traditional support services to its subsidiary consistent with the Bank Holding Company Act, which specifically contemplates that bank holding companies may provide such services to their subsidiaries. 12 U.S.C. 1843(c)(1)(C).

The Board staff has advised the Board that, in staff's opinion, an absolute prohibition on the provision of services by the parent to its nonbank bank would not appear necessary to carry out the purposes of the *U.S. Trust* conditions. The provision by a parent or its affiliates to a nonbank bank of such internal administrative services does not impair the prohibition on linking demand deposits and commercial loans, particularly since it does not involve contact of the affiliate with customers of the nonbank bank. Nor, in staff's opinion, does the provision of these services result in an integration of the banking activities of the nonbank bank with those of its other affiliates in a manner that would cause the nonbank bank to fall within the present definition of "bank" in the Bank Holding Company Act. In the situation of the parent providing limited administrative services to the subsidiary nonbank bank, the staff has pointed out that the parent is not using the nonbank bank to further its other business activities, and the parent and its affiliates are not customers of the nonbank bank; nor do they use the nonbank bank to obtain access to banking products or services.

The Board is requesting public comment on whether the provision of the internal administrative support services requested should be allowed and whether the provision of such administrative services would lead to a commingling of banking and commerce when a nonbanking company provides such support services to its nonbank bank subsidiary.

Trust Company Agreements and Arrangements. Several bank holding companies also have urged that they be permitted to continue trust service and investment agreements or arrangements with their nonbank banks where the nonbank bank was originally a limited purpose trust company. Such agreements and arrangements generally allow an affiliate to prepare account statements and tax returns, keep custody of securities, maintain records, collect income and other monies due and collectable from securities, credit and disburse income as directed by the nonbank bank, execute investment orders, redeem maturing securities, and make recommendations to the nonbank bank relating to investments and proxies and render other advice. In addition, such arrangements would allow customers of the nonbank bank to continue to invest in common trust funds maintained by affiliated banks.

In all cases, these trust and investment service agreements predated the conversion of a limited purpose trust company to a nonbank bank and are permissible under the Board's Regulation Y authorizing bank holding companies to provide trust and investment services.

The Board is requesting comment on whether such preexisting trust and investment service arrangements should be allowed.

Common Officers and Directors. The question of whether a nonbank bank may share common officers and directors with affiliates also has been raised by several bank holding companies. Such interlocking management relationships raise issues of consistency with the *U.S. Trust* conditions.

The Board is soliciting comments on whether some limitations on common officers and directors are necessary in order to avoid integrated operations involving demand deposits and commercial loans or, in the case of nonbanking concerns, commingling of banking and commerce. In particular, the Board requests comments on whether such issues should be resolved on a case by case basis subject to general guidelines for management interrelationships. The Board requests comment on whether such guidelines should require that a majority of a nonbank bank's directors could not be officers, directors, or employees of the parent holding company or any other subsidiary of that company, and, with respect to officers, that no officer of a nonbank bank could be an officer, director or employee of any affiliate engaged in a demand deposit or commercial lending activity prohibited to the nonbank banks.

The Board believes that a public comment period on these issues would be appropriate in view of the public interest in nonbank bank and their operations generally. The Conference of State Bank Supervisors has requested that the Board provide a public comment period. In addition, the Independent Bankers Association of America has requested an opportunity to submit its views on this matter to the Board.

List of Subjects in 12 CFR Part 225

Banks, banking.

By Order of the Board of Governors of the Federal Reserve System, January 11, 1985.

William W. Wiles,

Secretary of the Board.

[FR Doc. 85-1263 Filed 1-14-85; 8:45 am]

BILLING CODE 6210-01-M

Corporation, 71 Federal Reserve Bulletin 55 (1985); *Suburban Bancorporation*, 71 Federal Reserve Bulletin 61 (1985) *First National State Bancorporation*. (Order of December 19, 1984).

DEPARTMENT OF TRANSPORTATION

Federal Aviation Administration

14 CFR Part 39

[Docket No. 84-ASW-44]

Airworthiness Directives; Hughes Helicopters, Inc., Model 369 Series Helicopters

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: This notice proposes to adopt an airworthiness directive (AD) which requires a one-time inspection to identify and remove from service certain main rotor blades which contain leading edge abrasion strips which were installed or replaced without FAA design approval on Hughes Helicopters, Inc., Model 369 series helicopters. The proposed AD is needed to detect and remove from service helicopter main rotor blades which do not meet FAA-approved type design.

DATE: Comments must be received on or before March 1, 1985.

ADDRESSES: Comments on the proposal may be mailed in duplicate to: Office of the Regional Counsel, Southwest Region, Federal Aviation Administration, P.O. Box 1689, Fort Worth, Texas 76101, or delivered in duplicate to: Office of the Regional Counsel, Southwest Region, Room 158, Building 3B, Federal Aviation Administration, 4400 Blue Mound Road, Fort Worth, Texas 76106. Comments delivered must be marked: Docket No. 84-ASW-44. Comments may be inspected in Room 158, Building 3B, between 8 a.m. and 4:30 p.m., Monday through Friday, except Federal holidays.

A copy of each document supporting the proposed AD is contained in the Rules Docket at the Office of the Regional Counsel, Federal Aviation Administration, Southwest Region, Room 158, Building 3B, 4400 Blue Mound Road, Fort Worth, Texas 76106.

FOR FURTHER INFORMATION CONTACT: Jerry Sullivan, Aerospace Engineer, Airframe Section, Western Aircraft Certification Office, Northwest Mountain Region, FAA, P.O. Box 92007, Worldway Postal Center, Los Angeles, California 90009-2007 telephone (213) 536-6166.

SUPPLEMENTARY INFORMATION: Interested persons are invited to participate in the making of the proposes rule by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket number and be submitted in duplicate to the address specified above. All communications received on or before the closing date for comments will be considered by the Director before taking action on the proposed rule. The proposal contained in this notice may be changed in light of comments.

Comments are specifically invited on the overall regulatory, economic, environmental, and energy aspects of the proposed rule. All comments submitted will be available, both before and after the closing date for comments, in the Office of the Regional Counsel, Southwest Region, 4400 Blue Mound Road, Fort Worth, Texas 76106, for examination by interested persons. A report summarizing each FAA-public contact, concerned with the substance of the proposed AD, will be filed in the Rules Docket.

Commenters wishing the FAA to acknowledge receipt of their comments submitted in response to this notice must submit a self-addressed, stamped postcard on which the following statement is made: "Comments to Docket Number 84-ASW-44." The postcard will be date/time stamped and returned to the commenter.

The FAA has determined that a repair station has installed or replaced leading edge abrasion strips on 38 Hughes Helicopters, Inc., Model 369 series main rotor blades without FAA design approval. At least one of these abrasion strip installations have been analyzed and determined not to meet all criterial considered necessaryfor an acceptable abrasion strip-to-rotor blade adhesive bond on similar approved installations.

Since this condition is likely to exist on other helilcopters of the same type design, the proposed AD would require removing from service main rotor blades with unauthorized abrasion strips from Model 369 series helicopters.

The FAA has determined that this proposed regulation affects only nine entities, and it is estimated that the total one time cost of compliance is less than $310,000. Therefore, I certify that this action (1) is not a "major rule" under Executive Order 12291; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and (3) if promulgated, will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the draft evaluation prepared for this action is contained in the regulatory docket. A copy of it 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.

The Proposed Amendment

Accordingly, the Federal Aviation Administration proposes to amend § 39.13 of Part 39 of the Federal aviation Regulations (14 CFR 39.13) by adding the following new AD:

Hughes Helicoptes, Inc., (Hughes Helicopters): Applies to certain Model 369A(OH-6A), 369D, E, H, HM, HS, and HE helicopters certificated in all categories.

Compliance is required within the next 100 hours' time in service after the effective date of this AD, unless already accomplished.

To detect and remove from service helicopter main rotor blades which do not meet FAA-approved type design, accomplish the following:

(a) For Models 369D and 369E with Part Number 369D21100 series main rotor blades installed, remove main rotor blades having the following serial numbers from service: 1030, 1069, 1355, 2690, 3312, 3318, 3371, 3399, 3412, 3949, 3954, 5260, 5312, 5337, 5371, 5374, 5383, 5609, 5731, 5795, 5800, 5878, 5943, 5981, 6077, 6419, 6446, 7585, 7604, 7609.

(b) For Models 369A (OH-6A), H, HE, HM, and HS with Part Number 369A1100 series main rotor blades installed, remove main rotor blades having the following serial numbers from service: 1747, 6457, C898, R766, U673, U667, V454, V484.

(c) Blades removed in accordance with paragraphs (a) and/or (b) may be returned to service after being restored to original or other FAA-approved type design.

(Secs. 313(a), 601, and 603, Federal Aviation Act of 1958, as amended 49 U.S.C. 1354(a), 1421, and 1423); 49 U.S.C. 106(g) (Revised, Pub. L. 97-449, January 12, 1983); 14 CFR 11.85.)

Issued in Fort Worth, Texas, on October 22, 1984.

C.R. Melugin, Jr.,

Director, Southwest Region.

[FR Doc. 85-1069 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

14 CFR Part 39

[Docket No. 84-NM-114-AD]

Airworthiness Directives; Airbus Industrie Model A300 B2 and B4 Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: This notice proposed an airworthiness directive (AD) that would require inspection of the shims at the flap track/beam No. 2 rear attachment for damage and replacement of the bolts on Airbus Industrie Model A300 B2 and B4 series airplanes. Loose bolts have been found in this structure which could result in bolt failure. This condition can lead to flap asymmetry and create a hazardous flight condition.

DATE: Comments must be received no later than March 5, 1985.

ADDRESSES: The applicable service information may be obtained from Airbus Industrie, Airbus Support Division, Centreda, Avenue Didier Daurat, 31700 Blagnac, France, or may also be examined at the Seattle Aircraft Certification Office, FAA, Northwest Mountain Region, 9010 East Marginal Way South, Seattle, Washington.

FOR FURTHER INFORMATION CONTACT:

Mr. Sulmo Mariano, Foreign Aircraft Certification Branch, Seattle Aircraft Certification Office; telephone (206) 431–2979. Mailing address: FAA, Northwest Mountain Region, 17900 Pacific Highway South, C–68966, Seattle, Washington 98168.

SUPPLEMENTARY INFORMATION:

Comments Invited

Interested persons are invited to participate in the making of the proposed rule by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket number and be submitted in duplicate to the address specified below. All communications received on or before the closing date for comments specified above will be considered by the Administrator before taking action on the proposed rule. The proposals contained in this notice may be changed in light of the comments received. All comments submitted will be available, both before and after the closing date for comments, in the Rules Docket for examination by interested persons. A report summarizing each FAA-public contact concerned with the substance of this proposal will be filed in the Rules Docket.

Availability of NPRM

Any person may obtain a copy of this Notice of Proposed Rulemaking (NPRM) by submitting a request to the FAA, Northwest Mountain Region, Office of the Regional Counsel, Attention: Airworthiness Rules Docket No. 84–NM–114–AD, 179000 Pacific Highway South, C–68966, Seattle, Washington 98168.

Discussion

The French Civil Aviation Authority (DGAC) has issued a Consigne de Navigabilite which mandates compliance with the requirements of Airbus Industrie Service Bulletin A300–57–107.

Bolts have been found loose at the flap track/beam No. 2 rear attachment to the wing. Loose bolts may be the result of sealant extrusion under flight loads, causing reduction in bolt tension. Loose bolts will result in fretting between the flap beam rear attachment packing block and wing bottom skin, causing a rapid reduction in fatigue life of the bolts due to ground loads. Bolt failure can cause loss of flap track beam support leading to flap asymmetry and creating a potentially hazardous flight condition. The service bulletin prescribes inspection of the shims at the flap track/beam No. 2 rear attachment for damage and replacement of four titanium bolts and nuts with new steel bolts and nuts.

This airplane model is manufactured in France and type certificated in the United States under the provisions of § 21.29 of the Federal Aviation Regulations and the applicable airworthiness bilateral agreement.

Since these conditions are likely to exist or develop on airplanes of this model registered in the United States, an AD is proposed that would require the action previously described.

It is estimated that 24 U.S. registered airplanes would be affected by this AD, that it would take approximately 14 manhours per airplane to accomplish the required actions, and that the average labor cost would be $40 per manhour. Repair parts are estimated at $1,500 per airplane. Based on these figures, the total cost impact of this AD to U.S. operators is estimated to be $49,440.

For the reasons discussed above, the FAA has determined that this document (1) involves a proposed regulation which is not major under Executive Order 12291, and (2) is not a significant rule pursuant to the Department of Transportation Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and it is certified under the criteria of the Regulatory Flexibility Act that this proposed rule, if promulgated, will not have a significant economic impact on a substantial number of small entities because few, if any, Airbus Industrie Model A300 airplanes are operated by small entities. A copy of a draft regulatory evaluation prepared for this action is contained in the regulatory docket. A copy may be obtained by contacting the person identified under the caption **"FOR FURTHER INFORMATION CONTACT."**

List of Subjects in 14 CFR Part 39

Aviation safety, aircraft.

The Proposed Amendment

Accordingly, the Federal Aviation Administration proposes to amend § 39.13 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) by adding the following new airworthiness directive:

Airbus Industrie: Applies to Model A300 B2 and B4 series airplanes listed in Airbus Industrie Service Bulletin A300–57–107, Revision 2, dated July 15, 1982, certificated in all categories. To prevent flap asymmetry, within 120 days after the effective date of this AD accomplish the following, unless previously accomplished:

A. Inspect the shims at the flap track/beam No. 2 rear attachment for damage and replace the four titanium bolts with steel bolts in accordance with the accomplishment instructions of the service bulletin. If the shims are found to be damaged or displaced, repeat the inspection of the new bolts at intervals not to exceed 2,500 landings.

B. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, Seattle Aircraft Certification Office, FAA, Northwest Mountain Region.

C. Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate airplanes to a base for the accomplishment of inspections and/or modifications required by this AD.

(Secs. 313(a), 314(a), 601 through 610, and 1102 of the Federal Aviation Act of 1958 (49 U.S.C. 1354(a), 1421 through 1430, and 1502); 49 U.S.C. 106(g) (Revised, Pub. L. 97–449, January 12, 1984); and 14 CFR 11.85)

Issued in Seattle, Washington, on January 4, 1985.

Charles R. Foster,

Director, Northwest Mountain Region.

[FR Doc. 85–1076 Filed 1–14–85; 8:45 am]

BILLING CODE 4910–13–M

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14 CFR Part 39

[Docket No. 82–ANE–46]

Airworthiness Directives; Rolls-Royce Limited RB211–22B and –524 Series Turbofan Engines

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Withdrawal of notice of proposed rulemaking (NPRM).

SUMMARY: This document withdraws an NPRM which proposed the adoption of an airworthiness directive (AD) that would have reduced the cyclic life limit of certain high pressure compressor rotor stage 4 to 6 shaft assemblies. The

shaft assemblies were suspected to have suffered a reduction in material properties due to overtemperature during heat treating in manufacture. Additional analysis has proven that the suspected reduction in material properties was negligible. Subsequently, Rolls-Royce Limited, with the concurrence of the United Kingdom Civil Aviation Authority (CAA), has withdrawn the life restriction. Upon further consideration of the additional findings, the FAA has determined that the proposed AD is not required and, accordingly, the NPRM is withdrawn.

DATES: The withdrawal is effective January 25, 1985.

FOR FURTHER INFORMATION CONTACT: Mark C. Fulmer, Transport Engine Branch, ANE-141, Engine Certification Office, Aircraft Certification Division, New England Region, Federal Aviation Administration, 12 New England Executive Park, Burlington, Massachusetts 01803, telephone (617) 273-7120.

SUPPLEMENTARY INFORMATION: A proposal to amend Part 39 of the Federal Aviation Regulations to include an AD which requires a reduction in the cyclic life limit for certain high pressure compressor rotor stage 4 to 6 shaft assemblies on Rolls-Royce Limited RB211-22B and -524 series turbofan engines was published in the **Federal Register** on November 22, 1982, (47 FR 52466). Comments were requested from the public and none were received.

The FAA determined that as a result of a vaccum furnace problem during manufacture, 60 high pressure compressor rotor stage 4 to 6 shaft assemblies, part number LK73317, entered service having been subject to a post-weld heat treatment that was in excess of the specified temperature. The effect of this heat treatment on the material properties was suspected to have caused the material at the rim of the shaft assemblies to suffer unacceptable loss of fatigue life. Because it was not possible to identify the affected assemblies by non-destructive inspection techniques, it was proposed to reduce the life limit for those assemblies. Subsequent laboratory tests and stress analysis caused the FAA to conclude that the reduction in disk material properties of the affected assemblies is negligible. Rolls-Royce Limited, with United Kingdom CAA concurrence, has withdrawn the life restriction imposed by Rolls-Royce Service Bulletin RB211-72-6420. The FAA concurs with the CAA findings and withdraws NPRM of Rules Docket No. 82-ANE-46.

Conclusion

Since this action only withdraws an NPRM, it may be made effective in less than 30 days. It is neither a proposed nor final rule, and therefore, is not covered under Executive Order 12291, the Regulatory Flexibility Act, or DOT Regulatory Policies and Procedures (44 FR 11034; February 26, 1979).

Withdrawal of this NPRM constitutes only such action and does not preclude the FAA from issuing another notice or commit the FAA to any course of action in the future.

List of Subjects in 14 CFR Part 39

Engines, Air transportation, Aircraft, Aviation safety.

The Withdrawal

In consideration of the foregoing, and pursuant to the authority delegated to me by the Administrator, the proposed AD, Rules Docket No. 82-ANE-46, published in the **Federal Register** on November 22, 1982, (47 FR 52466), is hereby withdrawn.

(Sec. 313(a), 601, and 603, Federal Aviation Act of 1958, as amended (49 U.S.C. 1354(a), 1421, and 1423); 49 U.S.C. 106(g) (Revised, Pub. L. 97-449, January 12, 1983); 14 CFR 11.85)

Issued in Burlington, Massachusetts, on January 3, 1985.

Robert E. Whittington,

Director, New England Region.

[FR Doc. 85-1068 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

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14 CFR Part 39

[Docket No. 84-ANE-14]

Airworthiness Directives; Rolls-Royce Limited RB211-22B and -524 Series Turbofan Engines

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: This notice proposes to adopt an airworthiness directive (AD) which would require modification of the low pressure rotor location bearing area on Rolls-Royce RB211-22B and RB211-524 series turbofan engines in accordance with Rolls-Royce Mandatory Service Bulletin (SB) RB211-72-6847. The proposed AD is needed to prevent internal oil fires caused by low pressure rotor location bearing failures which can result in an uncontained engine failure.

DATES: Comments must be received on or before March 24, 1985.

ADDRESSES: Comments on the proposal may be mailed in duplicate to: Federal Aviation Administration, New England Region, Office of the Regional Counsel, Attention: Rules Docket No. 84-ANE-14, 12 New England Executive Park, Burlington, Massachusetts 01803, or delivered in duplicate to Room No. 311 at the above address.

Comments delivered must be marked: Docket No. 84-ANE-14.

Comments may be inspected at the New England Regional Office, Office of the Regional Counsel, Room No. 311, between the hours of 8:00 a.m. and 4:30 p.m. Monday through Friday, except Federal holidays.

The applicable SB may be obtained from Rolls-Royce Limited, Technical Publications Department, P.O. Box 31, Derby DE2 8BJ, England. A copy of the SB is contained in Rules Docket No. 84-ANE-14 in the Office of the Regional Counsel, New England Region, Federal Aviation Administration, 12 New England Executive Park, Burlington, Massachusetts 01803.

FOR FURTHER INFORMATION CONTACT: Mark C. Fulmer, Transport Engine Branch ANE-141, Engine Certification Office, Aircraft Certification Division, New England Region, Federal Aviation Administration, 12 New England Executive Park, Burlington, Massachusetts 01903, Telephone (617) 273-7120.

SUPPLEMENTARY INFORMATION: Interested persons are invited to participate in making of the proposed rule by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket number and be submitted in duplicate to the address specified above. All communications received on or before the closing date for comments will be considered by the Director before taking action on the proposed rule. The proposal contained in this notice may be changed in light of comments received.

Comments are specifically invited on the overall regulatory, economic, environmental, and energy aspects of the proposed rule. All comments submitted will be available for examination in the Rules Docket, both before and after the closing date for comments, at the address given above. A report summarizing each FAA-public contact, concerned with the substance of the proposed AD, will be filed in the Rules Docket.

Commenters wishing the FAA to acknowledge receipt of their comments submitted in response to this notice must submit a self-addressed, stamped postcard on which the following statement is made: "Comments to

Docket Number 84-ANE-14". The postcard will be date/time stamped and returned to the commenter.

The FAA has determined that the failure of the low pressure rotor location bearing on certain Rolls-Royce RB211-22B and -524 series turbofan engines can result in an internal oil fire and subsequent failure of the low pressure compressor rotor shaft. Failure of the low pressure compressor rotor shaft results in loss of load transfer from the low pressure turbine to the low pressure compressor and can cause the low pressure turbine rotor to overspeed leading to an uncontained failure of the turbine roto assembly. Since this condition is likely to exist or develop on other engines of the same type design, the proposed AD would require incorporation of low pressure rotor location bearing area modifications as specified in Rolls-Royce Mandatory SB RB211-72-6847, Revision 2, dated March 30, 1984, on Rolls-Royce RB211-22B and RB211-524B, -524C, and -524D series turbofan engines.

Conclusion

The FAA has determined that this proposed regulation involves 120 Lockheed L1011 aircraft and 433 Rolls-Royce RB211-22B and -524 series turbofan engines at an approximate total cost of 6.1 million dollars. Less than 11 small entities will be affected by this proposed regulation. Therefore, I certify that this action (1) is not a "major rule" under Executive Order 12291; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11043; February 26, 1979); and (3) if promulgated, will not have a significant economic impact on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the draft evaluation prepared for this action is contained in the regulatory docket. A copy may be obtained by contacting the person identified under the caption "**FOR FURTHER INFORMATION CONTACT**".

List of Subjects in 14 CFR Part 39

Engines, Air transportation, Aircraft, Aviation safety, Incorporation by reference.

The Proposed Amendment

Accordingly, the FAA proposes to amend § 39.13 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) by adding the following new AD:

Rolls-Royce Limited: Applies to Rolls-Royce RB211-22B and RB211-524B, -524C, and -524D series turbofan engines.

Compliance is required as indicated unless already accomplished.

To prevent an internal oil fire, failure of the low compressor rotor shaft, and subsequent low turbine rotor overspeed leading to an uncontained rotor failure, accomplish the following:

Prior to April 1, 1986, incorporate low pressure rotor location bearing area modifications as specified in Rolls-Royce Mandatory Service Bulletin (SB) RB211-72-6847, Revision 2, dated March 30, 1984, or FAA approved equivalent.

Upon request, an equivalent means of compliance may be approved by the Manager, Engine Certification Office, Aircraft Certification Division, New England Region, Federal Aviation Administration, 12 New England Executive Park, Burlington, Massachusetts 01803.

The FAA will request the permission of the **Federal Register** to incorporate by reference the manufacturer's SB identified and described in this document.

(Sec. 313(a), 601, and 603, Federal Aviation Act of 1958, as amended (49 U.S.C. 1354(a), 1421, and 1423); 49 U.S.C. 106(g) (Revised, Pub. L. 97-449, January 12, 1983); 14 CFR 11.85)

Issued in Burlington, Massachusetts, on January 3, 1985.

Robert E. Whittington,

Director, New England Region.

[FR Doc. 85-1074 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

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14 CFR Part 39

[Docket No. 84-NM-102-AD]

Airworthiness Directives; Fairchild Model F27 and FH227 Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: This amendment proposes a new airworthiness directive (AD), applicable to Fairchild Model F27 and FH227 series airplanes which would require a repetitive inspection and repair, if required, of the rod ends on the rudder control push-pull tubes. Cracks in these rod ends have been reported. These cracks, if allowed to grow undetected, could cause failure of the rudder control system and possible loss of control of the airplane. The inspections are necessary to detect cracks before failure occurs.

DATE: Comments must be received no later than March 5, 1985.

ADDRESSES: Send comments to the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington 98168.

The applicable service information specified in this AD may be obtained from Fairchild Industries, Inc., Fairchild Republic Division, Hagerstown, Maryland 21740. This information may also be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington.

FOR FURTHER INFORMATION CONTACT: Mr. Alfred A. Maila, ANE-172, New York Aircraft Certification Office, 181 S. Franklin Avenue, Room 202, Valley Stream, New York 11581; telephone (516) 791-6220.

SUPPLEMENTARY INFORMATION:

Comments Invited

Interested persons are invited to participate in the making of the proposed rule by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket and be submitted in duplicate to the address specified under the caption "Availability of NPRM." All communications received on or before the closing date for comments specified above will be considered by the Administrator before taking action on the proposed rule. The proposals contained in this notice maybe changed in light of the comments received. All comments submitted will be available, both before and after the closing date for comments, in the Rules Docket for examination by interested persons. A report summarizing each FAA-public contact concerned with the substance of this proposal will be filed in the Rules Docket.

Availability of NPRM

Any person may obtain a copy of this Notice of Proposed Rulemaking (NPRM) by submitting a request to the FAA, Northwest Mountain Region, Office of the Regional Counsel, Attention: Airworthiness Rules Docket No. 84-NM-102-AD, 17900 Pacific Highway South, C-68966, Seattle, Washington 98168.

Discussion

There have been reports of failure of two rod ends of the rudder torque tube push rod assembly on Fairchild FH227 series airplanes operated by the French Airline Transport Aerien Transregional (TAT). Investigation of 17 aircraft in the TAT fleet indicated the following results (**Note:** 4 rod assemblies per aircraft for a total of 68 rods):

Nine (9)—Cracked
Two (2)—Corroded Rod Ends
Three (3)—Bearing Seized.

Investigation has revealed that the probable cause of the failed rod ends indicated that a potentially corrosive atmosphere exists below the floor where the lower rod end is installed. Fairchild has issued Service Bulletins (S/B) FH227-27-31 and S/B F27-27-76 which requires repetitive inspections and repair, if necessary, of the riveted rod end assembly, P/N 27-727404-11, on rudder control push-pull tubes, P/N's 27-727402-11 (or -41) and -31 (or -51).

The FAA has examined the available information related to the issuance of Fairchild's S/B Nos. FH227-27-31 and F27-27-76. Based on the foregoing, the FAA has determined that the condition addressed by the Fairchild Service Bulletins Nos. FH227-27-31 and F27-27-76 is an unsafe condition that may exist on other products of the same type design certificated for operation in the United States. The extent and severity of the condition is not known. In order to factually determine the severity of this unsafe condition, a report as to the findings, either positive or negative, obtained by the initial inspection, would be sent to the FAA. This reporting requirement is approved by the Office of Management and Budget under OMB No. 2120-0056.

Therefore, in consideration of the hazardous consequence of cracking in the rod ends on the rudder control push-pull tubes, an AD is being proposed which would require a repetitive visual inspection and repair, if necessary, of the riveted rod end assembly, P/N 27-727404-11, on the rudder contol push-pull tubes, P/N's 27-727402-11 (or -41) and -31 (or -51), on Fairchild FH227 and F27 series airplanes. Upon replacement of the riveted rod end assembly with a new riveted rod end assembly the repetitive inspections may be terminated.

Cost Estimate

It is estimated that 125 airplanes of U.S. registry would be affected by the proposed AD, that it would take 8 manhours per airplane to accomplish the required inspection, and that the average labor cost would be $40 per manhour. Repair parts (4 torque tube rod assemblies) are estimated at $1200 per airplane. Based on these figures, the total cost impact of this AD to U.S. operators is estimated to be $190,000.

For these reasons, the proposed rule is not considered to be a major rule under the criteria of Executive Order 12291. Few, if any, small entities within the meaning of the Regulatory Flexibility Act would be affected.

List of Subjects 14 CFR Part 39

Aviation safety, Aircraft.

The Proposed Amendment

Accordingly, the Federal Aviation Administration proposes to amend § 3913 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) by adding the following new airworthiness directive:

Fairchild: Applies to all Model F27 and FH227 series airplanes certificated in all categories. Compliance required as indicated.

To detect cracks due to stress corrosion in the riveted rod end assembly part number (P/N) 27-727404-11 on rudder control push-pull tubes, P/N 27-727402-11 (or -41) and -31 (or -51), accomplish the following:

A. Within the next 50 hours time in service after the effective date of this AD, unless already accomplished within the last 150 hours time in service, and thereafter at intervals not to exceed 200 hours time in service from the last inspection, inspect the riveted rod end (P/N 27-727404-3) of the rudder control push-pull tubes [P/N 27-727402-11 (or -41), and -31 (or -51)] for cracks, in accordance with Fairchild Service Bulletin (S-B) FH227-27-31 for Model FH227 S/N's 501 through 578, and S/B F27-27-76 for Model F27 (S/N's 1 through 128).

B. If cracks are found, the rod assembly must be replaced before further flight with a rod of the same part number or equivalent, inspected and found serviceable in accordance with paragraph A., above, or replaced before further flight with a new rod end asembly, P/N 27-727404-31 or equivalent.

C. The repetitive inspection interval specified in paragraph A., above, may be cancelled upon installation of the new assembly, P/N 27-727404-31.

D. Aircraft maintenance record entries must be made and a report in writing of the initial inspection findings, positive or negative, must be submitted to the FAA, New York Aircraft Certification Office, Room 202, Attention: ANE-170, 181 South Franklin Avenue, Valley Stream, New York 11581. The report must state the location and length of any crack found during the initial inspection, and include the total time in service of the component at the time the crack was discovered. (Reporting requirement approved by the Office of Management and Budget under OMB No. 2120-0056.)

E. Upon the request of an operator, an FAA Maintenance Inspector, subject to prior approval by the Manager, New York Aircraft Certification Office, FAA, New England Region, may adjust the inspection times specified in this AD to permit compliance at an established inspection period of that operator if the request contains substantiating data to justify the change for that operator.

F. Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate airplanes to a base in order to comply with the inspection requirements of this AD.

G. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, New York Aircraft Certification Office, FAA, New England Region.

All persons affected by this proposal who have not already received these documents from the manufacturer may obtain copies upon request to Fairchild Industries, Inc., Fairchild Republic Division, Hagerstown, MD 21740. These documents also may be examined at the FAA, Northwest Mountain Region, 17900 Pacific Highway South, Seattle, Washington, or at the FAA, New England Region, New York Aircraft Certification Office, 181 S. Franklin Avenue, Room 202, Valley Stream, New York.

(Secs. 313(a), 314(a), 601 through 610 and 1102 of the Federal Aviation Act of 1958 (49 U.S.C. 1354(a), 1421 through 1430, and 1502) (49 U.S.C. 106(g) (Revised Pub. L. 97-449, January 12, 1983); and 14 CFR 11.89))

Note: For the reasons discussed earlier in the preamble, the FAA has determined that this document (1) involves a proposed regulation wiich is not major under Executive Order 12291 and (2) is not a significant rule pursuant to the Department of Transportation Regulatory Policies and Precedures (44 FR 11034; February 26, 1979); and it is certified under the criteria of the Regulatory Flexibility Act that this proposed rule, if promulgated, will not have a significant economic impact on a substantial number of small entities because few, if any, Model F27 or FH227 airplanes are operated by small entities. A copy of a draft regulatory evaluation prepared for this action is contained in the regulatory docket. A copy may be obtained by contacting the person identified under the caption "**FOR FURTHER INFORMATION CONTACT.**"

Issued in Seattle, Washington, on January 4, 1985.

Charles R. Foster,

Director, Northwest Mountain Region.

[FR Doc. 85-1067 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

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14 CFR Part 39

[Docket No. 84-NM-122-AD]

Airworthiness Directives; Boeing Model 757 Series Airplanes

AGENCY: Federal Aviation Administration (FAA), DOT.

ACTION: Notice of proposed rulemaking (NPRM).

SUMMARY: This notice proposes a new airworthiness directive that would require replacement of the existing forward and aft cargo compartment blowout panels with new panels incorporating an improved retention system. The cargo compartment blowout panels are designed to blow out in case of a decompression in order to minimize the differential pressure of floor panels. Operators have reported blowout panels becoming dislodged. In a survey of

seven airplanes, 50% of the blowout panels were either taped in place, missing, or had substitute panels taped in place. Missing blowout panels reduce fire containment and fire suppression capability of the cargo compartment.

DATE: Comments must be received on or before February 2, 1985.

ADDRESSES: Send comments to the FAA, Northwest Mountain Region, 17900 Pacific Highway South, C-68966, Seattle, Washington 98168.

The applicable service bulletin may be obtained from the Boeing Commercial Airplane Company, P.O. Box 3707, Seattle Washington 98124. This information may also be examined at the Seattle Aircraft Certification Office, FAA, Northwest Mountain Region, 9010 East Marginal Way South, Seattle, Washington.

FOR FURTHER INFORMATION CONTACT: Mr. Robert C. McCracken, Systems & Equipment Branch, ANM-130S, Seattle Aircraft Certification Office; telephone (206) 431-2947. Mailing address: FAA, Northwest Mountain Region, 17900 Pacific highway South, C-68966, Seattle, Washington 98168.

SUPPLEMENTARY INFORMATION:

Comments Invited

Interested persons are invited to participate in the making of the proposed rule by submitting such written data, views, or arguments as they may desire. Communications should identify the regulatory docket number and be submitted in duplicate to the address specified below. All communications received on or before the closing date for comments specified above will be considered by the Administrator before taking action on the proposed rule. The proposal contained in this notice may be changed in light of the comments received. All comments submitted will be available, both before and after the closing date for comments, in the rules docket for examination by interested persons. A report summarizing each FAA/public contact concerned with the substance of this proposal will be filed in the rules docket.

Availability of NPRM

Any person may obtain a copy of this Notice of Proposed Rulemaking (NPRM) by submitting a request to the Federal Aviation Administration, Northwest Mountain Region, Office of the Regional Counsel, Attention: Airworthiness Directive Rules Docket No. 84-NM-122-AD, 17900 Pacific Highway South, C-68966, Seattle, Washington 98168.

Discussion

Opeators of Boeing Model 757 airplanes have reported that blowout panels in the forward and aft cargo compartments have become dislodged. There are 4 panels in each airplane. During a survey of seven airplanes, 50% of the panels were taped in place, missing completely, or had substitute panels taped in place. The blowout panels are designed to blow out in case of a decompression, and serve to minimize the differential pressure of floor structure. Missing blowout panels reduce fire containment capability of the compartment liners, and affect the fire suppression capability of the cargo compartment fire protection system.

Since all Model 757 airplanes are equipped with cargo compartment liners which are subject to becoming dislodged, an airworthiness directive is being proposed which would require replacement of the existing panels with new panels which employ improved retention methods.

It is estimated that 15 airplanes of U.S. registry are affected by this AD; that it will take approximately 4 manhours per airplane to accomplish the required replacement, and that the average labor cost would be $40 per manhour. The kits for accomplishing the replacement are being furnished by Boeing at no charge. Based on these figures, the total cost impact of this AD would be $2400. For these reasons, the proposed rule is not considered to be a major rule under the criteria of Executive Order 12291. No small entities within the meaning of the Regulatory Flexibility Act would be affected.

List of Subjects in 14 CFR Part 39

Aviation safety, Aircraft.

The Proposed Amendment

Accordingly, the Federal Aviation Administration proposes to amend § 39.13 of Part 39 of the Federal Aviation Regulations (14 CFR 39.13) by adding the following new airworthiness directive:

Boeing: Applies to Boeing Model 757 airplanes listed in the Boeing Service Bulletin 757-25A0036, Revision 1, dated September 21, 1984. To prevent degradation of fire protection capability in the cargo compartments, accomplish the following within 120 days after the effective date of this AD, unless already accomplished:

A. Replace the existing cargo compartment blowout panels in accordance with Boeing Service Bulletin 757-25A0036, Revision 1, dated September 21, 1984, or later FAA approved revision.

B. Alternate means of compliance which provide an equivalent level of safety may be used when approved by the Manager, Seattle Aircraft Certification Office, FAA, Northwest Mountain Region.

C. Special flight permits may be issued in accordance with FAR 21.197 and 21.199 to operate airplanes to a base for the accomplishment of replacements required by this AD.

All persons affected by this directive who have not already received the above specified service bulletins from the manufacturer may obtain copies upon request to the Boeing Commercial Airplane Company, P.O. Box 3707, Seattle, Washington 98124, or they may be examined at the FAA, Northwest Mountain Region, 9010 East Marginal Way South, Seattle, Washington.

(Secs. 313(a), 314(a), and 601 through 610, and 1102 of the Federal Aviation Act of 1958 [49 U.S.C. 1354(a), 1421 through 1430, and 1502]; 49 U.S.C. 106(g) (Revised Pub. L. 97-449, January 12, 1983); and 14 CFR 11.85)

Note: For the reasons discussed earlier in the preamble, the FAA has determined that this document (1) involves a proposed regulation which is not major under Executive Order 12291 and (2) is not a significant rule pursuant to the Department of Transportation Regulatory Policies and Procedures (44 FR 11034; February 26, 1979); and it is certified under the criteria of the Regulatory Flexibility Act that this proposed rule, if promulgated, will not have a significant economic impact on a substantial number of small entities, since few, if any, Model 757 series airplanes are operated by small entities. A copy of a draft regulatory evaluation has been prepared for this action and has been placed in the regulatory docket. A copy may be obtained by contacting the person identified under the caption **"FOR FURTHER INFORMATION CONTACT."**

Issued in Seattle, Washington, on December 19, 1984.

Wayne J. Barlow,

Acting Director, Northwest Mountain Region.

[FR Doc. 85-1066 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-13-M

DEPARTMENT OF COMMERCE

International Trade Administration

15 CFR Part 377

[Docket No. 50101-5001]

Short Supply Regulations Covering "Petroleum Partly Refined for Further Refining"

AGENCY: Office of Industrial Resource Administration, Commerce.

ACTION: Advance notice of proposed rulemaking with request for comments.

SUMMARY: The Short Supply Regulations, administered by the Office of Industrial Resource Administration, ("OIRA"), classify commodities as

refined "petroleum products" only if they are exported for use as a finished product. If they are to be further refined abroad they are treated as crude oil, regardless of the extent of processing in the United States. This "end use" test helps enforce the stringent, Congressionally mandated export controls on crude oil. It also results in automatically precluding the export of many petroleum products while allowing the export of the same products if they are to be used without further refining. The revision under consideration would classify petroleum commodities as refined petroleum products, regardless of end-use. An alternative being considered is a "distillation" test. If commodities have been subjected to a specific distillation process in the United States they will be classified in the refined petroleum products categories. Furthermore, in the event that the stated end-use of a product is further refining abroad, the exporter will be required to identify the U.S. facility where the distillation took place. This requirement is designed to ensure that petroleum products that are exported have been subjected to distillation in the U.S. and are not crude petroleum or blends thereof. Comments on this test as well as other alternatives are requested. The proposed revisions are intended to continue to implement Congress' mandate to vigorously control the export of crude oil, but without unnecessarily restricting exports of refined petroleum products.

DATE: Comments must be received by February 14, 1985.

ADDRESS: Department of Commerce, Resource Assessment Division, P.O. Box 663, Washington, D.C. 20044.

FOR FURTHER INFORMATION CONTACT: Steven C. Goldman, Director, Resource Assessment Division, International Trade Administration (Telephone: 202/377–4060).

SUPPLEMENTARY INFORMATION: The Department of Commerce is considering revisions to the short supply regulations concerning the classification of commodities as "petroleum partly refined for further refining" as set forth in section 377(d)(1) and Supplement No. 2 to Part 377 of the Export Administration Regulations. ("EAR")

Under existing regulations, petroleum commodities are classified as refined petroleum products only if they are to be used abroad as finished products. Such refined petroleum products have been exported on a routine basis since the lifting of quantitative restrictions on petroleum product exports in 1981. In contrast, petroleum commodities that are exported for further refining abroad are subject to the stringent statutory export restrictions that apply to crude oil. This "end-use" test has produced the anamolous result of classifying the same petroleum products in different export control categories because of their stated end-use abroad.

OIRA's objective is to continue to enforce the statutory restrictions on crude oil exports without imposing unwarranted controls on refined petroleum product exports. Accordingly, OIRA is soliciting comments from the public regarding the following proposal to amend the short supply regulations:

- The "end-use" test would no longer be applied to determine whether a commodity was to be treated as crude oil or as a refined product. Crude oil export restrictions would not be applied automatically to petroleum products that will be further refined abroad.
- Refined petroleum products would be defined as those products that have been processed from crude oil through a "distillation process" in the United States. This "distillation process" must yield at least two distinct refined petroleum products listed in Supplement No. 2 to Part 377 of the EAR and total at least one-half of the crude charge. Petroleum that has not been distilled in the United States in this manner would be treated as crude oil. The category "petroleum partly refined for further refining" would be eliminated from the Group A category of the EAR.
- All petroleum products that have been through the "distillation process" in the United States will be classified in Groups B through N of Supplement No. 2 to Part 377 of the EAR, and could be exported in accordance with § 377.6(d)(2) and (3) of the EAR.
- However, if the stated end-use of such a product is further refining abroad, the exporter would be required to identify the name and location of the facility in the United States where the required distillation took place.

Comments should include an analysis of the practicality of the "distillation test," any alternatives to it, and the economic impact of the proposed change.

The period of submission of comments will close one month from the publication of this notice. All comments received before the close of the comment period will be considered by OIRA. While comments received after the end of the comment period will be considered if possible, their consideration cannot be assured. Public comments will become a matter of public record, and will be available for public inpsection and copying. Communications from agencies of the United States Government or foreign governments will not be made available for public inspection.

The public record concerning this notice will be maintained in the International Trade Administration Freedom of Information Records Inspection Facility, Room 4001–B, U.S. Department of Commerce, 14th Street and Pennsylvania Avenue, NW., Washington, DC. 20230. Records in this facility may be inspected and copied in accordance with regulations published in Part 4 of Title 15 of the Code of Federal Regulations. Information about the inspection and copying of records at the facility may be obtained from Patricia L. Mann, the International Trade Administration Freedom of Information Officer, at the above address or by calling 202/377–3031.

Authority: Secs. 203, 206, Pub. L. 95–223, as amended (50 U.S.C. 1702, 1704); E.O. 12470 of March 30, 1984 (49 FR 13099, April 3, 1984); sec. 103, Pub. L. 94–163 as amended (42 U.S.C. 6212); E.O. 11912 of April 13, 1976 (41 FR 15825, as amended); sec. 201 (10), Pub. L. 94–258 amending 10 U.S.C. 7430.

January 10, 1985.

John A. Richards,

Director, Office of Industrial Resources Administration.

[FR Doc. 85–1120 Filed 1–14–85; 8:45 am]

BILLING CODE 3510-25-M

FEDERAL TRADE COMMISSION

16 CFR Part 13

[File No. 822–3153]

Craftmatic/Contour Organization, Inc., et al.; Proposed Consent Agreement With Analysis To Aid Public Comment

AGENCY: Federal Trade Commission.

ACTION: Proposed consent agreement.

SUMMARY: In settlement of alleged violations of federal law prohibiting unfair acts and practices and unfair methods of competition, this consent agreement, accepted subject to final Commission approval, would require two Bensalem, Pa. sellers of electric adjustable beds and their individual owner, among other things, to cease denying responsibility of their written warranties; failing to fully and promptly honor valid warranty claims; and failing to disclose relevant information concerning any other guarantor. The firms would be required to clearly and prominently disclose in advertisements and promotional materials offering any product warranty, either the nature and extent of all material limitations and exclusions of the warranty (including any requirement that consumers seeking

to obtain warranty performance are obliged to arrange for shipping and/or pay shipping charges) or a statement advising that the warranty contains major limitations and exclusions and should be consulted by the prospective buyer prior to purchase. The Order would also bar the companies from disseminating to their door-to-door sellers written promotional materials that do not contain copies of all written warranties offered and disclose to prospective buyers that the sales representative has copies of such warranties available for the consumer's inspection. The companies would be further required to comply fully with the Pre-Sale Availability Rule; maintain specified records concerning warranty performance for a period of four years; and provide their current distributors and retailers with a copy of the Order and the attached notice.

DATE: Comments must be received on or before March 18, 1985.

ADDRESS: Comments should be directed to: FTC/Office of the Secretary, Room 136, 6th St. and Pa. Ave., NW., Washington, D.C. 20580.

FOR FURTHER INFORMATION CONTACT: Rachel Miller, FTC/H 236, Washington, D.C. 20580. (202) 523-1670.

SUPPLEMENTARY INFORMATION: Pursuant to section 6(f) of the Federal Trade Commission Act, 38 Stat. 721, 15 U.S.C. 46 and § 2.34 of the Commission's Rules of Practice (16 CFR 2.34), notice is hereby given that the following consent agreement containing a consent order to cease and desist and an explanation thereof, having been filed with and accepted, subject to final approval, by the Commission, has been placed on the public record for a period of sixty (60) days. Public comment is invited. Such comments or views will be considered by the Commission and will be available for inspection and copying at its principal office in accordance with § 4.9(b) of the Commission Rules of Practice (16 CFR 4.9(b)(14)).

List of Subjects in 16 CFR Part 13

Electric adjustable beds, Trade practices.

Before Federal Trade Commission

[File No. 822 3153]

Agreement Containing Order To Cease and Desist

In the matter of Craftmatic/Contour Organization, Inc., Craftmatic Comfort Mfg. Corp., corporations, and Stanley Kraftsow, individually and as an officer and director of said corporations.

The Federal Trade Commission having initiated an investigation of certain acts and practices of Craftmatic/Contour Organization, Inc., and Craftmatic Comfort Mfg. Corp., corporations, and Stanley Kraftsow, individually and as an officer and director of said corporations, and it now appearing that Craftmatic/Contour Organization, Inc., and Craftmatic Comfort Mfg. Corp., corporations, and Stanley Kraftsow, individually and as an officer and director of said corporations, ("proposed respondents") are willing to enter into an agreement containing an order to cease and desist from the use of the acts and practices being investigated.

It is hereby agreed by and between Craftmatic/Contour Organization, Inc., and Craftmatic Comfort Mfg. Corp., corporations, and Stanley Kraftsow, individually and as an officer and director of said corporations, by their duly authorized officers and their attorney, and counsel for the Federal Trade Commission that:

1. Proposed respondent Craftmatic/Contour Organization, Inc., ("Craftmatic/Contour") is a corporation organized, existing and doing business under and by virtue of the laws of the Commonwealth of Pennsylvania. Proposed respondent Craftmatic/Contour is wholly owned by below-named proposed respondent Stanley Kraftsow. Proposed respondent Craftmatic/Contour was formerly named Craftmatic Wholesale, Inc., ("CWI") and was a wholly-owned subsidiary of Kraftsow Organization, Inc., ("KOI"), a Delaware corporation, which in turn was wholly owned by proposed respondent Stanley Kraftsow. On or about April 1, 1984, CWI was merged with KOI and with Contour Inc. of Pa. ("Contour"), a former Pennsylvania corporation and wholly-owned subsidiary of KOI. Prior to January 1, 1982, Contour was wholly owned by proposed respondent Stanley Kraftsow.

Proposed respondent Craftmatic Comfort Mfg. Corp. ("CCM") is a corporation organized and existing under and by virtue of the laws of the Commonwealth of Pennsylvania. Prior to January 1, 1982, proposed respondent CCM was wholly owned by proposed respondent Stanley Kraftsow. From January 1, 1982 to April 1, 1984, proposed respondent CCM was a wholly-owned subsidiary of KOI. Since April 1, 1984, proposed respondent CCM has been a wholly-owned subsidiary of Contour Chair-Lounge Co., Inc., a Missouri corporation whose common stock is wholly owned by proposed respondent Stanley Kraftsow.

The principal office and place of business of the two corporate proposed respondents is 1726 Winchester Road, Bensalem, PA 19020.

Proposed respondent Stanley Kraftsow ("Kraftsow") is an individual and is, and for some time past has been, the principal officer and director of proposed respondents CCM and Craftmatic/Contour. Proposed respondent Kraftsow was also the principal officer and director of Contour and KOI during their existence. Proposed respondent Kraftsow also is and has been the sole shareholder of proposed respondent Craftmatic/Contour and of Contour Chair-Lounge Co., Inc. Individually, or in concert with others, he has directed, controlled and formulated the business practices of proposed respondents Craftmatic/Contour and CCM, and of Contour and KOI during their existence, including the acts and practices alleged in this complaint. His business address is the same as that of the corporate respondents. His residential address is 120 Surrey Road, Melrose Park, PA 19126.

2. Proposed respondents admit all the jurisdictional facts set forth in the draft of complaint here attached.

3. Proposed respondents waive:

(a) Any further procedural steps;

(b) The requirement that the Commission's decision contain a statement of findings of fact and conclusions of law;

(c) All rights to seek judicial review or otherwise to challenge or contest the validity of the order entered pursuant to this agreement; and

(d) All claims under the Equal Access to Justice Act.

4. This agreement shall not become part of the public record of the proceeding unless and until it is accepted by the Commission. If this agreement is accepted by the Commission it, together with the draft of complaint contemplated thereby, will be placed on the public record for a period of sixty (60) days and information in respect thereto publicly released. The Commission thereafter may either withdraw its acceptance of this agreement and so notify the proposed repondents, in which event the Commission will take such action as it may consider appropriate, or the Commission may issue and serve its complaint (in such form as the circumstances may require) and decision, in disposition of the proceeding.

5. This agreement is for settlement purposes only and does not constitute an admission by proposed respondents that the law has been violated as

alleged in the draft of complaint here attached.

6. This agreement contemplates that, if it is accepted by the Commission, and if such acceptance is not subsequently withdrawn by the Commission pursuant to the provisions of § 2.34 of the Commission's Rules, the Commission may, without further notice to proposed respondents, (a) issue its complaint here attached and its decision containing the following order to cease and desist in disposition of the proceeding, and (b) make information public in respect thereto. When so entered, the order to cease and desist shall have the same force and effect and may be altered, modified or set aside in the same manner and within the same time provided by statute for other orders. The order shall become final upon service. Delivery by the U.S. Postal Service of the complaint and decision containing the agreed-to order to proposed respondents' address as stated in this agreement shall constitute service. Proposed respondents waive any right they may have to any other manner of service. The complaint may be used in construing the terms of the order, and no agreement, understanding, representation, or interpretation not contained in the order or the agreement may be used to vary or contradict the terms of the order.

7. Proposed responsents have read the proposed complaint and order contemplated hereby. They understand that once the order has been issued they will be required to file one or more compliance reports showing that they have fully complied with the order. Proposed respondents further understand that they may be liable for civil penalties in the amount provided by the law for each violation of the order after it becomes final.

Order

The definition of "commerce" contained in section 4 of the Federal Trade Commission Act, 15 U.S.C. 44, shall apply to this order.

The definitions of "written warranty," "consumer," and "consumer product" contained in section 101 of the Magnuson-Moss Warranty Act ("Warranty Act"), 15 U.S.C. 2301, shall apply to this order except as noted below.

The definitions of "consumer product," "written warranty," "seller," "door-to-door sale," and "prospective buyer" contained in the Federal Trade Commission's Rule on Pre-Sale Availability of Written Warranty Terms ("Pre-Sale Availability Rule"), 16 CFR Part 702, implementing section 102(b)(1)(A) of the Warranty Act, shall apply to Part IV of this order.

I

It is ordered that respondents Craftmatic/Contour Organization, Inc., and Craftmatic Comfort Mfg. Corp., corporations, and Stanley Kraftsow, individually and as an officer and director of said corporations, their successors and assigns, and their officers, agents, representatitives, and employees, directly or through any corporation, subsidiary, division, or other device, in connection with the distribution, advertising, offering for sale or sale of any bed or other consumer product in or affecting commerce, do forthwith cease and desist from representing, directly or by implication, that any such product carries a written warranty, if that warranty is offered or issued by anyone other than a respondent, its successor or assign, without:

a. Disclosing, clearly and prominently with such representation, that the warranty is not offered or issued by any respondent, its successor or assign; and

b. Identifying, clearly and prominently with such representation, who does offer the warranty.

II

It is further ordered that respondents, their successors and assigns, and their officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division, or other device, in connection with the offering or issuance of any written warranty with respect to any consumer product distributed, advertised, offered for sale or sold in or affecting commerce, do forthwith cease and desist from:

a. Denying that respondents, their successors and assigns are responsible for performance of such written warranty; and

b. Failing to honor and satisfy, fully and within a reasonable time, every valid claim arising under such written warranty;

Provided that, if any respondent, its successor or assign designates any representative to perform duties under a written warranty, that respondent or its successor or assign and that representative may allocate among themselves costs for warranty performance in any manner consistent with the requirements of section 107 of the Warranty Act, 15 U.S.C. 2307, but such designation or allocation shall not relieve respondents, their successors and assigns, and their officers, agents, representatives, and employees of their direct obligation to honor and satisfy, fully and within a reasonable time, every valid claim arising under the written warranty, and

Provided further that, if any such product is offered for sale or sold with a warranty that clearly and prominently identifies that selling dealer as the sole warrantor obligated to honor the warranty, and if the selling dealer for that product is not a respondent, its successor or assign, then this provision of the order shall not apply to that warranty on that product.

III

It is further ordered that respondents, their successors and assigns, and their officers, agents, representatives and employees, within thirty (30) days after receiving notice of a request for such satisfaction, shall honor and satisfy fully every valid claim arising under any outstanding written or implied warranty offered or issued by any respondent, its successor or assign with respect to any adjustable bed or chair, or component or accessory thereof, in or affecting commerce, if that claim was originally lodged with any distributor, retailer or respondent, its successor or assign, orally or in writing, prior to the date of service of this order; and, upon concluding reasonably and in good faith that any person requesting such satisfaction for such a claim is not entitled to all or part of the relief requested under any applicable written or implied warranty, and upon choosing to deny the request in whole or in part based upon such conclusion, shall send to the requester a written notice explaining the denial and the reasons therefor (a signed statement from the requester, or from another person with such knowledge, that such claim was lodged prior to the date of service of this order, shall be sufficient evidence of such lodging for purposes of this order provision); provided that, if any respondent, its successor or assign designates any representative to perform duties under any warranty, that respondent or its successor or assign and that representative may allocate among themselves costs for warranty performance in any manner consistent with the requirements of section 107 of the Warranty Act, 15 U.S.C. 2307, but such designation or allocation shall not relieve respondents, their successors and assigns, and their officers, agents, representatives, and employees of their direct obligation to honor and satisfy claims and provide notice of denials as specified herein.

IV

It is further ordered that respondents their successors and assigns, and

officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division, or other device, in connection with the distribution, advertising, offering for sale or sale of any consumer product in or affecting commerce, do forthwith cease and desist from:

a. Failing to give to every buyer of any such consumer product in a door-to-door sale, prior to or upon execution of the sale, a copy of every written warranty offered or issued with respect to that consumer product, provided that, giving to a buyer a copy of a sales contract with such a written warranty printed clearly and legibly on the reverse side, and with a clear and prominent reference on the face to the warranty on the reverse side, shall satisfy this requirement as to that warranty for that buyer.

b. Disseminating to any door-to-door seller any written materials intended to be shown to any prospective buyer of any such consumer product in a door-to-door sale offer, that fail to contain:

i. Copies of every written warranty offered or issued with respect to that consumer product; and

ii. A clear and prominent disclosure that the sales representative has copies of such warranties, which may be inspected by the prospective buyer at any time during the sales presentation.

c. Failing to comply fully with the Pre-Sale Availability Rule, as amended from time to time.

V

It is further ordered that respondents, their successors and assigns, and their officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division, or other device, in connection with the preparation, approval or dissemination of any advertising or promotional material that is mailed, shipped or shown to any consumer and that describes any written warranty offered or issued with respect to any consumer product distributed, advertised, offered for sale or sold in or affecting commerce, do forthwith cease and desist from failing to disclose, clearly and prominently, either:

a. The nature and extent of all material limitations and exclusions of the warranty, including any requirement that consumers arrange or pay any charge for shipping, or pay a servicer or truck travel or similar charge, in order to obtain performance under the warranty; or

b. The following:

i. That there are other major limitations and exclusions of the warranty and that customers should consult the warranty before making a purchase; and

ii. Where any such material describes the warranty as free of charge for parts and labor and the warranty requires any consumer to arrange or pay any charge for shipping, or to pay a servicer or truck travel or similar charge, in order to obtain performance under the warranty; the fact that there may be costs for shipping or such other requirement.

VI

It is further ordered that respondents, their successors and assigns, and their officers, agents, representatives, and employees, directly or through any corporation, subsidiary, division, or other device, do forthwith cease and desist from requiring any consumer who purchased any adjustable bed, bed component, or bed accessory prior to the date of service of this order to arrange or pay any charge for shipping, or to pay any servicer or truck travel or similar charge, in order to obtain performance under any written warranty.

VII

It is further ordered that respondents shall, within thirty (30) days of the date of service of this order, send to each current distributor and retailer of respondents' consumer products, a copy of this order together with the attached notice.

VIII

It is further ordered that respondents and their successors and assigns shall maintain for at least four (4) years after the date of each record's generation, and upon request shall make available to the Federal Trade Commission for inspection and copying, the following records as to each consumer who purchases a consumer product with a written warranty offered or issued by any respondent, its successor or assign, or its officer, agent, representative or employee, directly or through any corporation, subsidiary, division or other device:

a. The name and address of the consumer;

b. The name of the dealer from whom the product is purchased; and

c. For each request for service or other action under any such written warranty or under any implied warranty, and for each complaint concerning any such written warranty or any implied warranty, whether submitted in writing or orally:

i. A description of the problem, the action requested, the firm or firms receiving the request or complaint, and the date or dates of receipt;

ii. A copy or description of all replies given to the request or complaint, and by whom; a description of all actions taken, and by whom, in response to the request or complaint; and the date of each such reply and of each such action;

iii. A description of any payment sought from a consumer, the reason for seeking the payment, and the amount received from the consumer, if any; and

iv. Any later service requested or complaint made by or on behalf of the consumer concerning the product.

IX

It is further ordered that respondents shall distribute a copy of this order to all of respondents' divisions and to all present and future officers, agents, representatives, and employees of respondents having responsibilities with respect to the subject matter of this order.

X

It is further ordered that the corporate respondents shall notify the Commission at least thirty (30) days prior to any proposed change such as dissolution, assignment or sale resulting in the emergence of a successor corporation, the creation or dissolution of subsidiaries or any other change in the corporate respondent which may affect compliance obligations arising out of the order.

XI

It is further ordered that respondent Stanley Kraftsow shall promptly notify, as described herein, the Commission of any discontinuance of his present business or employment and of his affiliation with any new business or employment, and that, for a period of ten (10) years from the date of service on him of this order, respondent Stanley Kraftsow shall promptly notify, as described herein, the Commission of each affiliation with a new business or employment whose activities include the offering or issuance of written warranties, or of his affiliation with any new business or employment in which his own duties and responsibilities involve offering or issuance of written warranties. Such notice shall include respondent Stanley Kraftsow's new business address and a statement of the nature of the business or employment in which respondent Kraftsow is newly engaged as well as a description of respondent Kraftsow's duties and responsibilities in connection with the business or employment.

XII

It is further ordered that respondents shall, within sixty (60) days after service upon them of this order, file with the Commission a report, in writing, setting forth in detail the manner and form in which they have complied with this order.

Attachment to Order

To All Our Distributors and Dealers

Craftmatic has recently signed an agreement with the Federal Trade Commission concerning our warranty policies. A copy of that agreement is attached for your information. The discussion below summarizes the agreement and tells you how the agreement affects you.

Warranty Performance on Warranties now in the Field

We have agreed that we are responsible for making sure these warranties are fully and promptly honored, even where one of you has sold the product. Under the terms of our arrangement with you, you are responsible for providing full and prompt performance of these warranties. You should understand that when you handle these warranties, you do so as our representative, and we are required to make sure they are handled properly. We will keep you informed of all our policies and procedures for handling claims for these warranties.

We have also agreed to make sure that any outstanding warranty claims from any of your customers are properly taken care of within 30 days after we learn of such a claim. Please help us handle these claims, for any customer in your area.

In addition we have agreed that certain records about warranty performance under the outstanding Craftmatic warranty will be kept. You need to keep these records for your customers who receive that warranty. We are sure that these records will assist you in performing under the warranty and accounting for your performance should that ever become necessary. As to each customer you have sold, please keep:

The customer's name and address.

A record of each request for service or other action under warranty, and of each warranty complaint, regardless of whether it is made orally or in writing, including:

A description of the problem, what the customer asked for, and the date you received the request or complaint;

A copy or description of every reply made, and the date;

A description of every action taken about the matter, and the date;

Any charge (whether or not collected); the reason for the charge and the amount collected;

If the request or complaint was received or handled in any way be Craftmatic (Pennsylvania) or any other firm, similar records of such receipt and handling; and

Any later request for service or complaints by or on behalf of that customer.

Keep in the file any letters you receive and a copy of any letter you send.

Issuance of Future Warranties

As you know, under our agreement with you, you have always been responsible to your customers for full and prompt performance of their warranties. We have decided that in the future any warranties on the products you sell will clearly states they are offered not by Craftmatic but by you. You will be responsible to your customers for performance of those warranties. We will only warrant the products we sell to our retail customers.

We plan to rewrite the warranty to make it clear that the warrantor, the only firm obligated to honor the warranty, is the selling dealer in each case. A sample copy of the revised warranty document is enclosed.

Of course, if you have a problem with a claim for warranty performance that you cannot handle comfortably, please feel free to contact us. We will still do our utmost to help you resolve the problem.

We also suggest that you continue to keep records like those described above for customers to whom you offer your warranty. Such records can assist you in ongoing performance of your warranty.

Warranty Availability Before Sale

We have agreed to give a copy of our warranty, at the sales presentation, to every customer who buys from us.

We have also agreed to include a copy of our warranty in every pitch book we send you, and to add to the sales pitch and sales materials we send you a statement that the warranty is available for customers to read before buying our products. You should know that, under federal law, door-to-door sellers must bring copies of any warranties on the products they sell to the sales presentation, and must disclose, both orally and in any written materials, that the customer can read the warranties before buying. We have enclosed revised sales materials that include the statement and the warranty itself. You should let us know how many sets of materials you need. Also, you must be sure to make these disclosures in every sales call.

Advertising and Brochure

We are revising our advertisements and sales materials to delete any impression that we offer a warranty on the products sold by selling dealers other than us. We have agreed that, if we make any reference in these materials to a warranty, we will make it clear who actually gives the warranty. You should be careful also, in your sales presentations, not to let your customers think that the warranty is from Craftmatic.

Also, we have agreed that, if we discuss a warranty in our brochure, New Dimensions in Bedroom Luxury, we will disclose any warranty term requiring customers with warranty claims to return the defective part at their cost. This would apply to any other mailer that discuss a warranty as well. We have enclosed samples of the revised brochure.

Transportation Charges

We have agreed not to charge for transportation or truck travel for any warranty service needed, for beds now in the field. Since you do warranty service under our old warranty, this means that you will not be able to make those charges either. Beds sold after the date of this agreement are not subject to this restriction.

[signature]

Analysis of Proposed Consent Order To Aid Public Comment

The Federal Trade Commission has accepted an agreement to a proposed concent order from Craftmatic/Contour Organization, Inc., Craftmatic Comfort Manufacturing Corporation, and Stanley Kraftsow.

The proposed consent order has been placed on the public record for sixty (60) days for reception of comments by interested persons. Comments received during this period will become part of the public record. After sixty (60) days, the Commission will again review the agreement and the comments received and will decide whether it should withdraw from the agreeemnt or make final the agreement's proposed order.

The named companies designed, formerly manufactured, and now wholesale and retail the Craftmatic electric adjustable bed. They are the largest sellers of electric adjustable beds for residential use. These are beds whose head and foot can be raised by pushbutton operation.

The individual named, Stanley Kraftsow, is and has been the president, director, and owner of the named companies. The complaint alleges that the three respondents have cooperated as a single business entity in the adjustable bed business and, specifically, in the practices cited in the complaint.

The Commission complaint alleges that the respondents issued warranties both to its retail customers and to buyers through distributors, but that on many occasions it failed and refused to honor its warranties fully and promptly to the distributors' customers. The complaint also alleges that on many occasions the respondents denied that they were responsible for the warranties to those customers, although in fact, under section 107 of the Magnuson-Moss Warranty Act and other laws, they are responsible for those warranties. The complaint states that such practices violate section 5(a) of the Federal Trade Commission Act.

The complaint also alleges that on many occasions the respondents failed to make their warranty available to their retail customers as required by the Commission's Rule on Pre-Sale Availability of Warranties (16 CFR Part 702), implementing the Magnuson-Moss Warranty Act. The respondents also failed on many occasions to provide distsributors with copies of the warranty as necessary for the distributors to meet their obligations under the same Rule, according to the complaint. Such failures violate the Warranty Pre-Sale Availability Rule, the Warranty Act, and section 5(a) of the Federal Trade Commission Act.

In addition, the complaint alleges that the respondents' promotional brochure and other materials misrepresented the terms of the warranty offered. Specifically, the complaint alleges, those materials purported to disclose all the major terms of the mattress warranty, but failed to disclose the warranty's shipping requirement; that customers must return a defective mattress, at their own cost, for warranty service.

The agreed-upon order would require the respondents to cease denying their responsibility for warranties, and to honor their warranty fully and promptly. The respondents would also be required to resolve every outstanding claim, within 30 days of its being brought to their attention, by honoring the claim if it is valid and by notifying the claimant if they believe in good faith that the claim is invalid. In addition, the repondents would be required to keep specific records of their warranty performance. Also, if a respondent were to make any representation that any of the respondents' products is warranted, where the warranty was not from any of the respondents, they would be obligated to make it clear that the warranty is not theirs, and explain who actually offers the warranty.

The order would also require the respondents to give a copy of any applicable warranty, prior to or upon purchase, to each consumer purchaser at retail from a respondent. The respondents would also be obligated to include the warranty in point-of-sale materials supplied to distributors, and to comply with the Warranty Pre-Sale Availability Rule. In addition, the respondents could not require any customer seeking warranty service under an outstanding warranty to arrange or pay for shipping or similar service.

Finally, the respondents would be required to make certain disclosures if they advertise a warranty without disclosing all its material terms. A shipping or similar requirement would be considered a material term in this case. Any advertisement making such a partial disclosure would require a further disclosure that not all the major warranty terms are stated, and that consumers should see the warranty itself. Also, if such a partially disclosed warranty with a shipping or similar requirement were described as free of charge for parts and labor, the respondents would be required to disclose specifically that there may be costs for that requirement.

The respondents would send notices to their distributors explaining how the order would affect them.

The purpose of this analysis is to facilitate public comment on the proposed order, and it is not intended to constitute an official interpretation of the agreement and proposed order or to modidy in any way their terms.

Emily H. Rock,

Secretary.

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BILLING CODE 6750-01-M

POSTAL SERVICE

39 CFR Part 10

Proposed Express Mail International Service to Denmark, Portugal, Turkey and United Arab Emirates

AGENCY: Postal Service.

ACTION: Proposed rule.

SUMMARY: Pursuant to agreements with the postal administrations of Denmark, Portugal, Turkey and United Arab Emirates, the Postal Service intends to begin Express Mail International Service with these countries at postage rates indicated in the tables below. The proposed services are scheduled to begin on March 21, 1985.

DATE: Comments must be received on or before February 14, 1985.

FOR FURTHER INFORMATION CONTACT: Leon W. Perlinn [202] 245-4414.

ADDRESS: Written comments should be directed to the General Manager, Rate Development Division, Office of Rates, Rates and Classification Department, U.S. Postal Service, Washington, D.C. 20260-5350. 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 8620, 475 L'Enfant Plaza West, SW., Washington, DC 20260-5350.

SUPPLEMENTARY INFORMATION: The International Mail Manual is incorporated by reference in the Code of Federal Regulations, 39 CFR 10.1. Additions to the manual concerning the proposed new service, including the rate tables reproduced below, will be made in due course. Accordingly, although 39 U.S.C. 407 does not require advance notice and the opportunity for submission of comments on international service, and the provisions of the Administrative Procedure Act regarding proposed rulemaking [5 U.S.C. 553] do not apply [39 U.S.C. 410 [a]], the Postal Service invites interested persons to submit written data, views or arguments concerning the proposed Express Mail International Service to Denmark, Portugal, Turkey and United Arab Emirates at the rates indicated in the tables below.

List of Subjects in 39 CFR Part 10

Postal Service, Foreign relations.

DENMARK

[Express mail international service]

Custom designed service [1] [2]—up to and including		On demand service [2]—up to and including	
Pounds	Rate	Pounds	Rate
1	$31.00	1	$23.00
2	35.90	2	27.90
3	40.80	3	32.80
4	45.70	4	37.70
5	50.60	5	42.60
6	55.50	6	47.50
7	60.40	7	52.40
8	65.30	8	57.30
9	70.20	9	62.20
10	75.10	10	67.10
11	80.00	11	72.00
12	84.90	12	76.90
13	89.80	13	81.80
14	94.70	14	86.70
15	99.60	15	91.60
16	104.50	16	96.50
17	109.40	17	101.40
18	114.30	18	106.30
19	119.20	19	111.20
20	124.10	20	116.10

DENMARK—Continued

[Express mail international service]

Custom designed service [1] [2]—up to and including		On demand service [2]—up to and including	
Pounds	Rate	Pounds	Rate
21	129.00	21	121.00
22	133.90	22	125.90
23	138.80	23	130.80
24	143.70	24	135.70
25	148.60	25	140.60
26	153.50	26	145.50
27	158.40	27	150.40
28	163.30	28	155.30
29	168.20	29	160.20
30	173.10	30	165.10
31	178.00	31	170.00
32	187.90	32	174.90
33	187.80	33	179.80
34	192.70	34	184.70
35	197.60	35	189.60
36	202.50	36	194.50
37	207.40	37	199.40
38	212.30	38	204.30
39	217.20	39	209.20
40	222.10	40	214.10
41	227.00	41	219.00
42	231.90	42	223.90
43	236.80	43	228.80
44	241.70	44	233.70

[1] Rates in this table are applicable to each piece of International Custom Designed Express Mail shipped under a Service Agreement providing for tender by the customer at a designated Post Office.

[2] Pickup is available under a Service Agreement for an added charge of $5.60 for each pickup stop, regardless of the number of pieces picked up. Domestic and International Express Mail picked up together under the same Service Agreement incurs only one pickup charge.

PORTUGAL

[Express mail international service]

Custom designed service [1] [2]—up to and including		On demand service [2]—up to and including	
Pounds	Rate	Pounds	Rate
1	$31.00	1	$23.00
2	34.80	2	26.80
3	38.60	3	30.60
4	42.40	4	34.40
5	46.20	5	38.20
6	50.00	6	42.00
7	53.80	7	45.80
8	57.60	8	49.60
9	61.40	9	53.40
10	65.20	10	57.20
11	69.00	11	61.00
12	72.80	12	64.80
13	76.60	13	68.60
14	80.40	14	72.40
15	84.20	15	76.20
16	88.00	16	80.00
17	91.80	17	83.80
18	95.60	18	87.60
19	99.40	19	91.40
20	103.20	20	95.20
21	107.00	21	99.00

PORTUGAL—Continued

[Express mail international service]

Custom designed service [1] [2]—up to and including		On demand service [2]—up to and including	
Pounds	Rate	Pounds	Rate
22	110.80	22	102.80
23	114.60	23	106.60
24	118.40	24	110.40
25	122.20	25	114.20
26	126.00	26	118.00
27	129.80	27	121.80
28	133.60	28	125.60
29	137.40	29	129.40
30	141.20	30	133.20
31	145.00	31	137.00
32	148.80	32	140.80
33	152.60	33	144.60

[1] Rates in this table are applicable to each piece of International Custom Designed Express Mail shipped under a Service Agreement providing for tender by the customer at a designated Post Office.

[2] Pickup is available under a Service Agreement for an added charge of $5.60 for each pickup stop, regardless of the number of pieces picked up. Domestic and International Express Mail picked up together under the same Service Agreement incurs only one pickup charge.

TURKEY

[Express mail international service]

Custom designed service [1] [2]—weight not over		On demand service [2]—weight not over	
Pounds	Rate	Pounds	Rate
1	$31.00	1	$23.00
2	35.90	2	27.90
3	40.80	3	32.80
4	45.70	4	37.70
5	50.60	5	42.60
6	55.50	6	47.50
7	60.40	7	52.40
8	65.30	8	57.30
9	70.20	9	62.20
10	75.10	10	67.10
11	80.00	11	72.00
12	84.90	12	76.90
13	89.80	13	81.80
14	94.70	14	86.70
15	99.60	15	91.60
16	104.50	16	96.50
17	109.40	17	101.40
18	114.30	18	106.30
19	119.20	19	111.20
20	124.10	20	116.10
21	129.00	21	121.00
22	133.90	22	125.90

[1] Rates in this table are applicable to each piece of International Custom Designed Express Mail shipped under a Service Agreement providing for tender by the customer at a designated Post Office.

[2] Pickup is available under a Service Agreement for an added charge of $5.60 for each pickup stop, regardless of the number of pieces picked up. Domestic and International Express Mail picked up together under the same Service Agreement incurs only one pickup charge.

UNITED ARAB EMIRATES

[Express mail international service]

Custom designed service [1] [2]—up to and including		On demand service [2]—up to and including	
Pounds	Rate	Pounds	Rate
1	$31.00	1	$23.00
2	35.90	2	27.90
3	40.80	3	32.80
4	45.70	4	37.70
5	50.60	5	42.60
6	55.50	6	47.50
7	60.40	7	52.40
8	65.30	8	57.30
9	70.20	9	62.20
10	75.10	10	67.10
11	80.00	11	72.00
12	84.90	12	76.90
13	89.80	13	81.80
14	94.70	14	86.70
15	99.60	15	91.60
16	104.50	16	96.50
17	109.40	17	101.40
18	114.30	18	106.30
19	119.20	19	111.20
20	124.10	20	116.10
21	129.00	21	121.00
22	133.90	22	125.90
23	138.80	23	130.80
24	143.70	24	135.70
25	148.60	25	140.60
26	153.50	26	145.50
27	158.40	27	150.40
28	163.30	28	155.30
29	168.20	29	160.20
30	173.10	30	165.10
31	178.00	31	170.00
32	182.90	32	174.90
33	187.80	33	179.80

[1] Rates in this table are applicable to each piece of International Custom Designed Express Mail shipped under a Service Agreement providing for tender by the customer at a designated Post Office.

[2] Pickup is available under a Service Agreement for an added charge of $5.60 for each pickup stop, regardless of the number of pieces picked up. Domestic and International Express Mail picked up together under the same Service Agreement incurs only one pickup charge.

An appropriate amendment to 39 CFR 10.3 to reflect these changes will be published when the final rule is adopted.

(39 U.S.C. 401, 404, 407)

W. Allen Sanders,

Associate General Counsel, Office of General Law and Administration.

[FR Doc. 85-1119 Filed 1-14-85; 8:45 am]

BILLING CODE 7710-12-M

Notices

Federal Register
Vol. 50, No. 10
Tuesday, January 15, 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 AGRICULTURE

Agricultural Marketing Service

Hop Marketing Advisory Board; Public Meeting

Pursuant to the Federal Advisory Committee Act (Pub. L. 92-426; 86 Stat. 770), notice is given of a meeting of the Hop Marketing Advisory Board at 8:15 a.m., local time, January 23, 1985, in Seattle, Washington, at the Westin Hotel.

The purpose of the meeting is to discuss marketing policy, and related matters. The meeting will be open to the public.

The Hop Marketing Advisory Board is established under Marketing Order No. 991, as amended (7 CFR Part 991), regulating the handling of hops of domestic production. The marketing order is effective under the Agricultural Marketing Agreement Act of 1937, as amended (Secs. 1-19, 48 Stat. 31, as amended; 7 U.S.C. 601-674).

The names of Board members, agenda, summary of the meeting, and other information pertaining to the meeting may be obtained from Robert H. Eaton, Hop Administrative Committee, 330 Dayton Building, 838 SW. 1st Avenue, Portland, Oregon, 97204, telephone (503) 224-1823.

Dated: January 10, 1985.

William T. Manley,

Deputy Administrator, Marketing Programs.

[FR Doc. 85-1144 Filed 1-14-85; 8:45 am]

BILLING CODE 3410-02-M

Forest Service

Medicine Bow National Forest Grazing Advisory Board; Meeting

The annual meeting of the Medicine Bow National Forest Grazing Advisory Board will be February 22, 1985, at 10 a.m. in the Medicine Bow National Forest Supervisor's Office, 605 Skyline Drive, Laramie, Wyoming.

The agenda for the meeting will include: (1) Accepting new board members; (2) acquaint new members with the function of the Board; (3) recommendations concerning the development of allotment management plans and the utilization of range betterment funds; (4) location and agenda for the summer tour; and (5) amend by-laws regarding election of board members.

The meeting will be open to the public. Persons who wish to attend and participate should notify Ladd Frary (307/745-8971) Laramie, Wyoming, prior to meeting. Public members may participate in discussions at any time during the meeting, or may file a written statement following the meeting.

Dated: January 7, 1985.

Sonny J. O'Neal,

Forest Supervisor.

[FR Doc. 85-1127 Filed 1-14-85; 8:45 am]

BILLING CODE 3410-11-M

DEPARTMENT OF COMMERCE

Office of the Secretary

Economic Advisory Board; Meeting

Pursuant to the provisions of section 10(a) (2) of the Federal Advisory Committee Act, as amended, 5 U.S.C. App. (1976), notice is hereby given that the meeting of the Department of Commerce Economic Advisory Board will be held on Monday, February 4, 1985, from 9:30 a.m. to 4:00 p.m. in Room 4830, Herbert C. Hoover Building, 14th Street and Constitution Avenue, NW., Washington, D.C. 20230.

The Board was established by the Secretary of Commerce on January 13, 1967. The purpose of the Board is to advise the Secretary of Commerce on economic policy issues. The intended agenda for this meeting is as follows:

- A review of the economic outlook by major sector.
- A discussion of the outlook for prices and employment and of strategies for sustaining noninflationary economic growth.

A limited number of seats will be available to the public on a first-come, first-served basis. Public participation will be limited to requests for clarification of items under discussion. Additional statements or inquiries may be submitted to the chair before or after the meeting. Copies of the minutes will be available on request 30 days after the meeting.

Additional information concerning this meeting may be obtained by contacting Mrs. Virginia R. Marketti, Office of the Under Secretary for Economic Affairs, Room 4836, Department of Commerce, Washington, D.C. 20230 (202) 377-3523.

Dated: January 10, 1985.

Sidney L. Jones,

Under Secretary for Economic Affairs.

[FR Doc. 85-1116, Filed 1-14-85; 8:45 am]

BILLING CODE 3510-18-M

Travel and Tourism Administration

Travel and Tourism Advisory Board; Meeting

Pursuant to section 10(a)(2) of the Federal Advisory Committee Act, 5 U.S.C. (App. 1976) notice is hereby given that the Travel and Tourism Advisory Board of the U.S. Department of Commerce will meet on February 7, 1985, at 9:30 a.m., in Room 4830 of the Main Commerce Building, 14th and Constitution Avenue, NW., Washington, D.C. 20230.

Established March 19, 1982, the Travel and Tourism Advisory Board consists of 15 members, representing the major segments of the travel and tourism industry and state tourism interests, and includes one member of a travel labor organization, a consumer advocate, an academician and a financial expert.

Members advise the Secretary of Commerce on matters pertinent to the Department's responsibilities to accomplish the purpose of the National Tourism Policy Act (Pub. L. 97-63), and provide guidance to the Assistant Secretary for Tourism Marketing in the preparation of annual marketing plans.

Agenda items are as follows:

I. Call to Order
II. Approval of the Minutes
III. Old Business
  A. Update on Automated System
  B. Tourism Policy Council
  C. Approval of 1984 Annual Report
  D. International Marketing Meeting
IV. New Business
  A. USTTA Consumer Surveys
  B. Cooperative Advertising Theme
  C. FY-1986 Marketing Plan

V. Election of Officers
VI. Adjournment

A limited number of seats will be available to observers from the public and the press. The public will be permitted to file written statements with the Committee before or after the meeting. To the extent time is available, the presentation of oral statements is allowed.

Karen M. Cardran, Committee Control Officer, United States Travel and Tourism Administration, Room 1865, U.S. Department of Commerce, Washington, D.C. 20230 (telephone: 202–377–0140) will respond to public requests for information about the meeting.

Donna Tuttle,

Under Secretary for Travel and Tourism, U.S. Department of Commerce.

[FR Doc. 85–1115 Filed 1–14–85; 8:45 am]

BILLING CODE 3510–11–M

International Trade Administration

[C–484–015]

Tomato Products From Greece; Final Results of Administrative Review and Revocation of Countervailing Duty Order

AGENCY: International Trade Administration/Import Administration, Commerce.

ACTION: Notice of final results of administrative review and revocation of countervailing duty order.

SUMMARY: On March 29, 1984, the Department of Commerce published the preliminary results of its administrative review of the countervailing duty order on tomato products from Greece. The review covers the period January 1, 1982, through December 31, 1982.

We gave interested parties an opportunity to comment on the preliminary results. After review of all of the comments received, the final results are the same as the preliminary results.

On October 29, 1984, the International Trade Commission notified the Department that an industry in the United States would not be injured by reason of imports of Greek tomato products if the order were revoked. The Department consequently is revoking the countervailing duty order. All entries of this merchandise made on or after March 22, 1982, shall be liquidated without regard to countervailing duties.

EFFECTIVE DATE: January 15, 1985.

FOR FURTHER INFORMATION CONTACT: Al Jemmott or Philip Otterness, Office of Compliance, International Trade Administration, U.S. Department of Commerce, Washington, D.C. 20230; telephone: (202) 377–2786.

SUPPLEMENTARY INFORMATION:

Background

On March 29, 1984, the Department of Commerce ("the Department") published in the **Federal Register** (49 FR 12291) the preliminary results of its administrative review of the countervailing duty order on tomato products from Greece (37 FR 6360, March 28, 1972). The Department has now completed that administrative review, in accordance with section 751 of the Tariff Act of 1930 ("the Tariff Act").

On March 22, 1982, the International Trade Commission ("the ITC") notified the Department that the Government of Greece had requested an injury determination for this order under section 104(b) of the Trade Agreements Act of 1979 ("the TAA"). It was not necessary for the Department, upon notification by the ITC, to suspend liquidation of entries of the merchandise pursuant to that section of the TAA, since previous suspensions remained in effect.

On October 29, 1984, the ITC notified the Department of its determination (49 FR 44561) that an industry in the United States would not be materially injured, or threatened with material injury, by reason of imports of Greek tomato products if the countervailing duty order were revoked.

Scope of Review

Imports covered by the review are shipments of Greek tomato paste and sauce, peeled tomatoes and tomato juice. Such merchandise is currently classifiable under items 141.6520, 141.6540, 141.6600 and 166.3000 of the Tariff Schedules of the United States Annotated. The review covers the period January 1, 1982, through December 31, 1982, and one program: "production aid" to processors of tomatoes.

Analysis of Comments Received

We gave interested parties an opportunity to comment on our preliminary results. We received written comments from one importer, S.A. Laraja & Sons, Inc.

Comment 1: Laraja argues that the process applied by the Department in administering the countervailing duty law is unfair, unreasonable and constitutes a threat to the solvency of importers operating in good faith. It is most threatening for a firm which essentially acts as a broker, creating a liability in excess of the commission earned on a *bona fide* commercial operation completed two years previously.

Department's Position: The administrative review process was established by the provisions of the TAA and the Commerce Department regulations. Under that body of law, at the time of importation, importers post only a cash deposit of estimated countervailing duty. The final amount of countervailing duty to be assessed can only be determined after completion of the subsequent administrative review.

Comment 2: Laraja argues that the Department has not realistically taken cognizance of the pricing of Greek tomato products since 1982.

Department's Position: For purposes of this law, the calculation of the countervailable benefit is based on the net subsidy granted to the Greek tomato products processors and not on the processors' subsequent prices to their consumers.

Comment 3: Laraja states that the countervailing duty order on tomato products from Greece concerned an export subsidy instituted and financed by the Greek government. Between 1972 and 1981 this subsidy continued to be in effect. When Greece became a member of the European Communities ("the EC") on January 1, 1981, the Greek national export subsidy was replaced by a "production aid" program funded by EC grants. The Department "essentially is countervailing against an export subsidy which has to all intents and purposes expired."

Department's Position: Subsidy programs discovered during a proceeding are countervailable, even if not included in the original investigation. Although the program originally investigated in this case no longer exists, it has been replaced with a second countervailable program.

Comment 4: Relying on the International Trade Commission's June 1980, negative injury determination on EC tomato products, and the fact that the "production aid" afforded to Greek tomato processors is funded by the same EC source as that to Italian and French tomato growers and processors, Laraja suggests that no countervailing duties should be imposed on Greek tomato products.

Department's Position: The Department has addressed this issue in a previous administrative review of this order (48 FR 30420, July 1, 1983). Because the ITC has now reached a negative injury determination on this order, we are revoking the order effective March 22, 1982.

Final Results of the Review

After consideration of all of the comments received, the final results of our review are the same as those presented in the preliminary results. We determine that the net subsidies conferred on Greek tomato products during 1982 are those shown in the appendix to this notice.

The Department will instruct the Customs Service to assess countervailing duties, as indicated in the appendix, on all shipments of Greek tomato products exported on or after January 1, 1982, and entered, or withdrawn from warehouse, for consumption before March 22, 1982.

As a result of the ITC finding of no injury, the Department is revoking the countervailing duty order concerning Greek tomato products effective on or after March 22, 1982, the date the ITC notified the Department of the request for a section 104(b) injury determination. The Department will further instruct the Customs Service to proceed with liquidation of all unliquidated entries of this merchandise entered, or withdrawn from warehouse, for consumption on or after March 22, 1982, without regard to countervailing duties and to refund any estimated countervailing duties collected with respect to those entries.

This administrative review, revocation, and notice are in accordance with section 751(a)(1) of the Tariff Act (19 U.S.C. 1675(a)(1)), section 104(b)(4)(B) of the TAA (19 U.S.C. 1671 note), and § 355.41 of the Commerce Regulations (19 CFR 355.41).

Dated: January 8, 1985.

Alan F. Holmer,

Deputy Assistant Secretary for Import Administration.

Appendix

For January 1, 1982 through December 31, 1982.

(1) Tomato Paste and Sauce:

Concentration (percent)		Drachmas per gross kilogram (packing size)				
Not less than	But less than	More than 1.5 kg	From 1.5 to 0.7 kg	From 0.7 to 0.25 kg	From 0.25 to 0.15	0.15 and less
12	14	10.16	11.91	12.88	15.28	17.56
14	16	11.10	13.01	14.07	15.61	19.18
16	18	12.03	14.11	15.26	18.49	20.80
18	20	12.99	15.23	16.47	19.96	22.45
20	22	13.92	16.33	17.66	21.39	24.06
22	24	14.86	17.42	18.85	22.83	25.68
24	26	15.80	18.52	20.04	24.27	27.30
26	28	16.73	19.62	21.22	25.71	28.92
28	30	17.76	20.72	22.41	27.15	30.54
30	32	18.61	21.81	23.60	28.59	32.16
32	34	19.54	22.91	24.79	30.03	33.78
34	36	20.48	24.01	25.97	31.47	35.39
36	38	21.42	25.11	27.16	32.91	37.01
38	40	22.37	26.23	28.37	34.37	38.66
40	42	23.31	27.33	29.56	35.81	40.28
42	93	24.24	28.43	30.75	37.25	41.90
93	100	68.91	68.91	68.91	68.91	68.91

(2) Tomato Juice: 5.62 drachmas per gross kilogram.

(3) Peeled Tomatoes: San Marzano Variety—9.19 drachmas per gross kilogram.

Roma and Similar Varieties—7.02 drachmas per gross kilogram.

[FR Doc. 85-1080 filed 1-14-85; 8:45 am]

BILLING CODE 3510-05-M

Articles of Quota Cheese; Annual Listing of Foreign Government Subsidies

AGENCY: International Trade Administration, Import Administration, Commerce.

ACTION: Publicaton of Annual List of Foreign Government Subsidies on Articles of Quota Cheese.

SUMMARY: The Department of Commerce, in consultation with the Secretary of Agriculture, has prepared its annual list of foreign government subsidies on articles of quota cheese. We are publishing the current listing of those subsidies that we have determined exist.

EFFECTIVE DATE: January 1, 1985.

FOR FURTHER INFORMATION CONTACT: Patricia W. Stroup or Susan Silver, Office of Compliance, International Trade Administration, U.S. Department of Commerce, Washington, D.C. 20230; telephone: (202) 377-2786.

SUPPLEMENTARY INFORMATION: Section 702(a) of the Trade Agreements Act of 1979 ("the TAA") requires the Department of Commerce ("the Department") to determine, in consultation with the Secretary of Agriculture, whether any foreign government is providing a subsidy with respect to any article of quota cheese, as defined in section 701(c)(1) of the TAA, and to publish an annual list and quarterly updates of the type and amount of those subsidies.

The Department has developed, in consultation with the Department of Agriculture, information on subsidies (as defined in section 702(h)(2) of the TAA) being provided either directly or indirectly on articles of quota cheese. The appendix to this notice lists the country, the subsidy program or programs, and the gross and net amount of each subsidy on which information is currently available.

The Department will incorporate additional programs which are found to constitute subsidies, and additional information on the subsidy programs listed, as the information is developed.

The Department encourages any person having information on foreign government subsidy programs which benefit articles of quota cheese to submit such information in writing to the Deputy Assistant Secretary for Import Administration, U.S. Department of Commerce, 14th Street and Constitution Avenue, NW., Washington, D.C. 20230.

This determination and notice are in accordance with section 702(a) of the TAA (19 U.S.C. 1202 note).

Alan F. Holmer,

Deputy Assistant Secretary for Import Administration.

Appendix

QUOTA CHEESE SUBSIDY PROGRAMS

Couuntry and program(s)	Gross [1] subsidy (per pound)	Net [2] subsidy (per pound)
Belgium: European Community (EC) restitution payments	0.0¢	0.0¢
Canada: Export assistance on certain types of cheese	26.5¢	26.5¢
Denmark: EC restitution payments	0.2¢	0.2¢
Finland:		
Export subsidy	33.7¢	33.7¢
Indirect subsidies	14.5¢	14.5¢
Total	48.2¢	48.2¢
France: EC restitution payments	0.9¢	0.9¢
Ireland: EC restitution payments	.0¢	.0¢
Italy: EC restitution payments	13.9¢	13.9¢
Luxembourg: EC restitution payments	.0¢	.0¢
Netherlands: EC restitution payments	.0¢	.0¢
Norway:		
Indirect (milk) subsidy	13.8¢	13.8¢
Consumer subsidy	30.6¢	30.6¢
Total	44.4¢	44.4¢
Switzerland: Deficiency payments	57.9¢	57.9¢
U.K.: EC restitution payments	.0¢	.0¢
W. Germany: EC restitution payments	.0¢	.0¢

[1] Defined in 19 U.S.C. 1677(5).
[2] Defined in 19 U.S.C. 1677(6).

[Fr Doc. 85-1079 Filed 1-14-85; 8:45 am]

BILLING CODE 3510-05-M

Minority Business Development Agency

Financial Assistance Application Announcement; Texas

AGENCY: Minority Business Development Agency, Commerce.

ACTION: Notice—Project No.: 06-10-85007-01.

SUMMARY: The Minority Business Development Agency (MBDA) announces that it is soliciting competitive applications unders its Minority Business Development Center

(MBDC) Program to operate an MBDC for a 3-year period, subject to available funds. The cost of performance for the first eight *(8) months* is estimated at *$394,785* for the project performance of *05-1-85 to 12-31-85*. The MBDC will operate in the *Dallas, Texas Metropolitan Statistical Area (MSA), and the Waco, Texas Metropolitan Statistical Area*. The first year cost for the MBDC will consist of *$335,567* in Federal funds and a minimum of *$59,218* in non-Federal funds (which can be a combination of cash, in-kind contribution and fees for services).

The funding instrument for the MBDC will be a cooperative agreement and competition is open to individuals, nonprofit and for-profit organizations, local and state governments, American Indian tribes and educational institutions.

The MBDC will provide management and technical assistance to eligible clients for the establishment and operation of businesses. The MBDC program is designed to assist those minority businesses that have the highest potential for success. In order to accomplish this, MBDA supports MBDC programs that can: coordinate and broker public and private sector resources on behalf of minority individuals and firms; offer them a full range of management and technical assistance; and serve as a conduit of information and assistance regarding minority business.

Applications will be judged on the experience and capability of the firm and its staff in addressing the needs of minority business individuals and organizations; the resources available to the firm in providing management and technical assistance; the firm's proposed approach to performing the work requirements included in the application; and the firm's estimated cost for providing such assistance. It is advisable that applicants have an existing office in the geographic region for which they are applying.

The MBDC will operate for a 3-year period with periodic reviews culminating in annual evaluations to determine if funding for the project should continue. Continued funding will be at the discretion of MDBA based on such factors as an MBDC's satisfactory performance, the availability of funds, and Agency priorities.

DATE: Clsoing Date: The closing date for aplication is 2/11/85. Applications must be postmarked on or before February 11, 1985.

ADDRESS: MBDA Dallas Regional Office, 1100 Commerce Street, Suite 7B23, Dallas, Texas 75242-0790.

FOR FURTHER INFORMATION CONTACT: Irene Campos, Dallas Regional Office, 1100 Commerce Street, Suite 7B23, Dallas, Texas 75242-0790, 214/767-8001.

SUPPLEMENTARY INFORMATION: Questions concerning the preceding information, copies of application kits and applicable regulations can be obtained at the above address.

11.800 Minority Business Development (Catalog of Federal Domestic Assistance)

Melda Cabrera,

Acting Regional Director, MBDA Dallas Regional Office.

December 20, 1984.

[FR Doc. 85-1135 Filed 1-14-85; 8:45 am]

BILLING CODE 3510-21-M

DEPARTMENT OF EDUCATION

Office of Postsecondary Education

National Direct Student Loan Program

AGENCY: Department of Education.

ACTION: Notice of closing date for filing report of defaulted loans for the period ending December 31, 1984 (Form E40-1P; formerly ED Form 574).

The Secretary gives notice of the deadline for filing the National Direct Student Loan (NDSL) Program Report of Defaulted Loans for the period ending December 31, 1984 (Form E40-1P; formerly ED Form 574) (Report). The Secretary takes this action under section 463(a)(4) of the Higher Education Act of 1965, as amended (20 U.S.C. 1087cc(a)(4)) which provides that an institution participating in the NDSL Program must report to the Secretary at least semi-annually the total number of loans it made under the NDSL Program that are in default. Those loans that are in default but have already been assigned to and accepted by the Department of Education are not to be included in this Report. An institution must file this Report if it is participating in the National Direct Student Loan Program, regardless of whether it is currently making loans under the Program. An institution must submit the Report and one copy of the Report. (OMB Number 1849-0129).

Closing Date: The Report must be mailed or hand-delivered by February 15, 1985.

Reports delivered by mail: The Report sent by mail must be addressed to the Department of Education, Office of Student Financial Assistance, Campus Based Programs Branch, DPO, 400 Maryland Avenue, SW., Washington, D.C. 20202.

An institution must show proof of mailing its Report. Proof of mailing consists of one of the following: (1) A legible mail receipt with the date of mailing stamped by the U.S. Postal Service, (2) a legibly dated U.S. Postal Service postmark, or (3) any other proof of mailing acceptable to the Secretary of Education.

If the Report is sent through the U.S. Postal Service, the Secretary does not accept either of the following as proof of mailing: (1) A private metered postmark, or (2) a mail receipt that is not dated by the U.S. Postal Service. An institution should note that the U.S. Postal Service does not uniformly provide a dated postmark. Before relying on this method, an institution should check with its local post office. An institution is encouraged to use certified or at least first-class mail.

Reports delivered by hand: A Report that is hand delivered must be taken to the Department of Education, Office of Student Financial Assistance, Division of Program Operations, Campus-Based Programs Branch, 7th and D Streets, SW., Room 4613, Regional Office Building 3, Washington, D.C. The Campus-Based Programs Branch will accept hand-delivered Reports between 8:00 a.m. and 4:30 p.m. daily (Washington, D.C. time), except Saturdays, Sundays and Federal holidays. A Report that is hand-delivered will not be accepted after 4:30 p.m. on the closing date.

FOR FURTHER INFORMATION CONTACT: Program Services Section, Division of Program Operations (202) 245-2991.

(20 U.S.C. 1087cc(a)(4))

(Catalog of Federal Domestic Assistance No. 84.038, National Direct Student Loan Program)

Dated: January 11, 1985.

Sven Groennings,

Acting Assistant Secretary for Postsecondary Education.

[FR Doc. 85-1231 Filed 1-14-85; 8:45 am]

BILLING CODE 4000-01-M

DEPARTMENT OF ENERGY

Office of the Secretary

Spent Fuel and Nuclear Waste Transportation Business Planning; Meeting

AGENCY: Office of Civilian Radioactive Waste Mangement, DOE.

ACTION: Notice of a Workshop to Assist in the Development of a Transportation Business Plan in Support of Shipping

Under the Nuclear Waste Policy Act of 1982.

SUMMARY: The Office of Civilian Radioactive Waste Management (OCRWM), U.S. Department of Energy, is developing a Transportation Business Plan related to responsibilities assigned by the Nuclear Waste Policy Act of 1982 (NWPA). The document will provide information on the plans and strategies for the development and operations of the projected system to transport spent fuel or high-level waste as authorized by the NWPA. As a framework for strategy decisions that will appear in the Business Plan, a *Transportation Business Plan: Strategy Options Document* was released for public comment in December 1984.

This notice is to announce a workshop to assist in the development of the strategies to be included in the Transportation Business Plan. The previously issued Strategy Options Document will serve as a basis for discussion.

This workshop, which is one of a series of meetings to address transportation-related concerns, will only cover business issues related to cask development, fleet procurement, and related service requirements for transporting spent fuel and high-level waste from civilian nuclear powerplants to repositories or storage facilities. Broader institutional issues related to the transport of these materials will not be considered in this particular forum. Representatives from industrial transportation equipment and service suppliers and other affected commercial entities are encouraged to attend. However, since the format of the meeting is one of small working groups to discuss business strategies, attendance by a company should be limited to key personnel.

The meeting will be held in Albuquerque, New Mexico, on February 19–21, 1985. Additional information, including a registration form, may be obtained from Kenneth Golliher, U.S. Department of Energy, Albuquerque Operations Office, P.O. Box 5400, Albuquerque, New Mexico 87115, (505) 846–2334.

Issued in Washington, D.C., January 8, 1985.

Robert H. Bauer,

Associate Director for Resource Management, Office of Civilian Radioactive Waste Management.

[FR Doc. 85–1175 Filed 1–14–85; 8:45 am]

BILLING CODE 6450–01–M

Office of Assistant Secretary for International Affairs and Energy Emergencies

International Atomic Energy Agreements; European Atomic Energy Community; Proposed Subsequent Arrangements

Pursuant to section 131 of the Atomic Energy Act of 1954, as amended (42 U.S.C. 2160) notice is hereby given of proposed "subsequent arrangements" under the Additional Agreement for Cooperation Between the Government of the United States of America and the European Atomic Energy Community (EURATOM) Concerning Peaceful Uses of Atomic Energy, as amended, and the Agreements for Cooperation Concerning Civil Uses of Atomic Energy, as amended, Between the Government of the United States of America and the Governments of Canada and Japan.

The subsequent arrangements to be carried out under the above mentioned agreements involve approval of the following sales: Contract Number S–EU–828, with Gesellschaft fur Schwerionenforschungh mbh, Darmstadt, West Germany, 0.02 grams of plutonium–244, for use as standard reference material.

Contract Number S–CA–367, with Atomic Energy of Canada, Ltd., 42.387 grams of natural uranium, for use as standard reference material.

Contract Number S–JA–352, with Marubeni Corp., Tokyo, Japan, 6.001 grams of plutonium–239, and 0.0098 grams of uranium–235, for use as standard reference materials.

In accordance with section 131 of the Atomic Act of 1954, as amended, it has been determined that these subsequent arrangements will not be inimical to the common defense and security.

These subsequent arrangements will take effect no sooner than fifteen days after the date of publication of this notice.

For the Department of Energy.

Dated: January 9, 1985.

George J. Bradley, Jr.,

Deputy Assistant Secretary for International Affairs.

[FR Doc. 85–1086 Filed 1–14–85; 8:45 am]

BILLING CODE 6450–01–M

International Atomic Energy Agreement; Hungary; 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" under general license issued by the U.S. Nuclear Regulatory Commission.

The subsequent arrangement to be carried out under the above authority involves approval for the following sale:

Contract S–IA–136, 0.0996 grams of uranium, enriched to 99.8195% in U-235, for use as standard reference material by the Institute of Isotopes, Hungarian Academy of Sciences, Budapest, Hungary.

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.

For the Department of Energy.

Dated: January 9, 1985.

George J. Bradley, Jr.,

Deputy Assistant Secretary, for International Affairs.

[FR Doc. 85–1085 Filed 1–14–85; 8:45 am]

BILLING CODE 6450–01–M

International Atomic Energy Agreements; Mexico; 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" under general license issued by the U.S. Nuclear Regulatory Commission.

The subsequent arrangement to be carried out under the above mentioned authority involves approval of the following sale: Contract Number S–IA–135, to the Institute Nacional de Investigaciones Nucleares, Mexico, 300.71 grams of natural uranium, for use as standard reference material.

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.

For the Department of Energy.

Dated: January 9, 1985.

George J. Bradley, Jr.,

Deputy Assistant Secretary, for International Affairs.

[FR Doc. 85–1087 Filed 1–14–85; 8:45 am]

BILLING CODE 6450–01–M

Office of Hearings and Appeals

Implementation of Special Refund Procedures

Correction

In FR Doc. 84-29329 beginning on page 44541 in the issue of Wednesday, November 7, 1984, make the following correction on page 44543: In the middle column of text, the last line, "not" should read "now".

BILLING CODE 1505-01-M

Energy Information Administration

Industrial Emissions of Sulfur and Nitrogen Oxides; Extension of Comment Period on Survey Design

AGENCY: Office of Energy Markets and End Use, Energy Information Administration, DOE.

ACTION: Notice of extension of comment period.

SUMMARY: The Energy Information Administration (EIA) issued a notice which appeared in the December 17, 1984, issue of the **Federal Register** (49 FR 48960, December 17, 1984). The notice solicited comments on the design of a survey to gather information for research purposes from industrial sources of emissions of sulfur and nitrogen oxides. A 30-day comment period was specified for receipt of comments. This notice extends the due date for receipt of comments from January 16, 1985 to January 31, 1985.

DATE: Comments should be submitted by January 31, 1985.

ADDRESS: Comments should be submitted in writing to: Ms. Loretta Beaumont, Office of Energy Markets and End Use, EI-652, Room 1F-093, Energy Information Administration, 1000 Independence Avenue, SW., Washington, D.C. 20585.

FOR FURTHER INFORMATION CONTACT: Loretta Beaumont, (202) 252-1129.

Issued in Washington, D.C., January 10, 1985.

Dr. H. A. Merklein,

Administrator, Energy Information Administration.

[FR Doc. 85-1232 Filed 1-14-85; 8:45 am]

BILLING CODE 6450-01-M

ENVIRONMENTAL PROTECTION AGENCY

Science Advisory Board

[SAB-FRL-2757-1]

Environmental Engineering Committee; Open Meeting

Under Pub. L. 92-463, notice is hereby given that a two-day meeting of the Waste Banning Subcommittee of the Environmental Engineering Committee (EEC) of the Science Advisory Board will be held in Conference Room 3906/3908, Waterside Mall, U.S. Environmental Protection Agency, 401 "M" Street SW., Washington, D.C. on January 31 and February 1, 1985. The meeting will begin at 9:00 a.m. each day and last until approximately 5:00 p.m. on January 31, and until 12:00 noon on February 1.

The purpose of the meeting is to continue review of Agency criteria for determining which wastes should be restricted from land disposal. The meeting is open to the public. Any member of the public wishing to participate or obtain further information about the meeting should contact Harry C. Torno, Executive Secretary, at (202) 382-2552, or Terry F. Yosie, Staff Director, Science Advisory Board, at (202) 382-4126. Public comment will be accepted at the meeting. Written comments will be accepted in any form, and there will be opportunity for brief oral statements. Anyone wishing to make such comments must contact Mr. Torno prior to January 28, 1985 in order to be placed on the agenda.

In order to minimize any inconvenience due to EPA visitor control procedures, persons wishing to attend the meeting are requested to call Mrs. Brenda Browne at (202) 382-2552, so that they may be included on a roster that will be prepared for the building security guards.

Dated: January 9, 1985.

Terry F. Yosie,

Director, Science Advisory Board.

[FR Doc. 85-1088 Filed 1-4-85; 8:45 am]

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FEDERAL COMMUNICATIONS COMMISSION

[Gen Docket 84-467; FCC 84-644]

Preparation for an International Telecommunication Union Region 2 Administrative Radio Conference for the Planning of Broadcasting in the 1605-1705 kHz Band, Second Notice of Inquiry

Adopted: December 20, 1984.
Released: January 9, 1985.

By the Commission.

Purpose

1. The Commission is issuing this *Second Notice of Inquiry* as a means to inform the public and to obtain comments of interested parties on the FCC recommended United States Preliminary Views for the first session of the Regional Administrative Radio Conference (RARC) to establish a plan for the broadcasting service in the band 1605-1705 kHz in Region 2.[1] Those FCC recommended Preliminary Views for the first session of that RARC are attached as Appendix 1. They have been developed in response to the earlier notice in this proceeding. We emphasize that these FCC recommended Preliminary Views are of an iterative nature; they will be modified during this proceeding, evolving into the FCC recommended proposals for the conference to be submitted to the Department of State for forwarding to the RARC first session.

Background

2. The International Telecommunication Union (ITU) Regional Administrative Radio Conference (RARC) will be held to establish a plan for the broadcasting service in the 1605-1705 kHz band in the Western Hempishere. The RARC first session, April 14-May 2, 1986, will develop the technical criteria and planning method or methods for submission to the second session in the third quarter of 1988. The second session will develop the plan for broadcasting use of the 1605-1705 kHz spectrum

[1] These Preliminary Views, developed by the FCC, set out initial proposals in those areas where consensus has been reached. In other areas, they merely explain the issue in an attempt to further narrow the consideration process. We will use these Preliminary Views at forthcoming international meetings as a means to evoke comment and reaction. See paragraph 5 herein.

based on that earlier submission. The Agenda for that RARC first session was shown in Appendix 1 to our *First Notice*. This expanded Am broadcasting band is essentially an outgrowth of the United States proposals to the 1979 World Administrative Radio Conference. By recent Commission action, our domestic frequency allocations table now provides for AM broadcasting within 1615–1705 kHz, subject to the results of the plan to be developed by the 1986/1988 RARC.[2] Implementation of AM broadcasting in the 1605–1705 kHz band in the Western Hemisphere, however, is dependent upon the results of the plan to be developed for this band by the Region 2 Administrative Radio Conference.

Background

3. On May 10, 1984, the Commission adopted a *First Notice of Inquiry (Notice)* concerning the above entitled proceeding.[3] It was released on May 16, 1984. The dates for filing comments and reply comments were established as June 29, 1984, and July 30, 1984, respectively.[4]

4. In that *Notice* we discussed several of the issues that need to be explored as part of our preparatory process, such as international activities leading up to the first session, and United States and international use of the 1605–1705 kHz band. We also pin-pointed a number of specific issues that must be addressed in order to develop a set of United States proposals to go forward to the ITU conference. These include the satisfaction of broadcasting requirements, determining the power limits and classes of stations, determining protection requirements, developing ground-wave and sky-wave propagation curves that will best meet those needs, and how to bring AM broadcasting into fruition in the band.

Development of Proposals

5. Based on the comments and reply comments received in response to our *First Notice*, and in coordination with the Executive Branch agencies, we have developed the recommended Preliminary Views attached hereto as Appendix 1.[5] We expect to use these Preliminary Views in any bilateral or multilateral international discussions that may be held in the next few months. Using information obtained at those meetings, as well as comments to this *Second Notice*, we expect to refine our recommended proposals and seek comments on them in a subsequent notice of inquiry sometime in early to mid-1985. We further expect to adopt the recommended United States Proposals in late 1985 or early 1986 for transmission to the Department of State as the United States Proposals for the first session of the RARC.

Preliminary Views Presentation

6. The recommended United States Preliminary Views, Appendix 1, set out, in a few areas, initial proposals and associated rationale. In other areas, only the issues and a discussion of possible alternatives are given. We request comments on those Preliminary Views and also on the discussion that follows.

I. Broadcasting Requirements

7. One of the key issues identified in the *First Notice* was that of developing the United States broadcasting requirements. There was a consensus in the comments received that there is in fact a need to develop a requirements list along the lines of the list that was prepared for the Region 2 Conference in Rio de Janeiro.[6] Commenting parties cautioned, however, that the list prepared for the Rio Conference needs to be updated because several recent Commission actions have caused some of the requirements contained in the list to change.[7] We agree with these recommendations, and believe that the types of broadcasting needs that formed the basis for the development of the list remain valid, and that preparation of an updated list of requirements will assist the FCC in making decisions related to recommendations for the United States Proposals to the RARC.[8] This is the approach we intend to follow.

8. As was noted in the *First Notice*, the Advisory Committee on Radio Broadcasting played an important role in assisting the FCC in developing the earlier requirements list. We believe that this is again an appropriate issue for the advisory Committee on Radio Broadcasting to address. As noted elsewhere in this *Notice*, this Advisory Committee can greatly assist the Commission in its conference preparations. We have recommended to GSA that the charter of the Committee be modified to specifically include preparatory activities for the RARC. It is intended that the Allocations Subgroup of that Advisory Committee be continued in order to address issues such as updating the requirements list.

II. Planning Methods and Guidelines for the Agreement

9. In the *First Notice* we raised the issue of the types of categories of service that should be provided in the expanded band as well as the interference protection levels that should be provided. A review of the comments filed in response shows that there are somewhat differing views regarding the best use of the expanded AM broadcasting band. The Progressive Broadcasting Corporation proposed to set aside certain channels in the expanded band for different classes of stations. The National Radio Broadcasters Association believed that the expanded band should be used to satisfy the incompatibilities resulting from the Rio plan.[9] The Corporation for Public Broadcasting recommended that a number of channels should be set aside for non-commercial public educational broadcast service in those areas where there is no such service or where additional channels are needed. The Great Southern Broadcasting Company, Incorporated, indicated that only Class IV should be used.[10] The

[2] *Second Report and Order*, General Docket No. 80–739, FCC 83–511, 49 F.R. 2358.

[3] FCC 84–195, 49 F.R. 21419.

[4] On June 26, 1984, a *Petition for Extension of Time Within Which to File Comments* was submitted by John A. Landin, President, on behalf of the Association of Federal Communications Consulting Engineers (AFCCE). This *Petition* indicated that additional time was necessary to develop comments on several of the technical issues raised in the *Notice*. An *Order*, (FCC 5199) was released by the Chief Scientist on July 3, 1984, denying that petition, primarily because of the need to meet deadlines with respect to the submission dates of proposals to the ITU and exchange of proposals among administrations, and because we would continue the examination of issues in further notices of inquiry. AFCCE was urged to pursue its studies and to submit its findings in response to further *Notices of Inquiry* in this proceedings.

[5] Para. 25. of the *Notice, supra.*, at,[3] indicated that the Interdepartment Radio Advisory Committee has established a special sub-committee, Ad Hoc 193, to prepare for this conference. It is an inter-agency committee providing advice to the Department of Commerce's National Telecommunication and Information Administration. The public has no direct access to the activities of this ad hoc sub-committee. The FCC staff, however, represents the non-government interests in this forum.

[6] Three parties responded to the issue of using the existing requirements list. All three, the Corporation for Public Broadcasting, the National Association of Broadcasters, and the National Black Media Coalition, indicated that the list should be used but that it requires revision.

[7] For example, MM Docket 84–231, *Notice of Proposed Rule Making*, FCC 84–66, 49 FR 11214, which began the implementation of the new FM policies developed in BC Docket No. 80–90. Docket 84–231 listed 684 communities as proposed locations for new FM channel assignments.

[8] As we indicated in Paragraph 17 in the *First Notice*, that list contained a total of some 3,000 communities which lacked local aural service, had one or more AM stations that could operate only during daytime hours, or for which an interest for minority or public radio service has been indicated. In Docket 84–231 above, at paragraph 5, we indicated that approximately 1400 communities had been identified from this list for consideration in the FM omnibus proceeding.

[9] The Rio Plan has two separate lists: (1) List A includes the assignments whose caused and received interference are accepted; and (2) List B includes the assignments whose caused and recieved interference are *not* accepted. It is this second category of stations that are referred to as the "incompatibilities" resulting from the Rio Plan.

[10] Class IV is a station operating on a local channel designed to render service primarily to a

Continued

National Association of Broadcasters opposed Class IV, and indicated that the channels should be used by foreign stations to resolve incompatibilities resulting from the Rio Plan. The engineering firm of du Treil-Rackley indicated that Class IV should be used with extended hours of operation, proposing that this be a new Class V. By this approach, it would also permit one or more Class IB stations.[11] The National Black Media Coalition indicated an idea of Class IV for new service to smaller towns, and Class III for competitive larger areas, and also the establishment of a new class somewhat comparable to the existing Class IV.[12] Ronald F. Schatz in his reply comments opposed use of a new Class V and Class IB as suggested by du Treil-Rackley. To meet these varied needs it seems that particular attention should be given to maintaining the maximum degree of flexibility in any plan to be developed. This, or course, would have to be consistent with the need to satisfy the United States broadcasting requirements and to obtain adequate protection for such use.

10. To achieve this flexibility principle in the plan, we must first decide on the type of planning that should be used. Possibilities include the adoption of an allotment plan, an assignment plan, or one using features of both.[13] For the purpose of this initial discussion, the essential difference between these two forms of plans lies in the specification of the location of the station. In an allotment plan, an area can be specified within which the station may be located and afforded protection. In an assignment plan, a specific transmitter site is given for each station in the plan. From a regulatory point of view, changing the site of a station in an assignment plan requires a modification of the plan. In an allotment plan, implementing a station within a given allotment area would not require any prior modification of the plan as long as the agreed protection is provided to all of the other allotments appearing in the plan. Comments are requested on the best planning method for satisfying U.S. broadcasting requirements.

11. After the form of the plan is decided, the planning method must be developed. Since the primary goals of planning that will be developed by the first session will be to accommodate the broadcasting requirements of Region 2 administrations and obtain international recognition for stations implemented in accordance with the interference protection provided by the plan, the planning method will have to be tailored to the form of the plan, either utilizing the allotment or assignment method or some combination of both. These two cases are discussed below and further amplified in Appendix 2.

A. *Allotment plannning.* 12. The successive stages of allotment planning would be to: (1) Develop a list of allotments based upon the general requirements of administrations: (2) determine the conformity of the allotments with the agreed interference objectives of the conference: and (3) adopt an adjusted list of allotments that has been accepted by all—the plan. Associated closely with such an allotment plan would be a set of implementation criteria, which would define the regulatory and administrative conditions to be met and the steps to be taken in bringing into use stations in conformity with the plan. These conditions would specify a simple way to detemine whether a station would exceed the interference levels accepted by the conference. If the agreed interference levels are exceeded, the allotment plan would have to be modified in accordance with the procedures adopted by the conference. Specific methods will need to be developed to facilitate the several stages of allotment planning. For example, it might be possible to bring into use one or more stations within the allotment area without modifying the plan as long as the agreed protection level to the allotments of other countries was not exceeded. In contrast with the assignment planning case, emphasis would be on methods of distribution of radio frequency channel resources, and *not* the resolution of interference levels between specific stations. Any necessary resolution of such interference level incompatibilities between stations would take place in the plan modification stage after the conference, when specific station requirements by exact location become known and station assignments are made. This would simplify the procedures reducing the administrative burden. Resolution of incompatibilities would only be required if administrations exceeded the interference levels in the allotment plan. See Appendix 2 for further discussion.

B *Assignment Planning.* 13. The successive stages of assignment planning would be to: (1) Develop a list of stations based upon the specific requirements of administrations: (2) identify and resolve the resulting incompatibilities; and (3) adopt an adjusted list of station assignments that has been accepted by all—the plan. The interference levels specified within the plan form the basis for procedures for the subsequent modification of the plan. As a result of assignment planning, administrations obtain the right to bring into use specific stations listed in the plan. Bringing into use assignments differing from those specified in the plan would require modification of the plan. The precise conditions under which modificaitons could be made are to be negotiated at the conference; in past similar planning exercises within the ITU, however, the agreement of other countries has generally been required only if the interference levels accepted in the plan are exceeded by the difffering assignment. Specific methods will need to be developed to facilitate the different stages of assignment planning. Major emphasis would be on the resolution of incompatibilities between stations. See Appendix 2 for further discussion.

C. *Guidelines for the agreement.* 14. The dicision on the form of the plan will determine the appropriate nature of the associated regulatory procedures—the agreement. These procedures have been discussed above within the description of the planning methods.

III. Technical standards

15. In the *First Notice* we raised the question as to whether the 1605 kHz to 1705 kHz band should be treated as an expansion of the existing band or as a new band. Commenters clearly favored treating the 1605–1705 kHz band as an expansin of the existing band, principally because receivers that will be developed for the expanded band will be similar to existing receivers.

16. We agree that the 1605–1705 kHz band should be treated as an expansion of the existing AM Broadcasting band from 535–1605 kHz. We have developed the FCC recommended United States

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city or town and the suburban and rural areas contiguous thereto. The power level does not exceed 1 kW. This type of station is defined in the Rio Plan as Class C.

[11] Class I is a dominant station operating on a clear channel rendering primary and secondary service over an extended area and at relatively long distances. The power level does not exceed 50 kW. In the Rio Plan, this type of station is defined as a Class A station, except that the Rio Plan did not set aside specific channels for this type of service.

[12] Case III stations operate on regional channels designed to render service primarily to a principal center of population and the rural areas contiguous thereto. The power level does not exceed 5 kW. In the Rio Plan this type of station would be a Class B.

[13] In the ITU Radio Regulations, an allotment plan is defined as the designation of a frequency channel in an agreed plan, adopted by a competent conference, for use by one or more administrations for a radiocommunication service in one or more identified countries or geographic areas and under specified conditions. An assignment plan is defined as the designation of a radio *station* in an agreed plan to use a radio frequency or radio frequency channel under specified conditions.

Preliminary Views accordingly. Thus, we propose that protection ratios, class of emission, and bandwidth of emissions should remain the same. We believe that this would enhance the availability of receivers making this band available to the United States public in the most expeditious and least costly manner. Three primary technical issues, however, remain to be resolved. They are: (1) What power limits and station class or classes should be proposed for inclusion in the plan; (2) determining the ground wave curves that should be employed; and (3) determining a sky-wave prediction method to permit a most effective method of spectrum utilization. These issues are discussed in greater detail below.

A. *Power limits and station class.* 17. In response to the *First Notice*, a number of comments were received on this subject. As shown elsewhere in this *Notice*, the comments generally appeared to favor stations similiar to the present Class III and Class IV categories, which approximates Classes B and C in the Rio Plan. Only one comment was received that suggested that the expanded band be used to provide additional Class A (Class 1 domestically) stations. In addition, one comment strongly urged that the expanded band not be used for additional Class IV stations. Thus, the majority of the comments fell somewhere in between the extremes of high and low power stations. In order to facilitate the development of the United States techncial proposals to the confernece, as well as the development of a planning mechanism for the extended spectrum, it is necessary for the FCC to determine with greater specificity the types of stations, operating powers, and expected service for this expanded spectrum, so that the public needs can be met. Further comments are requested in this regard. Additionally, it is believed that the Advisory Committee on Radio Broadcasting will be able to develop recommendations on this subject to meet those needs.

18. In exploring this issue further, it is beneficial to consider some examples of the extent of service and interference that might be experienced by stations in this expanded band of frequencies. In the following example, it is assumed that the stations are operating with non-directional antennas and that there is a three-station lattice around the reference station. If the stations operate with quarter-wave antennas with a uniform ground conductivity of 6 millisiemens/metre (mS/m), then the following table indicates the approximate distance, in miles, to the daytime service and interfering contours. (These calculations were made using the ground-wave curves computed for 1655 kHz, which are referred to elsewhere in this *Notice*.)

Power	Service contour distance (0.5 mV/m) (miles)	Interference contour distance (0.025 mV/m) (miles)	Separation distance between stations (miles)
100 W	14.2	55.9	70.1
250	17.68	66.7	84.38
500	20.13	77.0	97.13
1 kW	24.2	86.82	111.02
2.5	30.0	103.8	133.8
5	34.3	115.6	149.9
10	41.2	132.1	173.3
25	50.1	146.7	196.8
50	58.2	161.8	220.0

19. If these stations were permitted to operate with the same power day and night with the separation determined by the daytime 0.5 mV/m and 0.025 mV/m service and interfering groundwave contours, respectively, the nighttime minimum usable field strength of the subject station, calaculated by the root sum square (RSS) method, as described in Annex 2, Chapter 4 of the Rio Final Acts, would be as follows (sky-wave field factors were obtained from Annex 2, Chapter 3 of the Rio Final Acts):

Power	Night minimum usable field strength (mV/m)	Distance to the contour from the station transmitter (miles)
100	7.23	3.6
250	10.7	3.9
500	14.2	4.0
1 kW	19.4	4.1
2.5	29.5	4.3
5	38.7	4.4
10	52.0	4.5
25	78.0	4.6
50	103.9	4.8

20. As is evident from the above, the extent of the nighttime service for a station on this frequency is relatively small. If a decision were to be made that the reference station must be protected to its 10 mV/m nighttime contour, through use of directional antennas, etc., the extent of service for the reference station would be as follows:

Power	Distance to the contour from the station transmitter, (miles)
100 W	3.0
250	4.0
500	4.9
1 kW	5.9
2.5	7.6
5	8.9
10	10.5
25	13.0
50	14.7

21. Under these propagation conditions, the additional service that may be obtained in the expanded band is not as great as might be anticipated. At lower conductivities, the service will be even less. The above illustrates that even utilizing different power levels associated with the various classes does not change the service areas significantly.

22. Consideration of the above information results in several questions upon which comments are requested:

1. What would be the advantage or disadvantage of using the entire expanded spectrum for a single class of stations?

2. If more than one class of station should be permitted in the expanded spectrum, should the classes of station be intermixed on the same channels, or should the channels be subdivided by class?

3. What power levels and protection standards should be applied for these classes of stations during daytime hours? Similarly, what power levels and protection standards should be applied during nighttime hours?

4. To what degree do the United States broadcasting requirements to be identified in this proceeding affect the choice of power levels and other technical standards, including the use of more than one class of station?

B. *Ground-wave propagation.* 23. The basis for the FCC ground-wave propagation curves is set forth in § 73.184 of the FCC Rules and Regulations. These curves for the 535 to 1605 kHz band have been in use for many decades. During these years, many thousands of field strength measurements have been made in this band by consulting engineers and analyzed through application of the FCC curves. This extensive experience has shown that, except where some drafting errors had occurred in the preparation of the ground-wave curves, correlation between the curves and measured data is good.

24. In our preparations for the Region 2 Conference on AM broadcasting in the 535–1605 kHz, band, Buenos Aires, 1980, and Rio de Janeiro 1981, the FCC recomputed the ground-wave curves using the same basis as the original FCC curves and replotted them by computer

in metric format. The correlation between the new metric curves and the original FCC curves was good, and previous drafting errors were eliminated. Those differences that did occur were essentially the result of greater accuracy possible today in performing calculations through use of a digital computer. These metric curves were formally adopted at Rio de Janeiro and equivalent curves have been incorporated in the new United States-Canadian AM Broadcasting Agreement. Additionally, the Commission has proposed in MM Docket No. 84–752 to adopt equivalent curves in the FCC Rules and Regulations.[14]

25. The FCC is of the preliminary view that the basis used for calculating the curves for the 535 to 1605 kHz band is also applicable in the extended spectrum from 1605 to 1705 kHz. Calculations have been performed for a new family of ground-wave curves for use in the extended spectrum. The curves were calculated for a center frequency of 1655 kHz using a dielectric constant of 15, which is typically used in computing the land path. The calculated points for these curves are attached to this *Notice* as Appendix 3 and comments are invited on their application to the extended band.[15]

C. *Sky-wave propagation.* 26. Sky-wave propagation is also a very important aspect of our preparatory work for the forthcoming RARC. It is more important today than it was in 1980–81 for a number of reasons: (1) The expanded band is to be shared by different services in different regions of the world. Inter-regional inter-service interference will be an important consideration in the planning process; (2) Sky-wave propagation at MF is now much better understood than in 1980; (3) A more accurate and realistic sky-wave field strength prediction method may be the single most viable and promising approach to achieve the most efficient use of the spectrum; and (4) Intra-regional sharing between broadcasting and other permitted services, e.g., fixed and mobile, will also require a good skywave prediction model.

27. At this stage, there appear to be three issues concerning sky-wave propagation. They are:

A. *Prediction Method:* Undoubtedly, some administrations will prefer the extension of the current method for Region 2 to cover the expanded band. Admittedly, the current method can be extended to cover the new band without introducing additional significant errors. However, more accurate and easy-to-use methods are available and are being further developed.[16] These should be carefully studied before the United States proposals are finalized.

B. *Diurnal Variation of Field Strengths:* In the 1980 Report (Buenos Aires), a single curve for all frequencies is given (Chapter 3, Figure 9, source: CCIR). After the 1980/81 RARC, the Commission initiated a rule-making proceeding (BC Docket 82–538) to allow pre-sunrise and post-sunset services by certain AM stations. This necessitated a study of diurnal variation. FCC, with support from the Advisory Committee on Radio Broadcasting, developed a set of improved curves and formulas to quantify this highly frequency-dependent phenomenon.[17] The new FCC diurnal variation curves were later endorsed by the Communication Research Center of Canada and became part of the new United States-Canadian AM Broadcasting Agreement. The Commission also adopted these curves in September 1983.[18] There are two questions that have to be answered: (1) Do we need to address diurnal variation in the United States proposal at all? This depends on how we propose to use the expanded band (e.g. class of station); and (2) If the answer is yes, shall we, for the purpose of simplicity, propose a single curve calculated for the center of the expanded band, e.g. 1655 kHz, or treat each channel separately?

C. *Field Strengths of Short Paths:* The sky-wave curves in Part 73 of the FCC Rules and Regulations stops at 100 miles. Occasionally there is a need to calculate field strengths for shorter paths. A standardized procedure may be desirable.

IV. Regional Sharing

A. *Intra-regional sharing.* 28. In the *First Notice* we addressed the issue of sharing the 1605–1705 kHz band between the services allocated by the 1979 WARC. Recommendation No. 504 from that WARC recommended that a Region 2 conference be convened to plan the broadcasting service in the 1605–1625 kHz and 1625–1705 kHz bands. It also recommended that the CCIR develop intra-regional sharing criteria between the broadcasting service and other services allocated in the band. The 1979 WARC adopted a primary broadcasting allocation in both bands for Region 2. The WARC also provided a primary allocation for the fixed, mobile, and aeronautical radionavigation services, and a secondary allocation to the radiolocation service, until a date that is to be decided by this 1986/1988 regional administrative radio conference. After that time, the 1605–1625 kHz band will be allocated on an exclusive basis to the broadcasting service, and the 1625–1705 kHz band will be allocated on a primary basis to the broadcasting service, in a permitted basis to the fixed and mobile services, and on a secondary basis to the radiolocation service. Recognizing the provisions of No. 419 of the International Radio Regulations, which states that permitted and primary services have equal rights, except that primary services will have prior choice of frequencies in the preparation of frequency plans, we have initially examined sharing criteria that might be necessary among these services in order to develop a meaningful broadcasting plan. Specifically, we are concerned with what protection criteria should be applied by the permitted services to protect the broadcasting service after the plan has been established, as well as the protection criteria to be applied by the broadcasting service to protect the permitted services when the plan is modified.

29. After reviewing existing reports that address sharing in this band, however, it does not appear that any sharing of the 1605–1705 kHz band can be accomplished without requiring excessive restrictions on the broadcasting service. Therefore, we are proposing in our FCC recommended Preliminary Views that the permitted services within 1625–1705 kHz not be assigned frequencies in the band until it is demonstrated that they can share this spectrum without placing excessive restrictions on the broadcasting service. Comments are invited.

B. *Inter-regional sharing.* 30. In our FCC recommended Preliminary Views, we have proposed Recommendation A, which, while a first draft, outlines the situation regarding inter-regional sharing. The Recommendation promotes cooperation so that the different regional services can continue to operate without causing harmful interference. It leaves resolution of the matter open, however, and should receive further consideration and

[14] FCC 84–372, adopted July 21, 1984.

[15] There are two other models widely used for calculating ground-wave propagation. These are the model described in CCIR Report 714 and a model used by ITS in Boulder, Colorado. There has been no systematic investigation, however, of any differences between these models and the FCC model, or of the effects of spectrum planning resulting from any possible differences.

[16] Paper presented by J. H. Wang, FCC, at IEEE LATINCOM 84, Mexico City, Mexico, July, 1984, "Skywave Propagation Considerations Related to the 1605–1705 kHz Broadcasting Conference."

[17] FCC Technical Memorandum, OST 83–4, June, 1983.

[18] 48 FR 133, September 20, 1983.

evaluation nationally and internationally. Comments are invited.

V. Existing Domestic Users

31. In the *First Notice*, we pointed out that there are a number of existing domestic users in the 1605–1705 kHz band. The Commission has, however, adopted policies for reaccommodation of existing users in the Radiolocation, and Alaska Fixed and Maritime Services.[19] Cordless telephones that utilize frequencies in this band are not to be manufactured after October 1, 1984.[20] The 525–535 kHz and 1605–1615 kHz bands are currently allocated in the United States Table of Allocations as mobile service bands but are limited to distribution of public service information from Traveler's Information Stations (TIS) operating at 530 and 1610 kHz, respectively. Internationally, however, TIS is considered to be a broadcasting service.[21] TIS operations on 530 kHz are beyond the scope of this proceeding. As described below, however, consideration does need to be given to TIS operations at 1610 kHz in the expanded band.

32. Over 200 federal and non-federal government TIS installations have been authorized in the 1605–1615 kHz portion of the expanded band. The federal, state and local governments that operate such stations have indicated that they have increasing requirements for such services. They believe that at least two TIS channels (*viz*, 530 and 1610 kHz) are necessary because, in many of the areas where TIS service is desired, one of the channels is likely to be unavailable due to the authorized operation of a standard AM broadcast station on the adjacent channel. However, since AM broadcast stations are not required to protect TIS operations, this situation could affect both channels. In addition, consideration will need to be given to the additional impact new broadcast operations on 1610 kHz or elsehwere in the expanded band would have on TIS operations. Various alternatives to continuing TIS operations on 1610 kHz have been suggested in the comments and by government users. Some of these are currently under study by the Commission and the National Telecommunication and Information Administration. Because of the inter-relationship between TIS and the expanded band, the preparation of the United States proposals for the 1986/1988 Broadcasting RARC must necessarily take into account the mutual-impact between TIS and the future radio broadcasting services to be offered inthe 1605–1705 kHz expanded band as part of the overall evaluations. Consequently, we are soliciting further comments addressing the status of TIS operations on 1610 kHz within the context of this proceeding to assist the Commission in forming its input to the United States proposals. Any needed change in the TIS allocation would be made in a separate domestic proceeding.

Public Advisory Committee

33. Several parties commented favorably on the suggestion that the Advisory Committee on Radio Broadcasting be expanded to include preparations for the RARC. The Advisory Committee on Radio Broadcasting has provided invaluable assistance in the past for preparations for the Region 2 MF Conference, as well as subsequent bilateral negotiations. There are a number of significant areas in this instant proceeding in which we believe an advisory committee can greatly assist our efforts, including such items as the development of United States broadcasting requirements and method(s) of planning. To make this possible, the Commission believes it is appropriate to modify the Charter of the Advisory Committee on Radio Broadcasting to include preparations for the RARC and to establish a structure that will insure that the various communications issues, both broadcasting as well as nonbroadcasting, can be fully considered by the Committee. The Commission has done this in connection with the upcoming renewal of the Charter for the Advisory Committee on Radio Broadcasting.

Administrative Matters

34. Pursuant to sections 4(i) 303, and 403 of the Communications Act of 1934, as amended, it is ordered that this *Second Notice of Inquiry* is hereby *ADOPTED.*

35. Interested parties may file comments on or before February 6, 1985, and reply comments on or before March 6, 1985. Although § 1.419 of the Commission's Rules and Regulations requires that an original and five copies of all statements, briefs, or comments be filed in response to this *Inquiry*, ten additional copies would be useful. All relevant and timely comments and reply comments filed in this proceeding, as well as other pertinent information available to the Commission, will be considered. It should be recognized that the purpose of this proceeding is to invite comments to assist the FCC in recommending possible changes to the international Radio Regulations and development of multinational agreements it does not involve Commission Rules and Regulations, even though changes to our Rules may later occur through domestic rulemaking as a result of conference action.

36. Point of contact on this matter is Edward R. Jacobs, International Staff, Office of Science and Technology (202) 653–8102.

Federal Communications Commission.

William J. Tricarico,

Secretary.

Note.—Appendices 1, 2, and 3 (Subject matter mentioned below) will not be printed herein due to the Commission's ongoing effort to minimize publishing costs. However, copies of the complete Second Notice of Inquiry may be obtained from the International Transcription Service, 1918 M St., NW., Washington, D.C. 20036, Tel. (202) 296–7322. A copy is also available for public inspection in the FCC Dockets Branch, Rm. 239, and the FCC Library, Rm. 639, both located at 1919 M St., NW., Washington, D.C.

Appendix 1

FCC Recommended Preliminary Views of the United States of America for the First Session of the International Telecommunication Union Regional Administrative Radio Conference To Establish A Plan For the Broadcasting Service in the Band 1605–1705 kHz in Region 2; Geneva, April 14–May 2, 1986 (pp. 1–11);

Appendix 2

Additional Consideration for Allotment Planning and Assignment Planning (pp. 1–2); and

Appendix 3

Calculations for a New Family of Ground-Wave Curves Tentatively To Be Used for the Extended Band at 1605–1705 kHz (pp. 1–18).

[FR Doc. 85–1166 Filed 1–14–85; 8:45 am]

BILLING CODE 6712-01-M

[19] *Second Report and Order*, General Docket No. 80-739, *supra* at 2 (Radiolocation); See paragraph 11 *Notice*, and also *Notice of Proposed Rule Making*, PR docket No. 84–874, adopted September 5, 1984, as regards Radiolocation; *Report and Order*, PR Docket No. 83–464, adopted July 30, 1984 (Alaska Fixed/Maritime); as regards Industrial users which no longer have an allocation in the band, see *Report and Order*, General Docket No. 82–625, adopted June 29, 1983.

[20] *Report and Order*, General Docket No. 83–325, adopted December 22, 1983.

[21] *First Notice*, *supra* at 3.

Public Information Collection Requirements Submitted to Office of Management and Budget for Review

January 8, 1985.

The Federal Communications Commission has submitted the following information collection requirements to OMB for review and clearance under

the Paperwork Reduction Act of 1980, Pub. L. 96–511.

Copies of the submissions are available from Doris Peacock, Agency Clearance Officer, (202) 632–7513. Persons wishing to comment on these information collections should contact Marty Wagner, Office of Management and Budget, Room 3235 NEOB, Washington, D.C. 20503, (202) 395–4814.

OMB Number: 3060–0094
Title: Section 22.501(L)(10)(ii), Common Carrier Land Mobile Channel Loading Measurement
Action: Extension
Respondents: Businesses (including small businesses)
Estimated Annual Burden: 11 Respondent; 88 Hours

OMB Number: 3060–0119
Title: Section 90.145, Special Temporary Authority
Action: Extension
Respondents: Individuals or households, state or local governments, businesses (including small businesses), and non-profit institutions
Estimated Annual Burden: 6,000 Respondents; 3,000 Hours

OMB Number: 3060–0274
Title: Section 94.45, Modification of License
Action: Extension
Respondents: Individuals or households, state or local governments, businesses (including small businesses), and non-profit institutions
Estimated Annual Burden: 40 Respondents; 7 Hours

OMB Number: 3060–0282
Title: Section 94.17(d), Cooperative use of stations
Action: Extension
Respondents: State or local governments, business (including small businesses), and non-profit institutions
Estimated Annual Burden: 300 Recordkeepers; 225 Hours

OMB Number: 3060–0270
Title: Section 90.443, Content of Station Records
Action: Extension
Respondents: Individuals or households, state or local governments, businesses (including small businesses), and non-profit institutions
Estimated Annual Burden: 57,180 Recordkeepers; 4,765 Hours

William J. Tricarico,
Secretary, Federal Communications Commission.

[FR Doc. 85–1168 Filed 1–14–85; 8:45 am]
BILLING CODE 6712–01–M

Public Information Collection Requirements Submitted to Office of Management and Budget for Review

January 8, 1985.

The Federal Communications Commission has submitted the following information collection requirements to OMB for review and clearance under the Paperwork Reduction Act of 1980, Pub. L. 96–511.

Copies of these submissions are available from Doris R. Peacock, Agency Clearance Officer, (202) 632–7513. Persons wishing to comment on any information collection should contact Marty Wagner, Office of Management and Budget, Room 3235 NEOB, Washington, D.C. 20503, (202) 395–4814.

OMB No.: 3060–0108
Title: Emergency Broadcast System (EBS) Activation Report
Form No.: FCC 201
Action: Extension
Estimated Annual Burden: 350 Responses; 30 Hours.

OMB No.: 3060–0070
Title: Request for Waiver of Re-examination Waiting Period and Notification of Action
Form No.: FCC 757–B
Action: Extension
Estimated Annual Burden: 200 Responses; 17 Hours.

William J. Tricarico,
Secretary, Federal Communications Commission.

[FR Doc. 85–1169 Filed 1–14–85; 8:45 am]
BILLING CODE 6712–01–M

[Report No. DS–359]

Advisory Committee in Reduced Orbital Spacing; Meeting

January 8, 1985.

A meeting of the FCC Advisory Committee on Reduced Orbital Spacings will take place on January 22, 1985 as indicated below. The purpose of this advisory committee is to obtain expert technical and operational advice on how to better implement 2° spacings in the 4/6 GHz and 12/14 GHz bands.

Date: January 22, 1985.
Time: 9:30 AM.
Place: Room 856, Federal Communications Commission, 1919 M Street NW., Washington, D.C.

Agenda

1. Adoption of agenda.
2. Adoption of minutes from last meeting.
3. Report from nominating committee.
4. Installation of Advisory Committee officers.
5. Committee work plan.
6. Organization of working groups.
7. Other business.

This meeting is open to the public. For more information contact Roger Herbstritt at the FCC on (202) 634–1624.

William J. Tricarico,
Secretary, Federal Communications Commission.

[FR Doc. 85–1170 Filed 1–14–85; 8:45 am]
BILLING CODE 6712–01–M

FEDERAL MEDIATION AND CONCILIATION SERVICE

Labor-Management Cooperation Program; Application Solicitation

AGENCY: Federal Mediation and Conciliation Service.

ACTION: Final FY 1985 Program Announcement/Application Solicitation.

SUMMARY: The Federal Mediation and Conciliation Service (FMCS) published the draft Fiscal Year 1985 Application Solicitation for the Labor Management Cooperation Program in the November 29, 1984, issue (49 FR 46951) of the **Federal Register.** As no public comments were received, no changes have been made in this final version.

FOR FURTHER INFORMATION CONTACT: Peter L. Regner, Director, Labor-Management Grant Programs, FMCS, 2100 K Street, NW., Washington, D.C. 20427.

SUPPLEMENTARY INFORMATION:

Labor-Management Cooperation Program Application Solicitation—FY 1985

A. Introduction

The following is the final solicitation for the Fiscal Year 1985 cycle of the Labor-Management Cooperation Program. These guidelines represent the fifth year of efforts of the Federal Mediation and Conciliation Service to implement the provisions of the Labor-Management Cooperation Act of 1978 which was approved in October 1978.

The Act generally authorized FMCS to:

Provide assistance in the establishment and operation of plant, area, public sector, and industrywide 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 Act also prohibited FMCS from awarding any grants or contracts under the following three circumstances:

(1) No assistance can be given for plant labor-management committees unless the employees in that plant are represented by a labor organization and there is in effect at that plant a collective bargaining agreement;

(2) No assistance can be given for an area, public sector, or industrywide labor/management committee unless its participants include any labor organizations certified or recognized as the representative of the employees of an employer participating in such a committee. However, employers whose employees are not represented by a labor organization may participate on such area or industrywide committees; and

(3) No assistance can be given to any committee which FMCS finds to have as one of its purposes the discouragement of the exercise of rights contained in section 7 of the National Labor Relations Act (29 U.S.C. 157) or the interference with collective bargaining in any plant or industry.

With respect to item (2) above, applicants for area, public sector, or industrywide grants should offer committee memberships to every labor organization having a collective bargaining contract with any employer participating on the committee. Any labor organization so desiring may voluntarily elect not to participate on the Committee. Documentation of all this (i.e., the listing of each participating employer and corresponding labor organizations and written declinations by those labor organizations not electing to participate on the committee) should be included as part of the application.

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, areawide, industry, or public sector labor-management committee. Directions for obtaining an application kit may be found in Section H.

B. Program Description

Objectives

The Labor-Management Cooperation Act of 1978 identified 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 employers 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 plant, 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 and operation 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 and conform to the restrictions noted in Section A (Introduction). These committees may be found at either the 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 labor 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. 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 FY85, competition will be open to plant, area, private industry, and public sector committees. In-plant committee applications must offer an innovative or unique effort.

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 objectives 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 applications 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 resumes 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 commitees (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 Milestones*—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 specific 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 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.

7. *Other Requirements*—Applicants are also responsible for the following:

(a) The submission of data indicating 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 breakout of annual operating costs and identification of all sources and levels of financial support;

(c) A detailed budget narrative based on policies 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 justified 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 inplant applicants, this section will address the degree of innovativeness 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 of the government of the application in light of the overall objectives of the Labor-Management Cooperation Act of 1978. This includes such factors as innovativeness, 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 private 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 FY85 appropriation of $1 million for the Labor-Management Cooperation program. 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 category. After these applications are selected for award, the remaining applications will be awarded according to highest score without regard to category.

FMCS reserves the right to retain up to 5 percent of the FY85 appropriation to contract for program support purposes. In addition, $60,000 will be reserved for support of the Third National Labor-Management Conference.

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 in-plant 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 committees 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 FY85, 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 also 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 previously made available for these purposes. Also, under no circumstances will business or labor officials participating on a labor-management committee be paid or otherwise compensated out of grant funds for time spent at committee meetings or time spent in training sessions.

For a more complete discussion of cost allowability, applicants are encouraged to consult the FY85 FMCS Financial and Administrative Grants Manual which will be included in the application kit.

G. Application Submission and Review Process

Applications must be postmarked no later than May 10, 1985. No applications or supplementary materials can be accepted after the deadline. An original 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.

After the deadline has passed, all eligible applications will be reviewed and scored initially by an FMCS Grant Review Board. The Director, Labor-Management Grant Programs, will finalize the scoring and place the application in one of the following three categories: (a) Unacceptable for funding, (b) potentially acceptable for funding but funds are unavailable, and (c) recommended for funding.

All FY85 grant applicants will be notified of results, and all grant awards will be made, prior to September 30, 1985. Applications submitted after the deadline dates or that fail to adhere to eligibility or other major requirements will be administratively rejected prior to the convening of the Grant Review Board.

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. 85–1142 Filed 1–14–85; 8:45 am]

BILLING CODE 6732–01–M

FEDERAL MARITIME COMMISSION

Information Collection Item Submitted for OMB Review

The Federal Maritime hereby gives notice that the following item has been submitted to OMB for review pursuant to the Paperwork Reduction Act of 1980 (44 U.S.C. 3501, et seq.). Requests for information, including copies of the collection of information and supporting documentation, may be obtained from Francis C. Hurney, Agency Clearance Officer, Federal Maritime Commission, 1100 L Street, NW., Room 11101, Washington, D.C. 20573, telephone number (202) (523–5725). Comments may be submitted to the Office of Information and Regulatory Affairs, Office of Management and Budget, Attention: Desk Officer for the Federal Maritime Commission, within 10 days after the date of the **Federal Register** in which the notice appears.

Summary of Item Submitted for OMB Review

Tariff Data/Information Needs Study Questionnaire

As part of a study of the foreign freight rate tariff filing system of the Federal Maritime Commission, two voluntary questionnaires were developed to consider the separate opinions of the ocean shipping industry and shipping public. 46 CFR Part 580 requires that every common carrier by water and conference of such carriers engaged in the foreign commerce of the United States file with the Commission and keep open to public inspection tariffs showing rates and charges for transportation between U.S. and foreign ports and between points on any through route which is established. One survey was developed to target ocean common carriers, conferences, and non-vessel operating common carriers; the other shipper associations, freight forwarders and custom house brokers.

The Commission estimates that the one time only surveys will solicit about 100 respondents for a burden of 350 hours. Total estimated cost to the government is $8,000; cost to the public is estimated at $6,300.

Bruce A. Dombrowski,

Assistant Secretary.

[FR Doc. 85–1124 Filed 1–14–85; 8:45 am]

BILLING CODE 6730–01–M

Ocean Freight Forwarder License; Revocations; A.R. Pradillo, et al.

Notice is hereby given that the following ocean freight forwarder licenses have been revoked by the Federal Maritime Commission pursuant to section 19 of the Shipping Act of 1984 (46 U.S.C. app. 1718) and the regulations of the Commission pertaining to the licensing of ocean freight forwarders, 46 CFR Part 510.

License Number: 1423
Name: A. R. Pradillo
Address: #2 Canal Street, ITM Bldg., Suite 2011 New Orleans, LA 70130
Date Revoked: January 1, 1985
Reason: Voluntarily requested revocation

License Number: 1308–R

Name: Alpha Cargo Service Corporation
Address: 1222 East Imperial Avenue, El Segundo, CA 90245
Date Revoked: January 2, 1985
Reason: Failed to maintain a valid surety bond
License Number: 1499
Name: Anderson Bros. Storage & Moving Co.
Address: 3141 North Sheffield Ave., Chicago, IL 60667
Date Revoked: January 4, 1985
Reason: Failed to maintain a valid surety bond

Eugene P. Stakem,
Deputy Director, Bureau of Tariffs.

[FR Doc. 85-1164 Filed 1-14-85; 8:45 am]
BILLING CODE 6730-01-M

Ocean Freight Forwarder License; Applicants; LMB Transport, Inc., et al.

Notice is given that the following applicants have filed with the Federal Maritime Commission applications for licenses as ocean freight forwarders pursuant to section 19 of the Shipping Act of 1984 (46 U.S.C. app. 1718 and 46 CFR Part 510).

Persons knowing of any reason why any of the following applicants should not receive a license are requested to communicate with the Director, Bureau of Tariffs, Federal Maritime Commission, Washington, D.C. 20573.

LMB Transport, Inc., 44 West 54th Street Bayonne, NJ 07702.
Officer:
Lawrence M. Buck, President

Four Winds International, Inc., 4275 Campus Point Court, San Diego, CA 92121.
Officers:
R. W. Arendsee, Chairman of Board of Directors
F. W. Kircher, Executive Vice President/Director
Douglas Cruikshank, Vice President
Hugh Crumpler, Vice President
Han Helders, Senior Vice President
Harry House, Vice President
Peter J. Malatesta, Vice President
Charles H. Purviance, Senior Vice President
Catherine N. Sirpis, Secretary/Director
Paul D. Smith, President

Morgan Overseas Service, Ltd., 120 Broadway, New York, NY 10271.
Officers:
Eleonora A. Torp, President/Treasurer/Director
Willy Rufenacht, Secretary/Director

Rapid Movements Ltd., 1180 Pratt Avenue, Elk Grove Village, IL 60007.
Officers:
Edward B. Moore, President
Lawrence C. Cantello, Senior Vice President
Ingrid M. MacCready, Vice President
Kenneth E. Moore, Secretary
Franklyn Sheps, 14823 SW. 84th Terrace, Miami, FL 33193.

By the Federal Maritime Commission.
Dated: January 10, 1985.

Bruce A. Dombrowski,
Assistant Secretary.

[FR Doc. 1165 Filed 1-14-85; 8:45 am]
BILLING CODE 6730-01-M

FEDERAL RESERVE SYSTEM

Angola State Bancorp, et al.; Formations of; Acquisitions by; and Mergers of Bank Holding Companies

The companies listed in this notice have applied for the Board's approval under section 3 of the Bank Holding Company Act (12 U.S.C. 1842) and § 225.14 of the Board's Regulation Y (12 CFR 225.14) to become a bank holding company or to acquire a bank or bank holding company. The factors that are considered in acting on the applications are set forth in section 3(c) of the Act (12 U.S.C. 1842(c)).

Each application is available for immediate inspection at the Federal Reserve Bank indicated. Once the application has been accepted for processing, it will also be available for inspection at the offices of the Board of Governors. Interested persons may express their views in writing to the Reserve Bank or to the offices of the Board of Governors. Any comment on an application that requests a hearing must include a statement of why a written presentation would not suffice in lieu of a hearing, identifying specifically any questions of fact that are in dispute and summarizing the evidence that would be presented at a hearing.

Unless otherwise noted, comments regarding each of these applications must be received not later than February 6, 1985.

A. **Federal Reserve Bank of Chicago** (Franklin D. Dreyer, Vice President) 230 South LaSalle Street, Chicago, Illinois 60690:

1. *Angola State Bancorp*, Angola, Indiana; to become a bank holding company by acquiring 100 percent of the voting shares of Angola State Bank, Angola, Indiana.

2. *Comprehensive Investment Company*, Coon Rapids, Iowa; to acquire The Farmers State Bank, Bayard, Iowa.

B. **Federal Reserve Bank of San Francisco** (Harry W. Green, Vice President) 101 Market Street, San Francisco, California 94105:

1. *Salt Lake Holding Corp.*, Salt Lake City, Utah; to become a bank holding company by acquiring 100 percent of the voting shares of Sandy State Bank, Sandy, Utah.

Board of Governors of the Federal Reserve System, January 9, 1985.

James McAfee,
Associate Secretary of the Board.

[FR Doc. 85-1092 Filed 1-14-85; 8:45 am]
BILLING CODE 6210-01-M

Chemical New York Corp., et al.; Applications To Engage De Novo in Permissible Nonbanking Activities

The companies listed in this notice have filed an application under § 225.23(a)(1) of the Board's Regulation Y (12 CFR 225.23(a)(1)) for the Board's approval under section 4(c)(8) of the Bank Holding Company Act (12 U.S.C. 1843(c)(8)) and § 225.21(a) of Regulation Y (12 CFR 225.21(a)) to commence or to engage *de novo*, either directly or through a subsidiary, in a nonbanking activity that is listed in § 225.25 of Regulation Y as closely related to banking and permissible for bank holding companies. Unless otherwise noted, such activities will be conducted throughout the United States.

Each application is available for immediate inspection at the Federal Reserve Bank indicated. Once the application has been accepted for processing, it will also be available for inspection at the offices of the Board of Governors. Interested persons may express their views in writing on the question whether consummation of the proposal can "reasonably be expected to produce benefits to the public, such as greater convenience, increased competition, or gains in efficiency, that outweigh possible adverse effects, such as undue concentration of resources, decreased or unfair competition, conflicts of interests, or unsound banking practices." Any request for a hearing on this question must be accompanied by a statement of the reasons a written presentation would not suffice in lieu of a hearing, identifying specifically any questions of fact that are in dispute, summarizing the evidence that would be presented at a hearing, and indicating how the party commenting would be aggrieved by approval of the proposal.

Unless otherwise noted, comments regarding the applications must be received at the Reserve Bank indicated or the offices of the Board of Governors not later than February 4, 1985.

A. **Federal Reserve Bank of New York** (A. Marshall Puckett, Vice President), 33

Liberty Street, New York, New York 10045:

1. *Chemical New York Corporation*, New York, New York; to engage *de novo* in the activity of making credit related involuntary unemployment insurance available.

2. *Republic New York Corporation*, New York, New York; *Saban, S.A.*, Panama City, Republic of Panama; *Republic Holding, S.A.*, City of Luxembourg, Grand Duchy of Luxembourg; *Trade Development Finance (Netherlands Antilles), N.V.*, The Netherlands Antilles; *Trade Development Hollard Holding, N.V.*, Amsterdam, The Netherlands; to engage *de novo* through their subsidiary, Republic New York Trust Company of Florida, N.A., Miami, Florida, in the performance of trust services, including estate administration; testamentary trust administration; investment advisory and management services; custodianship; guardianship (property); escrow; and life insurance trust administration.

Board of Governors of the Federal Reserve System, January 10, 1985.

James McAfee,

Associate Secretary of the Board.

[FR Doc. 85-1093 Filed 1-14-85; 8:45 am]

BILLING CODE 6210-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Alcohol, Drug Abuse, and Mental Health Administration

American Indian Mental Health Research and Development Center; Request for Applications

AGENCY: The National Institute of Mental Health, HHS.

ACTION: Issuance of request for Applications for American Indian Mental Health Research and Development Center.

SUMMARY: The National Institute of Mental Health through the Center for Studies of Minority Group Mental Health, Division of Prevention and Special Mental Health Programs, will award a grant to support an American Indian Mental Health Research and Development Center which will develop and carry out innovative, multi-disciplinary studies on the mental health problems and needs of American Indians; serve as a resource for the training of new and established American Indian mental health researchers; disseminate information stemming from the Center's ongoing research programs; and provide an environment which will assure high-level research leadership in the area of American Indian mental health. Support may be requested for up to 5 years. It is expected that the maximum support for the Center will be $250,000 (direct costs) per year.

DATE: Receipt date of applications for FY 1985 funding: March 1, 1985. (This is a one-time only submission date for this Request for Applications.)

FOR FURTHER INFORMATION CONTACT: Dr. James R. Ralph, Chief, Center for Studies of Minority Group Mental Health, Division of Prevention and Special Mental Health Programs, National Institute of Mental Health, Room 11-95 Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, Telephone: (301) 443-3724.

Donald Ian Macdonald, M.D.,

Administrator, Alcohol, Drug Abuse, and Mental Health Administration.

[FR Doc. 85-1137 Filed 1-14-85; 8:45 am]

BILLING CODE 4160-20-M

Food and Drug Administration

Micro Blenders, Inc.; withdrawal of Approval of NADA's

Correction

In FR Doc. 85-11 beginning on page 347 in the issue of Thursday, January 3, 1985, make the following correction:

On page 348, first column, in **"SUPPLEMENTARY INFORMATION"**, third line, "2109" should have read "210".

BILLING CODE 1505-01-M

Health Resources and Services Administration

National Advisory Council on Health Professions Education; Filing of Annual Report of Federal Advisory Committee

Notice is hereby given that pursuant to section 13 of Pub. L. 92-463, the Annual Report for the following Health Resources and Services Administration Federal Advisory Committee has been filed with the Library of Congress:

National Advisory Council on Health Professions Education

Copies are available to the public for inspection at the Library of Congress, Newspaper and Current Periodical Reading Room, Room 1026, Thomas Jefferson Building, Second Street and Independence Avenue, SE, Washington, D.C., or weekdays between 9:00 a.m. and 4:30 p.m. at the Department of Health and Human Services, Department Library, North Building, Room 1436, 330 Independence Avenue, SW, Washington, D.C. 20201, Telephone (202) 245-6791. Copies may be obtained from Mr. Robert L. Belsley, Executive Secretary, National Advisory Council on Health Professions Education, Health Resources and Services Administration, Room 8C-22, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, Telephone (301) 443-6880.

Dated: January 9, 1985.

Jackie E. Baum,

Advisory Committee Management Officer, HRSA.

[FR Doc. 85-1077 File 1-14-85; 8:45 am]

BILLING CODE 4160-16-M

National Council on Health Planning and Development; Filing of Annual Report of Federal Advisory Committee

Notice is hereby given that pursuant to section 13 of Pub. L. 92-463, the Annual Report for the following Health Resources and Services Administration Federal Advisory Committee has been filed with the Library of Congress:

National Council on Health Planning and Development

Copies are available to the public for inspection at the Library of Congress, Newpaper and Current Periodical Reading Room, Room 1026, Thomas Jefferson Building, Second Street and Independence Avenue, SE, Washington, D.C., or weekdays between 9:00 a.m. and 4:30 p.m. at the Department of Health and Human Services, Department Library, North Building, Room 1436, 330 Independence Avenue, SW, Washington, D.C. 20201, Telephone (202) 245-6791. Copies may be obtained from Ms. Diane McMenamin, Interim Executive Secretary, National Council on Health Planning and Development, Health Resources and Services Administration, Room 174-55, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, Telephone (301) 443-4686.

Dated: January 9, 1985.

Jackie E. Baum,

Advisory Committee Management Office, HRSA.

[FR Doc. 85-1078 Filed 1-14-85; 8:45 am]

BILLING CODE 4160-16-M

Centers for Disease Control

National Institute for Occupational Safety and Health; Public Health Service; Grants for Education Programs in Occupational Safety and Health; Availability of Funds for Fiscal Year 1985

The National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control (CDC), announces the availability of funds in Fiscal Year 1985 for training grants in occupational safety and health as authorized by section 21(a)(1) of the Occupational Safety and Health Act of 1970 (29 U.S.C. 670(a)(1)). Regulations applicable to this program are in Part 86, "Grants for Education Programs in Occupational Safety and Health," of Title 42, Code of Federal Regulations (42 CFR). The objective of this grant program is to award funds to eligible institutions or agencies to pay part or all of the costs of the combination of long-term and short-term training activities in occupational safety and health.

Approximately $8,760,000 will be available in Fiscal Year 1985 to award 15 continuation and renewal educational resource center grants ranging from approximately $300,000 to $700,000 with the average award being $520,000, and to award approximately 15 continuation and new or competing renewal project grants ranging from approximately $10,000 to $150,000 with the average award being $58,000.

Grants are usually awarded for a 3- to 5-year project period. Continuation awards within the project period are made on the basis of satisfactory progress in meeting project objectives and on the availability of funds.

Applications are subject to review as detailed in 42 CFR Part 86. Program guidelines, information on application and review procedures, deadlines, and the consequences of late submission may be obtained from the individuals listed below.

FOR FURTHER INFORMATION CONTACT:

David Thelen, Training Grant Coordinator, Division of Training and Manpower Development, MIOSH, CDC, 4676 Columbia Parkway, Cincinnati, Ohio 45226, Telephone: (513) 684-8241 or FTS 684-8241

Leo A. Sanders, Chief, Grants Management Branch, Procurement and Grants Office, Centers for Disease Control, 255 East Paces Ferry Road, NE., Room 321, Atlanta, Georgia, 30305, Telephone: (404) 262-6575 or FTS 236-6575.

(This program is described in the Catalog of Federal Domestic Assistance Program No. 13.263, Occupational Safety and Health Training Grants.)

Dated: January 7, 1985.

L. W. Sparks,

Acting Director, National Institute for Occupational Safety and Health.

[FR Doc. 85-1134 Filed 1-14-85; 8:45 am]

BILLING CODE 4160-19-M

Office of Human Development Services

Revised Fiscal Year 1985 Federal Allotments to States for Social Services Expenditures Pursuant to Title XX; Block Grants to States for Social Services

AGENCY: Office of Policy And Legislation, Office Of Human Development Services (HDS), Department of Health and Human Services.

ACTION: Notification of Revised Federal Allotments to States under title XX, the Social Services Block Grant program, for fiscal year 1985, including increases pursuant to Pub. L. 98-473 regarding the prevention of child abuse and neglect.

SUMMARY: Public Law 98-473, enacted October 12, 1984, among other things, increased the fiscal year 1985 authorization and appropriation for title XX, to $2.725 billion, an increase of $25 million. This notice sets out the conditions for use of these funds and lists each State's proportional allotment.

EFFECTIVE DATE: The allotments are effective October 1, 1984.

FOR ADDITIONAL INFORMATION CONTACT:

(1) David A. Rust, (202) 245-7027 or Janet Hartnett, (202) 245-2892.

(2) The Department of Justice for questions regarding: the development of State statutes and/or regulations in accordance with Pub. L. 92-544 and 28 CFR Part 20 Subpart C and information on nationwide criminal record checks: Mr. William H. Garvie, Identification Division, Federal Bureau of Investigation, Washington, D.C. 20537, (202) 324-5456.

SUPPLEMENTARY INFORMATION: Title IV, Section 401, of Pub. L. 98-473 increased the authorized and appropriated levels of the Social Services Block Grant Program (title XX of the Social Security Act (Act)) by $25 million, from $2.7 billion to $2.725 billion, in FY 1985.

Each State's allotment has been computed at the same proportion of the $25 million as the State's proportional share of other title XX funds for fiscal year 1985, as determined under section 2003 of the Act.

Expenditures of these funds follow the Department's block grant program rules, 45 CFR 96.14, which require that any payments to a State from its allotment for any fiscal year must be expended by the State in that fiscal year or in the succeeding fiscal year.

Section 401(b) of Pub. L. 98-473 contains the following requirements regarding the use of these funds:

(1) These funds must be used only for the purpose of providing training and retraining (including training in the prevention of child abuse in child care settings) to:

- Providers of licensed or registered child care services;
- Operators and staffs (including those receiving in-service training) of facilities where licensed or registered child care services are provided;
- State licensing and enforcement officials; and
- Parents.

(2) Section 401(b)(2) of Pub. L. 98-473 provides that these funds must be expended only to supplement the level of any funds that would, in the absence of the additional funds appropriated under section 401(a), be available from other sources (including any amounts available under title XX of the Act without regard to that section) for the purposes specified in (1) above, and shall in no case supplant such funds from other sources or reduce the level thereof; and

(3) These funds must be separately accounted for in the reports and audits provided for in seciton 2006 of the Act.

Section 401(c)(2)(A) of Pub. L 98-473 provides that any State receiving an additional allotment shall have in effect not later than September 30, 1985 for all operators, staff or employees or prospective operators, staff or employees of child care facilities (including any facility or program having primary custody of children for 20 hours or more per week), and juvenile detention correcton or treatment facilities the following:

(1) Procedures established by State law or regulations to provide for employment history and background checks; and

(2) Provisions of State law enacted in accordance with the provisions of Pub. L. 92-544 (86 Stat. 115) requiring nationwide criminal record checks. (See also 28 CFR 20.33)

If any State does not meet these requirements by September 30, 1985, that State's allotment for fiscal year 1986 or 1987 shall be reduced by an amount equal to one half of the amount by which such State's allotment under the statute was increased for fiscal year

1985. Therefore, in order to enable HDS to determine whether a State is in compliance with these provisions, each State (as well as the District of Columbia, Guam, Puerto Rico, the Virgin Islands, and the Commonwealth of the Northern Marianas) must submit to the appropriate Regional Administrator, HDS, on or before July 31, 1986 a copy of the State law(s) and regulation(s) documenting compliance as of September 30, 1985.

We encourage States to coordinate the expenditure of these additional funds with the State agency receiving State grants under the Child Abuse Prevention and Treatment Act.

The Department has received many inquiries concerning definitions of terms in and requests for interpretation of the requirements in Pub. L. 98–473. In line with the discretion provided to States under the SSBG and the Department's block grant regulations (45 CFR 96.50(e)), however, we intend that States, not the Department, will define terms (e.g., child care settings, juvenile detention facilities) and activities (e.g., training) in the context of their own services programs and needs. In addition, the Department will accept any State law regarding nationwide criminal record checks that meets the requirements of Pub. L. 92–544.

The additional $25 million is allotted to the States as set forth in Column 2 below. The initial allotment of $2.7 billion (published in the **Federal Register**, December 13, 1983 (45 FR 55514)) is set forth in Column 1, and the total allotment for the year is set forth in Column 3.

REVISED FISCAL YEAR 1985 FEDERAL ALLOTMENTS—TITLE XX SOCIAL SERVICES BLOCK GRANTS

	Column 1—Authorized Level Pub. L. 98–135	Column 2—Authorized Level Pub. L. 98–473	Column 3—Total
Total	$2,700,000,000	$25,000,000	$2,725,000,000
Alabama	45,725,250	423,382	46,148,632
Alaska	5,079,295	47,031	5,126,326
Arizona	33,166,172	307,094	33,473,266
Arkansas	26,567,727	245,997	26,813,724
California	286,713,437	2,654,754	289,368,191
Colorado	35,311,536	326,959	35,638,495
Connecticut	36,583,965	338,555	36,902,520
Delaware	6,981,131	64,640	7,045,771
District of Columbia	7,317,432	67,754	7,385,186
Florida	120,789,806	1,118,424	121,908,230
Georgia	65,393,022	605,491	65,998,513
Guam	465,517	4,310	469,827
Hawaii	11,526,984	106,731	11,633,715
Idaho	11,190,684	103,617	11,294,301
Illinois	132,757,460	1,229,236	133,986,696
Indiana	63,444,799	587,452	64,032,251
Iowa	33,688,017	311,926	33,999,943
Kansas	27,924,525	258,560	28,183,085
Kentucky	42,524,599	393,746	42,918,345
Louisiana	50,584,210	468,372	51,052,582
Maine	13,138,906	121,657	13,260,563
Maryland	49,459,344	457,957	49,917,301
Massachusetts	67,039,734	620,738	67,660,472
Michigan	105,633,098	978,084	106,611,182
Minnesota	47,928,597	443,783	48,372,380
Mississippi	29,582,834	273,915	29,856,749
Missouri	57,414,586	531,617	57,946,203
Montana	9,288,848	86,008	9,374,856
Nebraska	18,392,150	170,298	18,562,448
Nevada	10,216,573	94,598	10,311,171
New Hampshire	11,028,332	102,114	11,130,446
New Jersey	86,255,240	798,660	87,053,900
New Mexico	15,759,730	145,923	15,905,653
New York	204,783,716	1,896,146	206,679,862
North Carolina	69,799,716	646,294	70,446,010
North Dakota	7,769,698	71,942	7,841,640
No. Mariana Islands	93,104	862	93,966
Ohio	125,138,517	1,158,690	126,297,207
Oklahoma	36,842,282	341,132	37,183,414
Oregon	30,719,297	284,438	31,003,735
Pennsylvania	137,593,227	1,274,011	138,867,238
Puerto Rico	13,965,517	129,310	14,094,827
Rhode Island	11,109,508	102,866	11,212,374
South Carolina	37,143,793	343,924	37,487,717
South Dakota	8,013,225	74,197	8,087,422
Tennessee	53,935,617	499,404	54,435,021
Texas	177,195,491	1,640,699	178,836,190
Utah	18,021,060	166,862	18,187,922
Vermont	5,983,827	55,406	6,039,233
Virgin Islands	465,517	4,310	469,827
Virginia	63,676,730	589,599	61,266,329
Washington	49,227,412	455,809	49,683,221
West Virginia	22,590,106	209,168	22,799,274
Wisconsin	55,257,625	511,645	55,769,270
Wyoming	5,821,475	53,903	5,875,378

Dated: December 10, 1985.

David A. Rust,

Director, Office of Policy and Legislation.

Approved: December 10, 1985.

Dorcas R. Hardy,

Assistant Secretary for Human Development Services.

[FR Doc. 85-1207 Filed 1-14-84; 8:45 am]

BILLING CODE 4130-01-M

DEPARTMENT OF THE INTERIOR

Office of the Secretary

Alaska Land Use Council; Meeting

As required by the Alaska National Interest Lands Conservation Act, (ANILCA), Pub. L. 96-487, dated December 2, 1980, section 1201, Paragraph (h), the Alaska Land Use Council will meet Thursday, February 14, 1985, at 9:00 A.M., in the Governor's Conference Room, Third Floor, Capitol Building, Juneau, Alaska.

The proposed agenda will include Council consideration of:

- —The Steese and White Mountains Resource Management Plans;
- —Proposed Council Work Program Item on Trespass
- —Council's 1984 Annual Report;
- —Status Report on the Competitive Events Study;
- —Report on Subsistence and Land Use Decisions, Phase II;
- —Cadastral Survey Work Group Recommendations;
- —Kenai National Wildlife Refuge Plan;
- —Status report on the Federal Bristol Bay Regional Management Plan; and
- —Other items that may come before the Council.

For further information contact: Alaska Land Use Council, P.O. Box 100120, Anchorage, Alaska 99510-0120 (907) 272-3422 (FTS) 271-5485.

The public is invited to attend.

Vern Wiggins,

Federal Cochairman, Alaska Land Use Council.

January 9, 1985.

[FR Doc. 85-1059 Filed 1-14-85; 8:45 am]

BILLING CODE 4310-10-M

Privacy Act of 1974—Revision and Deletion of Notices of Systems of Records

This notice updates and revises the information which the Department of the Interior has published describing systems of records maintained which are subject to the requirements of Section 3 of the Privacy Act of 1974, as amended, 5 U.S.C. 552a. Changes are being made to two Office of the Secretary systems of records notices as described below.

Th notice titled "Motor Vehicle Operator's Identification Card Applications—Interior, Office of the Secretary-50", which was previously published in the **Federal Register** on May 3, 1983 (48 FR 19947), is deleted from the inventory of notices describing systems of records maintained by the Department. A recent review indicates that records on the issuance of identification cards are no longer maintained or retrieved in a manner identifiable to a particular individual. Records on applications for motor vehicle identification cards and driving records are maintained in the individual's Official Personnel Folder which is covered under a governmentwide system of records notice published by the Office of Personnel Management (OPM/GOVT-1).

Recently, the Department coverted the provision of services for official employee travel in the Washington, D.C. area from an "in-house" operation to a contract-operated activity. Travel services are now provided by a contractor pursuant to a General Services Administration contract. Therefore, the system notice titled "Travel Management Records—Interior, Office of the Secretary-52", previously published in the **Federal Register** on May 3, 1983 (48 FR 19948), is being revised to delete references to travel related information other than passports and visas. The title of the system notice is also being revised to reflect that only passport and visa records are included in the records system. The revised notice is published in its entirety below.

5 U.S.C. 552a(e)(11) requires that the public be provided a 30-day period in which to comment. Therefore, written comments on these proposed changes can be addressed to the Department Privacy Act Officer, Office of the Secretary (PIR), U.S. Department of the Interior, Washington, D.C. 20240. Comments received on or before February 14, 1985, will be considered. The notice published below shall be effective as proposed without further notice at the end of the comment period, unless comments are received which would require a contrary determination.

Dated: January 4, 1985.

Oscar W. Mueller,

Director, Office of Information Resources Management.

INTERIOR-OS-52

SYSTEM NAME:

Passport and Visa Records—Interior, Office of the Secretary—52.

SYSTEM LOCATION:

Division of General Services, Office of Administrative Services (PMO), Office of the Secretary, U.S. Department of the Interior, 18th and C Streets, NW., Washington, D.C. 20240.

CATEGORIES OF INDIVIDUALS COVERED BY THE SYSTEM:

Employees or individuals who travel on official business on behalf of the Department of the Interior, and Independent Agencies, Councils, and Commissions who are provided administrative support.

CATEGORIES OF RECORDS IN THE SYSTEM:

The records system contains passports and visas.

AUTHORITY FOR MAINTENANCE OF THE SYSTEM:

5 U.S.C. 5701, et seq.

ROUTINE USE OF RECORDS MAINTAINED IN THE SYSTEM, INCLUDING CATEGORIES OF USERS AND THE PURPOSES OF SUCH USES:

The primary use of the records are to initiate and maintain passports and visas. Disclosures outside the Department are (1) the transfer of passports and visas to other Federal agencies, (2) to the U.S. Department of Justice when related to litigation or anticipated litigation, and (3) of information indicating a violation or potential violation of a potential violation of a statute regulation, rule, order or license, to appropriate Federal, State, local or foreign agencies responsible for investigating or prosecuting the violation or for enforcing or implementing the statute rule, regulation, order or license, and (4) from the record of an individual in response to an inquiry from a Congressional office made at the request of that individual.

POLICIES AND PRACTICES FOR STORING, RETRIEVING, ACCESSING, RETAINING, AND DISPOSING OF RECORDS IN THE SYSTEM:

STORAGE:

Passports and visas are maintained in a locked safe.

RETRIEVABILITY:

Passports and visas are filed by name.

SAFEGUARDS:

Passports and visas are stored in a locked room in manipulation proof three way combination lock steel safes. Access granted only to designated personnel.

RETENTION AND DISPOSAL:

General Records Schedule No. 9, Item No. 4.

SYSTEM MANAGER(S) AND ADDRESSES:

Chief, Division of General Services, Office of Administrative Services, Department of the Interior, 18th and C Street, NW., Washington, D.C. 20240.

NOTIFICATION PROCEDURES:

A written and signed request stating that the requester seeks information concerning records pertaining to him/her. See 43 CFR 2.60.

RECORD ACCESS PROCEDURES:

Submit request to the System Manager. The request must be in writing, signed by the requester, and meet the content requirements of 43 CFR 2.63.

CONTESTING RECORD PROCEDURES:

A petition for amendment shall be addressed to the System Manager and must meet the requirements of 43 CFR 2.71.

RECORD SOURCE CATEGORIES:

Federal employees and individuals who travel on behalf of the Department.

[FR Doc. 85-1133 filed 1-14-85; 8:45 am]

BILLING CODE 4310-10-M

Bureau of Land Management

[F-14913-A; 5-00262-GP5-028]

Alaska Native Claims Selection; Gana-a 'Yoo, Ltd.

In accordance with Departmental regulation 43 CFR 2650.7(d), notice is hereby given that a decision to issue conveyance (DIC) under the provisions of sec. 12 of the Alaska Native Claims Settlement Act of December 18, 1971 (ANCSA), 43 U.S.C. 1601, 1611 (1976), will be issued to Gana-a 'Yoo, Limited, for approximately 3 acres. The lands involved are within U.S. Survey No. 724, containing approximately 3 acres.

Upon issuance, the DIC will be published once a week, for four (4) consecutive weeks, in the Fairbanks Daily News-Miner. For information on how to obtain copies, contact the Bureau of Land Management, Alaska State Office, 701 C Street, Box 13, Anchorage, Alaska 99513.

Any party claiming a property interest which is adversely affected by the decision shall have until February 14, 1985, to file an appeal. However, parties receiving service by certified mail shall have 30 days from the date of receipt to file an appeal. Appeals must be filed in the Bureau of Land Management, Division of Conveyance Management (960), address identified above, where the requirements for filing an appeal can be obtained. Parties who do not file an appeal in accordance with requirements in 43 CFR Part 4, Subpart E (1983) (as amended, 49 FR 6371, February 21, 1984) shall be deemed to have waived their rights.

Helen Burleson,

Section Chief, Branch of ANCSA Adjudication.

[FR Doc. 85-1118 Filed 1-14-85; 8:45 am]

BILLING CODE 4310-JA-M

[F-14944-A; 5-000262-GP5-026]

Alaska Native Claims Selection; Tozitna, Ltd.

In accordance with Departmental regulation 43 CFR 2650.7(d), notice is hereby given that a decision to issue conveyance (DIC) under the provisions of sec. 12 of the Alaska Native Claims Settlement Act of December 18, 1971 (ANCSA), 43 U.S.C. 1601, 1611 (1976), will be issued to Tozitna, Limited, for approximately 0.236 acre. The lands involved are lot 7, Block 11, U.S. Survey No. 2754A and B, Townsite of Tanana, Alaska.

Upon issuance, the DIC will be published once a week, for four (4) consecutive weeks, in the TUNDRA TIMES. For information on how to obtain copies, contact the Bureau of Land Management, Alaska State Office, 701 C Street, Box 13, Anchorage, Alaska 99513.

Any party claiming a property interest which is adversely affected by the decision shall have until February 14, 1985, to file an appeal. However, parties receiving service by certified mail shall have 30 days from the date of receipt to file an appeal. Appeals must be filed in the Bureau of Land Management, Division of Conveyance Management (960), address identified above, where the requirements for filing an appeal can be obtained. Parties who do not file an appeal in accordance with the requirements in 43 CFR Part 4, Subpart E (1983) (as amended, 49 FR 6371, February 21, 1984) shall be deemed to have waived their rights.

Helen Burleson,

Section Chief, Branch of ANCSA Adjudication.

[FR Doc. 85-1117 Filed 1-14-85; 8:45 am]

BILLING CODE 4310-JA-M

Realty Action; Recreation and Public Purposes Classification in Kanabec County, MN

AGENCY: Bureau of Land Management, Interior.

ACTION: Land Classification for Recreation and Public Purposes, ES-31821 and ES-31822.

SUMMARY: The following public lands have been examined and found to be suitable for classification and sale under the Recreation and Public Purposes Act of June 14, 1926, as amended (43 U.S.C. 869):

Fourth Principal Meridian, Minnesota

1. *ES-31821*, T. 39 N., R. 24 W., Sec. 34, Lot 7; a 0.30 acre island in Fish Lake
2. *ES-31822*, T. 39 N., R. 24 W., Sec. 28, SE¼SW¼

The Minnesota Department of Natural Resources has applied for these lands so that they can be added to the State Wildlife Management Area system to be used for wildlife habitat and recreational purposes.

The lands are physically suited to the proposed use and are not of national significance. Since the lands are valuable for a State program they are considered chiefly valuable for public purposes and therefore suitable for classification and sale under the Recreation and Public Purposes Act. This action is consistent with local and Federal government plans, programs and policies.

Any patent issued under this notice shall be subject to the provisions in 43 CFR 2741.8. In the event of noncompliance with the terms of the patent, title to the land shall revert to the United States.

The classification of these lands will segregate them from all appropriation except as to applications under the mineral leasing laws and the Recreation and Public Purposes Act. Segregation will terminate upon issuance of a patent; or eighteen (18) months from the date of this notice; or upon publication of a notice of termination, whichever occurs first.

COMMENTS: For a period of 45 days from the date of first publication of this notice, interested parties may submit comments to: District Manager,

Milwaukee District Office, Bureau of Land Management, P.O. Box 631, Milwaukee, Wisconsin 53201–0631. Any adverse comments will be evaluated by the District Manager who may vacate or modify this classification. In the absence of any action by the State Director, this Realty Action will become the final determination of the Department of Interior.

FOR FURTHER INFORMATION CONTACT: Detailed information concerning these applications is available for review at the Milwaukee District Office, Suite 225, 310 W. Wisconsin Ave., Milwaukee, Wisconsin 53201, or by calling Priscilla McLain at (414) 291–4427.

Chuck Steele,

District Manager.

[FR Doc. 85–1145 Filed 1–14–85; 8:45 am]

BILLING CODE 4310–84–M

[500252 GP–5–037]

New Mexico; Filing of Plat of Survey

January 7, 1985.

The plat of survey described below was officially filed in the New Mexico State Office, Bureau of Land Management, Santa Fe, New Mexico, effective at 10 a.m. on January 8, 1985.

New Mexico Principal Meridian

The dependent resurvey of a portion of the south boundary of the Nuestra Senora del Rosario San Fernando y Santiago Grant, portions of the north and southwest boundaries of the Santiago de Cundiyo Grant, a portion of the subdivisional lines, the subdivision of sections 6, 20 and 21, and the dependent resurvey of certain small holding claim boundaries in Township 20 North, Range 10 East, NMPM, New Mexico, under Group 781, accepted December 28, 1984.

This survey was requested by Albuquerque District, Bureau of Land Management.

The plat will be in the open files of the New Mexico State Office, Bureau of Land Management, P.O. Box 1449, Santa Fe, New Mexico 87501. Copies of the plat may be obtained from that office upon payment of $2.50 per sheet.

Gary S. Speight,

Chief, Branch of Cadastral Survey.

[FR Doc. 85–1139 Filed 1–14–85; 8:45 am]

BILLING CODE 4310–FB–M

[5–00258–GP5–107]

Colorado; Craig District Grazing Advisory Board Meeting

Notice is hereby given in accordance with Pub. L. 92–463, that a meeting of the Craig District Grazing Board will be held on February 28, 1985, at the District Office of the Bureau of Land Management, 455 Emerson Street, Craig, Colorado. The meeting will convene at 10:00 a.m.

The agenda for the meeting will include:

(1) FY86 projects for feasibility and survey and design.

(2) Status of FY85 projects.

(3) Status of Little Snake Resource Management Plan.

(4) Status of Kremmling rangeland improvement program implementation.

(5) The expenditure of advisory board funds for range improvement.

The meeting is open to the public. Interested persons may make oral statements to the board between 10:00 and 11:00 a.m. on February 28, 1985, or file written statements for the board's consideration. Depending on the number of persons wishing to make oral statements, a per person time limit may be established by the District Manager.

Dated: January 4, 1985.

William J. Pulford,

District Manager.

[FR Doc. 85–1136 Filed 1–14–85; 8:45 am]

BILLING CODE 4310–JB–M

Susanville District Advisory Council; Meeting

AGENCY: Bureau of Land Management, Interior.

ACTION: Notice of meeting.

SUMMARY: Notice is hereby given in accordance with Pub. L. 94–579 (FLPMA) that a meeting of the Susanville District Advisory Council will be held on February 1, 1985.

The meeting will begin at 1:00 p.m. on February 1, in the Conference Room of the Bureau of Land Management, Susanville District Office, 705 Hall Street, Susanville, California.

The Purpose of the meeting is to design a citizens involvement process to attempt to resolve the current conflicts surrounding the Fort Sage Off Highway Vehicle Area near Doyle California.

The meeting is open to the public and time will be provided for public comment. Summary minutes of the Council meeting will be maintained in the District Office and will be available for public inspection and reproduction within 30 days following the meeting.

C. Rex Cleary,

Susanville District Manager.

[FR Doc. 85–1140 Filed 1–14–85; 8:45 am]

BILLING CODE 4310–40–M

[C–019106, C–28243; 5–00258–GP5–020]

Colorado; Proposed Modification of Bureau of Reclamation Collbran Project

January 4, 1985.

AGENCY: Bureau of Land Management, Interior.

ACTION: Notice.

SUMMARY: The Bureau of Reclamation proposes that those orders which withdrew lands for the Collbran Project be modified to expire 20 years from the date of the final order insofar as they affect 163.45 acres of public and national forest system lands. The lands will remain closed to surface entry and mining but have been and will continue to be open to mineral leasing.

DATE: Comments should be received within 90 days of publication date.

ADDRESS: All comments should be addressed to State Director, Colorado State Office, 2020 Arapahoe Street, Denver, Colorado 80205.

FOR FURTHER INFORMATION CONTACT: Richard D. Tate, BLM Colorado State Office, 303–294–7626.

The Bureau of Reclamation proposes that portions of the existing land withdrawals made by Secretarial Order of October 14, 1948, as amended, Bureau Order of June 11, 1957, as amended, and Bureau Order of September 15, 1958, as amended, be modified to expire 20 years from the date of the final order pursuant to section 204 of the Federal Land Policy and Management Act of 1976, 90 Stat. 2751, 43 U.S.C. 1714, insofar as they affect the following described public and national forest system lands:

Sixth Principal Meridian

T. 10 S., R. 93 W.,
Sec. 7, lot 12.
T. 10 S., R. 94 W.,
Sec. 2, S½NW¼SE¼.
T. 10 S., R. 95 W.,
Sec. 33, S½NE¼SW¼.

Grand Mesa National Forest

Sixth Principal Meridian

T. 11 S., R. 94 W.,
Sec. 9, SE¼SW¼;
Sec. 16, NW¼NE¼.

The areas described aggregate 83.45 acres of public land and 80 acres of national forest system lands in Mesa County, Colorado.

The purpose of these withdrawals is for the administration and protection of the Collbran Reclamation Project. No change is proposed in the purpose or segregative effect of the withdrawals. The land will continue to be withdrawn

from surface entry and mining, but not from mineral leasing.

For a period of 90 days from the date of publication of this notice, all persons who wish to submit comments in connection with the proposed withdrawal modification may present their views in writing to the State Director, Colorado State Office.

The authorized officer of the Bureau of Land Management will undertake such investigations as are necessary to determine the existing and potential demand for the land and its resources. A report will also be prepared for consideration by the Secretary of the Interior, the President, and Congress, who will determine whether or not the withdrawals will be continued and, if so, for how long. The final determination on the modification of the withdrawals will be published in the **Federal Register**. The existing withdrawals will continue until such final determination is made.

Richard E. Richards,

Acting Chief, Branch of Lands and Minerals Operations.

[FR Doc. 85-1141 Filed 1-14-85; 8:45 am]

BILLING CODE 4310-JB-M

[M59847; 5-00254]

Montana; Modification of Notice of Realty Action; Exchange

AGENCY: Bureau of Land Management, Butte District Office, Interior.

ACTION: Modification of Notice of Realty Action M59847, Exchange of Public and Private Lands in Lewis & Clark, Jefferson, Broadwater, Gallatin, Park, and Sweet Grass Counties.

SUMMARY: This notice modified the original Notice of Realty Action for M59847 published on December 12, 1984 (49 FR 48391). The legal description for tract B-4 as noted in the original notice is corrected as follows: B-4—T. 9N., R. 2 E., Section 20 SW¼NW¼NE¼, NW¼Sw¼NE¼, N½SE¼NW¼, SW¼se¼NW¼, 50 acres.

Dated: December 27, 1984.

Paul E. Peek,

Acting District Manager, Butte District.

[FR Doc. 85-1128, Filed 1-14-85; 8:45 am]

BILLING CODE 4310-DN-M

Minerals Management Service

Development Operations Coordination Document; Chevron U.S.A. Inc.

AGENCY: Minerals Management Service, Interior.

ACTION: Notice of the Receipt of a Proposed Development Operations Coordination Document (DOCD).

SUMMARY: Notice is hereby given that Chevron U.S.A. Inc. has submitted a DOCD describing the activities it proposes to conduct on Lease OCS-G 4112, Block 256, South Marsh Island Area, offshore Louisiana. Proposed plans for the above area provide for the development and production of hydrocarbons with support activities to be conducted from an onshore base located at Morgan City, Louisiana.

DATE: The subject DOCD was deemed submitted on January 4, 1985. Comments must be received within 15 days of the date of this Notice or 15 days after the Coastal Management Section receives a copy of the DOCD from the Minerals Management Service.

ADDRESSES: A copy of the subject DOCD is available for public review at the Office of the Regional Director, Gulf of Mexico OCS Region, Minerals Management Service, 3301 North Causeway Blvd., Room 147, Metairie, Louisiana (Office Hours: 9 a.m. to 3:30 p.m., Monday through Friday). A copy of the DOCD and the accompanying Consistency Certification are also available for public review at the Coastal Management Section Office located on the 10th Floor of the State Lands and Natural Resources Building, 625 North 4th Street, Baton Rouge, Louisiana (Office Hours: 8 a.m. to 4:30 p.m., Monday through Friday). The public may submit comments to the Coastal Management Section, *Attention OCS Plans*, Post Office Box 44396, Baton Rouge, Louisiana 70805.

FOR FURTHER INFORMATION CONTACT: Mr. Michael J. Tolbert; Minerals Management Service; Gulf of Mexico OCS Region; Rules and Production; Plans, Platform and Pipeline Section; Exploration/Development Plans Unit; Phone (504) 838-0876.

SUPPLEMENTARY INFORMATION: The purpose of this Notice is to inform the public, pursuant to section 25 of the OCS Lands Act Amendments of 1978, that the Minerals Management Service is considering approval of the DOCD and that it is available for public review. Additionally, this Notice is to inform the public, pursuant to § 930.61 of Title 15 of the CFR, that the Coastal Management Section/Louisiana Department of Natural Resources is reviewing the DOCD for consistency with the Louisiana Coastal Resources Program.

Revised rules governing practices and procedures under which the Minerals Management Service makes information contained in DOCDs available to affected states, executives of affected local governments, and other interested parties became effective December 13, 1979 (44 FR 53685). Those practices and procedures are set out in revised § 250.34 of Title 30 of the CFR.

Dated: Janaury 4, 1985.

John L. Rankin,

Regional Director, Gulf of Mexico OCS Region.

[FR Doc. 85-1129, Filed 1-14-85; 8:45 am]

BILLING CODE 4310-MR-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 January 5, 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 30, 1985.

Carol D. Shull,

Chief Of Registration National Register.

ARIZONA

Cochise County

Bisbee, *Bisbee Woman's Club Clubhouse*, 74 Quality Hill

Douglas, *Douglas Historic District*, Roughly bounded by Pan American, H, and F Aves. along 8th, 10th, 11th, 12th, and 13th Sts. and G Ave.

COLORADO

Archuleta County

Arboles vicinity, *Labo Del Rio Bridge (Vehicular Bridges in Colorado TR)*, Cty. Rd. F40 over Piedra River

FLORIDA

Duval County

Jacksonville, *House at 3325 Via De La Reiva (San Jose Estates TR)*, 3325 Via De La Reiva

Jacksonville, *House at 3335 Via De La Reina (San Jose Estates TR)*, 3335 Via De La Reina

Jacksonville, *House at 3500 Via De La Reina (San Jose Estates TR)*, 3500 Via De La Reina

Jacksonville, *House at 3609 Via De La Reina (San Jose Estates TR)*, 3609 Via De La Reina

Jacksonville, *House at 3685 Via De La Reina (San Jose Estates TR)*, 3685 Via De La Reina

Jacksonville, *House at 3703 Via De La Reina (San Jose Estates TR)*, 3703 Via De La Reina
Jacksonville, *House at 3764 Ponce De Leon Avenue (San Jose Estates TR)*, 3764 Ponce De Leon Ave.
Jacksonville, *House at 7144 Madrid Avenue (San Jose Estates TR)*, 7144 Madrid Ave.
Jacksonville, *House at 7207 Ventura Avenue (San Jose Estates TR)*, 7207 Ventura Ave.
Jacksonville, *House at 7217 Ventura Avenue (San Jose Estates TR)*, 7217 Ventura Ave.
Jacksonville, *House at 7227 San Pedro (San Jose Estates TR)*, 7227 San Pedro Rd.
Jacksonville, *House at 7245 San Jose Boulevard (San Jose Estates TR)*, 7245 San Jose Blvd.
Jacksonville, *House at 7246 San Carlos (San Jose Estates TR)*, 7246 San Carlos
Jacksonville, *House at 7246 St. Augustine Road (San Jose Estates TR)*, 7246 St. Augustine Rd.
Jacksonville, *House at 7249 San Pedro (San Jose Estates TR)*, 7227 San Pedro Rd.
Jacksonville, *House at 7288 San Jose Boulevard (San Jose Estates TR)*, 7288 San Jose Blvd.
Jacksonville, *House at 7306 St. Augustine Road (San Jose Estates TR)*, 7306 St. Augustine Rd.
Jacksonville, *House at 7317 San Jose Boulevard (San Jose Estates TR)*, 7317 San Jose Blvd.
Jacksonville, *House at 7330 Ventura Avenue (San Jose Estates TR)*, 7330 Ventura Ave.
Jacksonville, *House at 7356 San Jose Boulevard (San Jose Estates TR)*, 7356 San Jose Blvd.
Jacksonville, *House at 7400 San Jose Boulevard (San Jose Estates TR)*, 7400 San Jose Blvd.
Jacksonville, *San Jose Administration Building (San Jose Estates TR)*, 7423 San Jose Blvd.
Jacksonville, *San Jose County Club (San Jose Estates TR)*, 7529 San Jose Blvd.
Jacksonville, *San Jose Hotel (San Jose Estates TR)*, 7400 San Jose Boulevard

Hillsborough County

Brandon, *Moseley Homestead*, 1820 W. Brandon Blvd.

Pinellas County

St. Petersburg, *Casa De Muchos Flores*, 1446 Park St. N.

GUAM

Agana, *Agana Historic District (Agana Houses TR)*, Roughly bounded by 2nd S., 3rd S., and 9th W., Santa Cruz and Legaspi Sts.

LOUISIANA

East Baton Rouge Parish

Baton Rouge, *Magnolia Cemetery*, Bounded by Main, 19th, Florida, and 22nd Sts.

St. James Parish

Convent vicinity, *Manresa House of Retreat/ Jefferson College*, LA 44

Tangipahoa Parish

Ponchatoula vicinity, *Mount's Villa*, Off LA 22

MICHIGAN

Genesee County

Flint, *Capital Theatre Building*, 140 E. 2nd St.

Ionia County

Ionia vicinity, *Sessions Schoolhouse*, Riverside Dr.

Oakland County

Pontiac, *Fairgrove Avenue Historic District*, Along Fairgrove Ave. between N. Saginaw and Edison Sts.

Sanilac County

Lexington, *Divine, John, Law Office/Moore Public Library*, 7239 Huron Ave.

Shiawassee County

Owosso, *Duff Building (Owosso MRA)*, 118 W. Exchange St.
Owosso, *Crow Block (Owosso MRA)*, 120–122 W. Exchange St.

St. Clair County

Yale, *McColl, James, House*, 205 S. Maine St.

Wayne County

Detroit, *Redford Theatre Building*, 17354 Lahser Ave.

MISSOURI

Marion County

Hannibal, *Green Double House (Hannibal Central Business District)*, 113–115 S. 3rd St.

NEBRASKA

Lancaster County

Lincoln vicinity, *Pioneers Park*, W. Van Dorn and S. Coddington

Benton County

Corvallis vicinity, *Fiechter, John, House*, William L. Finley National Wildlife Refuge

PENNSYLVANIA

York County

Delta, *Coulsontown Cottages Historic District*, Ridge Rd. and Main

Berks County

Reading, *Grimshaw Silk Mill*, 1200 N. 1100 St.

Bucks County

Buckingham and Wrightstown Townships, *Wycombe Village Historic District*, Roughly bounded by Township Line, Mill Creek and Forest Grove Rds., Cherry Lane, Washington and Park Aves.

Crawford County

Titusville, *Titusville Historic District*, Roughly bounded by Petroleum, Spruce, Franklin, Perry, Monroe, Main and Spring Sts.

Philadelphia County

Philadelphia, *Pennsylvania Institute for the Deaf and Dumb*, 7500 Germantown Ave.

SOUTH DAKOTA

Bon Homme County

Tyndall, *ZCBJ Hall*, Nebraska and Washington Sts.

Day County

Webster, *Havens, William, House*, 915 E. First St.

Edmunds County

Bowdle, *Bank of Bowdle*, 3026 Main St.

Minnehaha County

Sioux Falls, *Apartments at 411–415 N. Prairie Avenue*, 411–415 N. Prairie Ave.

Union County

Beresford, *Chicago and Northwestern Railroad Depot*, 1 Depot Square

Yanktown County

Yanktown, *Schnauber, Fred, House*, 717 Walnut St.

TEXAS

Travis County

Auston, *Barton Springs Archeological and Historic District*.

[FR Doc. 85–1075 Filed 1–14–85; 8:45 am]
BILLING CODE 4310-70-M

DEPARTMENT OF JUSTICE

[AAG/A Order No. 21–84]

Privacy Act of 1974; New System of Records

Pursuant to the provisions of the Privacy Act of 1974 (5 U.S.C. 552a), notice is given that the Department of Justice proposes to establish a new system of records to be maintained by the Immigration and Naturalization Service (INS).

The Freedom of Information Act/ Privacy Act (FOIA/PA) Case Tracking and Reporting System (JUSTICE/INS–010) is a new system of records for which no public notice consistent with the provisions of 5 U.S.C. 552a(e) (4) and (11) has been published in the **Federal Register**. The system will be used to document, control, and account for all FOIA/PA initial requests received by INS nationwide.

5 U.S.C. 552 (e) (4) and (11) provide that the public be given a 30-day period in which to comment; the Office of Management and Budget (OMB), which has oversight responsibility under the Act, requires a 60-day period in which to review the system before it is implemented. However, a waiver of the 60-day requirement has been requested of OMB. If the waiver is granted, the system will be fully implemented no later than 30 days from the publication date of this notice. Therefore, comments should be submitted by February 14, 1985. The public, OMB, and the Congress are invited to submit comments to Thomas F. O'Leary, Assistant Director, Administrative

Services Staff, Justice Management Division, Department of Justice, Room 6314, 10th and Constitution Avenue, NW., Washington, D.C. 20530.

A report of the proposed system has been provided to the Director, OMB; the President of the Senate; and the Speaker of the House of Representatives.

Dated: December 17, 1984.

Anthony C. Liotta,

Assistant Attorney General for Administration.

JUSTICE/INS-010

SYSTEM NAME:

Freedom of Information Act/Privacy Act (FOIA/PA) Case Tracking and Reporting System (JUSTICE/INS-010).

SYSTEM LOCATION:

Central, Regional, District, and other Files Control Offices of the Immigration and Naturalization Service (INS) in the United States as detailed in JUSTICE/INS-999.

CATEGORIES OF INDIVIDUALS COVERED BY THE SYSTEM:

Individuals making requests, individuals designated to receive responses, and individuals whose records are requested by others under the provisions of the Freedom of Information Act and/or Privacy Act.

CATEGORIES OF RECORDS IN THE SYSTEM:

Information extracted from FOIA/PA requests and the documentation provided by INS personnel of actions taken on the requests. The data base consists of data such as the names of requesters, record subjects, or persons designated to receive responses to requests; mailing addresses to send responses; date of receipt of requests; assigned request control numbers; date responses are due; interim and final action(s) taken on requests and the date(s) of final and/or interim actions; the persons or offices assigned action on requests; the types of requests; fee data; alien file numbers; specific exemptions applied in denial actions; offices where requests are transferred for referral or consultations; and the names/titles of officials responsible for denials.

AUTHORITY FOR MAINTENANCE OF THE SYSTEM:

This system is maintained pursuant to 44 U.S.C. 3101 and 8 U.S.C. 1103 to implement the provisions of 5 U.S.C. 552 and 5 U.S.C. 552a.

ROUTINE USES OF RECORDS MAINTAINED IN THE SYSTEM, INCLUDING CATEGORIES OF USERS AND THE PURPOSES OF SUCH USES:

This system of records is used to record, control, and determine the status of FOIA/PA requests, and produce statistical reports required by both Acts. Information from the system may be provided to the record subject, the requester or other persons designated by the requester, and to other Federal agencies and Department of Justice components receiving INS referrals or with whom consultations are required in order to complete the processing of requests. All other uses are internal within INS.

Release of information to Members of Congress: Information in this system may be disclosed as is necessary to appropriately respond to congressional inquiries on behalf of constituents.

Release of information to the National Archives and Records Service: A record from this system of records may be disclosed as a routine use to the National Archives and Records Service (NARS) in records management inspections conducted under the authority of 44 U.S.C. 2904 and 2906.

POLICIES AND PRACTICES FOR STORING, RETRIEVING, ACCESSING, RETAINING, AND DISPOSING OF RECORDS IN THE SYSTEM:

STORAGE:

Records may be stored on magnetic disks and tapes.

RETRIEVABILITY:

Records are indexed and retrieved by control number or by name of requester or subject.

SAFEGUARDS:

Records are safeguarded in accordance with Deparatment of Justice Security regulations governing Privacy Act systems of records. Access to the automated system is controlled by restricted password from remote terminals in secured areas.

RETENTION AND DISPOSAL:

Records are maintained for five years after date of last action and then destroyed.

SYSTEM MANAGER(S) AND ADDRESS:

The Associate Commissioner, Information Systems, Immigration and Naturalization Service, Central Office, 425 I Street, NW., Washington, D.C. is the sole manager of the system.

NOTIFICATION PROCEDURE:

Inquiries should be addressed to the system manager listed above.

RECORDS ACCESS PROCEDURE:

In all cases, requests for access to a record from this system shall be in writing. If a request for access is made by mail, the envelope and letter shall be clearly marked "FOIA/PA Request." Requests should be submitted to the INS office where the request which is the subject of the inquiry was sent, or to the Immigration and Naturalization Service, Attention: FOIA/PA Section, 425 I Street, NW., Washington, D.C. 20536. The requester shall include the control number or name of the requester and/or name of the record subject, and the date and place of submission of the request. The requester shall also provide a return address for response to the inquiry.

CONTESTING RECORD PROCEDURE:

Any individual desiring to contest or amend information maintained in the system should direct his request to the system manager or to the INS office where the request which is the subject of the inquiry was submitted. The request should state clearly what information is being contested, the reason(s) for contesting it, and the proposed amendment to the information.

RECORDS SOURCE CATEGORIES:

Individuals requesting information under FOIA/PA, and INS officials and employees engaged in processing or making determinations on FOIA/PA requests.

SYSTEMS EXEMPTED FROM CERTAIN PROVISIONS OF THE ACT:

None.

[FR Doc. 85-1148 Filed 1-14-85; 8:45 am]

BILLING CODE 4410-10-M

[AAG/A Order No. 1-85]

Privacy Act of 1974; Modified System of Records

Pursuant to the provisions of the Privacy Act of 1974 (5 U.S.C. 522a), notice is hereby given that the Department of Justice proposes to modify the system of records entitled "Central Criminal Division Index File and Assoicated Records, JUSTICE/CRM-100," which is maintained by the Criminal Division.

This system is a system of records for which public notice was published in the **Federal Register** on September 30, 1977, consistent with provisions of 5 U.S.C. 552a(e) (4) and (11). However, the Criminal Division now proposes to automate certain summary-type data, e.g., name of individual, file number, data of correspondence, etc., to assist in its efforts to track and control correspondence, cases and matters, and to improve its ability to determine the status thereof. Revisions are being made to various sections of the notice to reflect changes due to the automation effort. The "Storage" and "Retrievability" sections indicate that

certain summary data will be stored on magnetic disks and retrieved by on-line searches of individual names and file or docket numbers to locate the required file; the "Safeguards" section reflects increased security for the automated system; and the "Retention and Disposal" section has been revised to reflect that a retention and disposal schedule for the automated records is under review. In addition, changes have been made to clarify the "Legislative authority for maintenance of the system" section.

The Office of Management and Budget (OMB), which has oversight responsibility under the Act, requires a 60-day period in which to review the proposal to partially automate this system. Therefore, OMB, the Congress, and the public are invited to submit written comments on this system. Comments should be addressed to thomas F. O'Leary, Assistant Director, Administrative Services Staff, Justice Management Division, Department of Justice, Room 6314, 10th and Constitution Avenue NW., Washington, D.C. 20530. If no comments are received from either the public, OMB, or the Congress by March 18, 1985, the proposed modifications will be implemented without further notice in the Federal Register.

Dated: January 2, 1985.

Anthony C. Liotta,

Assistant Attorney General for Administration.

JUSTICE/CRM-001

SYSTEM NAME:

Central Criminal Division Index File and Associated Records.

SYSTEM LOCATION:

U.S. Department of Justice; Criminal Division, 10th and Constitution Avenue NW.; Washington, D.C. 20530, and, Federal Records Center; Suitland, Maryland 20409.

CATEGORIES OF INDIVIDUALS COVERED BY THE SYSTEM:

Persons referred to in potential or actual cases and matters of concern to the Criminal Division and correspondents on subjects directed or referred to the Criminal Division.

CATEGORIES OF RECORDS IN THE SYSTEM:

The system consists of alphabetical indices bearing individual names, and the associated records to which they relate, arranged either by subject matter or individual identifying number containing the general and particular records of all Criminal Division correspondence, cases, matters, and memoranda, including but not limited to, investigative reports, correspondence to and from the Division, legal papers, evidence, and exhibits. The system also includes items classified in the interest of national security with such designations as confidential, secret, and top secret received and maintained by the Department of Justice. This system may also include records concerning subject matters more particularly described in other systems of records of the Criminal Division.

AUTHORITY FOR MAINTENANCE OF THE SYSTEM:

This system is established and maintained pursuant to 44 U.S.C. 3101 to implement all functions assigned to the Criminal Division in 28 CFR 0.55 through 0.64–2.

ROUTINE USES OF RECORDS MAINTAINED IN THE SYSTEM, INCLUDING CATEGORIES OF USERS AND THE PURPOSES OF SUCH USES:

A record maintained in this system of records may be disseminated as a routine use of such record as follows: (1) In any case in which there is an indication of a violation or potential violation of law, whether civil, criminal, or regulatory in nature, the record in question may be disseminated to the appropriate federal, state, local, of foreign agency charged with the responsibility for investigation or prosecuting such violation or charged with enforcing or implementing such law; (2) in the course of investigating the potential or actual violation of any law, whether civil, criminal, or regulatory in nature, or during the course of a trial or hearing or the preparation for a trial or hearing for such violation, a record may be disseminated to a federal, state, local, or foreign agency, or to an individual or organization, if there is reason to believe that such agency, individual, or organization possesses information relating to the investigation, trial, or hearing and the dissemination is reasonably necessary to elicit such information or to obtain the cooperation of a witness or an informant; (3) a record relating to a case or matter may be disseminated in an appropriate federal, state, local, or foreign court or grand jury proceeding in accordance with established constitutional, substantive, or procedural law or practice; (4) a record relating to a case or matter may be disseminated to a federal, state, or local administrative or regulatory proceeding or hearing in accordance with the procedures governing such proceeding or hearing; (5) a record relating to a case or matter may be disseminated to an actual or potential party or his attorney for the purposes of negotiation or discussion on such matters as settlement of the case or matter, plea bargaining, or informal discovery proceedings; (6) a record relating to a case or matter that has been referred by an agency for investigation, prosecution, or enforcement, or that involves a case or matter within the jurisdiction of an agency, may be disseminated to such agency to notify the agency of the status of the case or matter or of any decision or determination that has been made, or to make such other inquiries and reports as are necessary during the processing of the case or matter; (7) a record relating to a person held in custody pending or during arraignment, trial, sentence, or extradition proceedings, or after conviction or after extradition proceedings, may be disseminated to a federal, state, local, or foreign prison, probation, parole, or pardon authority, or to any other agency or individual concerned with the maintenance, transportation, or release of such a person; (8) a record relating to a case or matter may be disseminated to a foreign country pursuant to an international treaty or convention entered into and ratified by the United States or to an executive agreement; (9) a record may be disseminated to a federal, state, local, foreign, or international law enforcement agency to assist in the general crime prevention and detection efforts of the recipient agency or to provide investigative leads to such agency; (10) a record may be disseminated to a federal agency, in response to its request, in connection with the hiring or retention of an employee, the issuance of a security clearance, the reporting of an investigation of an employee, the letting of a contract, or the issuance of a license, grant, or other benefit by the requesting agency, to the extent that the information relates to the requesting agency's decision on the matter; (11) a record may be disseminated to the public, news media, trade associations, or organized groups, when the purpose of the dissemination is educational or informational, such as descriptions of crime trends or distinctive or unique modus operandi, provided that the record does not contain any information identifiable to a specific individual other than such modus operandi; (12) a record may be disseminated to a foreign country, through the United States Department of State or directly to the representative of such country, to the extent necessary to assist such country in apprehending and/or returning a fugitive to a jurisdiction which seeks his return; (13) a record that contains classified national security information

and material may be disseminated to persons who are engaged in historical research projects, or who have previously occupied policy making provisions to which they were appointed by the President, in accordance with the provisions codified in 28 CFR 17.60; (14) a record relating to an actual or potential civil or criminal violation of title 17, United States Code, may be disseminated to a person injured by such violation to assist him in the institution or maintainance of a suit brought under such title.

Release of information to the news media: Information permitted to be released to the news media and the public pursuant to 28 CFR 50.2 may be made available from systems of records maintained by the Department of Justice unless it is determined that release of the specific information in the context of a particular case would constitute an unwarranted invasion of personal privacy.

Release of information to Members of Congress. Information contained in systems of records maintained by the Department of Justice, not otherwise required to be released pursuant to 5 U.S.C. 552, may be made available to a Member of Congress or staff acting upon the Member's behalf when the Member or staff requests the information on behalf of and at the request of the individual who is the subject of the record.

ROUTINE USES OF RECORDS MAINTAINED IN THE SYSTEM, INCLUDING CATEGORIES OF USERS AND THE PURPOSES OF SUCH USES:

Release of information to the National Archives and Records Service: A record from a system of records may be disclosed as a routine use to the National Archives and Records Service (NARS) in records management inspections conducted under the authority of 44 U.S.C. 2904 and 2906.

POLICIES AND PRACTICES FOR STORING, RETRIEVING, ACCESSING, RETAINING, AND DISPOSING OF RECORDS IN THE SYSTEM:

STORAGE:

Paper documents are stored in file folders; selected summary data is stored on manual index cards and on magnetic disks.

RETRIEVABILITY:

Summary data, e.g., names, file numbers, subjects, dates of correspondence, dates of receipt, due dates of assignments, docket numbers, and synopses are retrieved from manual index cards for records received prior to 1980; for 1980 and subsequent years summary data is retrieved from magnetic disks.

File folders are retrieved through manual or automated indexes which are accessed through certain summary data, i.e., name or file and docket numbers.

SAFEGUARDS:

The records are safeguarded and protected in accordance with applicable Departmental rules. Security for the automated records include strictly controlled access codes and passwords. In addition, only authorized Criminal Division employees will have access to the system.

RETENTION AND DISPOSAL:

Currently there is an agreement with the Federal Records Center for retention and disposal after ten years applicable to approximately 20 percent of the Division records. All other paper records are currently retained indefinitely. A retention and disposal schedule for automated records will be under review in connection with a revised schedule for the paper records.

SYSTEM MANAGER(S) AND ADDRESS:

Assistant Attorney General, Criminal Division; U.S. Department of Justice; 10th and Constitution Avenue, NW.; Washington, D.C. 20530.

NOTIFICATION PROCEDURE:

The major part of this system is exempted from this requirement under 5 U.S.C. 552a (j)(2), (k)(1), or (k)(2). Inquiry concerning this system should be directed to the system manager listed above.

RECORD ACCESS PROCEDURES:

The major part of this system is exempted from this requirement under 5 U.S.C. 552a (j)(2), (k)(1), or (k)(2). To the extent that this system of records is not subject to exemption, it is subject to access and contest. A determination as to exemption shall be made at the time a request for access is received. A request for access to a record contained in this system shall be made in writing, with the envelope and the letter clearly marked 'Privacy Access Request.' Include in the request the name of the individual involved, his birth date and place, or any other identifying number or information which may be of assistance in locating the record, the name of the case or matter involved, if known, and the name of the judicial district involved, if known. The requestor will also provide a return address for transmitting the information. Access requests will be directed to the system manager listed above.

CONTESTING RECORD PROCEDURES:

Individuals desiring to contest or amend information maintained in the system should direct their request to the system manager listed above, stating clearly and concisely what information is being contested, the reasons for contesting it, and the proposed amendment to the information sought.

RECORD SOURCE CATEGORIES:

Department officers and employees, and other federal, state, local, and foreign law enforcement and non-law enforcement agencies, private persons, witnesses, and informants.

SYSTEMS EXEMPTED FROM CERTAIN PROVISIONS OF THE ACT:

The Attorney General has exempted this system from subsections (c)(3) and (4), (d), (e)(1), (2) and (e)(4)(G), (H) and (I), (e)(5) and (8), (f) and (g) of the Privacy Act pursuant to 5 U.S.C. 552a (j)(2). Rules have been promulgated in accordance with the requirements of 5 U.S.C. 553(b), (c) and (e) and have been published in the **Federal Register.**

[FR Doc. 85-1149 Filed 1-14-85; 8:45 am]

BILLING CODE 4410-01-M

Drug Enforcement Administration

Queens County Medical Society Drug Line Revocation of Registration

On October 30, 1984, the Deputy Assistant Administrator, Office of Diversion Control, Drug Enforcement Administration (DEA), directed an Order to Show Cause to the Queens County Medical Society Drug Line, 30-64 37th Street, Long Island City, New York, 11103, (Respondent), seeking to revoke DEA Certificate of Registration PQ0212972 and to deny any pending applications for registration as a narcotic treatment program under 21 U.S.C. 823(g). Respondent replied to the Order to Show Cause by a letter dated December 1, 1984, in which it specifically waived its opportunity for a hearing. Therefore, the Administrator finds that registrant waived its opportunity for a hearing and enters this final order on the record as it appears. 21 CFR 1301.54(d) and (e).

Respondent is a narcotic treatment program located in the Borough of Queens, New York. The Controlled Substances Act (21 U.S.C. 824(g)) requires that narcotic treatment programs maintain security of stocks of narcotic drugs for maintenance treatment and detoxification and to maintain records in accordance with 21 U.S.C. 827. After examining the record in this case, the Administrator finds that the Queens County Medical Society Drug Line has failed both to maintain adequate security of stocks of narcotic

drugs and to maintain records of stocks of controlled substances ordered, dispensed, maintained and administered. For the reasons set forth below, the Administrator revokes the registration held by Respondent and denies any pending applications for renewal.

Respondent has had a long history of violating the Controlled Substances Act and its attendant regulations. In February, 1974, an in-depth accoutability investigation conducted by DEA diversion investigators revealed a 6.06% overage in methadone accountability and a failure to take a physical inventory as required by 21 CFR 1304.13. A further in-depth accountability investigation in May, 1979, uncovered an overage of 3,810 mgs. of methadone. Again, Respondent failed to take the biennial inventory and also failed to properly execute official order forms. Following this investigation, the DEA sent a letter of admonition to the registrant pointing out these violations and warning that further violations could result in further administrative action against the registration of the clinic. By letter dated June 14, 1979, Dr. Philip Kaufman, the medical director of Respondent, assured DEA that he would take the required biennial physical inventory and would insure that DEA order forms were properly completed.

Another in-depth investigation conducted by DEA in February, 1982, revealed continuing violations and new violations of the CSA and its regulations. The registrant again failed to take a biennial physical inventory as required by 21 CFR 1304.13 and continued to fill out incomplete order forms in violation of 21 CFR 1305.09(e). In addition, there was an accountability overage of 18,405 mgs. of methadone, or 5.47%. Perhaps most disturbing was the inadequate security at the facility. DEA personnel informed Dr. Kaufman that due to the large quantities of methadone being stored, the former security precautions, including electronic security connected to the central station of a security firm via a telephone dialer, was inadequate. DEA personnel discussed all of these violations with Dr. Kaufman at an informal administrative hearing on April 7, 1982. As he had in the past, Dr. Kaufman informed DEA personnel that he would take steps to rectify the violations pointed out to him. DEA personnel informed Dr. Kaufman that either a direct line to the security station must be installed or a much smaller quantity of medication be maintained at the facility. Dr. Kaufman stated that he would notify DEA personnel in writing by April 21, 1982, as to whether he would reduce the amount of medication on hand or install a direct line. Following extensive correspondence between Dr. Kaufman and DEA, a security system was agreed upon.

Attached to the December 1, 1984 letter from Dr. Kaufman was a copy of a letter from a security company describing certain security features purportedly installed at Respondent's facility. This letter is dated November 26, 1984, three weeks after the receipt of the Order to Show Cause by Respondent as evidence by a return receipt signed by Dr. Kaufman on November 5, 1984. The letter states that the alarm system is connected to a wireless central system that cannot be defeated by cutting telephone lines.

The Administrator is not impressed by this belated attempt to comply with the security requirements for narcotic treatment programs. Respondent moved to install the improved security at its facility only after issuance of the Order to Show Cause in October 1984, two years after Dr. Kaufman agreed to install the security. Installation at this time is not enough to forestall revocation. Even if these arrangements do meet DEA requirements, they were not in place when needed. Respondent was fully aware of the need for improved security yet when DEA investigators were at the facility in June, 1984, there was no security system at all in place. In light of Respondent's past security violation, it is not unlikely that these new security devices will be removed or disconnected when DEA has turned its attention to other matters. Voluntary compliance with the applicable law and regulations is essential in DEA's regulation of legitimate handlers of controlled substances. The Administrator should not be left to wonder whether this registrant will provide the necessary security or maintain the required records. Protection of the public safety is the paramount responsibility of the Administrator. Considering Respondent's history of security violations, even the tardy installation of this new system cannot convince the Administrator that the public would be best served by the continued registration of Respondent.

The Administrator has carefully considered the other points raised by Dr. Kaufman in his brief letter. Dr. Kaufman states that all applicable regulations are "being complied with." While he admits that the 1982 daily records "were misplaced and lost," all the monthly records for 1982 are available. He states that all required 1983 and 1984 records are maintained "with scrupulously detailed daily inventory." Given the past history of this program, the administrator gravely doubts that the records are now scrupulously maintained. Dr. Kaufman's letter does not contain any evidence that Respondent has rectified its chronic recordkeeping violations. Indeed, the record clearly shows that these violations continue.

In March, 1984, investigators of the New York State Division of Substance Abuse Services (DSAS) conducted an inspection of Respondent's facilities. That inspection revealed violations of the applicable State of New York and Food and Drug Administration (FDA) regulations governing the detoxification and maintenance of drug addicts at narcotic treatment programs. This inspection revealed that, among other violations, the registrant failed to maintain daily narcotic inventories. The registrant also failed to properly maintain medication order sheets and dispensing records. As a result of the violations found at this inspection, DSAS withdrew permission for the registrant to use liquid methadone. Previous DSAS inspections in February and September, 1983, revealed similar deficiencies. The Administrator is not basing his revocation on these state regulatory violations but merely includes them to show the unwillingness and inability of Respondent to comply with either Federal or state law regarding controlled substances.

In a letter to DEA personnel dated June 2, 1984, Dr. Kaufman stated that his census of addicts had been decreased to 37 patients and his drug inventory reduced to 13 grams of methadone. On June 25, 1984, DEA diversion investigators conducted a physical inventory of all methadone on hand at the registrant. The inventory on that day was 309.25 methadone 40 ml. diskettes, totalling 12,370 mg. or 12.37 grams. No security system was in place. A follow-up investigation on September 4, 1984, by DEA diversion investigators revealed that Dr. Kaufman was unable to locate his 1982 dispensing records.

Diversion, and the potential diversion of methadone from narcotic treatment programs, is of grave concern to the Administrator. As his predecessor noted in *Metro Substance Abatement Program, Inc.*, 45 FR 78845 (1980), Congress enacted the Narcotic Addict Treatment Act after it had found that the rapid and widespread use of methadone in these programs had brought with it a proportional increase in the diversion of methadone for illegal use and sale. The DEA regulation and supervision of these programs is

intended to prevent the loss and diversion of methadone. The Administrator will not hesitate to revoke the registration of a narcotic treatment program that fails to meet its statutory and regulatory obligations to provide adequate security and recordkeeping. Respondent has a history of violation dating back to 1974. This Respondent, like the Respondent in *Metro Substance Abatement Program, Inc.*, manifests a casual indifference to its obligation to provide adequate security, to keep complete and accurate records, and to properly account for its supply of narcotic drugs. Respondent has been warned many times since 1974 of its obligation to maintain these records and maintain adequate security. Given the Respondent's unwillingness to keep the records required of narcotic treatment programs, DEA will never know whether methadone was diverted from this facility. The public should not be placed at the risk of such diversion any longer.

The Administrator finds that there is a lawful or statutory basis for the revocation of the Respondent's DEA Certificate of Registration. Accordingly, pursuant to the authority vested in the Attorney General by 21 U.S.C. 824(a) and redelegated to the Administrator of the Drug Enforcement Administration, the Administrator hereby orders that Certificate of Registration PQ0212972 be revoked, and any pending applications for renewal, be denied, February 14, 1985.

Dated: January 7, 1985.

Francis M. Mullen, Jr.,

Administrator.

[FR Doc. 85-1113 Filed 1-14-85; 8:45 am]

BILLING CODE 4410-09-M

DEPARTMENT OF LABOR

Employment and Training Administration

Determinations Regarding Eligibility To Apply for Worker Adjustment Assistance

In accordance with section 223 of the Trade Act of 1974 (19 U.S.C. 2273) the Department of Labor herein presents summaries of determinations regarding eligibility to apply for adjustment assistance issued during the period December 31, 1984–January 4, 1985.

In order for an affirmative determination to be made and a certification of eligibility to apply for adjustment assistance to be issued, each of the group eligibility requirements of section 222 of the Act must be met.

(1) That a significant number or proportion of the workers in the workers' firm, or an appropriate subdivision thereof, have become totally or partially separated,

(2) That sales or production, or both, of the firm or subdivision have decreased absolutely, and

(3) That increases of impacts of articles like or directly competitive with articles produced by the firm or appropriate subdivision have contributed importantly to the separations, or threat thereof, and to the absolute decline in sales or production.

Negative Determinations

In each of the following cases the investigation revealed that criterion (3) has not been met. A survey of customers indicated that increased imports did not contribute importantly to worker separations at the firm.

TA-W-15,516 and TA-W-15,517; Benham Knitwear, Inc., Kutztown, PA

TA-W-15,526; Anderson Shake & Shingle, Inc., Cathlamet, WA

TA-W-15,531; Van Vlaanderen Machine Co., Paterson, NJ

TA-W-15,530; Jung Hing Fashions, Inc., New York, NY

Affirmative Determinations

TA-W-15,423, Charles Parker Co. Div. of Union Manufacturing Co., Meriden, CT

A certification was issued covering all workers separated on or after October 1, 1983 and before August 12, 1984.

TA-W-15,513, Shamokin Dress Co., Shamokin, PA

A certification was issued covering all workers separated on or after December 1, 1983.

TA-W-15,529; General Portland, Inc., Dade County Plant, Miami, FL

A certification was issued covering all workers separated on or after June 1, 1984.

TA-W-15,503, TA-W-15,504, TA-W-15,505, Farah Manufacturing Co., Inc., El Paso, TX

A certification was issued covering all workers separated on or after October 4, 1983.

TA-W-15,431, Quintana Petrochemical Co., Corpus Christi, TX

A certification was issued covering all workers separated on or after January 1, 1984.

TA-W-15,532; Whirlpool Corp., Evansville Div., Evansville, IN

A certification was issued covering all workers separated on or after October 16, 1983.

TA-W-15,473 Cannon Shoe Co., Hagerstown Shoe Co. Div., Hagerstown, MD

A certification was issued covering all workers separated on or after September 2, 1984.

TA-W-15,509; LLB Fashions, Inc., Lakewood, NJ

A certification was issued covering all workers separated on or after October 12, 1983 and before September 1, 1984.

TA-W-15,521; Iroquois Bag Co., Div. of 463 Howard St., Inc., Buffalo, NY

A certification was issued covering all workers separated on or after December 17, 1983.

TA-W-15,489; Hyde Athletic Industries, Spot-Bilt, Inc., Bangor, ME

A certification was issued covering all workers engaged in the production of uppers and soles separated on or after August 25, 1984.

TA-W-15,464; Lorraine Manufacturing Corp., Bristol, VA

A certification was issued covering all workers separated on or after August 29, 1983.

TA-W-15,338; M.P. Goodkin, Inc., Irvington, NJ

A certification was issued covering all workers separated on or after May 16, 1983 and before August 31, 1984.

TA-W-15,512; Regina Footwear, Inc., Brooklyn, NY

A certification was issued covering all workers separated on or after April 1, 1984 and before October 30, 1984.

I hereby certify that the aforementioned determinations were issued during the period December 31, 1984—January 4, 1985. Copies of these determination are available for inspection in Room 6443, U.S. Department of Labor, 601 D Street, NW., Washington, D.C. 20213, during normal business hours or will be mailed to persons who write to the above address.

Dated: January 8, 1985.

Marvin M. Fooks,

Director, Office of Trade Adjustment Assistance.

[FR Doc. 85-1155 Filed 1-14-85; 8:45 am]

BILLING CODE 4510-30-M

Investigations Regarding Certifications of Eligibility To Apply for Worker Adjustment Assistance

Petitions have been filed with the Secretary of Labor under section 221(a) of the Trade Act of 1974 ("The Act") and are identified in the Appendix to this notice. Upon receipt of these petitions, the Director of the Office of Trade

Adjustment Assistance, Employment and Training Administration, has instituted investigations pursuant to section 221(a) of the Act.

The purpose of each of the investigations is to determine whether the workers are eligible to apply for adjustment assistance under Title II, Chapter 2, of the Act. The investigations will further relate, as appropriate, to the determination of the date on which total or partial separations began or threatened to begin and the subdivision of the firm involved.

The petitioners or any other persons showing a substantial interest in the subject matter of the investigations may request a public hearing, provided such request is filed in writing with the Director, Office of Trade Adjustment Assistance, at the address shown below, not later than January 25, 1985.

Interested persons are invited to submit written comments regarding the subject matter of the investigations to the Director, Office of Trade Adjustment Assistance, at the address shown below, not later than January 25, 1985.

The petitions filed in this case are available for inspection at the Office of the Director, Office of Trade Adjustment Assistance, Employment and Training Administration, U.S. Department of Labor, 601 D Street, NW., Washington, D.C. 20213.

Signed at Washington, D.C., this 7th day of January 1985.

Marvin M. Fooks,

Director, Office of Trade Adjustment Assistance.

APPENDIX

Petitioner: Union/worker or former workers of—	Location	Date received	Date of petition	Petition No.	Articles produced
Aors Manufacturing (ILGWU)	Baltimore, MD	12/26/84	12/3/84	TA-W-15,661	Raincoats.
B-G Shoe Co. (company)	Lititz, PA	12/24/84	12/19/84	TA-W-15,662	Shoes—infants.
Bates Fabrics, Inc. (workers)	Lewiston, ME	12/26/84	12/17/84	TA-W-15,663	Weave yarn.
Burlington Industries (company)	Franklinton, NC	12/21/84	12/10/84	TA-W-15,664	Linings for suits, coats, jackets, men's and women's clothing.
Globe Refractories, Inc. (company)	Newell, WV	12/21/84	12/17/84	TA-W-15,665	Bricks, ladle, clay.
Marlboro Footwear Corp. (workers)	Marlboro, MA	12/21/84	12/7/84	TA-W-15,666	Shoes, casual, women's.
Pako Corp. (workers)	Minneapolis, MN	12/27/84	12/21/84	TA-W-15,667	Equipment, processing, film, speed, high.
Roller Derby Skate Corp. (UFCW)	Litchfield, IL	12/24/84	12/18/84	TA-W-15,668	Skates, roller, ice.
Stedfast Rubber Co., Inc. (ILGWU)	North Easton, PA	12/26/84	12/18/84	TA-W-15,669	Linings, shoe.
U.S. Steel Corp., Tie Plate Division (workers)	Gary, IN	12/21/84	12/18/84	TA-W-15,670	Tie plates.
Western block (workers)	Lockport, NY	12/21/84	12/14/84	TA-W-15,671	Tackle blocks.
Westinghouse Electric Corp., power circuit breaker division (IUE).	Trafford, PA	12/21/84	12/17/84	TA-W-15,672	Breakers, circuit, power.
Oak Communications Systems (workers)	Elkhorn, WI	12/7/84	11/29/84	TA-W-15,673	Parts and boards for the repair of the cable T.V. converters.
Wasser & Fluhrer, Inc.	Kalama, WA	12/26/84	12/19/84	TA-W-15,674	Cedar shakes.

[FR Doc. 85-1154 Filed 1-14-85; 8:45 am]

BILLING CODE 4510-30-M

[TA-W-15,466]

Mayr Brothers Logging Co., Inc., Raymond, WA; Amended Certification Regarding Eligibility To Apply for Worker Adjustment Assistance

In accordance with section 223 of the Trade Act of 1974, the Department of Labor issued a Certification of Eligibility to Apply for Worker Adjustment Assistance on December 12, 1984, applicable to all workers at the Mayr Brothers Logging Company, Incorporated, Hoquiam, Washington. The Notice of Certification was published in the **Federal Register** on December 21, 1984 (49 FR 49733).

On the basis of additional information, the Office of Trade Adjustment Assistance, on its own motion reviewed the certification. The additional information revealed that the certification did not contain the subject firm's worker group in Raymond, Washington but established instead the headquarters in Hoquiam, Washington as the adversely affected worker group. All the sales, production and employment data collected by the Department were for the Raymond, Washington worker group.

The certification for workers at Mayr Brothers Logging Company, Inc., TA-W-15,466, therefore is amended by substituting the new location at Raymond Washington in the certification for the headquarters location at Hoquiam, Washington.

The Certification applicable to TA-W-15,466 is hereby amended and issued as follows:

"All workers of Mayr Brothers Logging Company, Incorporated, Raymond, Washington who became totally or partially separated from employment on or after April 1, 1984 are eligible to apply for adjustment assistance under Section 223 of the Trade Act of 1974."

Signed at Washington, D.C. this 2nd day of January 1985.

Harold A. Bratt,

Deputy Director, Office of Program Management, UIS.

[FR Doc. 85-1150 Filed 1-14-85; 8:45 am]

BILLING CODE 4510-30-M

[TA-W-15,330]

New B Manufacturing Corp., Hawthorne, PA; Amended Certification Regarding Eligibility To Apply for Worker Adjustment Assistance

In accordance with section 223 of the Trade Act of 1974, the Department of Labor issued a Certification of Eligibility to Apply for Worker Adjustment Assistance on December 3, 1984, applicable to all workers at the New B Manufacturing Corporation, Hawthorne, Pennsylvania. The Notice of Certification was published in the **Federal Register** on December 18, 1984 (49 FR 49187).

On the basis of additional information, the Office of Trade Adjustment Assistance, on its own motion reviewed the certification. The additional information revealed that permanent layoffs began in June 1983. It was the Department's intent to include all workers as eligible to apply for adjustment assistance who were laid off from the New B Manufacturing Corporation in Hawthorne, Pennsylvania.

The certification for workers at the New B Manufacturing Corporation, Hawthorne, Pennsylvania TA–W–15,330, therefore is amended by substituting a new impact date of June 1, 1983.

The Certification applicable to TA–W–15,330 is hereby amended and issued as follows:

"All workers of the New B Manufacturing Corporation, Hawthorne, Pennsylvania who became totally or partially separated from employment on or after June 1, 1983 are eligible to apply for adjustment assistance under Section 223 of the Trade Act of 1974."

Signed at Washington, D.C., this 3rd day of January 1985.

Harold A. Bratt,

Deputy Director, Office of Program Management, UIS.

[FR Doc. 85–1151 Filed 1–14–85; 8:45 am]

BILLING CODE 4510-30-M

[TA-W-15,283]

Reltoc Manufacturing Co., Forrest City, AR; Negative Determination Regarding Application for Reconsideration

By an application dated November 7, 1984 and after being granted a filing extension, the Amalgamated Clothing Workers of America (ACWA) requested administrative reconsideration of the Department of Labor's Negative Determination Regarding Eligibility To Apply for Worker Adjustment Assistance in the case of workers and former workers at Reltoc Manufacturing Company, Forrest City, Arkansas. The additional information promised by December 14, 1984 to support the union's case has not been forthcoming. The negative determination was published in the **Federal Register** on October 23, 1984 (49 FR 42653).

Pursuant to CFR 90.18(c) reconsideration may be granted under the following circumstances:

(1) If it appears on the basis of facts not previously considered that the determination complained of was erroneous;

(2) If it appears that the determination complained of was based on a mistake in the determination of facts previously considered; or

(3) If, in the opinion of the Certifying Officer, a misinterpretation of facts or of the law justified reconsideration of the decision.

The union objects to the time periods used by the Department in denying the worker petition and to the fact that a customer survey was not conducted by the Department. The union argues that had the Department conducted a survey of Reltoc's customers, it would have found that Reltoc's customers substituted imported slacks for those produced at the Forrest City plant.

The investigative case file shows that Reltoc operates four plants which produce men's slacks. The Forrest City plant was temporarily closed in July 1983 and reopened in March 1984 with an increasing monthly employment trend. The findings show that in 1983 when the Forrest City plant temporarily closed, the sales, production and employment criteria of the group eligibility requirements in section 222 of the Trade Act were satisfied. However, the "contributed importantly" test was not met.

Reltoc's other three plants in Alabama had increased production of men's slacks during the time of the Forrest City's plant closure. Reltoc did not import men's slacks nor use foreign contractors during the relevant period of the investigation. Reltoc's sole customer, however, imported slack sets which include a pair of slacks and a jacket or top which were sold together as a set. According to company officials, the imported slacks incorporated into slack sets are not comparable to the type of slacks produced by Reltoc. The fabric used in the imported slacks is of a higher quality and the slacks and tops of the set are made from the same fabric. The imported slack sets are geared toward a different market segment than are Reltoc's slacks. Reltoc has never produced slack sets.

Conclusion

After review of the application and the investigative file, I conclude that there has been no error or misinterpretation of the law which would justify reconsideration of the Department of Labor's prior decision. Accordingly, the application is denied.

Signed at Washington, D.C., this 21st day of December 1984.

Stephen A. Wandner,

Deputy Director, Office of Legislation and Actuarial Services, UIS.

[FR Doc. 85–1152 Filed 1–14–85; 8:45 am]

BILLING CODE 4510-30-M

Wage and Hour Division

Certificates Authorizing the Employment of Learners at Special Minimum Wages

Notice is hereby given that pursuant to section 14 of the Fair Labor Standards Act (52 Stat. 1062, as amended; U.S.C. 214), Reorganization Plan No. 6 of 1950 (3 CFR 1949–53 Comp., p. 1004), and Administrative Order No. 1–76 (41 FR 18949), the firms listed in this notice have been issued special certificates authorizing the employment of learners at hourly wage rates lower than the minimum wage rates otherwise applicable under section 6 of the Act. For each certificate, the effective and expiration dates, number or proportion of learners and the principal product manufactured by the establishment are as indicated. Conditions on occupations, wage rates and learning periods which are provided in certificates issued under the supplemental industry regulations cited in the captions below are as established in those regulations.

The following certificates were issued under the apparel industry learner regulations (29 CFR 522.1 to 522.9, as amended and 522.20 to 522.25, as amended). The following normal labor turnover certificates authorize 10 percent of the total number of factory production workers except as otherwise indicated.

Flushing Shirt Mfg. Co., Inc., Frostburg, MD; 10–24–84 to 10–23–85; 25 learners for plant expansion purposes. (Men's shirts)

McCreary Mfg. Co., Stearns, KY; 12–8–84 to 12–7–85. 10 percent of the total number of factory production workers for normal labor turnover purposes. (Men's shirts)

Monticello Mfg. Co., Inc. Monticello, KY; 12–8–84 to 12–7–85. 10 percent of the total number of factory production workers for normal labor turnover purposes. (Men's and boys' shirts)

The following certificate was issued under the knitted wear industry regulations (29 CFR 522.1 to 522.9, as amended and 522.30 to 522.35, as amended)

Junior Form Lingerie Inc., Boswell, PA; 10–11–84 to 10–10–85. 5 percent of the total number of factory production workers for normal labor turnover purposes. (Ladies' underwear and sleepwear)

Each learner certificate has been issued upon the representations of the employer which, among other things were that employment of learners at special minimum rates is necessary in order to prevent curtailment of opportunities for employment, and that experienced workers for the learners occupations are not available.

The certificate may be annulled or withdrawn as indicated therein, in the manner provided in 29 CFR Part 528. Any person aggrieved by the issuance of any of these certificates may seek a review or reconsideration thereof on or before January 30, 1985.

Signed at Washington, D.C., this 9th day of January 1985.

Arthur H. Korn,

Authorized Representative of the Administrator.

[FR Doc. 85-1153 Filed 1-14-85; 8:45 am]

BILLING CODE 4510-27-M

Office of Pension and Welfare Benefit Programs

[Application No. D-5276, et al.]

Proposed Exemptions; J.P. Stevens & Co., et al.

AGENCY: Pension and Welfare Benefit Programs, Labor.

ACTION: Notice of proposed exemptions.

SUMMARY: This document contains notices of pendency before the Department of Labor (the Department) of proposed exemptions from certain of the prohibited transaction restrictions of the Employee Retirement Income Security Act of 1974 (the Act) and/or the Internal Revenue Code of 1954 (the Code).

Written Comments and Hearing Requests

All interested persons are invited to submit written comments or requests for a hearing on the pending exemptions, unless otherwise stated in the Notice of Pendency, within 45 days from the date of publication of this **Federal Register** Notice. Comments and requests for a hearing should state the reasons for the writer's interest in the pending exemption.

ADDRESS: All written comments and requests for a hearing (at least three copies) should be sent to the Office of Fiduciary Standards, Pension and Welfare Benefit Programs, Room C-4526, U.S. Department of Labor, 200 Constitution Avenue NW., Washington, D.C. 20216. Attention: Application No. stated in each Notice of Pendency. The applications for exemption and the comments received will be available for public inspection in the Public Documents Room of Pension and Welfare Benefit Programs, U.S. Department of Labor, Room N-4677, 200 Constitution Avenue NW., Washington, D.C. 20216.

Notice of Interested Persons

Notice of the proposed exemptions will be provided to all interested persons in the manner agreed upon by the applicant and the Department within 15 days of the date of publication in the **Federal Register**. Such notice shall include a copy of the notice of pendency of the exemption as published in the **Federal Register** and shall inform interested persons of their right to comment and to request a hearing (where appropriate).

SUPPLEMENTARY INFORMATION: The proposed exemptions were requested in applications filed pursuant to section 408(a) of the Act and/or section 4975(c)(2) of the Code, and in accordance with procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). Effective December 31, 1978, section 102 of Reorganization Plan No. 4 of 1978 (43 FR 47713, October 17, 1978) transferred the authority of the Secretary of the Treasury to issue exemptions of the type requested to the Secretary of Labor. Therefore, these notices of pendency are issued solely by the Department.

The applications contain representations with regard to the proposed exemptions which are summarized below. Interested persons are referred to the applications on file with the Department for a complete statement of the facts and representations.

Retirement Pension of J.P. Stevens & Co., Inc. and Subsidiaries (the Retirement Plan); Hourly Employees' Pension Plan of J.P. Stevens & Co., Inc. (the Hourly Plan); and Foote & Davis, Inc. Retirement Plan (the F&D Plan; Collectively, the Plans) Located in New York, New York

[Application Nos. D-5276, D-5277 and D-5278]

Proposed Exemption

The Department is considering granting an exemption under the authority of section 408(a) of the Act and section 4975(c)(2) of the Code and in accordance with the procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). If the exemption is granted the restrictions of section 406(a) of the Act and the sanctions resulting from the application of section 4975 of the Code, by reason of section 4975(c)(1)(A) through (D) of the Code shall not apply to the proposed purchase by the Plans of an interest in certain real property from the National Life Insurance Company (National), in connection with formation of a partnership between the Plans and National, provided that the transaction is on terms at least as favorable to the Plans as the Plans could expect in an arm's-length transaction with an unrelated party.

Summary of Facts and Representations

1. The Retirement Plan and the Hourly Plan are defined benefit plans with 8,382 participants and 31,065 participants, respectively, as of March 15, 1984, and are sponsored by J.P. Stevens & Company, Inc. (JPS), a public corporation engaged in the manufacture and marketing of textiles. The F&D Plan is a defined benefit plan with 25 participants as of March 15, 1984 and is sponsored by Foote & Davis, Inc., a wholly-owned subsidiary of JPS engaged in printing and engraving. Each of the Plans participates in the Master Trust for Employees of J.P Stevens & Co., Inc. and Subsidiaries, the master trustee of which is Northern Trust Company (the Master Trustee), located in New York, New York. Discretionary authority with respect to investments of the Plans' assets, including authority to retain and discharge investment managers on behalf of the Plans, is held by the J.P. Stevens & Co., Inc. Investment Committee (the JPS Committee), which is comprised of officers and directors of JPS. None of the members of the JPS Committee have any proprietary interest in National. As of December 31, 1983, the Plans had total assets of approximately $300 million.

2. The JPC Committee has established as one of the investment objectives of the Plans the investment of $30 million in real estate investments. Toward this objective, the JPS Committee selected National as one of three real estate investment managers and designated National as investment manager for $10 million of the Plans' assets. National is a mutual life insurance company organized under the laws of the State of Vermont, with total assets of approximately $2.793 billion as of December 31, 1983. Neither JPS nor the Master Trustee is affiliated with National. In addition to a wide variety of insurance products and services, National offers funding, asset management and other services to employee benefit plans subject to the Act. Through its general and certain separate advisory accounts, National is a substantial investor in income-producing real estate, holding real estate investments for all of its accounts valued at approximately $85 million as of December 31, 1983. Among the real estate investments offered by National to its pension plan clients is National Pension Properties (NPP), a closed-end separate account managed by officers of National. Pursuant to the JPS Committee's designation of National as an investment manager for $10 million of the Plans' assets, as of December 31, 1983, $9 million of the Plans' assets has been deposited with National and allocated to NPP.

3. Among the real estate assets held in National's general account is the

Southside Shopping Center (the Property), located in St. Petersburg, Florida. Because of the close match between the Property's characteristics, the investment objectives of the Plans and the investment merits of the Property, National has proposed to the JPS Committee that the Plans acquire and interest in the Property. The JPS Committee approved a proposed transfer of the Property from National's general account directly to NPP, but this was subsequently rejected by National. Since National and the JPS Committee continue to believe that the Plans' acquisition of an interest in the Property would be in the best interests of the Plans, National is proposing that National and the Plans form a partnership (the Partnership) which would own and operate the Property. The investment by the Plans of $1 million to the Partnership would complete the investment of the $10 million for which the JPS Committee designated National as a real estate investment manager. The JPS Committee and National (collectively, the Applicants) are requesting an exemption to permit the Plans to acquire interests in the Property by participating in the Partnership under the terms and conditions described herein.

4. The Property is a 105,875 square foot neighborhood shopping center with major tenants which include Publix, a large regional supermarket chain, Eckerds, a national drug store chain, and Home Federal Savings and Loan Association. National purchased the Property for its general account in 1979, at which time the Property was operated under a master lease to one of the major tenants. In June, 1982 National negotiated a termination of the master lease and assumed control of all operations of the Property. The day-to-day management of the Property has been delegated to an experienced on-site property management firm which is not affiliated with National. The Property's fair market value was $2.7 million as of December 23, 1983, according to an appraisal performed by the independent real estate appraisal firm of Joseph J. Blake and Associates (Blake) of Miami, Florida.

5. The Partnership will be a limited partnership organized under the laws of the State of Vermont, to be known as the Southside Partnership. National will be the general partner and the Master Trustee, on behalf of the Plans, will be the sole limited partner. The sole purpose of the Partnership will be to own and operate the Property for income and capital appreciation. The Partnership will have a term of ten years and its objective will be to sell the Property in a time period consistent with the expected liquidation and distribution of the assets of NPP. The plans will contribute $1 million in cash to the Partnership. National will contribute the Property to the Partnership at an agreed value of $2.7 million, consistent with Blake's appraisal, and in return will receive a cash distribution from the Partnership in the amount of $700,000. However, the transfer value of the Property will be adjusted for any capital improvement made by National subsequent to Blake's appraisal and prior to the transfer. The amount and nature of such capital improvements will be certified to the Plans prior to the Partnership's formation, and the cash distribution to National will be increased by one-third of the amount of such improvements. All operating expenses of the Property for the period prior to its transfer to the Partnership will be paid by National, and no brokerage fees or sales commissions will be paid in connection with the transfer. The Plans, as limited partner, will have a one-third interest, and National, as general partner, will have a two-third interest, in the profits, losses and other attributes of ownership of the Partnership.

National has designated the investment committee of NPP to exercise the authority of National as general partner. Through that committee, National will exercise management authority over the day-to-day affairs of the Partnership including, for example, the approval of leases to new tenants and related tenant improvements, the approval of annual capital and operating budgets, selection and hiring of outside property management and other service providers and the determination of whether to proceed with additional construction (expansion) on the site. In exercising its management authority, National represents that it will undertake to operate the Partnership in the best interests of the Partnership and its limited partner, the Plans. In particular, National will analyze all partnership transactions on a "pre-tax" basis reflecting the tax exempt status of the Plans. For its managment services in connection with the Partnership, National, as general partner, will receive from the Partnership an annual fee of one percent of the value of the Property and .25 percent of any cash equivalent assets held by the Partnership. Both fees will be payable quarterly.[1]

[1] The Department is not proposing an exemption for the receipt of fees beyond that provided by section 408(b)(2) of the Act.

Consistent with applicable partnership law, the JPS Committee, acting on behalf of the Plans, will have the authority to review and approve in advance major transactions involving the Partnership. The Partnership Agreement enumerates thirteen types of transactions requiring prior approval of the JPS Committee. For example, the JPS Committee must approve the creation of any mortgage debt on the Property; the Property may not be sold without the approval of the JPS Committee; and no substitutions for or withdrawal of the general partner could occur without the approval of the JPS Committee. In the event that additional capital is required by the Partnership, the Plans will have the right, but not be obligated, to contribute a pro rata share of such capital. Additional non-prorated contributions of capital by either partner will result in adjustments to the interests of the partners in the Partnership in proportion to the total capital contribution of each partner.

6. Prior to approving the Plans' proposed participation in the Partnership, the JPS Committee was provided with a copy of the Partnership Agreement establishing the Partnership and specific information regarding the physical characteristics, history and income-producing capabilities of the Property. Based on all information provided, the JPS Committee has determined that the Plans' investment in the Partnership and National's transfer of the Property to the Partnership will be in the best interests of the Plans and consistent with the Plans' investment objectives, complementing the Plans' investment in NPP. Prior to the closing of the proposed transactions, the JPS Committee will review the terms of the transaction, including the Property's transfer price and any adjustments thereto, to ensure that such terms remain in the Plans' best interests. The Applicants note that prior to National's proposal of the subject transactions, the JPS Committee had already scrutinized National as one of three selected real estate investment managers for the Plans, carefully considering NPP's investment philosophy, strategy and guidelines. The Applicants represent that the investment by the Plans in the Partnership, as proposed herein, is fully consistent with the objectives which the JPS Committee sought to achieve by selecting National as an investment manager. The Applicants represent that even though National is a fiduciary with respect to the Plans, as an investment manager, the essential investment decisions on behalf of the Plans in the subject transactions have been and will

remain those of the JPS Committee. Specifically, the Applicants represent that National has not used any of the authority, control or responsibility which makes National a fiduciary to cause the Plans to enter into the proposed transactions. It is noted that the members of the JPS Committee are independent of and have no interest in National and have full discretionary authority to make the investment decisions here under consideration on behalf of the Plans.

7. In summary, the Applicants represent that the criteria of section 408(a) of the Act are satisfied in the proposed transactions because: (1) The investment decision on behalf of the Plans is made by the JPS Committee, which is independent of National; (2) the JPS Committee has determined that the proposed transactions will be in the best interests of the Plans, consistent with the investment objectives of the Plans, and complementary of the Plans' investment in NPP; (3) prior to the closing of the subject transactions, the JPS Committee will review the terms to ensure that they remain in the best interests of the Plans; (4) the JPS Committee will retain authority throughout the Partnership's operation to review and approve in advance major transactions involving the Partnership; and (5) National is not using any of the authority, control or responsibility which makes National a fiduciary to cause the Plans to enter into the proposed transactions.

The exemption proposed herein would cover only the purchase transaction specifically described. The Applicants would be proceeding with the formation and operation of the Partnership without an exemption from section 406(b) of the Act. The Applicants are assuming the responsibility of any violation of section 406(b) of the Act resulting from any transactions with respect to the Partnership.

For Further Information Contact: Ronald Willett of the Department, telephone (202) 523-8194. (This is not a toll-free number.)

Amended and Restated Profit Sharing Plan and Trust of Shorr Paper Products, Inc. (the Plan) Located in Aurora, Illinois

[Application No. D-5571]

Proposed Exemption

The Department is considering granting an exemption under the authority of section 408(a) of the Act and section 4975(c)(2) of the Code and in accordance with the procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). If the exemption is granted the restrictions of section 406(a) and 406 (b)(1) and (b)(2) of the Act and the sanctions resulting from the application of section 4975 of the Code, by reason of section 4975(c) (1) (A) through (E) of the Code shall not apply to (1) the continuation after June 30, 1984, of a ground lease (the Ground Lease) by the Plan to Trust No. 1535, whose beneficiaries are parties in interest with respect to the Plan, and (2) the possible future sale by the Plan to Trust No. 1535 of the land subject to the Ground Lease pursuant to certain options granted to both the Plan and Trust No. 1535 by the Plan trustees when the Ground Lease was executed; provided the terms of all these transactions are at least as favorable to the Plan as those the Plan could obtain in similar transactions with unrelated parties, and provided further that in the event of any such sale the sales price is not less than the fair market value of the above-mentioned land (the Land) on the date of the sale, disregarding any reduction in value attributable to Trust No. 1535's repurchase option.

Effective Date: If the proposed exemption is granted, the exemption will be effective July 1, 1984.

Summary of Facts and Representations

1. The Plan covered approximately 60 participants as of June 22, 1984 and has assets totaling $727,802 as of September 30, 1983, including the Land. The Plan holds no other investments related to Shorr Paper Products, Inc. (the Employer), according to the applicant. The Land is the only real estate currently held by the Plan. Messrs. Kenneth B. Shorr and Robert A. Shorr are the trustees of the Plan and also the sole beneficiaries of Trust No. 1535. Each of them owns 50% of the voting stock of the Employer and is an officer and employee of the Employer.

2. By agreement dated June 21, 1984 (the 6/84 Agreement), the Plan trustees appointed Mr. Robert H. Shelp (Mr. Shelp) to serve as real estate manager for the Plan. It is represented that Mr. Shelp is unrelated to the parties involved in the Ground Lease and the related building lease (described below). Mr. Shelp is an architect and registered real estate broker who has practiced in Aurora, Illinois for 28 years with particular experience in consulting on existing building problems. He is a member of the American Institute of Architects and has testified as an expert witness on various architectural and real estate matters. Mr. Shelp has had very little specific or direct experience with the provisions of the Act. However, he states that before accepting his appointment as a fiduciary with respect to the Plan, he consulted extensively with legal counsel experienced in matters under the Act, particularly the duties, responsibilities and liabilities imposed by the Act on plan fiduciaries. Mr. Shelp states that he understands and acknowledges such duties, responsibilities, and liabilities in acting as a fiduciary with respect to the Plan.

3. The Land consists of 6 lots, 360 feet by 165 feet, improved by the Employer's principal office and warehouse, located at 227-41 S. River Street, Aurora, Illinois. On April 16, 1973, the Employer, as lessee, entered into a lease with the Merchant's National Bank of Aurora, as trustee of Trust No. 1535 under Trust Agreement dated July 2, 1978, for proprty to serve as the Employer's principal office and warehouse facilities (the Building Lease). On February 24, 1974, the Plan purchased the ground rights of the property governed by the Building Lease, excluding all buildings and structures thereon (the Improvements), for $100,000. Also on February 24, 1974, the Plan, as lessor, entered into the Ground Lease with Trust No. 1535, as lessee. On the same date, Trust No. 1535 granted the Plan the right during the term of the Ground Lease to call upon Trust No. 1535 to repurchase the Land for $100,000 (the Put Option) and also reserved the right during the term of the Ground Lease to repurchase the Land from the Plan (Trust No. 1535's Repurchase Option) for the greater of $100,000 or the fair market value of the Land as determined by a qualified, licensed appraiser at the time of such repurchase. The applicant represents that such appraiser will not be related to the Employer or to the trustee or beneficiaries of Trust No. 1535 and that Trust No. 1535's Repurchase Option will not be exercised unless Mr. Shelp (see 2. above) approves of the sale if and when Trust No. 1535 wishes to exercise this option. The applicant represents that the Put Option will be exercised only if (a) the fair market value of the Land does not exceed $100,000, (b) Mr. Shelp determines that the exercise of the Put Option would be in the best interests of the Plan and its participants and beneficiaries, and (c) the $100,000 will be paid in a lump sum of cash on the date the Put Option is exercised. The applicant also represents that in connection with the exercise of the Put Option, the Plan would incur no brokerage commissions or other expenses related to the sale.

4. The term of the Ground Lease is March 1, 1974 through June 30, 1993. The Ground Lease provides that the initial rent for the Land shall be $12,000 per year, payable in monthly installments of $1,000. The applicant represents that the

rental rate under the Ground Lease will be adjusted every two years during the remaining term thereof to an amount equal to or in excess of the then fair rental value of the Land, as determined at that time by a qualified appraiser who is not related to the Employer, Trust No. 1534, Kenneth B. Shorr, or Robert A. Shorr. The Plan pays no expenses under the Ground Lease; all expenses are paid by Trust No. 1535.

5. The Ground Lease is subject to the Building Lease, which leases both the Land and the Improvements to the Employer. The Ground Lease is also subject and subordinate to the Trust Deed executed by the trustee of Trust No. 1535 and dated April 16, 1973 and recorded June 15, 1973 (the Mortgage). The Mortgage constitutes a first lien on both the Land and the Improvements in favor of Security Mutual Life Insurance Company of New York (Security Mutual), which is not a party in interest with respect to the Plan, according to the applicant. The applicant explains that these provisions of the Ground Lease reflect the history of the property and certain protections built in to protect the interests of the Plan. Trust No. 1535 originally owned both the Land and the Improvements. Since the Building Lease was executed April 16, 1973, the Plan's purchase on February 24, 1974 of the Land (which is covered by the Building Lease) was made subject to the Building Lease. As the Plan owns only the Land, and not the Improvements, the Plan cannot raze the Improvements during the term of the Ground Lease, which ends when the Building Lease term ends. Because the Ground Lease is subject to the Building Lease, the indemnification provisions of the Building Lease also apply to the Ground Lease. The Employer maintains insurance for this purpose and would be responsible to Trust No. 1535 and, ultimately, to the Plan, as the secondary lessor, for such indemnity for the liabilities described in the Building Lease, namely, for penalties, damages or charges imposed for legal violations, losses, costs, damages or expenses arising out of accidents or other similar occurrences on or about the premises. Similarly, the Building Lease provisions for review and adjustment of rent every two years by independent third parties to keep the rental rate competitive with that charged for similar properties in the Aurora Metropolitan area, also apply to the Ground Lease, according to the applicant, because the Ground Lease is subject to the Building lease. The applicant explains that the Ground Lease subjection and subordination to the Mortgage protects the Plan by obligating it to lease the Land only insofar as it has a right to the Land subject to the Mortgage, including any easements of record. As the Plan did not assume any portion of Trust No. 1535's obligation under the Mortgage, the Plan's right to the Land and the Plan's obligation to lease the Land to Trust No. 1535 are subject and subordinate to the security interests of Security Mutual under the Mortgage. The applicant represents that the ground Lease provisions subjecting it to the Building Lease and subjecting and subordinating it to the Mortgage have no force and effect upon the rights and obligations of the Plan under the Ground Lease other than as described above.

6. The Building Lease also provides for rental adjustments every two years, similar to those provided for by the Ground Lease (see 4, above) and for payment of expenses relating to the leased premises by the Employer. The Plan has no involvement in the Building Lease, which, therefore, is not a prohibited transaction, according to the applicant.[2]

7. The Plan has realized a rate of return under the Ground Lease in the past of approximately 12% annually. The applicant represents that neither the Ground Lease nor the Building Lease constituted prohibited transactions within the meaning of section 503(b) of the Code when they were entered into and that the terms of the Ground Lease, which was a binding contract in effect on (and before) July 1, 1974 are at least as favorable to the Plan as an arm's-length transaction with an unrelated party would be. (The applicant also represents that the terms of the Building Lease are comparable to those of an arm's-length transaction between unrelated parties.) Therefore, the applicant states that the Ground Lease was statutorily exempt until June 30, 1984 under section 414(c)(2) of the Act.[3]

8. Mr. John W. Moyer (Mr. Moyer), ASA-SRA-SR/WA #1879, of Central States Appraisal Company, Aurora, Illinois, has appraised the Land's fair market value as of January 1, 1984 at $109,000. The Land represented less than 15% of the Plan's total assets as of September 30, 1983. Mr. Moyer is a senior member of the American Society of Appraisers and the Society of Real Estate Appraisers, has been actively engaged in appraisal work since 1955, and, according to the applicant, has no relationship to the Employer or Trust No. 1535 or its beneficiaries. Mr. Moyer states that the Mortgage has no effect upon the value of the Land but may enhance the value of the property, especially if the Mortgage were assumable, by making the property more saleable in the open market. He also states that the current rental of $12,000 per year, being a net amount with no expenses further deducted, represents a fair, reasonable, and greater than average return on the Land. He asserts that the fact that the Employer occupies the Land does not result in the Land being of any additional value to the Employer so long as the Employer is the prime tenant and the rental provides a net income over the extended period of time prescribed in the Ground Lease (which expires June 30, 1993). The applicant represents that the Ground Lease rent has remained the same since its inception in February 1974 because the sale and rental values for commercial properties in the Aurora, Illinois community have remained relatively constant during the past 10 years but are now expected to increase in the near future. The applicant explains that this leveling of rental and sale values is partly attributable to the transition of the economic base of Aurora, Illinois during this period.

9. The 6/84 Agreement (see 2, above) requires Mr. Shelp to evaluate the past and present performance of all lessees under any leases of real property owned by the Plan in order to determine the appropriateness of continuing such leases for the exclusive benefit of the Plan participants and beneficiaries; to determine if the real property held by the Plan is an appropriate investment for the Plan; and to represent the interests of the Plan under its leases, performing all acts appropriate for proper and advantageous management and investment of the Plan's real estate holdings.

10. On June 21, 1984, Mr. Shelp certified that he had accepted appointment as fiduciary to the Plan with respect to the Land and that he has reviewed and evaluated the past

[2] The Department expresses no opinion herein as to whether or not the Building Lease is a prohibited transaction under section 406 of the Act. Although the applicant has requested an administrative exemption with respect to the Building Lease, as well as the Ground Lease, the proposed exemption relates to the Ground Lease only in view of the applicant's statement that the Building Lease is not a prohibited transaction. If the applicant subsequently determines that the Building Lease is a prohibited transaction, a separate exemption for the Building Lease may be requested.

[3] Section 414(c)(2) of the Act provided a transitional exemption ending June 30, 1984 for certain leases meeting specified conditions. The Department expresses no opinion herein as to the applicability of section 414(c)(2) to the Ground Lease.

performance of the Employer and Trust No. 1535 as lessees of the Building Lease and the Ground Lease, respectively. He stated that he has determined that such past performance has been excellent as both the Employer and Trust No. 1535 have paid rent timely and have met all their other obligations under these leases. Mr. Shelp certified further that he had also reviewed and evaluated the terms of these leases and their proposed continuation. He states that at that time he had reviewed the January 1, 1984 appraisal of the Land, indicating that the fair market value of the Land was $109,000. Since the $12,000 per year rental amount paid to the Plan represented an 11% annual rate of return to the Plan, a rate he states is usual and customary for commercial properties of a similar type in the Aurora, Illinois community, Mr. Shelp believed then (prior to July 1, 1984) that the rent to be paid pursuant to the Ground Lease from July 1, 1984 would represent fair rental value. Mr. Shelp certified that on June 21, 1984, he had determined, based upon all of the foregoing, that the Ground Lease will be an appropriate investment for the Plan as both leases have been and will be in the best interests and protective of the Plan participants and beneficiaries. Also on June 21, 1984, Mr. Shelp approved the continuation of the Ground Lease by the Plan. He agreed on that date to monitor the Ground Lease on behalf of the Plan, to direct the Plan trustees with respect to all actions to be taken by them with respect to the Ground Lease, and to act to enforce any and all rights of the Plan under the Ground Lease.

Mr. Shelp explains that although the Ground Lease indirectly benefits the Employer, he has concluded that the Ground Lease compares favorably with the terms of similar transactions between unrelated parties. He states that in forming his opinion regarding the desirability of the Plan's continued investment in the Ground Lease, he has examined the Plan's overall investment portfolio, considered the liquidity requirements of the Plan, examined the diversification of the Plan's assets in light of the Ground Lease, and considered whether the Ground Lease complies with the Plan's investment objectives and policies. He has concluded that the Plan's investment in the Ground Lease represents an income-producing investment which also provides for long-term appreciation and, therefore, is a desirable investment for the Plan, which has other liquid investments earning a fair rate of return. He states that while he is not responsible for the overall diversification of the Plan's assets, he believes that the Plan's investment in the Ground Lease allows the overall portfolio to be diversified prudently while not jeopardizing the Plan's liquidity requirements.

11. With respect to Trust No. 1535's Repurchase Option, Mr. Shelp represents that:

(a) Such option is appropriate and commercially reasonable in connection with a lease of this type;

(b) He will decide at such time as Trust No. 1535 elects to exercise such option whether or not the sale of the Land is in the Plan's best interests, and he will block the sale if it is not in the best interests of the Plan;

(c) He will determine that the sales price will not be less than the fair market value of the Land on the date of the sale, and, in determining such fair market value, any reduction in value attributable to Trust No. 1535's Repurchase Option will be disregarded; and

(d) The sales price will be paid in a cash lump sum on the date of the sale.

12. In summary, the applicant represents that the subject transaction satisfies the exemption criteria set forth in section 408(a) of the Act because (a) a qualified appraiser unrelated to the Employer, Trust No. 1535 or its beneficiaries has determined that the current rental rate, being a net amount with no expenses to be further deducted, represents a fair and reasonable return on the Land; (b) the rental rate will be adjusted every two years during the remaining term of the Ground Lease to an amount equal to or in excess of the then fair rental value of the Land, as determined at that time by a qualified appraiser who is not related to either the Employer or Trust No. 1535 or either of its beneficiaries; (c) the Plan will pay no expenses under the Ground Lease; (d) Mr. Shelp, an independent fiduciary to the Plan with respect to the Land, determined prior to July 1, 1984 that continuation of the Ground Lease is in the best interests and protective of Plan participants and beneficiaries; (e) Mr. Shelp agreed before July 1, 1984 to represent the interests of the Plan by monitoring the Ground Lease and acting to enforce all rights of the Plan thereunder; (f) Trust No. 1535's Repurchase Option may not be exercised unless Mr. Shelp approves of the sale if and when Trust No. 1535 wishes to exercise this option; (g) Mr. Shelp represents that Trust No. 1535's Repurchase Option is appropriate and commercially reasonable in connection with a lease of this type; (h) if Trust No. 1535's Repurchase Option is exercised, the sale price (I) will not be less than the fair market value of the Land on the date of the sale—disregarding, in determining such fair market value, any reduction in value attributable to such repurchase option, and (II) will be paid in a cash lump sum on the date of the sale; (i) the Put Option will not be excercised unless (I) the fair market value of the Land does not exceed $100,000, (II) Mr. Shelp determines that exercising the Put Option would be in the best interests of the Plan and its participants and beneficiaries, and (III) the $100,000 will be paid in a lump sum of cash on the date the Put Option is exercised; and (j) the Plan will incur no brokerage commissions or other expenses in connection with the exercise of the Put Option.

For Further Information Contact: Mrs. Miriam Freund, of the Department, telephone (202) 523-8971. (this is not a toll-free number.)

Ellerbe, Inc. and Affiliated Companies Profit Sharing Trust (the Plan) Located in Saint Paul, Minnesota

[Application No. D-5572]

Proposed Exemption

The Department is considering granting an exemption under the authority of section 408(a) of the Act and section 4975(c)(2) of the Code and in accordance with the procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). If the exemption is granted the restrictions of section 406(a), 406 (b)(1) and (b)(2) of the Act and the sanctions resulting from the application of section 4975 of the Code, by reason of section 4975(c)(1) (A) through (E) of the Code shall not apply to (1) the ground lease (the Lease) of certain unimproved real property (the Property) by the Plan to Ellerbe, Inc. (the Employer), a party in interest with respect to the Plan; and (2) the possible cash sale of the Property by the Plan to the Employer pursuant to a purchase option in the Lease, provided that the terms and conditions of the transactions are at least as favorable to the Plan as those obtainable in arm's length transactions between unrelated parties.

Effective Date: If granted, the exemption will be effective November 20, 1984.

Summary of Facts and Representations

1. The Plan is a qualified profit sharing plan which had approximately 370 participants and net assets of approximately $11,900,000 as of December 31, 1983. The Employer, an architectural and engineering firm, is a closely held corporation headquartered

in Bloomington, Minnesota. The trustees (the Trustees) of the Plan are Robert F. Jacobson, Wilton L. Wyatt, Douglas G. Wolfangle, Era B. Stevens and Gerald A. Simons, all of whom are directors, officers or employees of the Employer or its affiliates.

2. The Property was contributed to the Plan in 1972 by Ellerbe Architects, Inc. (the prior corporate name of the Employer) at an appraised value of $1.5 million. In connection with the contribution, a note was taken back from the Plan in the amount of $686,000 and was paid in full by the Plan in 1973. On June 12, 1973, the Plan entered into a ground lease (the Lease) of the Property with the Employer for an initial term of 31 years, 6 months and 24 days, commencing June 6, 1972 and terminating December 31, 2003. Rent under the Lease is payable in cash at the beginning of each year and is 10% of the fair market value of the Property as appraised once every five years over the term of the Lease. The Lease provides that the Employer must pay for any improvements which are placed upon the Property, all general taxes and installments of special assessments with respect to the Property, all insurance premiums, all maintenance and repair expenses and all other costs and expenses of whatever character or kind which may be necessary to the operation of the premises and the Employer's authorized use during the term of the Lease. Upon the expiration of the Lease, any improvements on the Property will belong to the lessor. The Lease also provides that the Employer bears the risk associated with all property of any kind on the premises, that the Plan is not liable to the Employer or any other person for any injury, loss or damage to any person or property on the premises or resulting from any equipment on the premises becoming out of repair or defective, or for any other cause. Additionally, the Employer covenants to hold the Plan harmless and indemnify the Plan from all such injury, loss or damage.[4] A purchase option in the Lease permits the Employer to purchase the Property for cash at any time upon giving 120 days notice to the lessor, for an amount which is the fair market value of the Property, as if bare and unencumbered, on the date such notice is given.

3. Since the contribution of the Property to the Plan, significant portions have been sold to various entities.[5] The Property owned by the Plan currently consists of a portion of Parcel 7 and Parcels 8 and 9. The application states that the Trustees intend that the Plan hold the Property only until it can be sold at an acceptable price and under acceptable terms and conditions. The Property is currently unimproved and the application states that neither the Trustees nor the Employer has any present intent to construct improvements on the Property. The Property was appraised on June 18, 1984 and October 9, 1984 by Mr. O.J. Janski, M.A.I., S.R.E.A. of O.J. Janski and Associates, Inc., Minneapolis, Minnesota, who has determined the fair market values of the parcels currently comprising the Property to be the following:

Parcel 7 (portion remaining in the Plan)	$232,000
Parcel 8	679,000
Parcel 9	5,600
Total	916,600

Mr. Janski states that the current fair market rental value of the Property, based on a triple net leasing arrangement, is 10% of its fair market value, or $91,660 per annum.[6] The Employer represents also that it will pay any excise taxes due as a result of the Lease for the period between June 30, 1984 and the effective date of the exemption, within sixty days of the publication of a grant of the exemption in the **Federal Register**. Based upon Mr. Janski's appraisal, the Property represents approximately 7.7% of the Plan's current assets.

4. On November 20, 1984, the Lease was amended as follows:

(a) The rental rate under the Lease is the greater of—(1) The fair market rental value of the Property as determined once every three years over the term of the Lease by an independent M.A.I. appraiser selected by the independent fiduciary for the Plan, or (2) ten percent of the fair market value of the Property as determined once every three years over the term of the Lease by such independent appraiser.

(b) No improvements may be constructed upon the Property without the prior approval of the independent fiduciary for the Plan.

(c) With respect to the Employer's purchase option, any exercise of the purchase option is subject to the approval of the independent fiduciary for the Plan and the sale price of any portion of the Property will be no less than its fair market value as determined by at least one independent M.A.I. appraiser appointed by the independent fiduciary or in such other manner as the independent fiduciary may determined.[7]

(d) No brokers fees or finders commissions will be paid by the Plan with respect to any exercise of the purchase option by the Employer.

(e) The parties to the Lease understand that any or all of the Property may be sold by the Plan if deemed to be in the Plan's best interest by the independent fiduciary.

5. First Trust Company of Saint Paul (First Trust), Saint Paul, Minnesota, has been appointed to act as the independent fiduciary for the Plan. First Trust has in the past and is now functioning as a trustee in certain industrial development bond transactions with which the Employer or one of its affiliates has been or is involved, but is otherwise independent of the Employer. Fees earned from this work constitute only approximately one-tenth of one percent of First Trust's annual revenue. No other commercial relationships exist between First Trust and the Employer or its affiliates and there are no common officers or directors. First Trust currently administers approximately $2.8 billion of employee retirement plan assets and represents that it is familiar with the Act and the fiduciary responsibilities, duties and liabilities prescribed therein.

On November 20, 1984, First Trust represented that it had examined the terms and conditions of the transactions, the appraisals, the Lease and Lease

[4] The applicant represents that the Lease between the Plan and the Employer was exempt until June 30, 1984, from the prohibited transaction provisions of section 406 of the Act by virtue of the relief provided by section 414(c)(2) of the Act. The Department expresses no opinion as to the applicability of section 414(c)(2) to the Lease.

[5] All of the past sales, except one, were to unrelated parties. The applicant states that the one sale to a party in interest with respect to the Plan occurred prior to June 30, 1984 and met the requirements of section 414(c)(3) of the Act. The Department expresses no opinion as to the applicability of section 414(c)(3) to that sale.

The most recent sale, which was of a portion of the Property known as Parcel 7, was closed on April 30, 1984. However, under a purchase agreement option, the buyers, who are unrelated to the Plan, elected to purchase and pay for only one-half of the parcel at closing and are obligated to purchase and pay for the remainder within one year from the April 30, 1984 closing. The application indicates that obligation of the buyer to purchase the remainder of Parcel 7 is absolute. In the interim, the buyer is obligated to pay all taxes due and payable in 1984. Until conveyance, the Employer will pay rent for the unconveyed portion and other costs and risks related to the unconveyed portion will continue to be paid and assumed by the Employer. Upon conveyance of the remaining portion of Parcel 7, the Employer will be entitled to a refund of unearned rent pro-rated to the date of closing on the conveyance.

[6] The Employer represents that it will pay back rent for the period after June 30, 1984, if and as determined to be due by an independent fiduciary for the Plan.

[7] It is not intended that this provision will apply to the unconveyed portion of Parcel 7, as that commitment to sell arose previously in a binding purchase agreement with an unrelated party executed on April 15, 1984.

amendments, the Property itself and the Plan documents and balance sheet and had determined that the transactions were and are in the best interest of the Plan. First Trust states that the transactions are protective of the Plan in that the Property constitutes less than 8% of the Plan's assets and does not impair the Plan's diversification and liquidity, the triple-net Lease will initially provide a net rate of return to the Plan of approximately 11.025% per annum, since the rent for an entire year is payable in advance at the beginning of each year, the rental under the Lease will be readjusted every three years to the greater of the then-current fair market rental value as determined by an independent M.A.I. appraiser selected by First Trust or ten percent of the fair market value of the Property as determined by such appraiser, and any exercise of the purchase option by the Employer will be at the then-current fair market value as determined by an independent M.A.I. appraiser selected by First Trust or in such other manner as First Trust may determine. First Trust will not consent to the construction of any improvements on the Property unless it determines that such improvements are in the best interest of the Plan, its participants and beneficiaries. Similarly, First Trust will not permit the exercise of any renewal option or of the purchase option unless in the best interest and protective of the Plan. First Trust may also, in its discretion, cause any or all of the Property to be sold to unrelated third parties at such price and under such terms as it deems to be in the Plan's best interest. In addition to monitoring the compliance by the Employer with the terms and conditions of the Lease and amendments, First Trust represents that it will take any enforcement actions necessary to protect the rights of the Plan with respect to the transactions and the Property.

6. In summary, the applicants represent that the transactions satisfy the requirements of section 408(a) of the Act because: (a) The Property represents less than 8% of the Plan's current assets and will produce a favorable rate of return for the Plan; (b) First Trust, as an independent fiduciary for the Plan, has reviewed the transactions in view of the needs of the Plan and has determined that they are protective of the Plan and in the best interest of the Plan's participants and beneficiaries; (c) the rental under the Lease will be no less than the fair market rental value as determined every three years by an M.A.I. appraiser selected by First Trust; (d) the Lease is a triple net lease with an indemnification clause; and (e) any exercise of the purchase option by the Employer must be approved in advance by First Trust and must be at a price no less than the then-current fair market value of the Property as determined by an M.A.I. appraiser selected by First Trust.

For Further Information Contact: Ms. Katherine D. Lewis of the Department, telephone (202) 523-8972. (This is not a toll-free number.)

Real Estate Collective Investment Fund Established Under the InterFirst Corporation Investment Trust for Employee Benefit Plans (the Dallas Fund); Employee Benefit Real Estate Equities Fund (the Fort Worth Equities Fund) and the Employee Benefit Real Estate Mortgage Fund (the Fort Worth Mortgage Fund) Established under the First National Bank of Fort Worth Collective Investment Trust

[Application No. D-5751]

Proposed Exemption

The Department is considering granting an exemption under the authority of section 408(a) of the Act and section 4975(c)(2) of the Code and in accordance with the procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). If the exemption is granted the restrictions of section 406(b)(2) of the Act shall not apply to the proposed merger of the Fort Worth Equities Fund into the Dallas Fund, and the proposed transfer of the Fort Worth Mortgage Fund into a new fund managed by InterFirst Bank Dallas, N.A., provided that the aggregate fair market value of the interests of each plan participating in any of these funds (collectively, the Funds), upon completion of the transactions, equals the aggregate fair market value of such plan's interests in the Funds immediately preceding the mergers.

Summary of Facts and Representations

1. InterFirst Corporation, a registered bank holding company under the Bank Holding Company Act of 1956, owns all of the capital stock (other than director's qualifying shares) of InterFirst Bank Dallas, N.A. (InterFirst Dallas) and InterFirst Bank Fort Worth, N.A. (InterFirst Fort Worth). InterFirst Dallas and InterFirst Fort Worth act as trustee, agent, investment manager or custodian of numerous employee benefit plans which hold units of participation in the Funds.

2. Both the Dallas Fund and the Fort Worth Equities Fund are authorized to invest directly or through interests in partnerships, corporations, or other entities, in real estate, in participations in real estate investments, in real estate mortgages, and in a variety of short-term investments. The Fort Worth Mortgage Fund is authorized to invest in mortgages secured by interests in real estate and in a variety of short-term investments. Approximately $76,435,859 in net assets were held in the Dallas Fund as of June 30, 1984. Approximatrely $10,855,053 of the net assets were invested in the Fort Worth Equities Fund as of July 31, 1984. Approximately $7, 782,658 of net assets were held in the Fort Worth Mortgage Fund as of July 31, 1984. As of June 30, 1984, 70 employee benefit plans participated in the Dallas Fund. As of July 31, 1984, 92 plans participated in the Fort Worth Equities Fund and 52 plans participated in the Fort Worth Mortgage Fund.

3. The applicants propose that the Fort Worth Equities Fund be merged into the Dallas Fund, and that the Fort Worth Equities Fund cease to exist. The merger will be accomplished by having the Fort Worth Equities Fund transfer all its assets to the Dallas Fund. In consideration for the transfer, new units of participation in the Dallas Fund will be created and will be allocated to the Fort Worth Equities Fund, based on the relative fair market value of the assets received from the Fort Worth Equities Fund to the fair market value of the assets in the Dallas Fund on the effective date of the merger. The new units of participation in the Dallas Fund will then be allocated proportionally to participants in the Fort Worth Equities Fund in exchange for such participants' units of participation in the Fort Worth Equities Fund. No fractional units of participation will be issued in the transaction, and the Dallas Fund will pay cash equal to the fair market value of any such fractional unit to which the participant would otherwise have been entitled. All accrued income of the Dallas Fund and the Fort Worth Equities Fund will be allocated to respective participants of the two Funds immediately prior to the merger.

4. The units of the Dallas Fund received by the former Fort Worth Equities Fund participants, plus cash received in lieu of fractional units, if any, will have a fair market value equal to the fair market value of their units in Fort Worth Equities Fund immediately prior to the merger. The value of units in the Dallas Fund held by participants in the Dallas Fund immediately prior to the merger will not change. However, as a result of the merger, each participant will hold units representing undivided interests in each and every investment formerly held by both Funds, rather than

in the investments of one Fund or the other. That is, the fair market value of each participant's units of the effective date of the merger will not change as a result of the merger, but the underlying investment represented by the units will be diversified. As result of the transaction, InterFirst Dallas will become solely responsible for the administration of the collective investment of all the assets previously held separately by the Dallas Fund and the Fort Worth Equities Fund. Neither InterFirst Dallas, InterFirst Fort Worth, nor any affiliated party will receive any fee or commission with respect to the transfer of the assets of the Fort Worth Equities Fund to the Dallas Fund.

5. It is also proposed that InterFirst Dallas be substituted for InterFirst Fort Worth as trustee of the Fort Worth Mortgage Fund, by merging the Fort Worth Mortgage Fund into a new fund. The transaction will be accomplished by having InterFirst Fort Worth, as trustee, transfer all of the assets of the Fort Worth Mortgage Fund to InterFirst Dallas as trustee. InterFirst Dallas will establish a new fund (the Dallas Mortgage Fund), in which the assets formerly held by the Fort Worth Mortgage Fund will be placed. There will be no assets in the Dallas Mortgage Fund immediately prior to the transfer. The Fort Worth Mortgage Fund will terminate. All of the participants in the Fort Worth Mortgage Fund will receive units of the Dallas Mortgage Fund having the same value and representing undivided interests in the same underlying assets immediately after the transaction as their units in the Fort Worth Mortgage Fund had immediately before the merger.

6. It is anticipated that InterFirst Forth Worth may continue to provide management services, including the collection of income from investments, with respect to the Forth Worth Mortgage Fund after it is transferred. InterFirst Forth Worth will act as agent for Interfirst Dallas in this regard. Any fees paid by InterFirst Dallas to InterFirst Forth Worth for the provision of these services will be treated as a cost of doing business and will not create any additional fees for the plans participating in the Fund.[9] As a result of these transactions, InterFirst Dallas will become solely responsible for the administration of the collective investment of all of the assets previously held by the Fort Worth Mortgage Fund, and the Fort Worth Mortgage Fund will cease to exist. Neither InterFirst Dallas, InterFirst Fort Worth, nor any affiliated party will receive any fee or commission with respect to the transfer of the assets of the Fort Worth Mortgage Fund to InterFirst Dallas as trustee.

7. The applicants represent that the combination of the Fort Worth Equities Fund and the Dallas Fund will result in a single, larger Fund with a greater diversity of investment than either separate Fund previously possessed. The banks believe that the existing Funds are adequately diversified. However, since plans participating in the Funds will hold units of participation representing aggregate undivided interests in each of the properties previously held separately by both the Funds, the diversification will benefit each and every plan involved. Moreover, the increase in the amount of assets held by the surviving Fund may broaden the range of possible investments and may enhance the Fund's ability to benefit from volume discounts on services it purchases.

8. The merger transactions will also permit more efficient and economical administration of the collective investment of the assets involved. The transactions are part of a broader effort to centralize the administration of all the collective investment funds of InterFirst Corporation affiliates and to use a uniform governing instrument for all such funds. The transactions will eliminate duplication of efforts at InterFirst Dallas and InterFirst Fort Worth and will help to centralize and enhance expertise in administering and managing the Funds.

9. In summary, the applicants represent that the proposed transactions meet the statutory criteria contained in section 408(a) of the Act because: (1) Neither InterFirst Dallas, InterFirst Fort Worth nor any affiliate will be receiving any commissions or fees in connection with the proposed mergers; (2) the fair market value of the participants' interests in the Funds will remain unchanged after the mergers; (3) the mergers will permit additional diversification of investments of the participating plans; and (4) the mergers will permit the InterFirst Corporation banks to manage the Funds more efficiently.

For Further Information Contact: Mr. Gary H. Lefkowitz of the Department, telephone (202) 523-8881. (This is not a toll-free number.)

Henry Meyersohn & Associates, Inc. D.B. Pension Plan (the Plan) Located in Miami, Florida

[Application No. D-5789]

Proposed Exemption

The Department is considering granting an exemption under the authority of section 408(a) of the Act and section 4975(c)(2) of the Code and in accordance with the procedures set forth in ERISA Procedure 75-1 (40 FR 18471, April 28, 1975). If the exemption is granted the restrictions of section 406(a) and 406 (b)(1) and (b)(2) of the Act and the sanctions resulting from the application of section 4975 of the Code, by reason of section 4975(c)(1) (A) through (E) of the Code shall not apply to the proposed cash sale by the Plan to the Plan trustees (the Trustees) of a certain condominium unit (the Property) for a price equal to the greater of the Property's fair market value or adjusted basis on the date or the sale.

Summary of Facts and Representations

1. The Plan, a defined benefit pension plan, covers three participants, all of whom are owners of the Plan sponsor and two of whom are also the Trustees. As of September 26, 1984, the Plan's assets totalled $870,000.

2. The Property is located at Wind River, Michael Drive, Unit #11, Teton Village, Teton County, Wyoming. The subdivision in which the Property is located is a major ski resourt, according to an appraisal of the Property by L.K. Benson, Associate Appraiser with Hoffman & Associates, Realtors and Appraisers. Mr. Benson has been employed as an independent associate since April 1977 in making fee appraisals in Teton County, Wyoming and has appraised unimproved land, single family residences, and individual condominium units, primarily for commercial lending institutions, in connection with a designated member of the American Institute of Real Estate Appraisers. Mr. Benson certifies that he has no personal interest or bias with respect to the Property or the participants to the sale. He estimates the fair market value of the Property as $257,000 as of June 7, 1984.

3. The Property was built in 1982 and was purchased by the Plan on August 19, 1982 from Dr. Paul M. Ellwood, Jr., who was neither a party in interest with

[9] No exemption from section 406 of the Act is being proposed for transactions related to the provision of services beyond that which is provided by the statutory exemption contained in section 408(b)(2) of the Act.

respect to the Plan nor related in any way to the Trustee or the Plan participants. The Plan paid $250,543.54 to acquire the Property and an additional $25,617.58 in aggregate capital expenditures regarding the Property (for furnishings). The Plan acquired the Property as an investment to generate income, hoping to sell it at a gain in a few years. The Plan attempted to rent the Property and received rental income therefrom in 1983 of $4,073. Rental expenses, however, exceeded rental income, and for this reason the Property was listed for sale in December 1983. However, the Plan has been unable to sell the Property and has incurred an aggregate net operating loss from renting the Property of $5,647 as of September 30, 1984.

4. The Trustees propose to purchase the Property for a price equal to the greater of the Property's adjusted basis or fair market value as of the date of the sale. For this purpose, the Property's adjusted basis is the sum of: (a) The price paid by the Plan to acquire the Property ($250,543.56), (b) the Plan's aggregate capital expenditures for the Property ($25,617.58), (c) the aggregate net operating loss incurred by the Plan from renting the Property, including the $5,647 aggregate net operating loss incurred thereafter and through the date of the proposed sale. The Trustees will make a single payment in cash to cover the proposed sale price and will also pay any selling expenses. The Plan will incur no commissions or other expenses in effecting the proposed sale. The applicant represents that the proposed sale is in the best interests of the Plan because it will permit the Plan to make other investments resulting in more liquidity and better diversification of Plan assets.

5. In summary, the applicant represents that the proposed transaction satisfies the exemption criteria set forth in section 408(a) of the Act because (a) the sale will be a one-time transaction for cash; (b) the sale price will equal the greater of the Property's fair market value or adjusted basis on the date of the sale, and such adjusted basis will equal the sum of the price paid by the Plan to acquire the Property plus the aggregate capital expenditures and net operating losses incurred by the Plan regarding the Property; (c) no commissions or other selling expenses will be charged to the Plan; and (d) the sale will enable the Plan to dispose of a non-income producing asset and to achieve greater liquidity and diversification of Plan assets.

For Further Information Contact: Mrs. Miriam Freund, of the Department, telephone (202) 523-8971. (This is not a toll-free number.)

General Information

The attention of interested persons is directed to the following:

(1) The fact that a transaction is the subject of an exemption under section 408(a) of the Act and/or section 4975(c)(2) of the Code does not relieve a fiduciary or other party in interest or disqualified person from certain other provisions of the Act and/or the Code, including any prohibited transaction provisions to which the exemption does not apply and the general fiduciary responsibility provisions of section 404 of the Act, which among other things require a fiduciary to discharge his duties respecting the plan solely in the interest of the participants and beneficiaries of the plan and in a prudent fashion in accordance with section 404(a)(1)(B) of the Act; nor does it affect the requirement of section 401(a) of the Code that the plan must operate for the exclusive benefit of the employees of the employer maintaining the plan and their beneficiaries;

(2) Before an exemption may be granted under section 408(a) of the Act and/or section 4975(c)(2) of the Code, the Department must find that the exemption is administratively feasible, in the interests of the plan and of its participants and beneficiaries and protective of the rights of participants and beneficiaries of the plan; and

(3) The proposed exemptions, if granted, will be supplemental to, and not in derogation of, any other provisions of the Act and/or the Code, including statutory or administrative exemptions and transitional rules. Furthermore, the fact that a transaction is subject to an administrative or statutory exemption is not dispositive of whether the transaction is in fact a prohibited transaction.

(4) The proposed exemptions, if granted, will be subject to the express condition that the material facts and representations contained in each application are true and complete, and that each application accurately describes all material terms of the transaction which is the subject of the exemption.

Signed at Washington, D.C., this 10th day of January 1985.

Elliot I. Daniel,

Acting Assistant Administrator for Regulations and Interpretations, Office of Pension and Welfare Benefit Programs, U.S. Department of Labor.

[FR Doc. 85-1172 Filed 1-14-85; 8:45 am]

BILLING CODE 4510-29-M

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

[Notice 85-05]

Aerospace Safety Advisory Panel; Meeting

AGENCY: National Aeronautics and Space Administration.

ACTION: Notice of meeting.

SUMMARY: In accordance with the Federal Advisory Committee Act, Pub. L. 92-463, as amended, the National Aeronautics and Space Administration announces a forthcoming meeting of the Aerospace Safety Advisory Panel.

DATE AND TIME: February 14, 1985, 2 p.m. to 4 p.m.

ADDRESS: National Aeronautics and Space Administration, 400 Maryland Avenue SW, Room 7002, Washington, DC 20546.

FOR FURTHER INFORMATION CONTACT: Mr. Gilbert L. Roth, Code LB, National Aeronautics and Space Administration, Washington, DC 20546 (202/453-8341).

SUPPLEMENTARY INFORMATION: The Panel will present its annual report to the NASA Administrator. This is pursuant to carrying out its statutory duties for which the Panel reviews, evaluates, and advises on those program activities, systems, procedures, and management policies that contribute to risk and the identification of assessment of these for management. Priority is given to those programs that involve the safety of manned flight. The major subjects will be the Space Shuttle Program, Space Flight Operations, and Aeronautical Operations. Visitors will be admitted to the meeting room up to its capacity, which is approximately 60 persons including Panel members and other participants. Visitors will be requested to sign a visitor's register.

Type of meeting: Open.

Richard L. Daniels,

Deputy Director, Logistics Management and Information, Programs Division, Office of Management.

January 9, 1985.

[FR Doc. 85-1062 Filed 1-14-85; 8:45 am]

BILLING CODE 7510-01-M

Notice 85-03

NASA Advisory Council; Meeting

AGENCY: National Aeronautics and Space Administration.

ACTION: Notice of meeting.

SUMMARY: In accordance with the Federal Advisory Committee Act, Pub. L. 92-463, as amended, the National

Aeronautics and Space Administration announces a forthcoming meeting of the NASA Advisory Council, Task Force on the Commercial Use of Space.

DATE AND TIME: January 30, 1985, 9 a.m. to 5 p.m.

ADDRESS: National Aeronautics and Space Administration, 600 Independence Avenue SW, Room 226A, Washington, DC 20546.

FOR FURTHER INFORMATION CONTACT: Mr. Carl R. Praktish, Code LB, National Aeronautics and Space Administration, Washington, DC 20546 (202/453-8335).

SUPPLEMENTARY INFORMATION: The NASA Advisory Council Task Force on the Commercial Use of Space was established under the NASA Advisory Council to council NASA on the development of the appropriate policies, programs, and research priorities to foster the commercial use of space and on the conduct of those programs. The Task Force, chaired by Thomas A. Vanderslice, has a total of 11 members. This meeting will provide a general review of NASA's program for materials processing research in microgravity. The meeting will be closed to the public from 2 p.m. to 5 p.m. During the closed session, the Task Force will discuss the qualifications of candidates for membership on new or existing committees to provide a more detailed technical review and prioritization of disciplines and research opportunities. Because this session will be concerned throughout with matters listed in 5 U.S.C. 552b(c)(6), it has been determined that this session should be closed to the public.

For the open session, visitors will be admitted to the meeting room up to its capacity, which is approximately 100 persons, including Task Force members and other participants. Visitors will be requested to sign a visitors's register.

Type of meeting: Open—except for the closed session as noted in the following agenda.

Agenda

January 30, 1985

9 a.m.—Review of Materials Processing Research in Microgravity.
2 p.m.—Executive Session (closed).
5 p.m.—Adjourn.

Richard L. Daniels,

Deputy Director, Logistics Management and Information, Programs Division, Office of Management.

January 7, 1985.

[FR Doc. 85-1060 Filed 1-14-85; 8:45 am]

BILLING CODE 7510-01-M

[Notice 85-04]

NASA Advisory Council (NAC); Life Sciences Advisory Committee Meeting

AGENCY: National Aeronautics and Space Administration.

ACTION: Notice of meeting.

SUMMARY: In accordance with the Federal Advisory Committee Act, Pub. L. 92-463, as amended, the National Aeronautics and Space Administration announces a forthcoming meeting of the NASA Advisory Council, Life Sciences Advisory Committee (LSAC).

DATE AND TIME: January 30, 1985, 8:30 a.m. to 4:30 p.m.; and January 31, 1985, 8 a.m. to 4:30 p.m.

ADDRESS: Lunar and Planetary Institute, Main Conference Room, Houston, Texas.

FOR FURTHER INFORMATION CONTACT: Henry V. Bielstein, MD., Code EB, National Aeronautics and Space Administration, Washington, DC 20546 (202/453-1546).

SUPPLEMENTARY INFORMATION: The Life Sciences Advisory Committee provides advice and coordination of NASA Life Sciences research programs. They assist in long-range planning for Spacelab, Space Station, and STS experiments, as well as ground-based biomedical research. The Committee, chaired by Dr. Robert E. Moser, is comprised of approximately 24 members.

Type of meeting: Open.

January 30, 1985

8:30 a.m.—Opening Remarks.
8:40 a.m.—Overview of NASA's Programs in Human Factors, Controlled Ecological Life Support System (CELSS), and the European Space Agency's (ESA) Life Sciences Advisory Council Activities.
1 p.m.—LSAC Planning Session.
4:30 p.m.—Adjourn.

January 31, 1985

8 a.m.—Presentation of Productivity Study, NASA Advanced Planning, and Hematology Research.
1 p.m.—LSAC Planning Session.
4:30 p.m.—Adjourn.

Richard L. Daniels,

Deputy Director, Logistics Management, and Information Programs Division, Office of Management.

January 9, 1985.

[FR Doc. 85-1061 Filed 1-14-85; 8:45 am]

BILLING CODE 7510-01-M

NUCLEAR REGULATORY COMMISSION

[Docket Nos. 50-250 and 50-251]

Florida Power and Light Co.; Environmental Assessment and Finding of No Significant Impact

The U.S. Nuclear Regulatory Commission (the Commission) is considering issuance of an exemption from the requirements of 10 CFR 50.48(c)(2), (c)(3) and (c)(4) to Florida Power and Light Company (the licensee), for the Turkey Point Plant, Units Nos. 3 and 4, located in Dade Country, Florida.

Environmental Assessment

Identification of Proposed Action

The exemption would grant the licensee schedular deferment for completion of four required modifications in Units 3 and 4 and one required modification in Unit 3 for 10 CFR Part 50, Appendix R, Section III.G. These modifications are both outage and non-outage related. The exemption would also grant schedular deferment in completion of alternate safe shutdown capability required by sections III.G.3 and III.L of Appendix R for Unit 3 only. This exempton is in response to the licensee's request dated November 16, 1984, and supplemented December 14, 1984.

The Need for the Proposed Action

Section 50.48 of 10 CFR Part 50 requires that licensed operating reactors be subject to the requirements in Appendix R of 10 CFR Part 50. Appendix R contains general requirements and some of the specific requirements for fire protection programs at licensed nuclear facilities. On February 17, 1981, the fire protection rule for nuclear power plants, 10 CFR 50.48 and Appendix R, became effective. This rule required all licensees of plants licensed prior to January 1, 1979, to submit plans and schedules for meeting the applicable requirements of Appendix R and a design description and schedules for any modifications proposed to provide alternate safe shut down capability pursuant to paragraph III.G.3 of Appendix R.

The licensee's plans for complying with Appendix R requirements and proposed modifications to provide alternate safe shutdown were approved by the Commission and the Safety Evaluations provided to the licensee by letters dated March 27, 1984 and April 16, 1984, respectively. The proposed schedules provided by the licensee for

implementing the modifications were in accordance with 10 CFR 50.48(c)(2) for modifications not requiring prior NRC approval and non-outage related, (c)(3) for modifications not requiring prior NRC approval and outage related, and (c)(4) for modifications pursuant to section III.G.3 of Appendix R which requires NRC approval and are both outage and non-outage related.

We indicated in our letter to the licensee dated July 9, 1984, that the proposed schedules were in compliance with the tolling requirements of 10 CFR 50.48 and no schedular exemptions were necessary. We further stated that if significant changes are required due to equipment procurement or other problems should occur, we be notified in a timely fashion and any required schedular exemptions, including supporting justification, be provided. By letter dated Novemer 16, 1984 and supplemented December 14, 1984, the licensee requested schedular exemptions in six areas and included the basis, justification and compensatory measures in support of the request.

The primary reason for the request is to limit the number of craft personnel on site during outage and non-outage related activities to assure reliability and safety of plant operations. In addition, the initial effort of vendor qualification and procurement of parts and materials has resulted in unanticpated delays in the engineering and scheduling of Appendix R related work. The licensee considered other ongoing plant modifications and integrated their needs in relation to the Appendix R fire protection related work. The other activities included TMI upgrades, safety-related equipment qualification and Performance Enhancement Program commitments.

Environmental Impacts of the Proposed Action

By using reasonable interim compensatory measures, the proposed schedular exemptions will provide a degree of fire protection such that there is no significant increase in the risk of fires at this facility. Consequently, the probability of fires has not been increased and the post-fire radiological releases will not be greater than previously determined nor does the proposed exemption otherwise affect radiological plant effluents. Therefore, the Commission concludes that there are no significant radiological environmental impact associated with this proposed exemption.

Since the Commission has concluded there is no measurable environmental impact associated with the proposed exemption, any alternatives either will have no environmental impact or will have a greater environmental impact. The principal alternative to the exemption would be to require literal schedular compliance with Sections (c)(2), (c)(3), and (c)(4) of 10 CFR 50.48. Such an action would not enhance the protection of the environment and could result in and substantial delays in other safety-related work at the facility.

Alternative Use of Resources

This action involves no use of resources not previously considered in the Final Environmental Statement (operating licenses) for the Turkey Point Plant, Unit Nos. 3 and 4.

Agencies and Persons Consulted

The Commission's staff reviewed the licensee's request and did not consult other agencies or persons.

Finding of no Significant Impact

Based upon the foregoing environmental assessment, we conclude that the proposed action will not have a significant effect on the quality of the human environment. The Commission has, therefore, determined not to prepare an environmental impact statement for the proposed exemption.

For further details with respect to this action, see the request for exemption dated December 16, 1984 and supplement dated December 14, 1984, which are available for public inspection at the Commission's Public Document Room, 1717 H Street, NW, Washington, D.C., and at the Environment and Urban Affairs Library, Florida International University, Miami, Florida 33199.

Dated at Bethesda, Maryland, this 3rd day of January 1985.

For the Nuclear Regulatory Commission.

Gus C. Lainas,

Assistant Director for Operating Reactors, Division of Licensing.

[FR Doc. 85-1162 Filed 1-14-85; 8:45 am]

BILLING CODE 7590-01-M

[Dockets Nos. 50-321 and 50-366]

Georgia Power Co. et al.; Environmental Assessment and Finding of No Significant Impact

The U.S. Nuclear Regulatory Commission (the Commission) is considering issuance of an exemption from the requirements of 10 CFR 50.48(c) to the Georgia Power Company, Oglethorpe Power Corporation, Municipal Electric Authority of Georgia, and the City of Dalton, Georgia (the licensees), for the Edwin I. Hatch Nuclear Plant, Units 1 and 2 located in Appling County, Georgia.

Environmental Assessment

Identification of Proposed Action

The exemption would grant the licensees a schedular deferment from the provisions of Appendix R, section III.G, fire protection of the equipment used for safe shutdown capability, from January 18, 1985, to November 30, 1986. The exemption is responsible to the licensees' application for exemption dated September 4, 1984, as supplemented by letters dated October 2, 1984, October 19, 1984, October 26, 1984, and December 20, 1984.

The Need for the Proposed Action

Appendix R, section III.G, requires a licensee authorized to operate a nuclear power reactor to provide fire protection for equipment used for safe shutdown. The schedular requirements of 10 CFR 50.48(c) call for the implementation of modifications for which a plant shutdown is not required within nine months after the effective date of this section. For Hatch Units 1 and 2, this nine-month period started on April 18, 1984, and ends on January 18, 1985.

In a submittal dated September 4, 1984, as supplemented by letters dated October 2, 1984, October 19, 1984, October 26, 1984, and December 20, 1984, the licensees requested that the implementation schedule for the proposed fire protection modification in certain areas at Hatch Units 1 and 2, not requiring plant shutdown for installation, be extended from January 18, 1985, to November 30, 1986.

The magnitude of the program associated with the fire protection modifications and with an equipment qualification program and other improvement programs with which the fire protection work must interface does not allow the 10 CFR 50.48(c) schedule requirements to be met. As an alternative to implementation of the required modifications by January 18, 1985, the licensees have proposed interim compensatory fire protection measures to be instituted until the modifications have been completed. These measures are being evaluated by the Commission's staff.

Environmental Impacts of the Proposed Action

By using reasonable interim compensatory measures, the proposed exemption will provide a degree of fire protection such that there is no significant increase in the risk of fire at this facility. Consequently, the probability of fires has not been

increased and the post-fire radiological releases will not be greater than previously determined nor does the proposed exemption otherwise affect radiological plant effluents. Therefore, the Commission concludes that there are no significant radiological environmental impacts associated with this proposed exemption.

With regard to potential nonradiological impacts, the proposed exemption involves features located entirely within the restricted area as defined in 10 CFR Part 20. It does not affect nonradiological plant effluents and has no other environmental impact. Therefore, the Commission concludes that there are no significant nonradiological environmental impacts associated with the proposed exemption.

Alternative Use of Resources

This action does not involve the use of resources not considered previously in connection with the Final Environmental Statements (FES) relating to this facility, *FES for Hatch Units 1 and 2*, USAEC (October 1972) and *FES for Hatch Unit 2*, NUREG–0417 (March 1978).

Agencies and Persons Consulted

The Commission's staff reviewed the licensees' request and did not consult other agencies or persons.

Finding of No Significant Impact

The Commission has determined not to prepare an environmental impact statement for the proposed exemption.

Based upon the foregoing environmental assessment, the Commission concludes that the proposed action will not have a significant effect on the quality of the human environment.

For further details with respect to this action, see the application for exemption dated September 4, 1984, as supplemented by submittals dated October 2, 1984, October 19, 1984, October 26, 1984, and December 20, 1984, which is available for public inspection at the Commission's Public Document Room, 1717 H Street, NW, Washington, D.C., and at the Appling County Public Library, 301 City Hall Drive, Baxley, Georgia.

Dated at Bethesda, Maryland, this 10th day of January 1985.

For the Nuclear Regulatory Commission.

Gus C. Lainas,

Assistant Director for Operating Reactors, Division of Licensing.

[FR Doc. 85–1159 Filed 1–14–85; 8:45 am]

BILLING CODE 7590–01–M

[Docket No. 50–321]

Georgia Power Co. et al.; Issuance of Amendment to Facility Operating License

The U.S. Nuclear Regulatory Commission (the Commission) has issued Amendment No. 105 to Facility Operating License No. DPR–57, issued to Georgia Power Company, Oglethorpe Power Corporation, Municipal Electric Authority of Georgia, and City of Dalton, Georgia (the licensees), which revised the Technical Specifications for operation of the Edwin I. Hatch Nuclear Plant, Unit No. 1, (the facility) located in Appling County, Georgia. The amendment was effective as of the date of its issuance.

This amendment revised the Technical Specifications to implement the Average Power Range Monitor/Rod Block Monitor/Technical Specification (ARTS) improvement Program.

The application for the amendment complies with the standards and requirements of the Atomic Energy Act of 1954, as amended (the Act), and the Commission's rules and regulations. The Commission has made appropriate findings as required by the Act and the Commission's rules and regulations in 10 CFR Chapter I, which are set forth in the license amendment.

Notice of Consideration of Issuance of Amendment and Opportunity for Prior Hearing in connection with this action was published in the **Federal Register** on May 16, 1984, 48 FR 20769 and October 24, 1984, 48 FR 42819. No request for a hearing or petition for leave to intervene was filed following this notice.

Also, in connection with this action, the Commission prepared an Environmental Assessment and Finding of No Significant Impact which was published in the **Federal Register** on December 21, 1984, 49 FR 49741.

For further details with respect to this action, see (1) the application for amendment dated February 6, 1984, as supplemented September 6, 1984, (2) Amendment No. 105 to License No. DPR–57, and (3) the Commission's related Safety Evaluation. All of these items are available for public inspection at the Commission's Public Document Room, 1717 H Street, NW, Washington, D.C. 20555, and at the Appling County Public Library, 301 City Hall Drive, Baxley, Georgia. A copy of items (2) and (3) may be obtained upon request addressed to the U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, Attention: Director, Division of Licensing.

Dated at Bethesda, Maryland, this 31st day of December 1984.

For the Nuclear Regulatory Commission.

John F. Stolz,

Chief, Operating Reactors Branch No. 4, Division of Licensing.

[FR Doc. 85–1160 Filed 1–14–84; 8:45 am]

BILLING CODE 7590–01–M

[Docket No. 50–322–OL]

Long Island Lighting Co. (Shoreham Nuclear Power Station, Unit 1); Resumption of Hearing on Diesel Generator Issues

January 10, 1985.

Before Administrative Judges: Lawrence Brenner, Chairman, Dr. George A. Ferguson, Dr. Peter A. Morris.

The evidentiary hearing on issues in controversy related to the emergency diesel generators manufactured by Transamerica Delaval, Inc. will resume on February 12, 1985, at 10:30 am, at the Nuclear Regulatory Commission's hearing room, located at: 4350 East-West Highway, 5th Floor, Bethesda, Maryland.

The hearings will continue, as necessary, on February 13–15 and 19–21. If necessary, further hearing sessions will be scheduled to resume the week of March 4, 1985, at a location to be determined.

It is so ordered.

Bethesda, Maryland, January 10, 1985.

For the Atomic Safety and Licensing Board.

Lawrence Brenner,

Chairman, Administrative Judge.

[FR Doc. 85–1163 Filed 1–14–85; 8:45 am]

BILLING CODE 7590–01–M

[Docket No. 50–346]

Toledo Edison Co. and the Cleveland Electric Illuminating Co.; Issuance of Amendment to Facility Operating License

The U.S. Nuclear Regulatory Commission (the Commission) has issued Amendment No. 83 to Facility Operating License No. NPF–3, issued to Toledo Edison Company and the Cleveland Electric Illuminating Company (the licensees), which revised the license for operation of the Davis-Besse Nuclear Power Station, Unit No. 1, (the facility) located in Ottawa County, Ohio. the amendment is effective as of the date of its issuance.

This amendment adds a new condition to the license which imposes three operational restrictions relating to the use of the startup feedwater pump.

The application for the amendment complies with the standards and

requirements of the Atomic Energy Act of 1954, as amended (the Act), and the Commission's rules and regulations. The Commission has made appropriate findings as required by the Act and the Commission's rules and regulations in 10 CFR Chapter I, which are set forth in the license amendment.

Notice of Consideration of Issuance of Amendment and Opportunity for Prior Hearing in connection with this action was published in the **Federal Register** on November 28, 1984, 49 FR 46833. No request for a hearing or petition for leave to intervene was filed following this notice.

Also, in connection with this action, the Commission prepared an Environmental Assessment and Finding of No Significant Impact which was published in the **Federal Register** on January 4, 1985, 50 FR 581.

For further details with respect to this action, see (1) the application for amendment dated November 12, 1984, (2) Amendment No. 83 to License No. NPF-3, and (3) the Commission's related Safety Evaluation. All of these items are available for public inspection at the Commission's Public Document Room, 1717 H Street, NW, Washington, D.C. 20555, and at the University of Toledo Library, Documents Department, 2801 Bancroft Avenue, Toledo, Ohio 43606. A copy of items (2) and (3) may be obtained upon request addressed to the U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, Attention: Director, Division of Licensing.

Dated at Bethesda, Maryland, this 8th day of January 1985.

John F. Stolz,

Chief, Operating Reactors Branch No. 4, DL, Division of Licensing.

[FR Doc. 85-1161 Filed 1-14-85; 8:45 am]

BILLING CODE 7590-01-M

[Docket No. 50-2]

University of Michigan; Consideration of Application for Renewal of Facility License

The United States Nuclear Regulatory Commission (the Commission or NRC) is considering renewal of Facility Operating License No. R-28 issued to the University of Michigan (the licensee) for the operating of the training and research reactor located on the North Campus in Ann Arbor, Michigan.

The renewal would extend the expiration date of Facility Operating License No. R-28 for twenty years from date of issuance, in accordance with the licensee's timely application for renewal dated November 30 1984.

Prior to a decision to renew the license, the Commission will have made the findings required by the Atomic Energy Act of 1954, as amended (the Act), and the Commission's regulations.

By February 14, 1985, the licensee may file a request for a hearing with respect to renewal of the subject facility license and any person whose interest may be affected by this proceeding and who wishes to participate as a party in the proceeding must file a written petition for leave to intervene. Request for a hearing and petition for leave to intervene shall be filed in accordance with the Commission's "Rules of Practice for Domestic Licensing Proceedings" in 10 CFR Part 2. If a request for a hearing or petition for leave to intervene is filed by the above date, the Commission or an Atomic Safety and Licensing Board designated by the Commission or by the Chairman of the Atomic Safety and Licensing Board Panel will rule on the request and/or petition and the Secretary of the designated Atomic Safety and Licensing Board will issue a notice of hearing or an appropriate order.

As required by 10 CFR 2.714, a petition for leave to intervene shall set forth with particularity the interest of the petitioner in the proceeding, and how that interest may be affected by the results of the proceeding. The petition should specifically explain the reasons why intervention should be permitted with particular reference to the following factors: (1) The nature of the petitioner's right under the Act to be made a party to the proceeding; (2) the nature and extent of the petitioner's property, financial, or other interest in the proceeding; and (3) the possible effected of any order which any be entered in the proceeding on the petitioner's interest. The petition should also identify the specific aspect(s) of the subject matter of the proceeding as to which petitioner wishes to intervene. Any person who has filed a petition for leave to intervene or who has been admitted as a party may amend the petition without requesting leave of the Board up to fifteen (15) days prior to the first prehearing conference scheduled in the proceeding, but such an amended petition must satisfy the specificity requirements described above.

Not later than fifteen (15) days prior to the first prehearing conference scheduled in the proceeding, the petitioner shall file a supplement to the petition to intervene which must include a list of the contentions which are sought to be litigated in the matter, and the bases for each contention set forth with reasonable specificity. Contentions shall be limited to matters within the scope of the renewal action under consideration. A petitioner who fails to file such a supplement with satisfies these requirements with respect to at least one contention will not be permitted to participate as a party.

Those permitted to intervene become parties to the proceeding, subject to any limitations in the order granting leave to intervene, and have the opportunity to participate fully in the conduct of the hearing, including the opportunity to present evidence and cross-examine witnesses.

A request for a hearing or a petition for leave to intervene shall be filed with the Secretary of the Commission, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, Attention: Docketing and Service Section, or may be delivered to the Commission's Public Document Room, at 1717 H Street, NW, Washington, DC. by the above date. Where petitions are filed during the last ten (10) days of the noticed period, it is requested that the peitioner or representative for the petitioners promptly so inform the Commission by a toll-free telephone call to Western Union at (800) 325-6000 (in Missouri (800) 342-6700). The Western Union operator should be given Datagram Identification Number 3737 and the following message addressed to Cecil O. Thomas: (petitioner's name and telephone number); (date petitions was mailed); (Univeristy of Michigan); and (publication date and page number of this **Federal Register** notice). A copy of the petition should also be sent to the Executive Legal Director, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555 and to Mr. Richard K. Daane, 4014 Fleming Administration Building, University of Michigan, Ann Arbor, Michigan 48109, attorney for the licensee.

Nontimely filings of petitions for leave to intervene, amended petitions, supplemental petitions and/or requests for hearing will not be entertained absent a determination by the Commission, the presiding officer or the Atomic Safety and Licensing Board designated to rule on the petition and/or request that the petition has made a substantial showing of good cause for the granting of a late petition and/or request. That determination will be based upon a balancing of the factors specified in 10 CFR 2.714(a)(1)(i)-(v) and 2.714(d).

For further details with respect to this action, see the application for renewal dated November 30, 1984, which is available for public inspection at the Commission's Public Document Room

15, 1717 H Street, NW, Washington, D.C. 20555.

Dated at Bethesda, Maryland, this 9th of January, 1985.

For the Nuclear Regulatory Commission.

Cecil O. Thomas,

Chief, Standardization and Special Projects Branch, Division of Licensing.

[FR Doc. 85-1158 File 1-14-85; 8:45 am]

BILLING CODE 7590-01-M

International Atomic Energy Agency Draft Safety Guide; Availability of Draft for Public Comment

The International Atomic Energy Agency (IAEA) is completing development of a number of internationally acceptable codes of practice and safety guides for nuclear power plants. These codes and guides are in the following five areas: Government Organization, Design, Siting, Operation, and Quality Assurance. All of the codes and most of the proposed safety guides have been completed. The purpose of these codes and guides is to provide guidance to countries beginning nuclear power programs.

The IAEA codes of practice and safety guides are developed in the following way. The IAEA receives and collates relevant existing information used by member countries in a specified safety area. Using this collation as a starting point, an IAEA working group of a few experts develops a preliminary draft of a code or safety guide which is then reviewed and modified by an IAEA Technical Review Committee corresponding to the specified area. The draft code of practice or safety guide is then sent to the IAEA Senior Advisory Group which reviews and modifies as necessary the drafts of all codes and guides prior to their being forwarded to the IAEA Secretariat and thence to the IAEA Member States for comments. Taking into account the comments received from the Member States, the Senior Advisory Group then modifies the draft as necessary to reach agreement before forwarding it to the IAEA Director General with a recommendation that it be accepted.

As part of this program, Safety Guide SG-D13, "Reactor Coolant and Associated Systems in Nuclear Power Plants," has been developed. The working group consisting of Mr. G. Ellia from France; Mr. C.N. Bapat from India; Mr. P.C. Dannatt from the United Kingdom; and Mr. W.H. D'Ardenne (General Electric Company) from the United States developed the initial draft of this guide from an IAEA collation. This draft was subsequently modified by the IAEA Technical Review Committee for Design and the Senior Advisory Group, and we are now soliciting public comment on a modified draft (Rev. 4, dated June 28, 1984). Comments received by the Director, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555, by February 15, 1985, will be particularly useful to the U.S. representatives to the Technical Review Committee and the Senior Advisory Group in developing their positions on its adequacy prior to their next IAEA meetings.

Single copies of this draft Safety Guide may be obtained by a written request to the Director, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, D.C. 20555.

(5 U.S.C. 522(a))

Dated at Washington, D.C., this 9th day of January 1985.

For the Nuclear Regulatory Commission.

Denwood F. Ross,

Deputy Director, Office of Nuclear Regulatory Research.

[FR Doc. 85-1156 Filed 1-14-85; 8:45 am]

BILLING CODE 7590-01-M

PENSION BENEFIT GUARANTY CORPORATION

Multiemployer Pension Plans; Effect of Withdrawal Following Sale of Assets

AGENCY: Pension Benefit Guaranty Corporation.

ACTION: Notice of consideration.

SUMMARY: This notice advises employers, multiemployer plan sponsors and other interested persons that the Pension Benefit Guaranty Corporation (PBGC) is considering issuing an interpretation concerning the effect that a prior sale of assets which meets the requirements of section 4204 of ERISA has on subsequent plan determinations with respect to complete and partial withdrawals, including the calculation of withdrawal liability. The PBGC expects to issue its interpretation in the form of an opinion letter. This notice establishes the procedures for public comment concerning the interpretation of the indicated statutory provisions.

DATE: Comments should be received on or before March 18, 1985.

ADDRESSES: Comments should be addressed to the General Counsel, Pension Benefit Guaranty Corporation, 2020 K Street, NW., Washington, D.C. 20006. Written comments will be available for public inspection at the PBGC, Suite 7100 at the above address between the hours of 9:00 a.m. and 4:00 p.m.

FOR FURTHER INFORMATION CONTACT: Terence G. Craig, Attorney, Legal Department, Code 250, 2020 K Street, NW., Washington, D.C. 20006, (202) 254-4873. (This is not a toll-free number.)

SUPPLEMENTARY INFORMATION:

The Statute

Under the Employee Retirement Income Security Act of 1974 as amended by the Multiemployer Pension Plan Amendments Act of 1980 (ERISA), an employer that withdraws from a multiemployer pension plan covered under Title IV of ERISA may be liable to the plan for a portion of the plan's unfunded vested benefits. In general a complete withdrawal from a plan occurs under section 4203 of ERISA if an employer either permanently ceases to have an obligation to contribute or permanently ceases all covered operations. A partial withdrawal occurs as described in section 4205. In the event of a withdrawal of an employer, the withdrawal liability of the employer to the plan is determined as described in section 4201(b) of ERISA. Section 4204 of ERISA provides that a complete or partial withdrawal of an employer does not occur solely as a result of a bona fide, arm's-length sale of assets to an unrelated party if three conditions are met:

(A) The purchaser has an obligation to contribute to the plan with respect to the operations for substantially the same number of contribution base units ("CBU's") for which the seller had an obligation to contribute to the plan;

(B) The purchaser provides to the plan for a period of 5 plan years commencing with the first plan year beginning after the sale of assets a bond or an amount held in escrow in an amount described in that section; and

(C) the contract for sale provides that, if the purchaser withdraws during such 5 plan years, the seller is secondarily liable for any withdrawal liability it would have had (but for the application of section 4204) if the liability of the purchaser is not paid.

Section 4204(b)(1) provides that withdrawal liability of the purchaser shall be determined as if the purchaser had been required to contribute to the plan in the year of the sale and the 4 plan years preceding the sale the amount the seller was required to contribute for such operations for such 5 plan years.

The Interpretation

On May 12, 1983, the PBGC published its opinion (PBGC Opinion Letter 83-10)

that in the event of a withdrawal of an employer subsequent to a sale of assets meeting the requirements of section 4204, the seller should be given a credit for the seller's withdrawal liability under sections 4211 and 4206 of ERISA. The purpose of the credit is to reflect Congress' intent that in the event of withdrawal by both the seller and the purchaser, the plan not recover twice based on the same contribution base units. The letter, however, did not describe how the amount of the credit is to be determined. As a result of the publication of Opinion Letter 83-10, the PBGC has received several inquires concerning the determination and application of credit to a seller in the event of a withdrawal subsequent to a section 4204 sale of assets. In light of these and earlier inquiries, the PBGC now wishes to clarify and to augment its interpretation by answering the following questions:

1. What credit should a seller receive to its contribution history for purposes of determining its allocation numerators under section 4211 of ERISA [see *e.g.* section 4211(b)(2)(E)(ii)(I); (b)(3)(B)(i); (c)(2)(B)((ii)(I); (c)(2)(C)(ii)(I); and (c)(3)(B)(i))?

2. What credit should a seller receive to its contribution base unit (CBU) history for purposes of determining its partial withdrawal reduction fraction under section 4206(a)(2) of ERISA?

3. What credit, if any, should a seller receive to its CBU history for purposes of determining whether a partial withdrawal occurs under section 4205(b)(1) (70% contribution decline)?

Public Comments

The PBGC hereby solicits public comment concerning these questions including any comments on related issues and the implications and practical effect that particular interpretations may have on employers, multiemployer pension plans and the pension insurance system. Comments should be addressed to the General Counsel, Pension Benefit Guaranty Corporation, 2020 K Street, NW., Washington, D.C. 20006.

Written comments will be available for public inspection at the above address, Suite 7100, between the hours of 9:00 a.m. and 4:00 p.m. Each person submitting comments should include his or her name, address, identify this notice, and give reasons for any recommendation.

(Sec. 4002(b)(3), Pub. L. 93-406, 88 Stat. 1004, as amended by sec. 403(1), Pub. L. 96-364, 94 Stat. 1302 (29 U.S.C. 1302))

Issued in Washington, D.C., this January 15, 1985.

C.C. Tharp,

Executive Director, Pension Benefit Guaranty Corporation.

[FR Doc. 85-1058 Filed 1-14-85; 8:45 am]

BILLING CODE 7708-01-M

POSTAL RATE COMMISSION

Alexandria VA, and Washington, DC; Post Office Visits

January 9, 1985.

Notice is hereby given that Commissioner Bonnie Guiton accompanied by Gerald Cerasale, Legal Advisor to the Chairman, will visit the Northern Virginia SCF and Alexandria, VA Post Office on January 10, 1985, and the Washington, D.C. Post Office January 11, 1985. A written report will be on file in the Commission's Docket Room.

Charles L. Clapp,

Secretary.

[FR Doc. 85-1063 Filed 1-14-85; 8:45 am]

BILLING CODE 7715-01-M

[Docket No. A85-13; Order No. 601]

Philomath, Georgia 30659 (Mrs. H. M. Callaway, et al., Petitioners); Notice and Order Accepting Appeal and Establishing Procedural Schedule

Issued: January 9, 1985.

Before Commissioners: Janet D. Steiger, Chairman; Henry R. Folsom, Vice-Chairman; John W. Crutcher; James H. Duffy; Bonnie Guiton.

Docket Number: A85-13.

Name of affected Post Office: Philomath, Georgia 30659.

Name(s) of petitioners(s): Mrs. H. M. Callaway, *et al.*

Type of determination: Consolidation.

Date of filing of appeal papers: December 31, 1984.

Categories of issues apparently raised:

1. Effect on the community [39 U.S.C. 404(b)(2)(A)].

2. Effect on postal services [39 U.S.C. 404(b)(2)(C)].

Other legal issues may be disclosed by the record when it is filed; or, conversely, the determination made by the Postal Service may be found to dispose of one or more of these issues.

In the interest of expedition within the 120-day decision schedule [39 U.S.C. 404(b)(5)] the Commission reserves the right to request of the Postal Service memoranda of law on any appropriate issue. If requested, such memoranda will be due 20 days from the issuance of the request; a copy shall be served on the Petitioner. In a brief of motion to dismiss or affirm, the Postal Service may incorporate by reference any such memorandum previously filed.

The Commission orders:

(A) The Secretary shall publish this Notice and Order and Procedural Schedule in the **Federal Register.**

By the Commission.

Charles L. Clapp,

Secretary.

December 31, 1984—Filing of Petitions.

January 9, 1985—Notice and Order of Filing of Appeal.

January 25, 1985—Last day for filing of petitions to intervene [*see* 39 CFR 3001.111(b)].

February 4, 1985—Petitioners' Participant Statement or Initial Brief [*see* 39 CFR 3001.115 (a) and (b)].

February 25, 1985—Postal Service Answering Brief [*see* 39 CFR 3001.115(c)].

March 12, 1985—(1) Petitioners' Reply Brief should petitioners choose to file one [*see* 39 CFR 3001.115(d)].

March 19, 1985—(2) Deadline for motions by any party requesting oral argument. The Commission will exercise its discretion, as the interest of prompt and just decision may require, in scheduling or dispensing with oral argument [*see* 39 CFR 3001.116].

April 30, 1985—Expiration of 120-day decisional schedule [*see* 39 U.S.C. 404(b)(5)].

[FR Doc. 85-1064 Filed 1-14-85; 8:45 am]

BILLING CODE 7715-1-M

DEPARTMENT OF TRANSPORTATION

Research and Special Programs Administration

Materials Transportation Bureau; Grants and Denials of Applications for Exemptions

AGENCY: Materials Transportation Bureau, DOT.

ACTION: Notices of grants and denials of applications for exemptions.

SUMMARY: In accordance with the procedures governing the application for, and the processing of, exemptions from the Department of Transportation's Hazardous Materials Regulations (49 CFR Part 107, Subpart B, notice is hereby given of the exemptions granted in December 1984. The modes of transportation involved are identified by a number in the "Nature of Exemption Thereof" portion of the table below as

follows: 1—Motor vehicle, 2—Rail freight, 3—Cargo vessel, 4—Cargo-only aircraft, 5—Passenger-carrying aircraft. Application numbers prefixed by the letters EE represent applications for Emergency Exemptions.

RENEWAL AND PARTY TO EXEMPTIONS

Application No.	Exemption No.	Applicant	Regulation(s) affected	Nature of exemption thereof
3004-P	DOT-E 3004	Big Three Industries, Inc., Houston, TX	49 CFR 173.302, 175.3	To become a party to Exemption 3004. (Modes 1, 2, 4, 5.)
3549-X	DOT-E 3549	U.S. Department of Energy, Washington, DC.	49 CFR 173.65(a), 173.77	To authorize use of DOT Specification 19B plywood boxes as an additional container. (Modes 1, 2.)
5038-X	DOT-E 5038	Synthatron Corp., Parsippany, NJ	49 CFR 173.119, 173.135(a)(6), 173.136(a)(5), 173.247(a)(1), 175.3.	To authorize shipment of dimethyldichlorosilane, trichlorosilane, other specifically identified flammable liquids and silicon tetrachloride in non-DOT specification type 304 stainless steel cylinders. (Modes 1, 2, 3, 4.)
5248-X	DOT-E 5248	3M Co., Austin, TX	49 CFR 173.431(a), 175.3	To authorize shipment of a certain quantity of polonium-210 in any DOT Specification approved outer Type A packaging. (Modes 1, 2, 4.)
5248-X	DOT-E 5248	U.S. Department of Energy, Washington, DC.	49 CFR 173.431(a), 175.3	To authorize shipment of a certain quantity of polonium-210 in any DOT Specification approved outer Type A packaging. (Modes 1, 2, 4.)
5649-P	DOT-E 5649	FMC Corp., Livonia, MI	49 CFR 173.154(a)	To become a party to Exemption 5649. (Modes 1, 2.)
5649-X	DOT-E 5649	Great Lakes Chemical Corp., Adrian, MI	49 CFR 173.154(a)	To authorize shipment of an oxidizer, in non-DOT specification polypropylene or polyethylene bags. (Modes 1, 2.)
6117-X	DOT-E 6117	Montana Sulphur & Chemical Co., Billings, MT	49 CFR 172.504, 173.314(c)	To authorize transport of hydrogen sulfide in DOT Specification 105A600W tank car tanks or proposed DOT Specification 120A600W tank car tanks. (Mode 2.)
6293-X	DOT-E 6293	Olin Corp., East Alton, IL	49 CFR 173.21(b), 173.248	To authorize transport of certain corrosive liquids, in DOT Specification MC-311 or MC-312 tank motor vehicles. (Mode 1.)
6293-X	DOT-E 6293	Hercules, Inc., Wilmington, DE	49 CFR 173.21(b), 173.248	To authorize transport of certain corrosive liquids, in DOT Specification MC-311 or MC-312 tank motor vehicles. (Mode 1.)
6349-X	DOT-E 6349	Airco Industrial Gases, Murray Hill, NJ	49 CFR 172.101, 173.315(a)	To authorize use of non-DOT specification insulated, containerized portable tanks, for shipment of certain flammable and nonflammable gases. (Modes 1, 2, 3.)
6349-X	DOT-E 6349	Union Carbide Corp., Danbury, CT	49 CFR 172.101, 173.315(a)	To renew, to make certain proper shipping name, weight limitations, retest and travel time changes in consonance with Docket HM-115 rulemaking. (Modes 1, 2, 3.)
6434-X	DOT-E 6434	Rhone-Poulenc, Inc., Monmouth Junction, NJ.	49 CFR 173.377(i)(1)	To authorize use of non-DOT specification paper bags, for transportation of a poisonous B solid material. (Modes 1, 2.)
6530-P	DOT-E 6530	Big Three Industries, Inc., Houston, TX	49 CFR 173.302(c)	To become a party to Exemption 6530. (Modes 1, 2.)
6543-X	DOT-E 6543	Synthatron Corp., Parsippany, NJ	49 CFR 173.119, 173.135(a)(6), 173.136(a)(5), 173.245, 173.247, 173.271, 175.3.	To authorize shipment of certain corrosive and flammable liquids in non-DOT specification 16 gauge, Type 304 stainless steel cylinders and/or 14 gauge Type 316 stainless steel cylinders. (Modes 1, 2, 3, 4.)
6543-X	DOT-E 6543	Union Carbide Corp., Danbury, CT	49 CFR 173.119, 173.135(a)(6), 173.136(a)(5), 173.245, 173.247, 173.271, 175.3.	To authorize shipment of certain corrosive and flammable liquids in non-DOT specification 16 gauge, Type 304 stainless steel cylinders and/or 14 gauge Type 316 stainless steel cylinders. (Modes 1, 2, 3, 4.)
6543-X	DOT-E 6543	Rohm and Haas Co., Philadelphia, PA	49 CFR 173.119, 173.135(a)(6), 173.136(a)(5), 173.245, 173.247, 173.271, 175.3.	To authorize shipment of certain corrosive and flammable liquids in non-DOT specification 16 gauge, Type 304 stainless steel cylinders and/or 14 gauge Type 316 stainless steel cylinders. (Modes 1, 2, 3, 4.)
6543-X	DOT-E 6543	Corning Glass Works, Corning, NY	49 CFR 173.119, 173.135(a)(6), 173.136(a)(5), 173.245, 173.247, 173.271, 175.3.	To authorize shipment of certain corrosive and flammable liquids in non-DOT specification 16 gauge, Type 304 stainless steel cylinders and/or 14 gauge Type 316 stainless steel cylinders. (Modes 1, 2, 3, 4.)
6762-P	DOT-E 6762	Carlin Laboratories, Jacksonville, FL	49 CFR 173.286(b)(2), 175.3	To become a party to Exemption 6762. (Modes 1, 2, 3, 4.)
6762-P	DOT-E 6762	DuBois Chemical Co., Cincinnati, OH	49 CFR 173.286(b)(2), 175.3	To become a party to Exemption 6762. (Modes 1, 2, 3, 4.)
6762-X	DOT-E 6762	Taylor Chemicals, Inc., Sparks, MD	49 CFR 173.286(b)(2), 175.3	To authorize transport of chemical kits in plastic inside bottles, packed in plastic boxes overpacked in fiberboard boxes. (Modes 1, 2, 3, 4.)
6762-X	DOT-E 6762	United Laboratories, Inc., Addison, IL	49 CFR 173.286(b)(2), 175.3	To authorize transport of chemical kits in plastic inside bottles, packed in plastic boxes overpacked in fiberboard boxes. (Modes 1, 2, 3, 4.)
6984-X	DOT-E 6984	Iraco Chemicals, Salt Lake City, UT	49 CFR 173.103(a), 173.65(g), 177.835(g)(2)(i).	To authorize packaging of 1,000 or less electric blasting caps in inside pastboard cartons or tubes, overpacked in an IME Standard 22 container. (Mode 1.)
7677-X	DOT-E 7677	San Diego Gas & Electric Co., San Diego, CA.	49 CFR 172.101, 173.315(a)	To authorize shipment of liquefied natural gas (methane in non-DOT specification vacuum insulated truck mounted portable tanks. (Mode 1.)
7777-X	DOT-E 7777	Lang Engineering Co., Inc., Rochester, WI.	49 CFR 173.248	To authorize use of DOT Specification 34 polyethylene containers, DOT Specification 12B or 12P corrugated fiberboard boxes, or DOT Specification 6D or 37M cylindrical steel overpacked with an inside Specification 2SL polyethylene containers, for shipment of spent sulfuric acid. (Modes 1, 2, 3.)
7862-X	DOT-E 7862	General Electric Co., Milwaukee, WI	49 CFR 173.302, 175.3	To authorize an additional xenon detector device similar to the one presently authorized. (Modes 1, 4, 5.)
7929-P	DOT-E 7929	Trojan Corp., Salt Lake City, UT	49 CFR 173.65	To become a party to Exemption 7929. (Modes 1, 2.)
8063-X	DOT-E 8063	Union Carbide Corp., Danbury, CT	49 CFR 173.304(a)	To renew and modify paragraph 4, proper shipping name to coincide with Docket HM-115. (Mode 1.)
8120-X	DOT-E 8120	Starflight, Inc., Smyrna, TN	49 CFR 172.101, 172.204(c)(3), 173.27, 175.30(a)(1), 175.320(b), Part 107, Appendix B.	To authorize carriage of certain Class A, B and C explosives that are not permitted for shipment by air or in quantities greater than those prescribed for shipment by air. (Mode 4.)
8126-X	DOT-E 8126	Fauvet-Giret, Paris, France	49 CFR 173.123, 173.315	To authorize use of non-DOT specification portable tanks, for transportation of certain liquefied petroleum gases and other gases classed as flammable gases and a flammable liquid. (Modes 1, 2, 3.)
8126-X	DOT-E 8126	SLEMI, Paris, France	49 CFR 173.123, 173.315	To authorize use of non-DOT specification portable tanks, for transportation of certain liquefied petroleum gases and other gases classed as flammable gases and a flammable liquid. (Modes 1, 2, 3.)
8580-X	DOT-E 8580	Priority Air, Inc., Sanford, FL	49 CFR 172.101, 172.204(c)(3), 173.27, 175.30(a)(1), 175.320(b), Part 107, Appendix B.	To authorize carriage of certain Class A, B and C explosives that are not permitted for air shipment or are in quantities greater than those prescribed for shipment by air. (Mode 4.)

RENEWAL AND PARTY TO EXEMPTIONS—Continued

Application No.	Exemption No.	Applicant	Regulation(s) affected	Nature of exemption thereof
8725-X	DOT-E 8725	CNG Cylinder Corp., Long Beach, CA	49 CFR 173.302(a)	To modify exemption to allow one test ring per heat treat load in place of 1 test ring per production lot of 200 cylinder or less. (Mode 1.)
8802-X	DOT-E 8802	EVA Eisenbahn-Verkehrsmittel GmbH, Dusseldorf, West Germany.	49 CFR 173.315	To authorize use of non-DOT specification IMO Type 5 portable tanks, for transportation of liquefied compressed gases. (Modes 1, 2, 3.)
8873-X	DOT-E 8873	Stauffer Chemical Co., Westport, CT	49 CFR 173.121	To authorize use of DOT Specification MC-312 cargo tanks, for transportation of carbon disulfide or carbon bisulfide. (Mode 1.)
8927-X	DOT-E 8927	HTL Industries, Inc., Duarte, CA	49 CFR 173.302(a), 175.3, 178.44	To authorize manufacture, marking and sale of non-DOT specification girth, welded steel spheres, for transportation of nonflammable gases. (Modes 1, 2, 4, 5.)
8939-X	DOT-E 8939	Hollice Clark Truck Fabrication, Inc., Odessa, TX.	49 CFR 173.119, 173.245, 178.259	To authorize manufacture, marking and sale of six non-DOT specification portable tanks manifolded together within a frame and securely mounted on a truck chassis, for transportation of flammable liquids and corrosive liquids. (Mode 1.)
9001-X	DOT-E 9001	Chesterfield Cylinder Co., Enid, OK	49 CFR 173.301, 173.302, 173.304, 175.3, 178.45.	To substitute a magnetic particle examination for the ultrasonic test of cylinder; to allow a reduction in wall thickness for cylinders of specified diameter. (Modes 1, 2, 3, 4.)
9233-P	DOT-E 9233	Allied Corp., Morristown, NJ	49 CFR 173.164	To become a party to Exemption 9233. (Mode 1.)
9319-X	DOT-E 9319	Dearborn Chemical Co., Lake Zurich, IL	49 CFR 173.245(a)(38)	To authorize DOT Specification 57 Type 304 or 316 stainless steel portable tanks, for water treatment compounds or boiler compounds, liquids that are not alkaline. (Modes 1, 2.)

NEW EXEMPTIONS

Application No.	Exemption No.	Applicant	Regulation(s) affected	Nature of exemption thereof
9263-N	DOT-E 9263	Liquid Air Corp., San Francisco, CA	49 CFR 172.101, 173.316	To authorize transport of a flammable cryogenic liquid, in DOT Specification 4L 200 cylinders. (Mode 1.)
9271-N	DOT-E 9271	Missouri Pacific Railroad Co., St. Louis, MO.	49 CFR 174.90	To authorize deviation from car separation requirements, for transportation of Class A and B explosives. (Mode 2.)
9271-N	DOT-E 9271	Union Pacific Railroad Co., Omaha, NE	49 CFR 174.90	To authorize deviation from car separation requirements, for transportation of Class A and B explosives. (Mode 2.)
9282-N	DOT-E 9282	Halocarbon Products Corp., Hackensack, NJ.	49 CFR 173.314(c)	To authorize use of DOT Specification 110A800W multi-unit tank car tanks except for safety relief devices, for shipment of trifluoroethylene. (Mode 1.)
9285-N	DOT-E 9285	Velsicol Chemical Corp., Chicago, IL	49 CFR 173.365	To authorize shipment of endosulfan, a poison B solid, in non-DOT specification metal drums with inside packaging consisting of four bags of nylon-reinforced polyethylene film. (Mode 1.)
9289-N	DOT-E 9289	Stauffer Chemical Co., Westport, CT	49 CFR 173.118a(b)(1)	To authorize shipment of certain herbicides in metal or polyethylene portable tanks considered to be an implement of husbandry, without shipping papers. (Mode 1.)
9345-N	DOT-E 9345	Wagner Brothers Containers, Inc., Baltimore, MD.	49 CFR 172.420, 175.3	To authorize manufacture, marking and sale of DOT Specification 12B fiberboard boxes bearing pre-printed labels not in full compliance with 172.420, for transportation of flammable solids. (Modes 1, 2, 3, 4, 5.)

EMERGENCY EXEMPTIONS

Application No.	Exemption No.	Applicant	Regulation(s) affected	Nature of exemption thereof
EE 9361-N	DOT-E 9361	Baker Sand Control, Houston, TX	49 CFR 172.101, 175.320(a)	To authorize transport of class A explosives with class C explosive and inert material on cargo aircraft only. (Mode 4).
EE 9362-N	DOT-E 9362	Nowsco Services, Inc., Houston, TX	49 CFR 172.101 column 8, 173.315, 175.30.	To authorize use of non-DOT specification portable tanks of not over 500 gallon capacity, for transportation of nitrogen, refrigerated liquid, nonflammable gas. (Mode 4.)

WITHDRAWALS

Application No.	Applicant	Regulation(s) affected	Nature of exemption thereof
6763-X	Pool Water Products, Garden Grove, CA.	49 CFR 173.217(a)(8)	To authorize use of non-DOT specification single-wall, double-faced corrugated fiberboard boxes, for shipment of certain oxidizers. (Modes 1, 2, 3.)

Denials

8795-X Request by The Marison Company, South Elgin, IL to authorize manufacture, marking and sale of non-DOT specification cylinders made in compliance with DOT Specification 4B240ET, for transportation of nonflammable gases denied December 26, 1984.

8921-X Request by Hoover Universal, Inc., Beatrice, NE to authorize use of non-reusable non-DOT specification polyethylene portable tanks subject to specific reconditioning steps denied December 18, 1984.

Issued in Washington, DC, on January 8, 1985.

J.R. Grothe,

Chief, Exemptions Branch, Office of Hazardous Materials Regulation, Materials Transportation Bureau.

[FR Doc. 85-1081 Filed 1-14-85; 8:45 am]

BILLING CODE 4910-60-M

VETERANS ADMINISTRATION

Agency From Under OMB Review

AGENCY: Veterans Administration.

ACTION: Notice.

The Veterans Administration has submitted to OMB for review the following proposal for the collection of information under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35). This document contains a new collection 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 form and supporting documents may be obtained from Patricia Viers, Agency Clearance Officer (732), Veterans Administration, 810 Vermont Avenue, NW., Washington, DC 20420, (202) 389–2146. Comments and questions about the item 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: January 8, 1985.

By direction of the Administrator:

Dominick Onorato,

Associate Deputy Administrator for Information Resources Management.

New

1. Department of Veterans Benefits
2. Vocational Training Application for VA Pensioners
3. VA Form 28–8966
4. On occasion
5. Individuals or households
6. 15,000 responses
7. 3,000 hours
8. Not applicable

[FR Doc. 85–1095 Filed 1–14–85; 8:45 am]

BILLING CODE 8320-01-M

Medical Care Reimbursement Rates for Fiscal Year 1985

In accordance with provisions of OMB Circular A–11, § 13.5(a), revised reimbursement rates have been established by the Veterans Administration for inpatient and outpatient medical care furnished to beneficiaries of other Federal Agencies during Fiscal Year 1985. These rates will be charged for such medical care provided at health care facilities under the direct jurisdiction of the Administrator on and after November 1, 1984.

Medicine	$308
Spinal cord injury	251
Surgery	332
Psychiatry	252
Drug and alcohol	129
Nursing home	114
Outpatient	61
Pharmacy-prescription refill	6.75
Hemodialysis:	
Hospital component	118
Physician component	12

The hospital component for hemodialysis will be charged in addition to the inpatient per diem rate except when billing Medicare for maintenance dialysis, in which case the physician component will be charged in addition to the hospital component. If other than maintenance dialysis care is provided to a Medicare beneficiary treated as a humanitarian emergency, an additional charge for an outpatient visit may be made by the VA.

Prescription refill charges in lieu of the outpatient visit rate will be charged when the patient receives no service other than the Pharmacy outpatient service. These charges apply if the patient receives the prescription refills in person or by mail.

When medical services for beneficiaries of other Federal Agencies are obtained by the Veterans Administration from private sources, the charges to the other Federal Agencies will be the actual amounts paid by the Veterans Administration for such medical services.

Dated: January 7, 1985.

Harry N. Walters,

Administrator.

[FR Doc. 85–1094 Filed 1–14–85; 8:45 am]

BILLING CODE 8320-01-M

Sunshine Act Meetings

Federal Register
Vol. 50, No. 10
Tuesday, January 15, 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).

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1

FARM CREDIT ADMINISTRATION

Federal Farm Credit Board; Special Meeting

AGENCY: Farm Credit Administration.

ACTION: Notice of meeting.

SUMMARY: Notice is hereby given, pursuant to the Government in the Sunshine Act (5 U.S.C. 552b(e)(3)), of a special meeting of the Federal Farm Credit Board ("Federal Board").

DATES AND TIMES: The special meeting is scheduled as follows: Sunday, January 20–9:00 a.m. to 5:00 p.m.; Monday, January 21—9:00 a.m. to 12 Noon; and Friday, January 25—8:30 a.m. to 3:00 p.m.

ADDRESS: Federal Farm Credit Board Special Meeting, Marriott Riverwalk Hotel, 711 East Riverwalk, San Antonio, Texas 78205.

FOR FURTHER INFORMATION CONTACT: Kenneth J. Auberger, Secretary to the Federal Farm Credit Board, 1501 Fram Credit Drive, McLean, VA 22102–5090, (703–883–4010).

SUPPLEMENTARY INFORMATION: A special meeting of the Federal Farm Credit Board has been called and will be held to discuss the Office of Examination and Supervision/General Counsel report regarding supervisory, financial, and legal matters related to the Federal Intermediate Credit Bank of Spokane and the Federal Intermediate Credit Bank of Omaha. The Federal Board will also meet with members of the Spokane district board to discuss supervisory matters related to the banks of the Twelfth Farm Credit District. The entire special meeting will be closed to the public. The matters to be considered at the special meeting are:

Sunday, January 20, 1985

*Office of Examination and Supervision/General Counsel-Report Regarding Supervisory, Financial, and Legal Matters related to the Federal Intermediate Credit Banks of Spokane and Omaha.

Monday, January 21, 1985

*Continuation—Office of Examination and Supervision/General Cousel—Report Regarding Supervisory, Financial, and Legal Matters related to the Federal Intermediate Credit Banks of Spokane and Omaha.

Friday, January 25, 1985

*Meeting with members of the Spokane District Board to discuss supervisory matters related to the banks of the Twelfth Farm Credit District.

Dated: January 10, 1985.

Donald E. Wilkinson,

Governor.

[FR Doc. 85–1249 Filed 1–11–85; 2:15 pm]

BILLING CODE 6705–01–M

2

FEDERAL RESERVE SYSTEM

"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT: Notice forwarded to **Federal Register** on January 8, 1985.

PREVIOUSLY ANNOUNCED TIME AND DATE OF THE MEETING: 10:00 a.m., Wednesday, January 16, 1985.

CHANGES IN THE MEETING: Addition of the following open item(s) to the meeting:

1. Proposal by the Federal Home Loan Bank Board to limit direct investments of institutions insured by the Federal Savings and Loan Insurance corporation.

CONTACT PERSON FOR MORE INFORMATION: Mr. Joseph R. Coyne, Assistant to the Board; (202) 452–3204.

Dated: January 11, 1985.

James McAfee,

Associate Secretary of the Board.

[FR Doc. 85–1188 Filed 1–11–85; 10:57 am]

BILLING CODE 6210–01–M

3

INTERNATIONAL TRADE COMMISSION

[USITC SE–85–04]

TIME AND DATE: 2:00 p.m., January 16, 1985.

PLACE: Room 117, 701 E Street, NW., Washington, D.C. 20436.

STATUS: Open to the public.

MATTERS TO BE CONSIDERED:

1. Agenda.
2. Minutes.
3. Ratifications.
4. Petitions and complaints.
(a) Certain frozen beverage dispensing machines (Docket No. 1128).
5. Any items left over from previous agenda.

CONTACT PERSON FOR MORE INFORMATION: Kenneth R. Mason, Secretary, (202) 523–0161.

[FR Doc. 85–1267 Filed 1–11–85; 4:00 pm]

BILLING CODE 7020–02–M

4

INTERNATIONAL TRADE COMMISSION

[USITC SE–85–05]

TIME AND DATE: 10:00 a.m., January 22, 1985

PLACE: Room 117, 701 E Street, NW., Washington, D.C. 20436.

STATUS: Open to the public.

MATTERS TO BE CONSIDERED:

1. Agenda.
2. Minutes.
3. Ratifications.
4. Petitions and complaints.
(a) Certain double-sided floppy disk drives and components thereof (Docket No. 1124).
5. Inv. Nos. 731–TA–169/182 [Final] (Carbon steel products from Argentina, Australia, Finland and Spain)—briefing and vote.
6. Any items left over from previous agenda.

CONTACT PERSON FOR MORE INFORMATION: Kenneth R. Mason, Secretary (202) 523–0161.

[FR Doc. 85–1265 Filed 1–11–85; 3:58 pm]

BILLING CODE 7020–02–M

5

POSTAL SERVICE

Vote to Close Meeting

At its meeting on January 7, 1985, the Board of Governors of the United States Postal Service unanimously voted to close to public observation its meeting scheduled for February 4, 1985, in San Diego, California. The meeting will involve a discussion of personnel matters.

The meeting is expected to be attended by the following persons:

*This session of the meeting will be closed to the public pursuant to the exemptions set forth in 5 U.S.C. 552b(c)(4), (8) and (9)(A).

Governors Babcock, Camp, Griesemer, McKean, Peters, Ryan, Sullivan and Voss; Postmaster General Carlin; Deputy Postmaster General Finch; Secretary to the Board Harris; General Counsel Cox; and Counsel to the Governors Califano.

The Board of Governors has determined that, pursuant to section 552b(c)(6) of Title 5, United States Code, and § 7.3(f) of Title 39, Code of Federal Regulations, the discussion of personnel matters is exempt from the open meeting requirement of the government in the Sunshine Act [5 U.S.C. 552b(b)], because it is likely to disclose information of a personal nature where disclosure would constitute a clearly unwarranted invasion of personal privacy. The Board also determined that the public interest does not require that the Board's discussion of this matter be open to the public.

In accordance with section 552b(f)(1) of Title 5, United States Code, and § 7.6(a) of Title 39, Code of Federal Regulations, the General Counsel of the United States Postal Service has certified that in his opinion the meeting to be closed may properly be closed to public observation, pursuant to section 552b(c)(6) of Title 5 United States Code, and § 7.3(f) of Title 39, Code of Federal Regulations.

David F. Harris,

Secretary.

[FR Doc. 85-1189 Filed 1-11-85; 10:57 am]

BILLING CODE 7710-12-M

federal register

Tuesday
January 15, 1985

Part II

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 334

Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 334

[Docket No. 78N-036L]

Laxative Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) laxative drug products are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal deals only with laxative drug products and is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determinations by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 21, 1975 (40 FR 12902), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC laxative, antidiarrheal, emetic, and antiemetic drug products, together with the recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. Interested persons were invited to submit comments by June 19, 1975. Reply comments in response to comments filed in the initial comment period could be submitted by July 19, 1975.

In a notice published in the **Federal Register** of March 21, 1980 (45 FR 18398), the agency advised that it had reopened the administrative record of OTC laxative drug products to allow for consideration of data and information that had been filed in the Dockets Management Branch after the date the administrative record previously had officially closed. The agency concluded that any new data and information filed prior to March 21, 1980 should be available to the agency in developing a proposed regulation in the form of a tentative final monograph.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. Data and information received after the administrative record was reopened have also been put on display in the Dockets Management Branch.

In response to the advance notice of proposed rulemaking, comments were received from 44 drug manfacturers, 2 trade associations, 3 consumers, 1 State government, and 1 university. Copies of the comments received are also on public display in the Dockets Management Branch.

The advance notice of proposed rulemaking, which was published in the **Federal Register** on March 21, 1975 (40 FR 12902), was designated as a "proposed monograph" in order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10). Similarly, the present document is designated in the OTC drug review regulations as a "tentative final monograph." Its legal status, however, is that of a proposed rule. In this tentative final monograph (proposed rule) to establish Part 334 (21 CFR Part 334), FDA states for the first time its position on the establishment of a monograph for OTC laxative drug products. Final agency action on laxative drug products will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC laxative drug products.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC laxative drug products as modified on the basis of the comments received and the agency's independent evaluation of the Panel's report. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) The Court in *Cutler* held that the OTC drug review regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register**. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e.,

conditions that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the advance notice of proposed rulemaking for OTC laxative drug products (published in the **Federal Register** of March 21, 1975; 40 FR 12902), the agency suggested that the conditions included in the monograph (Category I) be effective 30 days after the date of publication of the final monograph in the **Federal Register** and that the conditions excluded from the monograph (Category II) be eliminated from OTC drug products effective 6 months after the date of publication of the final monograph, regardless of whether further testing was undertaken to justify their future use. Experience has shown that relabeling of products covered by the monograph is necessary in order for manfacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experiences has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and reformulate their products and have them in compliance in the marketplace. However, if the agency determines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notice published in the **Federal Register** of February 8, 1973 (38 FR 3614) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

The Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic and Antiemetic Drug Products recommended that dioctyl calcium sulfosuccinate, dioctyl potassium sulfosuccinate, and dioctyl sodium sulfosuccinate (docusate salts) be classified in Category I as stool softener laxatives at adult oral dosages of 50 to 360 mg within a 24 hour period (see 40 FR 12912). However, after the Panel's report had been submitted, FDA became aware of information in animal studies raising questions about the Panel's conclusions and recommendations for these laxative ingredients (Ref. 1).

The time necessary to complete a full review and evaluation of these new studies could result in a considerable delay in the publication of the tentative final monograph for OTC laxative drug products. Accordingly, the agency has decided to remove all discussion of the safety and effectiveness of docusate salts from this document. The agency intends to publish a separate document in the **Federal Register** addressing the status of these ingredients.

Reference

(1) Teratology studies submitted to NDA 10-586.

I. The Agency's Tentative Conclusions on the Comments

A. General Comments

1. Two comments contended that FDA does not have the authority to establish substantive rules.

The agency responded to these comments in paragraph 4 of the preamble to the tentative final order for emetic active ingredients which was published in the **Federal Register** of September 5, 1978 (43 FR 39544) and reaffirms that response.

2. Several comments urged a greater role for pharmacists in the sale of OTC drug products. One comment recommended that OTC drug products be available only through pharmacies, and two suggested that any labeling suggesting consultation with a physician should mention a pharmacist as an alternative.

The agency responded to these comments in paragraph 5 of the preamble to the tentative final order for antiemetic active ingredients which was published in the **Federal Register** of July 13, 1979 (44 FR 41065) and reaffirms that response.

3. One comment stated that the Panel recommendations violate the objectives and philosophy of the OTC drug review in that the Panel appeared to be intent on undermining the concept of self-medication with OTC laxatives and that it failed to discharge its obligations by placing a number of long established laxative ingredients and laxative combinations in Category III.

The comment provided no basis for its statements. The Panel's recommendations for OTC laxative drug products are fully in accord with the objectives of the OTC drug review as stated in the applicable regulations (21 CFR Part 330). By placing laxative ingredients or combinations in Category III, the Panel simply concluded that the available data were insufficient to permit final classification at the time the Panel reviewed these drugs.

4. One comment objected to the Panel's recommendation that the quantity of each active ingredient be stated in OTC drug product labeling, on the basis that section 502(e)(1)(A) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(e)(1)(A)) provides for quantitative ingredient labeling only for prescription drug products.

FDA responded to this objection in paragraph 1 of the preamble to the tentative final order for emetic active ingredients (43 FR 39544) and reaffirms that conclusion.

5. Several comments objected to the Panel's recommendation that all inactive ingredients be listed on the labeling, arguing that such a listing would be meaningless, confusing, and misleading to most consumers.

The agency responded to these comments in paragraph 2 of the

preamble to the tentative final order for emetic active ingredients (43 FR 39544) and reaffirms that response.

6. One comment noted that on several pages of the Panel's recommended monograph the abbreviation "gm" is used for gram, yet 21 CFR 201.62(l) (formerly 21 CFR 1.102(d)) states that the only abbreviation that may be used for gram is "g".

The situation outlined in the comment was an editorial oversight. The OTC drug labeling regulations cited in the comment permit the use of "g" as the only abbreviation for gram. For clarity, metric units have been fully written out in this tentative final monograph.

B. General Comments on Laxatives

7. One comment noted that the product, Nature's Remedy Candy Coated, had been omitted from the "Data and Information Submissions" section of the Panel's report (40 FR 12903) and requested that this omission be corrected.

As noted by the comment the product was inadvertently omitted from the list of submitted products, but the product was considered by the Panel in reaching its conclusions on OTC laxative drug products.

8. A comment stated that the Panel report was generally "antilaxative" in attitude.

It was the intent of the Panel to set forth reasonable standards for the use of OTC laxatives. The Panel believed that many peopld have misconceptions about normal bowel function, particularly a fear of dire consequences if the bowel is not evacuated daily. The Panel believed that this fear is unfounded and leads to certain amount of unnecessary use of laxatives.

9. Comments stated that the Panel was confused on the role of OTC laxative medicines. The comments noted that it was the Panel's opinion that simple constipation could be corrected by a proper diet, and that there are few vaild indications for the use of laxatives. The comments stated that the Panel confused the prevention and medical treatment of constipation with its symptomatic relief. Contending that a consumer considering the use of an OTC laxative is suffering from constipation and is seeking relief through self-medication, the comments stated that it is not responsive to tell the consumer how the condition might have been prevented by eating proper foods or drinking more fluids. The consumer simply wants a laxative that will relieve the existing discomfort safely and effectively. The comments concluded that this overview of constipation was inappropriate.

One of the purposes of the Panel's general discussion was to present a broad view of the problem of constipation. The Panel recognized that prevention of a medical condition or disease is preferable to symptomatic relief, and the discussion of diet, adequate fluid intake, and exercise provides guidance to consumers on how to avoid or reduce constipation. The Panel believed, and the agency agrees, that the public ought to understand that the use of all laxatives should be minimized.

10. Comments stated that the Panel went beyond its charter in making statements concerning the advertising of laxative products, and that such statements regarding OTC laxative advertising were not only based upon inadequate information, but also were highly inappropriate for inclusion in a scientific report.

The OTC drug review procedures do not preclude a panel from expressing its concern about OTC drug advertising. The Federal Trade Commission (FTC) has the primary responsibility for regulating OTC drug advertising. FDA does, however, have the authority to regulate OTC drug advertising that constitutes labeling under the Federal Food, Drug, and Cosmetic Act. Under the act, a manufacturer can be prohibited from advertising a drug to treat a condition for which there are no adequate directions for use on the label. See, e.g., *United States* v. *Article of Drug . . . B-Complex Cholinos Capsules*, 362 F. 2d 923 (3d Cir. 1966); *V.E. Irons, Inc.* v. *United States*, 244 F. 2d 34 (10th Cir.), *cert. denied*, 354 U.S. 923 (1957). In addition, for an OTC drug to be generally recognized as safe and effective and not misbranded, the advertising for the drug must satisfy the FDA regulations at § 330.1(d) (21 CFR 330.1(d)), which state that the advertising may prescribe, recommend, or suggest the drug's use only under the conditions stated in the labeling.

11. Several comments objected to the Panel's statement that "the Panel found no evidence for claims that any laxative has a particular advantage for individuals simply on the basis of sex, age, or other demographic characteristics." (See 40 FR 12905.) The comments suggested that this sentence should not be interpreted as precluding a manufacturer's directing a promotional effort toward a particular demographic group of potential users, and that if a product has characteristics that may be preferred by a significant portion of a demographic group, then truthful statements to that effect should be allowed.

The agency agrees with the Panel. No evidence has been presented to justify labeling claims that any laxative has a particular advantage for individuals simply on the basis of sex, age, or other demographic characteristics. Nor is the agency aware of any characteristics of laxative products, e.g., form, taste, convenience, relative mildness, that may be preferred more by a significant portion of one demographic group than another. Such characteristics should be applicable regardless of the user of the product. However, the agency has no objection to manufacturers directing a promotional effort toward a particular demographic group of potential users as long as there is no claim of a particular advantage based on demographic characteristics.

12. A comment suggested that the monograph set specific dosages rather than express dosage requirements in terms of daily dose limits or ranges. The Comment further contended that the number of dosage units that could be used to deliver the required amount of ingredient did not have to be stated in the monograph. The comment cited as an example an ingredient whose daily dosage limit is 100 milligrams (mg) and stated that a recommended dosage of two 50-mg capsules once a day could be in compliance with the monograph, but that this specific dosage direction need not be in the monograph.

Some of the Panel's recommended dosages require clarification. For example, where the Panel recommended a daily dose of an ingredient without a dosage interval, the agency has clarified this to mean a single daily dose.

The monograph will not specify the number or type of dosage units, i.e., one or more tablets, capsules, teaspoons, needed to deliver the required amount of an active ingredient. Manufacturers will generally be free to choose whether a product should deliver the necessary amount of ingredient(s) in one or more dosage units.

13. Comments stated that the Panel's recommended labeling requirements when added to the general labeling requirements for OTC drugs, will result in a crowded and potentially confusing label that could defeat its intended purpose of informing the layman. Some of the comments stated that it would be very difficult to include all of the required information on the labeling of small size packages. One comment urged the Commissioner to carefully consider the need for each recommended statement with a view to eliminating or modifying the unessential statements.

The labeling of an OTC drug must contain information essential for the safe and effective use of the drug by the consumer. Labeling should not be needlessly crowded or confusing and, therefore, the agency has consolidated or deleted the Panel's recommended labeling wherever possible. The agency believes that any additional labeling statements proposed for laxative products will not be so numerous as to confuse the consumer. In addition, manufacturers are free to design ways of incorporating all required information on the package labeling, e.g., by using flap labels or redesigning packages.

14. One comment objected to the Panel's recommended indication for laxatives in proposed § 334.50(a)(1) "for the short-term relief of constipation". The comment argued that the phrase "short-term" duplicates the information provided in proposed § 334.50(c)(3), which warns against using OTC laxatives for longer than 1 week. The comment also argued that "short-term" refers to the period of laxative use and not to the degree of effectiveness of the laxative. Concluding that it was inaccurate and unnecessary to identify laxative products for "short-term relief," the comment recommended deleting "short-term" from the indication.

The agency agrees that "short-term" should refer to the period of laxative use and not to the degree of effectiveness. The agency also agrees that the 1-week use limitation warning adequately defines the period of time an OTC laxative may be used. The Panel utilized the phrase "short-term" in an attempt to qualify the indication for OTC laxatives, which are intended for the relief of occasional constipation and not in treating chronic constipation. Chronic constipation may be a sign of a serious condition that requires diagnosis and treatment by a doctor. Therefore, the indication in the tentative final monograph does not include the phrase "short-term," and the indication is revised to state "For the relief of occasional constipation."

15. comments objected to the Panel's view that the labeling claims "irregularity" and "regularity" are misleading. The Comments contended that these terms are readily understood by the consumer, that they serve a substitute for the socially unacceptable term "constipation," and that there is neither a practical nor a legal basis for banning their use.

The agency agrees with the comment that the term "irregularity" should be included in the monograph. The term has been widely used in the labeling and advertising of laxative drug products and is a term consumers readily understand. In addition, according to Webster's New Collegiate Dictionary (Ref 1) "irregularity " is synonymous with the term "constipation." Therefore, the agency has no objection to its use and is proposing its use in the tentative final monograph. However, the agency agrees with the Panel that the term "regularity" is inappropriate for use in the labeling of OTC laxative drug products. "Regular" is defined as recurring or functioning at fixed or uniform intervals (Ref. 1). When used in the context of bowel habits, the term "regularity" implies that laxatives are necessary to maintain an acceptable frequency of bowel movements. Because there is a normal range of frequency from three bowel movements a day to three per week (Ref. 2), "regular" bowel movements are not essential to health or well-being. Therefore, the agency agrees with the Panel that the term "regularity" is Category II.

References

(1) "Webster's New Collegiate Dictionary," G. & C. Merriam Co., Springfield, MA 1979, s.v. irregularity and regular.

(2) Connell, A.M., et al., "Variation of Bowel Habit in Two Population Samples," *British Medical Journal*, 2:1095–1099, 1965.

16. A comment took issue with the following statements in the Panel's report: "The Panel has no objection to statements regarding the source of the laxative ingredient. However, the suggestion that a laxative is somehow 'natural' because of its source is misleading, because it implies that the product or ingredient is a 'natural way' to induce laxation. It is not considered 'natural' to take any laxative." The comment argued that manufacturers should have the right to make truthful statements about the source of their products, i.e., that an ingredient is from a natural source if that is the case. The comment stated that the determination whether such a statement is misleading must be made within the total context of its use. Another comment stated that bran-rich cereals are natural laxatives, and their consumption is a natural way to provide the bulk in the diet that is necessary for normal laxation.

The agency agrees that a manufacturer should be allowed to make truthful statements in its labeling about the source of a laxative ingredient contained in the product. If an ingredient is in fact from a natural source, then there is no reason why such information may not appear in the labeling of the product so long as this information is not presented in such a way as to imply that it confers any advantage to the product in terms of safety or effectiveness or in any way encourages frequent or prolonged use of laxatives. The agency agrees with the comment that a determination as to whether such a statement is misleading must be made within the context of its use. It is the responsibility of the manufacturer to use information regarding the source of a product ingredient in a way that is not misleading.

17. Stating that many laxative products are prepared from unsterilized natural sources or contain ingredients that readily support microbiological growth, a comment urged that appropriate safety tests for contaminants like salmonella and staphylococcus be required for laxative drug products composed in whole or in part of natural ingredients.

The agency agrees with the comment; all drug products should be free from microbiological contamination. Manufacturing guidelines for preventing microbiological contamination are covered by the Current Good Manufacturing Practice Regulations (CGMPR) (21 CFR Part 211), and all OTC drug products are required to be manufactured in compliance with these regulations. The specific provisions of these regulations concerning the prevention of microbiological contamination are contained in 21 CFR 211.84(d)(6) and 211.113.

18. A comment stated that any regulation that purports to ban truthful and clearly understood alternative language in consumer labeling is arbitrary and capricious, and that such limitation is not authorized by the enabling statutes. The comment also urged that statements describing product attributes should not be regulated by OTC drug monographs.

During the course of the OTC drug review, the agency has maintained that the terms that may be used in an OTC drug product's labeling are limited to those terms included in a final OTC drug monograph. (This pol'cy has become known as the "exclusivity rule.") The agency's position has been that it is necessary to limit the acceptable labeling language to that developed and approved through the OTC drug review process in order to ensure the proper and safe use of OTC drugs. The agency has never contended, however, that any list of terms developed during the course of the review exhausts all the possibilities of terms that appropriately can be used in OTC drug labeling. Suggestions for additional terms or for other labeling changes may be submitted as comments to proposed or tentative final monographs within the specified time periods or through

petitions to amend monographs under § 330.10(a)(12). For example, the labeling proposed in this tentative final monograph has been expanded and revised in response to comments received.

During the course of the review, FDA's position on the "exclusivity rule" has been questioned many times in comments and objections filed in response to particular proceedings and in correspondence with the agency. The agency has also been asked by The Proprietary Association to reconsider its position. In a notice published in the **Federal Register** of July 2, 1982 (47 FR 29002), FDA announced that a hearing would be held to assist the agency in resolving this issue. On September 29, 1982, FDA conducted an open public forum at which interested parties presented their views. The forum was a legislative type administrative hearing under 21 CFR Part 15 that was held in response to a request for a hearing on the tentative final monographs for nighttime sleep-aids and stimulants (published in the **Federal Register** of June 13, 1978; 43 FR 25544). The agency's decision on this matter will be announced in the **Federal Register** following conclusion of its review of the material presented at the hearing.

Claims concerning nontherapeutic characteristics of drugs ("tastes good") or those unrelated to the characteristics of the drug itself ("4 out of 5 doctors recommend") are not dealt with in OTC drug monographs. Labeling claims of this type are, however, subject to regulatory actions initiated under the drug misbranding provisions of section 502 of the act (21 U.S.C. 352).

19. A comment suggested that recommended § 334.50(a)(1) be revised to read, "The labeling shall identify the product as a laxative (or other term of similar import)," and suggested "constipation remedy" or "for relief of constipation" as commonly understood and truthful alternatives that should be permitted.

The OTC drug review program establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. Two principal conditions examined during the review are allowable ingredients and allowable labeling. FDA has determined that it is not practical—in terms of time, resources, and other considerations—to set standards for all labeling found in OTC drug products. Accordingly, OTC drug monographs regulate only labeling related in a significant way to the safe and effective use of covered products by lay persons. OTC drug monographs establish allowable labeling for the following items: product statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action.

The term "remedy" has been used for many years to describe various OTC drug products. The agency believes this term is unrelated to the characteristics of the drug in question and, therefore, does not relate in a significant way to the drug's safe and effective use. Accordingly, the term is outside the scope of the OTC drug review. Such statements or terms will be evaluated by the agency on a product-by-product basis, under the provision of section 502 of the act (21 U.S.C. 352) relating to labeling that is false or misleading.

Moreover, any statement or term that is outside the scope of the monograph, even though it is truthful and not misleading, may not appear in any portion of the labeling required by the monograph and may not detract from such required information. However, statements and terms outside the scope of the monograph may be included elsewhere in the labeling, provided they are not false or misleading.

The phrase "for relief of constipation" is more appropriately an indication and the agency is proposing the indication "for relief of occasional constipation" in the indications section of this tentative final monograph. (See comment 14 above.)

20. A comment suggested that the Panel's definition of laxative, i.e., "any agent used for the relief of constipation," was too broad and could be misunderstood, especially when applied to stool softener and lubricant laxatives. According to the comment, the term "laxative aid" should apply to substances that act solely to modify the fecal contents and thereby aid or facilitate a laxative response; while the term "laxative" should apply only to agents that act upon the myoneural structures of the intestinal tract. The comment concluded that the terms "laxative" and "laxative aid" would more precisely set forth the pharmacologic activity of these different drugs.

The Panel's definition of laxative as "any agent used for the relief of constipation" includes all of the various mechanisms of action of OTC laxatives. The intended effect of these products is always laxation, even though this effect is achieved by different actions. Subdividing laxative ingredients into laxative and laxative aids would not be helpful and could be confusing to the consumer. The statements of identify, e.g. "bulk-forming," "stool-softener," etc. which will appear on the product's labeling, will adequately inform the consumer as to the product's characteristics. Therefore, a change to the definition of laxative is unnecessary.

21. A comment stated that it was not clear whether the labeling information in the professional labeling section (recommended § 334.80) is meant to supplement the labeling required for the OTC labeling of laxative products or is meant to be the only information required for health professionals. The comment argued that many warnings in recommended §§ 334.50 through 334.64 are unnecessary for health professionals, that recommended § 334.80 should specify that only the information contained in the professional labeling section need be provided to health professionals, and that information such as mode of action and definitions should be omitted from professional labeling, because health professionals should understand this information.

A similar issue was discussed in comment 56 of the preamble to the Antacid Tentative Final Monograph, published in the **Federal Register** of November 12, 1973 (38 FR 31264). There, the agency stated that the warning statements appearing on OTC products should be included in professional labeling. The health professional needs this information in order to best advise the consumer as to the safe and effective use of laxative drug products. Thus, the agency tentatively concludes that labeling intended for health professionals must include all labeling required for OTC products as well as the specialized professional labeling. The monograph has been amended accordingly.

22. A comment objected to the Panel's terms for classifying the mechanism of action of laxatives, stating that these terms are obsolete, confusing, and inaccurate. The comment argued that because most laxatives attract water into the stool, a laxative should be defined as any substance that increases water in the stool. The comment further argued that a separate classification is not needed for hyperosmotic, saline, or stool softener laxatives, and that stimulant laxatives do not stimulate anything, but act as the other laxatives. The comment suggested replacing the terms "stimulant," "saline," "hyperosmotic," and "stool softener," which were recommended by the Panel for classifying certain laxatives, with one of the following terms: "hydrophoric" (to carry water), "sodium-water retention," or "sodium-retention laxative." The comment stated

that these terms more accurately describe the mechanism of action of a large group of laxatives, which, amounts to preventing sodium and water absorption from the small and large intestines. The comment added that this group of laxatives could be subclassified into plant, synthetic, or inorganic chemical groups.

The comment offered no data to support a classification of laxatives based on a particular mechanism of action. Moreover, the Panel stated that the precise mechanisms of action of laxatives are unknown. With the exception of the term hyperosmotic, the Panel's recommended terms for classifying laxatives described the general ways in which these laxatives work and are understandable to most consumers. The word "hyperosmotic," which is applicable to only two rectal laxatives (glycerin and sorbitol), is probably not well understood by consumers. Consumers are more familiar with the dosage forms of these ingredients (enema and suppository) and the action that can be expected from these products. Because the word "hyperosmotic" is not needed and might be confusing, it will not be required on the labeling of these dosage forms. It will, however, be retained in the monograph for classification purposes only. The terms proposed by the comment do not appear to be more accurate than those recommended by the Panel, and a subclassification of laxative substances into plant, synthetic, and inorganic chemcial groups would not provide consumers with any useful information. Therefore, a reclassification of laxatives using different mechanism-of-action terminology does not appear to be warranted and will not be proposed at this time.

23. Numerous comments disagreed with recommended § 334.50(a)(1), which requires the labeling of laxatives to contain a statement identifying laxatives based on the action they have in the bowel, e.g., "stimulant laxative," "bulk-forming laxative," etc. The comments argued that identifying laxatives by their specific action is meaningless, confusing, and misleading to consumers, and "does not provide any useful information." Two of the comments also contended that requiring these identity statements in the labeling would violate the regulatory requirement that the identity statement be "in terms that are meaningful to the layman" and that requiring them was beyond FDA's statutory authority. One of the comments further added that it was not clear whether recommended § 334.50(a)(1) required only the identity statement, e.g., "stimulant laxative," "bulk-forming laxative," etc. to appear on the labeling or whether the definitions of the identity statements, contained in § 334.3, were also required on the labeling. Most of the comments recommended deleting the proposed identity statements; others recommended that laxatives be identified simply as substances or agents that increase the bulk or water content of the stool.

The agency does not agree that the identity statements for laxatives should be deleted from the monograph. Laxatives relieve constipation by various actions, depending on how a specific ingredient works in the bowel. The identity statements, such as "stimulant laxative," "bulk-forming laxative," etc., proposed in § 334.3, describe in nontechnical terms the effect a particular laxative product will have in the bowel or on the stool. Such information is necessary to provide consumers with adequate directions for using OTC laxative products safely and effectively, and is, therefore, within FDA's misbranding authority under section 502(f)(1) of the act (21 U.S.C. 352(f)(1)).

There appears to be no basis for including the definitions for each identity statement in the labeling, as originally recommended in the advance notice of proposed rulemaking in § 334.50(a)(1). The definitions will not increase consumers' understanding of a laxative's activity nor provide information that will increase the safety or effectiveness of OTC laxatives. Rather they may complicate and confuse laxative labeling. Therefore, any reference to definitions has been deleted from § 334.50(a)(1).

The agency has also determined that in addition to needing to know how a laxative acts, consumers should be aware of how soon a laxative is expected to work. Each type of laxative will generally work within a certain time (Refs. 1 and 2). For example, bulk-forming laxatives generally act within 12 to 72 hours; lubricant laxatives generally act within 6 to 8 hours. This information would increase a consumer's ability to properly select and use a particular laxative product. This information will also increase the safety of laxative products because consumers will be more likely to discontinue using a particular product and seek professional assistance if it does not act within a labeled time frame rather than increasing the specified dosage beyond safe and effective OTC levels.

Therefore, the agency is proposing in the laxative tentative final monograph, under the heading "Indications," the following time frames within which the different types of laxatives are expected to produce bowel movement:

Bulk laxatives—12 to 72 hours
Hyperosmotic laxatives—¼ to 1 hour
Lubricant laxatives:
  Oral dosage forms—6 to 8 hours
  Rectal dosage forms—2 to 15 minutes
Saline laxatives:
  Oral dosage forms—½ to 6 hours
  Rectal dosage forms—2 to 15 minutes
Stimulant laxatives:
  Oral dosage forms—6 to 12 hours
  Rectal dosage forms—¼ to 1 hour
Stool softener laxatives:
  Oral dosage forms—12 to 72 hours
  Rectal dosage forms—2 to 15 minutes
Carbon dioxide-releasing suppositories—5 to 30 minutes

References

(1) Darlington, R. C., "Laxative Products," *in* "Handbook of Nonprescription Drugs," American Pharmaceutical Association, 5th Ed., Washington, pp. 40–41, 1977.

(2) Barowsky, H., "A Rectal Suppository for Inducing Lower Bowel Evacuation," *American Journal of Gastroenterology*, 39:183–186, 1963.

24. A comment stated that grouping pharmacologically diverse and clinically contrasting laxatives into single categories has unfairly attributed the undesirable features of one ingredient to all the other ingredients in the group. The comment argued that pharmacologic grouping becomes arbitrary when label warnings, cautions, and limits of safe treatment are imposed for all ingredients of the group rather than on specific ingredients within the group.

In the tentative final monograph general warnings applicable to all laxative ingredients are supplemented by specific warnings for individual ingredients, thereby minimizing the possibility of unfair attribution as suggested in the comment. For example, stimulant laxatives must include all the applicable general warnings for laxatives; but bisacodyl, castor oil, and phenolphthalein (individual stimulant laxatives) must be labeled with additional specific warnings.

25. Several comments contended that the Panel's recommended 1-week use limitation warning (§ 334.50(c)(3)) is irrational, arbitrary, and unwarranted. The comments argued that the panel did not provide evidence that laxatives are harmful if taken for longer than 1 week. The comments also pointed out that the Panel recognized that laxative therapy may be necessary for longer than 1 week in some elderly persons and in persons on low fiber diets. Some of the comments recommended that the 1-

week limitation be changed to a "prolonged use" limitation. Others simply recommended deleting it.

The agency considers the recommended 1-week limitation on the use of laxatives to be a necessary warning for the safe use of these products. The comments provided no data to indicate that any other time restriction would be more appropriate. The suggestion to replace the proposed limitation with a "prolonged use" limitation is unacceptable. "A prolonged use" limitation would be defined differently by different people; some might interpret it to mean 1 week, others as continuous use over a year or longer. Constipation lasting longer than 1 week could signify a more serious condition, such as deverticular disease of the colon, irritable bowel, or cancer of the colon. In such cases it is essential that the person see a doctor at the earliest possible time so that the condition can be diagnosed and correctly treated. However, in some situations the long-term use of laxatives may be necessary, e.g., in some elderly persons suffering from certain disease conditions and in persons with heart ailments or other conditions where straining should be avoided. In these cases, laxative therapy should be carried out under the care and direction of a doctor so that regular therapy can be prescribed and the person's condition monitored regularly. Therefore, the agency proposes to retain the 1-week use limitation warning.

26. One comment suggested that the definition of "short-term use" (i.e., "use of a laxative for no longer than a 1-week period") in recommended § 334.3(k) should be revised by adding the word "daily" after the word "laxative" to define more explicitly "short-term use."

The definition of "short-term use" in § 334.3(k) as originally recommended has been deleted in this tentative final monograph. The use limitation warning (proposed § 334./50(b)(3) of the monograph) adequately explains the period of "short-term use;" therefore a definition of "short-term use" has not been included in the monograph.

27. Several comments stated that the signal word "warning" is too strong for the types of cautionary statements required for laxative products and suggested that the term "caution" be used instead. The comments argued that the word "warning" should be used only to highlight imminent physical hazards associated with normal storage or use of such consumer products as household cleaners, polishes, insecticides, and packaging forms such as aerosols. The comments suggested that the signal word " caution" in recommended §§ 334.50, 334.52, 334.54, 334.56, 334.60, 334.62, and 334.64.

Section 502(f)(2) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352 (f)(2)), states, in part, that any drug marketed OTC must bear in labeling ". . . such adequate warnings . . . as are necessary for the protection of users." Section 330.10(a)(4(v) of the OTC drug regulations provides that labeling of OTC drug products should include warnings against unsafe use, side effects, and adverse reactions. . . ."

The agency notes that historically there has not been a consistent usage of the signal words "warning" and "caution" in OTC drug labeling. For example, in §§ 396.20 and 396.21 (21 CFR 369.20 and 369.21), which list "warning" and "caution" statements for drugs, the signal words "warning" and "caution" are both used. In some instances, either of these signal words is used to convey the same or similar precautionary information.

FDA has considered which of these signal words would be most likely to attract consumers' attention to that information describing conditions under which the drug product should not be used or its use should be discontinued. The agency concludes that the signal word "warning" is more likely to flag potential dangers so that consumers will read the information being conveyed. Therefore, FDA has determined that the signal word "warning," rather than the word "caution," will be used routinely in OTC drug labeling that is intended to alert consumers to potential safety problems.

28. A comment suggested that the phrase "this product" in two of the warnings recommended by the Panel in § 334.50(c) (1) and (3) should be replaced by "laxatives" or "laxative products" to avoid creating the implication that these warning statements are applicable only to particular product. The comment noted that these warnings applied equally to all laxative products.

The agency agrees with the comment that these warnings apply to all laxative products. Accordingly, "laxative products" has been used instead of "this product" in proposed § 334.50(b) (1) and (3) of the monograph.

29. A comment recommended that the warning statements in recommended § 334.50(c) (2) and (3), "If you have noticed a sudden change in bowel habits that persists over a period of 2 weeks, consult a physician before using a laxative," and "This product should not be used for a period of longer than 1 week except under the advice and supervision of a physician," should be combined and reworded for clarity and brevity as follows: "A laxative should not be used longer than 1 week, except upon the advice of a physician. If a sudden change in bowel habits persists longer tha 14 days, a physician should be consulted."

The agency disagrees that these specific warnings should be combined. Two important and distinct issues are identified in these warnings, and each one should be treated separately. Patients who have noticed a change in bowel habits that has persisted for at least 2 weeks are instructed not to use a laxative at all without first consulting a physician. Patients who have temporary constipation are warned not to use the product for more than 1 week. If at the end of that time their bowel function has not returned to normal, they are instructed to consult a physician.

30. A comment suggested that the warning recommended by the Panel in § 334.50(c) (2), "If you have noticed a sudden change in bowel habits that persists over a period of 2 weeks, consult a physician before using a laxative," be changed to allow 1 month for change in bowel habits. The comment argued that 2 weeks is the normal duration of "ordinary intestinal upset," and the warning with an interval of only 2 weeks would cause unnecessary apprehension among many consumers.

The agency disagrees that the 2-week period in this warning should be changed to 1 month. Changes in regular bowel habits that persist for 2 weeks may be a sign of a serious underlying medical illness that requires diagnosis and care by a doctor. The comment provided no data demonstrating that "ordinary intestinal upset" usually lasts 2 weeks or any medical justification for extending the 2-week period to 1 month.

31. A comment suggested that croton seed oil and the kukula nut of Hawaii could be investigated for their laxative effect.

This suggestion is outside the scope of the OTC drug review process, which is intended to determine those ingredients that are generally recognized as safe and effective for OTC use. The comment included no data to substantiate the safe and effective use of these ingredients as OTC laxatives nor is the agency aware of such data. Investigation of new laxative agents is the responsibility of the drug industry, not FDA.

C. Comments on Bulk-Forming Laxatives

32. One comment objected to the Panel's definition of a bulk-forming laxative because the comment was not aware of bulk-forming laxatives

increasing bulk volume and water either more or less than other laxatives.

The Panel defined a bulk-forming laxative in recommended § 334.3(c) as an agent that promotes the evacuation of the bowel by increasing bulk volume and water content of the stools. In defining other types of laxatives, e.g., saline and hyperosmotic, the Panel did not attempt to quantify the amount of water increased in the stool, but only attempted to describe the action that occurs. The agency believes that the Panel's definition of a bulk-forming laxative is accurate.

33. A comment criticized as biased and scientifically unfounded the Panel's opinion that bulk-forming laxatives are among the safest of laxatives. The comment argued that the unsoundness and inconsistency of the Panel's position are illustrated by the Panel's own statement that "conclusive studies testing this hypothesis have not yet appeared". (See 40 FR 12907.)

The Panel, because of its scientific training and experience, had ample expertise on which to base an opinion that bulk-forming laxatives are among the safest of laxatives. The Panel's reasons for this opinion are that bulk-forming laxatives are not generally absorbed from the digestive tract, and that they increase the frequency of bowel movements and soften stools by holding water in the stool. The Panel cited bran as a good bulk-forming laxative, when accompanied with adequate fluid intake. The comment offered no evidence to support its statement that the Panel's opinion is scientifically unfounded, nor is the agency aware of any scientific data inconsistent with the Panel's statement. The Panel's statement that "conclusive studies testing this hypothesis have not yet appeared" was taken out of context by the comment. This statement is part of the Panel's comments on relationships between intraluminal pressure (p), tension of the bowel wall (t), and the radius of the bowel lumen (r), referred to as the Law of LaPlace. It was this relationship ($P=t/r$) about which the Panel stated that conclusive studies testing this hypothesis have not yet appeared.

34. Numerous comments stated that considering the safety of bulk-forming laxatives and their proven and potential benefits for various indications, there is no rational basis for restricting their unsupervised use to 1 week as recommended by the Panel in § 334.50(c)(3) or for characterizing them as appropriate only for short-term use as recommended in § 334.50(a)(1). The comments noted that these labeling requirements as applied to bulk-forming laxatives were not supported by a recommendation in the Panel's report. The comments also indicated that dietary bran and other bulk laxatives are essentially food derivatives that replace fiber in many diets, and as such are necessarily fit for longer use. Therefore, the comments concluded that bulk-forming laxatives should be exempt from the labeling in recommended § 344.50 (a)(1) and (c)(3).

Some of the ingredients in bulk-forming laxative drug products, especially those that are present at comparable levels in foods, may be ingested for periods of longer than 1 week without risk of untoward health effects. However, the agency believes that a decision that any laxative product should be used for longer than 1 week should be made by a doctor.

As discussed in comment 25 above, constipation lasting for longer than 1 week could be a sign of a more serious condition for which proper diagnosis and treatment may be warranted. Therefore, the 1-week use limitation warning will be retained for bulk-forming laxatives as well as all other OTC laxative drug products. The agency wishes to emphasize however, that this limitation is applicable only to laxative drug products and in no way applies to or is intended to reflect on the safety of any high fiber foods or food supplements such as bran or bran cereal.

35. Several comments pointed out that when the agency revoked the general warning requirement for OTC drugs in 21 CFR 330(i), i.e., "Warning: Do not take this product concurrently with a prescription drug except on the advice of a physician" (40 FR 11717), it stated that a general warning often goes unheeded and that a specific statement for a drug or class of drugs will be more effective. The comments stated that the Panel's suggested warning in § 334.52(b) for bulk laxatives derived from cellulose is virtually identical to this general warning and therefore is inappropriate. One comment asked that the reference to prescription drugs in this warning be replaced with the specific drugs that have been noted to react with bulk laxative ingredients. These drugs are digitalis, nitrofurantoins and salicylates. Two comments pointed out that the Panel stated that the clinical significance of the interaction between cellulose derivatives and these three drugs has not been established. Therefore, the warning should be deleted. In any case, the comments further suggested that when a specific drug interaction precaution is justified, it should be worded in such a manner as to allow a physician to override the warning.

The agency agrees that a specific warning statement is preferable to a general statement when a clinically significant adverse effect can be attributed to a specific drug. However, as the Panel stated in its report (40 FR 12907), the clinical significance of the interaction between digitalis, nitrofurantoins, and salicylates has not been determined. After evaluating several references concerning the reported interaction between these three drugs and cellulose derivatives, the agency tentatively concludes that these data do not warrant requiring a warning on the OTC labeling of cellulose derivative bulk laxatives (Refs. 1, 2, and 3). Johnson et al. (Ref. 1) and Kasper et al. (Ref. 2) report that the mean peak plasma concentration of digoxin taken following a dietary fiber, such as cellulose, does not vary significantly compared with digoxin when it is taken alone. The time for digoxin to reach its mean peak plasma concentration is longer when digoxin is taken following the ingestion of a dietary fiber. However, the clinical effects of the drug are not substantially altered. Seager (Ref. 3) suggests a similar occurrence with nitrofurantoins. Because the interaction between cellulose derivatives and other drugs does not appear to be clinically significant, the warning has not been included in this tentative final monograph.

References

(1) Johnson, B.F., et al., "Effects of a Standard Breakfast on Digoxin Absorption in Normal Subjects", *Clinical Pharmacology and Therapeutics*, 23(3):315–319, 1978.

(2) Kasper, H., et al., "The Effects of Dietary Fiber on Postprandial Serum Digoxin Concentration in Man," *The American Journal of Clinical Nutrition*, 32:2436–2438, 1979.

(3) Seager, H., "The Effects of Methylcellulose on the Absorption of Nitrofurantoin from the Gastrointestinal Tract," *Journal of Pharmacy and Pharmacology*, 20:968–969, 1968.

36. Several comments stated that the phrase "accompanied by adequate liquid intake" should be deleted wherever it appears in recommended § 334.10 for bulk-forming laxatives, and be replaced with a specification of what "adequate" liquid intake is, namely, "the ingestion of a full glass (8 ounces (oz)) of liquid with each dose." In conjunction, the comments requested that the warnings in recommended § 334.52(a)(1) "Drink a full glass (8 oz) of liquid with dose," and in recommended § 334.52(a)(2), for products containing karaya (sterculia gum), "Drink a full

glass (8 oz) of liquid immediately with each dose.", be deleted because these warnings essentially duplicate the labeling in recommended § 334.10. The comments also stated that a direction to drink liquid with each dose is properly part of the directions for use, and is not properly a caution.

The agency agrees with the comments. The phrase "accompanied by adequate liquid intake" in the directions for bulk-forming laxatives is revised to read "Drink a full glass (8 oz) of liquid with each dose." Because the phrase "adequate liquid intake" no longer appears in the labeling, the definition of adequate liquid intake in recommended § 334.3(a) is unnecessary and is not included in this tentative final monograph. The warnings for bulk-forming laxatives in recommended § 334.52(a) (1) and (2) that advised drinking a full glass of liquid with each dose repeat the labeling in § 334.10, and therefore are not included in this tentative final monograph.

37. One comment questioned the scientific basis for requiring in the labeling of certain laxatives that a full glass (8 oz) of water be taken with each dose. The comment contended that the requirement was unnecessary because the volume of fluid exchanged across the intestinal mucosa far exceeds any oral fluid ingestion.

The recommendation in the Panel's report for adequate fluid intake applies only to bulk-forming laxatives. It does not restrict the fluid to water, but calls for the ingestion of a full glass (8 oz) of liquid with each dose (40 FR 12096). The recommendation is part of the labeling that the Panel concluded was necessary for the proper use of bulk-forming laxatives because esophageal obstruction has occurred when bulk-forming laxatives have been swallowed dry, and the possibility exists that fecal impaction or intestinal obstructon may occur if adequate fluid intake is not assured. No data were submitted to show that a smaller amount of liquid, i.e., less that 8 oz of liquid, would be sufficient to prevent the potential dangers described above.

38. A comment recommended that dietary bran, such as is found in bran-rich ready-to-eat breakfast cereals, be specifically excluded from the proposed regulations, and that continued sale and promotion of bran-rich breakfast cereals as mild laxatives be permitted. Another comment made the statement that a breakfast cereal containing bran has for 50 years made laxative claims, and that these claims were permissible as "old drug claims" under the 1938 Food, Drug, and Cosmetic Act.

The meaning of "old drug claims" mentioned in the comment is unclear. Presumably, the commenter is referring to the "grandfather clause" of the 1938 act which exempts certain drugs from regulation as "new drugs" under section 201(p) of the act (21 U.S.C. 321(p)). The "grandfather clause" mentioned in the comment would not apply, however, unless the product in question were a drug. And, even if such a drug product did fall within the "grandfather clause" with respect to the product's status as a new drug, the product would remain subject to the other provisions of the act that apply to drugs. Moreover, to qualify for the "grandfather clause" a product's labeling must have remained unchanged from 1938 to the present time. The comment submitted no evidence that the labeling of these products has remained unchanged since 1938.

The Panel's reference to "dietary gran" has resulted in some confusion, including the impression that all high fiber food products, such as breakfast cereals, would be subject to regulation by the OTC laxative drug monograph. Bran cereals marketed solely as food products are not intended to be subject to regulation by the OTC laxative drug monograph. Therefore, "dietary bran" is not included in this tentative final monograph. The agency is aware, however, that bran has been marketed and labeled for use as a laxative. Therefore, "bran" is included in this tentative final monograph for those products that are marketed as laxative drug products. In order to avoid the impression that all high fiber food products regardless of labeling would be subject to the monograph, the term "bran", rather than "dietary bran" is used in the monograph.

A product that contains bran and that makes a laxative claim is subject to regulation as a drug. To avoid such regulations, it need merely drop the laxative claim. Laxative claims on a food product such as "the modern laxative" would bring the food product within the definition of "drug" in section 201(g)(1)(B) of the act (21 U.S.C. 321 (g)(1)(B)). In the absence of laxative claims, bran cereals and other bran products would be regulated as foods. Claims such as "contains fiber, which provides bulk to the diet," or "food-fiber cereal," generally would be considered to be descriptive statements of the cereal's food properties and would not be considered drug claims.

39. A comment contended that breakfast cereal containing dietary bran is always consumed with milk; therefore, the "adequate liquid intake" labeling in recommended § 334.10 is not necessary. The comment further stated that it is inappropriate to describe a bowl of cereal as a "dose," and suggested that the term "serving" would more completely describe the form in which cereal is consumed.

The required labeling statements for bulk-forming laxative drug products are not intended for breakfast cereals containing dietary bran that are sold as and designed to be consumed as foods. Thus the agency will not require such food products to bear the required labeling statements for bulk-forming laxatives, including the statement in § 334.10 regarding adequate liquid intake. However, as discussed in comment 38 above, if cereal products contain a drug claim the product is then subject to being regulated as a drug and must then conform to the monograph.

40. A comment stated that bran-rich breakfast cereals are not drugs, and restrictions on advertising that are appropriate for drugs are not appropriate for breakfast cereals. The comment stated that the Laxative Panel disapproved of any mention of a laxative product's good taste. The comment contended that bran-rich breakfast cereals with a laxative claim should not be forced to discontinue the use of "good taste" as an advertising claim.

As discussed in comment 38 above, the agency does not intend that bran cereal food products be subject to regulation by the laxative monograph. The Panel's statements regarding palatability of products concerned drug products. The agency does not object to truthful statements which accurately reflect inherent characteristics of a drug product, but agrees with the panel that they should not be used in a manner to support claims of effectiveness or to promote frequent or continued use.

41. A comment stated that recommended § 334.50(c) (4), (5), and (6), which pertain to the amount of sodium, potassium, and magnesium in the maximum recommended daily dose of a laxative product, should not be applicable to bran-rich cereals. The comment contended that recommended § 334.10 indicated no upper dosage limitation for dietary bran, and as such, recommended § 334.50(c) (4), (5), and (6) would be unworkable. The comments further contended that sodium and magnesium labeling is covered by nutritional labeling under food regulations and that it would be cumbersome and unnecessary to have comply with two sets of labeling on precisely the same elements.

As discussed in comment 38 above, bran-rich breakfast cereals would be

subject to the drug labeling requirements of the laxative monograph only if they make a laxative claim. If a product makes a drug claim there is no reason why that product should be exempt from any requirements applicable to similar drug products. If a bran cereal product wishes to avoid drug labeling requirements it need only avoid making a laxative claim.

42. One comment questioned whether the water-retaining properties of polycarbophil, in vitro, have a correlation with its laxative action.

The Panel presumed that polycarbophil acts by retaining water intraluminally and opposing dehydration in the bowel. The conclusion of effectiveness, however, was based on clinical studies that demonstrated that polycarbophil produced laxation. As stated in the response to comment 22, the exact mechanism by which most laxative agents produce laxation is unknown. Although knowledge of these mechanisms is desirable, it is not essential to a determination of safety and effectiveness.

43. A comment stated that it wanted to clarify that native carrageenan was an emulsifying agent and not an active ingredient of a particular product.

The Panel reviewed native carrageenan as an active ingredient because it was listed on the label of a product submitted for review. The Panel believed that because this ingredient is a hydrocolloid it had potential as a bulk-forming laxative. However, because of the lack of effectiveness data the Panel placed this ingredient in Category III. The agency agrees with the Panel that additional data are necessary before this ingredient can be considered a Category I laxative ingredient. Native carrageenan could be used as an inactive ingredient (emulsifying agent) because this ingredient is widely used in the food industry as a stabilizer and demulcent. FDA does not object to native carrageenan being included in laxative products as an inactive ingredient. However, its name should not be placed on the label in a manner that would mislead the consumer into thinking that it is an active ingredient.

44. One comment requested that recommended § 334.10(b) "Cellulose derivatives," be revised to include *alpha*-cellulose (powdered cellulose) as a Category I bulk laxative. The comment submitted data (Ref. 1) that, it claimed, demonstrate the safety and effectiveness of *alpha*-cellulose for OTC use as a bulk laxative.

After reviewing all of the available data, the agency believes that the data are inadequate to establish general recognition of safety and effectiveness of *alpha*-cellulose as an OTC laxative ingredient.

As evidenced by the FDA GRAS Food Ingredient Report (FDABF–GRAS–028), cellulose is generally recognized as a safe ingredient. *Alpha*-cellulose undoubtedly has potential as an OTC laxative ingredient, as several semisynthetic celluloses (methylcellulose and sodium carboxymethylcellulose) are already included in the proposed monograph for OTC laxative drug products. However, general recognition of effectiveness has not been demonstrated by the submitted studies. The subjects in the submitted studies were selected on the basis of slowest transit times and lowest daily fecal outputs, and do not meet the definition of constipated subjects (persons with not more than three spontaneous evacuations per week). Because laxatives are intended to relieve constipation, effectiveness cannot be established by studies in asymptomatic individuals.

While it could be argued that *alpha*-cellulose should be included in the monograph because of its similarity to the semisynthetic cellulose derivatives, the agency notes that the dose of the cellulose derivatives recommended by the Panel in the proposed monograph is 4 to 6 g whereas the dose used in the submitted studies was 14 g cellulose plus 6 g pectin. Although the comment concludes that pectin is an inactive ingredient, the difference in the dose of the cellulose is not explained. Therefore, the agency concludes that a clinical study, similar in design to those submitted (but in constipated subjects) is necessary before *alpha*-cellulose can be included in the monograph.

The agency's detailed comments and evaluation on the data and its recommendation for additional studies are on file in the Dockets Management Branch (Ref. 2).

References

(1) Comment No. CP, Docket No. 78N-036L, Dockets Management Branch.

(2) Letter from William E. Gilbertson, FDA, to Harold C. Anderson, Syntex Corporation, ANS LET 009, Docket No. 78N-036L, Dockets Management Branch.

D. Comments on Hyperosmotic Laxatives

45. Several comments requested clarification of the dosage for glycerin suppositories in recommended § 334.12(a). One comment pointed out that the Panel had concluded that glycerin is safe in the amounts usually used rectally, but then went on to establish a 3 g suppository as the only adult dose and a 1 to 1.5 g suppository dosage range for children under 6 years of age. One comment stated that it is unclear whether the dosage refers to the total weight of the suppository or to the weight of glycerin in each suppository. The comments stated that marketed adult glycerin suppositories range from 2 to 3 g of glycerin per suppositories range from 1 to 1.7 g of glycerin per suppository. The comments recommended that the monograph should more closely reflect what has been marketed. One comment also noted that recommended § 334.12(a) made no specific mention of dosage levels for infants or for children 6 to 12 years of age. The comment suggested that the dosage be clarified by revising the Panel's final sentence in § 334.12(a) to read "Adults and children 6 years or older . . ." and by revising the second sentence to read "Infants and children under 6 years of age . . . ."

The agency agrees that the dosages for glycerin suppositories should be clarified and believes that the Panel's recommended dosages for glycerin suppository refer to the weight of the glycerin in each suppository. Based on the information provided by the comments and the agency's independent survey of marketed glycerin suppository products (Ref. 1 through 4), the agency has determined that most glycerin suppositories are manufactured and marketed according to "The United States Pharmacopeia" (USP) specifications, and that adult suppositories contain between 2 and 3 g of glycerin, and children's suppositories contain between 1 and 1.75 g of glycerin. The tentative final monograph reflects these ranges.

Also, the dosages recommended by the Panel in § 334.12(a) need to be revised to indicate that the adult dosage range is the same as for children 6 years of age and over. However, as discussed in part II paragraph 2. below, constipation in children under 2 years of age should be diagnosed by a doctor. Therefore, dosages for children under 2 years of age are included in the monograph only under professional labeling.

References

(1) Letter from M. K. Laboratories to Michael Kennedy, FDA, November 6, 1981, OTC Volume 09LTFM, Docket No. 78N-036L, Dockets Management Branch.

(2) Letter from E. R. Squibb and Son, Inc., to Michael Kennedy, FDA, October 23, 1981, OTC Volume 09LTFM, Docket No. 78N-036L, Dockets Management Branch.

(3) Letter from Suppositoria Laboratories to Michael Kennedy, FDA, October 26, 1981.

OTC Volume 09LTFM, Docket No. 78N-036L, Dockets Management Branch.

(4) Letter from E.R. Squibb and Son, Inc., to Michael Kennedy, FDA, February 3, 1982, OTC Volume 09LTFM, Docket No. 78N-036L, Dockets Management Branch.

46. One comment recommended that the warning for products containing glycerin in recommended § 334.54(a)(1), i.e., "For rectal use only and not for oral use. Large doses of glycerin if taken orally can lead to serious toxic effects," be shortened to "For rectal use only." The comment stated that this shortened statement plus the mandatory warning in § 330.1(g), "In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately," are sufficient to convey the full intent of the warning, and that the other statements are redundant.

The agency agrees with the comment and is proposing that the warning read "For rectal use only." Consumers are generally aware of the mode of administration of suppository dosage forms. The phrase "for rectal use only" is sufficient for those who are unfamiliar with this dosage form. While it is unlikely that these products would be ingested, the mandatory warning in § 330.1(g) (21 CFR 330.1(g)) about accidental ingestion informs consumers of the proper action to take in case of accidental ingestion.

E. Comments on Lubricant Laxatives

47. Two comments suggested that the first phrase of the caution for mineral oil in recommended § 334.56(a)(1), "to be taken only at bedtime," should be deleted because this information is already provided in the "Directions for use" in recommended § 334.14(a).

Three other comments disagreed with the wording of the dosage for mineral oil emulsion in recommended § 334.14(b) which states, "Adult oral dosage is 15 mL to 45 mL of mineral oil component of emulsion administered orally twice daily with the first dose taken on arising and the second dose taken at bedtime and neither dose at mealtimes . . . ." The comments argued that this dosage statement could be misinterpreted to mean that 15 to 45 mL should be taken twice daily, giving a maximum daily dose of 30 to 90 mL, although the Panel clearly meant 15 to 45 mL to be the maximum daily dose, to be taken in two equally divided doses. The comments also pointed out that the children's dosage statment in recommended § 334.14(b) could be similarly misinterpreted. One of the comments suggested that recommended § 344.14(b) be revised to read, "Adult oral dosage is 15 mL to 45 mL daily of mineral oil component of emulsion administered orally twice daily in divided doses with the first dose taken on arising and the second dose taken at bedtime and neither dose at mealtimes."

The agency agrees that the warnings, dosage, and directions for use for both mineral oil and mineral oil emulsion are confusing and require clarification. The difference in directions for use between mineral oil and mineral oil emulsion is not adequately justified. Mineral oil emulsion is merely a different formulation of mineral oil; mineral oil is the active ingredient in mineral oil emulsion. Therefore, this tentative final monograph provides for warnings and directions for use for mineral oil only. The emulsion formulation is not included in this tentative final monograph, although manufacturers may choose to formulate mineral oil as either the plain oil or as an emulsion. The directions for use will provide for a minimum adult does of 15 mL with a total maximum daily dose of 45 mL. For children over 6 years of age, the minimum dose is 5 mL with a maximum total daily dose of 15 mL. Mineral oil is most often taken at bedtime, but restricting its administration to a particular time of day is unnecessary except that it should not be administered with meals because of potential interference with the absorption of fat-soluble vitamins. Because some persons prefer to take mineral oil in divided doses, the agency is proposing that directions for use provide that products may be labeled so that the dosage may be administered in either a single daily dose or in divided doses provided that no dose is taken at mealtimes. The agency believes that these directions more accurately reflect the current usage of mineral oil.

48. Two comments objected to the statement required for mineral oil products in recommended § 334.56(a)(1) that warns against the administration of mineral oil "to pregnant women, to bedridden or aged patients." The comments argued that the caution was unwarranted in view of the considerable body of evidence (Refs. 1 through 6) supporting the safe and effective use of mineral oil in such patients and in view of the general warning in recommended § 334.50(c)(3), which limits the OTC use of laxative products to 1 week. One of the comments argued that "since difficulties in absorbing vitamins A, D, E, and K occur very rarely and then only under conditions of chronic use of lubricant laxatives, the caution is not necessary because use is limited to 1 week."

The agency concludes that the studies submitted by the comments (Refs. 1 through 6) do not support deleting the statement in recommended § 334.56(a)(1) that warns against the use of mineral oil by pregnant women and bedridden patients. Only one of the submitted studies (Ref. 2) included pregnant women, and no mineral oil was administered in that study. Because data are lacking to support the comments' argument, the agency concurs with the Panel that lubricant laxatives should not be given to pregnant women. The Panel pointed out that ingested mineral oil may lower prothrombin levels, probably secondary to impaired vitamin K absorption, and therefore the regular use of mineral oil in pregnancy may predispose the newborn to hemorrhagic disease (40 FR 12912).

Additionally, only one of the submitted studies (Ref. 3) dealt extensively with bedridden patients, and, again, no mineral oil was administered. Because data are again lacking to support the comments' argument, the agency concurs with the Panel that lubricant laxatives should not be given to bedridden patients because the ingested mineral oil may be aspirated and cause lipid pneumonitis (40 FR 12912). In view of the lack of data, the agency does not believe that the 1-week limitation in recommended § 334.50(c)(3) would assure the safe use of mineral oil in pregnant women or bedridden patients.

The other submitted studies (Refs. 1, 4, 5, and 6) offer sufficient evidence to support the safe use of lubricant laxatives, such as mineral oil by aged patients. The Panel was primarily concerned that the absorption of a number of dietary nutrients, including fat-soluble vitamins, may be impaired by the ingestion of mineral oil during or after meals. Labeling that directs persons not to take mineral oil with meals can reduce the possibility of mineral oil interfering with the absorption of vitamins in aged patients. Also, the Panel's warning against the use of mineral oil by the aged apparently was based on a concern that aged patients have a debilitated or "worn out" gastrointestinal tract. The submitted studies, however, demonstrate that the gastrointestinal tract does not "wear out" with age and that clinical observation of gastrointestinal problems in older patients differs little from younger individuals (Refs. 1 and 6). Based on these data, the agency believes that a warning against the use of mineral oil laxatives by a particular group of adults because of their age is unwarranted without further sound medical rationale supporting specific age limitations. Therefore, the agency has deleted the

phrase "or aged" from the warning statement required for mineral oil products in this tentative final monograph.

In addition, in the Federal Register of December 3, 1982 (47 FR 54750), the agency published a final rule amending the general drug labeling provisions in Part 201 (21 CFR 201.63) to include a warning concerning the use by pregnant or nursing women of OTC drugs intended for systemic absorption. The final rule states that, where a specific warning relating to use during pregnancy or while nursing has been established for a particular drug product in an NDA or for a product covered by an OTC drug final monograph, the specific warning shall be used in place of the general warning, unless otherwise stated in the NDA or in the final OTC drug monograph. While the warning recommended by the Panel covers use of mineral oil during pregnancy, it does not refer to its use by nursing mothers. Therefore, the following additional statement is being proposed in this tentative final monograph for mineral oil: "As with any drug, if you are nursing a baby, seek the advice of a health professional before using this product." Accordingly, in this tentative final monograph the agency proposes that the specific pregnancy and nursing warnings discussed above for mineral oil supersede the general warning required under § 201.63.

References

(1) Mulinos, M.G., and A.J. Maloney, "Treatment of Constipation in the Aged," *The Journal of the Medical Society of New Jersey*, 66:619–622, 1969.

(2) Greenhalf, J.O., and H.S.D. Leonard, "Laxatives in the Treatment of Constipation in Pregnant and Breast-Feeding Mothers," *The Practitioner*, 210:259–263, 1973.

(3) Tirsch, H.S., and S. Rosenfeld, "Correction of Constipation in Severely Incapacitated Invalids and in Patients with Neurologic Diseases," *American Journal of Gastroenterology*, 31:702–705, 1959.

(4) Montilla, E., "Treatment of Chronic Constipation with an Emulsion of Milk of Magnesia and Mineral Oil," *Clinical Medicine*, 73:75–77, 1966.

(5) Cohen, T., and L. Gitman, "Clinical Evaluation of the Gastrointestinal Tract in the Aged," *The American Journal of Gastroenterology*, 32:422–434, 1960.

(6) Magnuson, C., "The Geriatric and Bedridden Patient and the Large Bowel," *Nebraska State Medical Journal*, 50:73–78, 1965.

49. Two comments maintained that the statement recommended for mineral oil products in § 334.56(a)(1) that warns against giving mineral oil "to persons having recent episodes of vomiting or regurgitation, or to persons having abdominal pain" is redundant and duplicates the general warning for all laxatives in recommended § 334.50(c)(1), which states, "Do not use this product when abdominal pain, nausea, or vomiting are present." The comments suggested revising the warning to eliminate the statement concerning vomiting, regurgitation, and abdominal pain from the specific mineral oil warnings in recommended § 334.56.

The agency agrees with the comments. Accordingly, recommended § 334.56 has been revised to delete the phrase "to persons having recent episodes of vomiting or regurgitation, or to persons having abdominal pain."

50. One comment requested that the phrase "except on the advice of a physician" be added to the drug interaction precaution in recommended § 334.56(a)(2), i.e., "Do not take this product if you are presently taking a stool softener laxative."

The agency agrees with the comment that situations may exist in which a physician might choose to use or combine drugs for a medical reason. In other recent tentative final monographs the agency has adopted the phrase "unless directed by a doctor" in place of phrases such as "except on the advice of a physician." Accordingly, the drug interaction precaution in recommended § 334.56 has been revised in the tentative final monograph to read, "Do not take this product if you are presently taking a stool softener laxative unless directed by a doctor." The tentative final monograph also includes the option of using either the word "physician" or the word "doctor" in OTC laxative labeling.

F. Comments on Saline Laxatives

51. Two comments stated that the warning for saline laxatives in recommended § 334.58(a), which states, "For occasional use only. Serious side effects from prolonged use or overdosage may occur," is unnecessary and redundant. The comments pointed out that the general warning in recommended § 334.50(c)(3), which states, "This product should not be used for a period of longer than 1 week except under the advice and supervision of a physician," restricts the prolonged use of any laxative. One comment further noted that the Panel's statement at 40 FR 12910 that saline laxatives should be restricted to occasional use only, as serious electrolyte disturbances have been reported with their long-term or daily use, is not supported by any of the references cited by the Panel for saline laxatives. The comment submitted a reference claiming to show that there is no serious disturbances to the electrolytic balance in the blood with the use of a kit containing magnesium citrate (Ref. 1). The comments concluded that there was no clinical justification for singling out saline laxatives such as magnesium citrate for disturbing electrolyte balance and recommended that § 334.58(a) be deleted from the monograph.

The agency has reviewed the data cited by the comment and believes that they do not provide a basis for deleting the warning. Magnesium citrate was administered once to each patient as part of a bowel cleansing regimen in preparing patients for barium x-ray. Although none of the patients experienced any electrolyte disturbances, the data do not provide information regarding the Panel's concerns about electrolyte disturbances from long-term use of saline laxatives. However, the general warning recommended by the Panel in § 334.50(c)(3) restricts the use of any laxative to not longer than 1 week. Therefore, the specific warning in recommended § 334.58(a) is unnecessary and is not included in the tentative final monograph.

Reference

(1) Irwin, G. A. L., J. E. Shields, and W. W. Wolff, "Clearer Roentgenographic Visualization of the Colon," *Gastroenterology*, 67:47–50, 1974.

52. Two comments noted that recommended § 334.16(a)(2) states that magnesium citrate products may be formulated in combinations with the sequestering agents, citric acid and anhydrous sodium citrate, to allow magnesium to be held in solution as a complex. The comments pointed out that the monograph for magnesium citrate solution in "The National Formulary" lists potassium bicarbonate in the prime formula and provides for sodium bicarbonate as an alternate ingredient (Ref. 1). The comments proposed that recommended § 334.16(a)(2) be revised to permit the use of potassium citrate as an alternate ingredient to sodium citrate.

Since submission of the comment, magnesium citrate oral solution has been added as an official article to the USP (Ref. 2). The agency has no objection to the use of different sequestering agents for magnesium citrate formulations because these ingredients are not active ingredients and do not contribute to the laxative effect of the product. The agency points out that the OTC drug review is primarily an active, not inactive ingredient review. Inactive ingredients are not usually included in the OTC drug monographs. They must, however, meet the requirements of § 330.1(e) (21 CFR

330.1(e)) that they be suitable ingredients that are safe and do not interfere with the effectiveness of the product. Because the purpose of the OTC drug review process is to determine the safety and effectiveness of OTC drugs, the OTC advisory review panels occasionally made recommendations with respect to inactive ingredients; these recommendations were made to call attention to those inactive ingredients that could potentially interfere with the safety and effectiveness of the product. In the case of the inactive ingredients in magnesium citrate solution, the agency is unaware of any evidence to demonstrate that they could potentially interfere with the safety and effectiveness of the product. Therefore, the specific sequestering agents for magnesium citrate solution which had been recommended by the Panel are not included in the tentative final monograph.

References

(1) "The National Formulary," 14th Ed., American Pharmaceutical Association, Washington, pp. 389–390, 1975.

(2) "The United States Pharmacopeia," 20th Revision, United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 459–460, 1980.

53. Two comments submitted a number of studies (Refs. 1 through 4) to show that one of the major professional uses of magnesium citrate solution is for the preparation of the colon for x-ray and endoscopic examination. Based on these studies, the comments requested that recommended § 334.80 be ameded to allow the following professional labeling claims for magensium citrate: "For the preparation of the colon for x-ray and endoscopic examination." One comment further proposed that the claim "for use in preparation of the patient for surgery" also be allowed.

The agency has reviewed the submitted studies and believes there is sufficient evidence to support the use of magnesium citrate as part of a bowel cleansing regimen in preparing the patient for surgery or for preparing the colon for x-ray or endoscopic examination. However, none of the studies used magnesium citrate solution alone to evacuate and cleanse the colon. In each of the studies, magnesium citrate solution was used with either bisacodyl, enemas, overhydration, or dietary restirctions as one part of an overall regimen in preparing the patients for surgery, or preparing the colon for x-ray or endoscopic examination.

Therefore, the agency is proposing in the tentative final monograph that the Category I professional labeling claim be limited to the following: "For use as part of a bowel cleansing regimen in preparing the patient for surgery or for preparing the colon for x-ray or endosopic examination."

The agency's comments and evaluation on the data are on file in the Dockets Management Branch (Refs. 5 and 6).

References

(1) Comment No. C00015, Docket No. 78N–036L, Dockets Management Branch

(2) Comment No. C00043, Docket No. 78N–036L, Dockets Management Branch.

(3) Sloan, R. D., et al., "What is the Best Way to Prepare the Colon for Radiological Study?" *Modern Medicine*, 38:198–201, 1970.

(4) Irwin, G. A. L., et al., "Clearer Roentgenorgraphic Visualization of the Colon," *Gastroenterology*, 67:47–50, 1974.

(5) Letter from William E. Gilbertson, FDA, to Richard Neimeth, National Magnesium Co., Coded ANS LET 012, Docket No. 78N–036L, Dockets Management Branch.

(6) Letter from William E. Gilbertson, FDA, to Warren L. Myers, Warren-Teed Pharmaceuticals Division of Adria Laboratories Inc., Coded ANS LET 011, Docket No. 78N–036L, Dockets Management Branch.

54. One comment requested that recommended § 334.16(b) be revised to include an infant dosage for milk of magnesia (magnesium hydroxide). The comment pointed out that an infant dosage for milk of megnesia was submitted to the Panel for evaluation, but that neither the Panel's minutes nor the preamble to the monograph reflect any consideration of this issue. Noting that its laxative product, which contains milk of magnesia and is labeled for use in infants, has been marketed for over 25 years, the comment argued that there is nothing in the medical literature that would cast doubt upon the continued use of an infant dosage for milk of magnesia.

Magnesium hydroxide has been used for the relief of constipation in infants. The available literature indicates that the magnesium hydroxide dosage generally recommended for infants is 0.035 to 0.043 gram per kilogram per dose (Refs. 1 and 2). However, as discussed in part II, paragraph 2, below, the agency believes that constipation in children under 2 years of age could be indicative of a more serious condition that should be diagnosed by a doctor. Therefore, dosages for children under 2 years of age are included in the tentative final monograph only under professional labeling.

References

(1) Fingl, E., "Laxatives and Cathartics," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A. Gilman, The Macmillan Publishing Co., New York, p. 1005, 1980.

(2) Shirkey, H.C., editor, "Pediatric Therapy," 6th Ed., The C.V. Mosby Co., St. Louis, p. 1219, 1980.

55. Two comments noted that the daily dosage range for magnesium citrate as expressed in milliequivalents (mEq) magnesium ion is listed in the recommended monograph as 77 to 126 mEq magnesium ion in § 334.16(a) under Subpart B—Active Ingredients and as 77 to 141 mEq magnesium ion at 40 FR 12910. The comments conteded that both calculations for mEq magnesium ion were incorrect and noted that the mEq stated for the magnesium ion neither conformed to the volume limits of the usual daily dosage range for magnesium citrate solution, nor to the magnesium oxide limits, as listed in the monograph for magnesium citrate solution in the "National Formulary" (Ref. 1). The comments further contended that the upper limit of 18 g for the daily dosage range of magnesium citrate recommended in § 334.16(a) should be extended to 25 g because the usual daily dosage of magnesium citrate solution varies from 200 to 350 mL.

The agency agrees with the comments that the daily dosage range for magnesium citrate as expressed in mEq magnesium ion is in error. However, the agency does not believe that there is a need to state the dosage for administration in milliequivalents because such information could be confusing to consumers. The agency also agrees that the upper limit of the daily dosage range of magnesium citrate should be extended to 25 g. Based on submissions to the agency, products currently marketed, and other available information, the agency notes that magnesium citrate, when used as a laxative, is usually formulated and administered as an oral solution within the requirements of the USP. Magnesium citrate oral solution, (see comment 52 above) contains in each 100 mL, 5.8 to 7.1 g of magnesium citrate equivalent to not less than 1.55 g and not more than 1.9 g of magnesium oxide (Ref. 2). The usual daily dosage for magnesium citrate oral solution is 200 to 350 mL. Based on the lower and higher limits of the amount of magnesium citrate in 100 mL of solution, the usual daily dosage would contain 11.6 to 24.8 g of magnesium citrate. The agency is expanding the dosage range for magnesium citrate for use as a laxative from 11 to 18 g to 11 to 25 g to be compatible with the USP requirements. Therefore, the following directions for use are included in the tentative final monograph for magnesium citrate:

"Adults and children 12 years of age and over: oral dosage is 11 to 25 grams. Children 6 to under 12 years of age: oral dosage is 5.5 to 12.5 grams. Children 2 to under 6 years of age: oral dosage is 2.7 to 6.25 grams. The dose may be taken as a single daily dose or in divided doses. Children under 2 years of age: consult a doctor."

References

(1) "The National Formulary," 14th Ed., American Pharmaceutical Association, Washington, pp. 389–390, 1975.

(2) "The United States Pharmacopeia," 20th Ed., United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 459–460, 1980.

56. Four comments objected to the phrase "taken in dividend doses" in the total daily dosage for magnesium citrate in recommended § 334.16(a) and for magnesium hydroxide in recommended § 334.16(b). Several of the comments stated that the phrase "in divided doses" is not applicable to the administration of magnesium citrate and magnesium hydroxide because these laxative ingredients are usually administered in single doses, that is, "once daily or at bedtime, or as directed by a physician." One of the comments pointed out that magnesium citrate solution is packaged in a single-dose container and each unit cannot be used more than once. Another comment stated that magnesium hydroxide when used as an antacid is given in divided doses, but when used as a laxative is given as a larger single dose. The comments pointed out that, in the absence of safety or effectiveness questions, there is no reason to prohibit a single-dose administration of these ingredients. Some of the comments requested that the dosage regimen permit both single and divided dosage directions. Others suggested a single dosage, once daily or at bedtime, or as directed by a physician.

Magnesium salts, magnesium citrate, magnesium hydroxide, and magnesium sulfate when used as laxatives are generally administered as a single dose once per day (Refs. 1, 2, and 3). The agency is not aware of any evidence contradicting the safety or effectiveness of these laxative ingredients when the recommended total daily dosage is administered either in a single dose once per day or in divided doses. Therefore, the tentative final monograph provides for both single daily doses or divided doses of the magnesium salts.

References

(1) Fingl, E., "Laxatives and Cathartics," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A. Gilman, The Macmillan Publishing Co., New York, p. 1005, 1980.

(2) Swinyard, E.A., "Gastrointestinal Drugs," *in* "Remington's Pharmaceutical Sciences," 16th Ed., edited by A. Osol et al., The Mack Publishing Co., Easton, PA, pp. 738 and 744, 1980.

(3) Aviado, D.M., "Krantz and Carr's Pharmacologic Principles of Medical Practice," 8th Ed., The Williams and Wilkins Co., Baltimore, p. 944, 1972.

57. Three comments requested a revision of recommended § 334.58(b), which provides for storage of magnesium citrate solution in a cold place (refrigerator temperature) to retard decomposition. The comments pointed out that this statement was appropriate for magnesium citrate solution prior to the modification of the manufacturing process in which a pasteurization step was introduced. The comments further pointed out that the requirements in the "National Formulary" for magnesium citrate solution call for storage at controlled room temperature or in a cool place (Ref. 1). Therefore, the comments requested that § 334.58(b) either be deleted or replaced with the storage statement in the "National Formulary".

Magnesium citrate in oral solution is an official article in the USP (Ref. 2). Therefore, the agency agrees that the storage conditions for magnesium citrate in oral solution should conform to the current official compendium, which requires storage at controlled room temperature or in a cool place. The USP defines "controlled room temperature" as between 59 and 86 °F (15 and 30 °C) and "cool place" as between 46 and 59 °F and (8 and 15 °C) (Ref. 2). Therefore, this tentative final monograph states that magnesium citrate when formulated in oral solution should be stored at temperatures between 46 and 86 °F (8 and 30 °C).

References

(1) "The National Formulary," 14th Ed., American Pharmaceutical Association, Washington, pp. 389–390, 1975.

(2) "The United States Pharmacopeia," 20th Revision, United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 8 and 459–460, 1980.

58. One comment submitted a number of references (Ref. 1) to show that the phosphate salts administered either orally or rectally are useful therapy for preparing the colon for x-ray, endoscopic examination, and for preparing the bowel for surgery. The comment requested that recommended § 334.80(a), which contains the professional labeling for products containing phosphate salts, be amended to allow the claim "For use in preparation of the patient for surgery or for preparation of the colon for x-ray and endoscopic examination." In addition, the comment requested that the upper limits for the daily dosage range for orally administered sodium biphosphate and sodium phosphate in recommended § 334.16(d) be expanded from 19.2 g to 21.3 g for sodium biphosphate and from 7.2 g to 8 g for sodium phosphate for these professional labeling indications.

The agency reviewed the submitted studies and agrees with the comment that phosphate salts are useful therapy for use in preparation of the colon for x-day and endoscopic examination or for the preparation of the patient for surgery. However, in most of the submitted studies phosphate salts were not used alone, but were used as part of an overall bowel cleansing regimen, which included overhydration, dietary restrictions, and/or other laxative agents. Accordingly, the professional labeling section of the monograph for phosphate salts, has been amended to include the following indication: "For use as part of a bowel cleansing regimen in preparing the patient for surgery or for preparing the colon for x-ray or endoscopic examination." Also, the studies submitted did not contain sufficient data to justify an increase in the upper limit of the dosage ranges for sodium phosphate and sodium biophosphate. However, in this tentative final monograph the agency is expanding the dosage ranges for phosphate salts to be compatible with the USP as follows: (1) *Sodium phosphate/sodium biophosphate solution. Oral dosage.* Adults and children 12 years of age and over: oral dosage is sodium phoshpate 3.42 to 7.56 grams, and sodium biphosphate 9.1 to 20.2 grams in a single daily dose. Children 10 to under 12 years of age: oral dosage is sodium phosphate 1.71 to 3.78 grams and sodium biphosphate 4.5 to 10.1 grams in a single daily dose. Children 5 to under 10 years of age: Oral dosage is sodium phosphate 0.86 to 1.89 grams and sodium biphosphate 2.2 to 5.05 grams in a single daily dose. Children under 5 years of age: consult a doctor. *Enema dosage.* Adults and children 12 years of age and over: enema dosage is sodium phosphate 6.84 to 7.56 grams and sodium biphosphate 18.24 to 20.16 grams in a single daily dose. Children 2 to under 12 years of age: enema dosage is sodium phosphate 3.42 to 3.78 grams and sodium biphosphate 9.12 to 10.08 grams in a single daily dose. Children under 2 years of age; consult a doctor.

(2) *Sodium phosphate.* Adults and children 12 years of age and over: oral dosage is 3.42 to 7.56 grams in a single

daily dose. Children 10 to under 12 years of age: oral dosage is 1.71 to 3.78 grams in a single daily dose. Children 5 to under 10 years of age: oral dosage is 0.86 to 1.89 grams in a single daily dose. Children under 5 years of age: consult a doctor.

(3) *Sodium biphosphate.* Adults and children 12 years of age and over: oral dosage is 4.5 to 20.2 grams in a single daily dose. Children 10 to under 12 years of age: oral dosage is 2.25 to 10.1 grams in a single daily dose. Children 5 to under 10 years of age: oral dosage is 1.12 to 5.05 grams in a single daily dose. Children under 5 years of age: consult a doctor.

The agency's comments and evaluation on the data and its recommendations are on file in the Dockets Management Branch (Ref. 2).

References

(1) Comment Nos. C00002 and C00022, Docket No. 78N–036L, Dockets Management Branch.

(2) Letter from William E. Gilbertson, FDA, to Fred T. Wickis, C. B. Fleet Co., ANS LET 008, Docket No. 78N–036L, Dockets Management Branch.

59. One comment stated that the usual daily dosages recommended for the phosphate salts (disodium phosphate, sodium phosphate, sodium biphosphate, and monosodium phosphate) as stated in the table at 40 FR 12911 and in recommended § 334.16(d) are unclear because disodium phosphate and monosodium phosphate are synonyms for sodium phosphate USP and sodium biphosphate USP, respectively. The comment recommended that the names monosodium phosphate and disodium phosphate, along with their corresponding dosages, be deleted. The comment suggested that the monograph state that only the USP names, with the designated chemical formulas and molecular weights for sodium phosphate and sodium biphosphate, be allowed in all labeling to avoid error in interpreting which salt is meant. Another comment stated that the milliequivalents expressed for the ionization products of the phosphate salts should have been calculated for the products resulting from ionization in aqueous solution, as would be ingested by the consumer, rather than the phosphate ion species released by alkaline degradation.

The agency agrees with the comment that the names and the dosages for the phosphate salts as stated at 40 FR 12911 and in recommended § 334.16(d) and § 334.35(a) are confusing. Disodium phosphate and monosodium phosphate are synonyms for sodium phosphate and sodium biphosphate, respectively. However, only the official names of these ingredients, i.e., sodium phosphate and sodium biphosphate, need to be designated in the monograph. Also, because these ingedients are official compendial articles there is no need to specify their molecular weight and chemical formula in the monograph.

Although the agency agrees with the comment that the milliequivalents expressed for the ionization of phosphate salts should have been calculated for the products existing in aqueous solution, in this tentative final monograph the agency states the dosage in grams of sodium phosphate and sodium biphosphate. (See comment 58 above.)

60. One comment submitted an unpublished study in response to the Panel's recommendations at 40 FR 12919 for further definitive, well-designed studies to establish a safe and effective laxative dose for tartaric acid and tartrate preparations (Ref. 1). The comment stated that the study supports the safety of tartaric acid and tartrate preparations and supports reclassifying them from Category III to Category I for use as a laxative.

The Panel recommended that the usual daily dose of tartrate preparations when used as laxatives (5 to 10 g) was probably safe, but that additional data were necessary to justify an increase in the total daily dose beyond 10 g. The submitted study was designed to determine the extent of absorption and metabolism of sodium ^{14}C-tartrate in the rat and in humans and to study quantitatively the effect of tartrate ingestion upon the acid-base status in humans. From the results in one phase of the study, consisting of the administration of sodium ^{14}C-*DL*-tartrate orally and parenterally to humans and rats, intestinal absorption was calculated as 18 percent of the dose in humans and 81 percent in rats, of which the greater portion in both humans (14 percent) and rats (70 percent) was excreted in the urine. Because the ^{14}C-labeled tartrate was excreted as respiratory carbon dioxide to a greater extent after oral than parenteral administration, the authors concluded that the main site of tartrate metabolism is in the intestine. Studies measuring tartrate metabolism and carbon dioxide liberation from intestinal bacteria confirmed this conclusion. In the acid-base studies, one subject was given 24 g and another 30 g per day of unlabeled sodium *L*-tartrate. The authors found no evidence of renal toxicity in the two subjects as assessed by maintenance of normal creatinine clearance and the absence of proteinuria. However, the authors indicated, based on the weight of the stools collected, that the laxative effect was slight and questioned the reputation of the tartrates as laxatives.

Although the study provides information to establish the safety of tartrate preparations in the dosages normally used in OTC laxative formulations, additional effectiveness data are needed before tartaric acid and tartrate preparations can be generally recognized as effective for oral use as OTC laxatives.

The agency's comments and evaluation on the data and its recommendation for additional studies are on file in the Dockets Management Branch (Ref. 2).

References

(1) Wrong, O. M., et al., "The Metabolism of Tartrate in Man and the Rat," draft of unpublished paper, Comment No. C0079, Docket No. 78N–036L, Dockets Management Branch.

(2) Letter from William E. Gilbertson, FDA, to Bernard Misek, Beecham Products, coded ANS C0082, Docket No. 78N–036L, Dockets Management Branch.

G. Comments on Stimulant Laxatives

61. One comment stated that there was ambiguity in the Panel's definition of "stimulant laxative" in recommended § 334.3(l), which states, "An agent that promotes bowel movement by one of more direct actions on the intestine," because this definition could conceivably be interpreted to include every clinically active laxative agent. According to the comment, saline and hyperosmotic laxatives would be included within the definition because they act directly on the intestine by increasing intestinal water content, thereby promoting bowel movement; bulk laxatives would be included because they increase motor activity of the colon through pressure stimulation by increasing intestinal bulk and water content. The lubricant laxatives would also be included because they exert one of more direct actions on the intestine by coating the intestinal wall to lubricate the passage of the intestinal contents. The comment recommended that stimulant laxative be defined as "an agent that promotes bowel movement by increasing peristalsis in the colon through direct stimulation of neuro-muscular components of the intestinal wall." The comment concluded that this definition does not include saline and hyperosmotic laxatives which do not increase peristaltic activity by direct neuro-muscular stimulation of the colon, but act through an intervening pharmacologic mechanism. Another comment stated that stimulant laxatives

do not "stimulate" anything, but act in the same manner as the other laxatives.

In defining stimulant laxative, the Panel provided a general definition that it felt would be applicable to all stimulant laxatives. The panel recognized that some of the so-called "stimulant laxatives" have recently been shown to promote laxation by means other than stimulation, but the exact mechanism by which they promote laxation is not known (40 FR 12906). Until the precise mechanisms for the "stimulant laxatives" have been defined, there is sound basis for changing the Panel's definition.

62. One comment disagreed with the Panel's recommendation that all stimulant laxatives bear the class warnings in recommended § 334.60(a) (1), (2), and (3). The comment argued that the ingredients classified as stimulant laxatives are markedly different from one another in terms of chemical composition, clinical pharmacology, and site of intestinal action. These differences result in wide variations in therapeutic response and clinical toxicity for the individual ingredients. The comment recommended amending the warnings and caution statements so that they properly reflect the clinical use experience reported for each ingredient, rather than have class warnings for the stimulant laxatives.

The agency agrees with the comment. The class warnings for stimulant laxatives contained in recommended § 334.60(a) (1), (2), and (3) are not included in this tentative final monograph. (See comments 63, 64, and 65 below.) The agency believes that the general warnings for OTC drugs in § 330.1(g) (21 CFR 330.1(g)), the general OTC laxative warnings in recommended § 334.50(c), and the ingredient-specific warnings for bisacodyl, castor oil, and phenolphthalein, will provide consumers with adequate warnings for the use of stimulant laxatives. The specific warnings are based on each ingredient's specific clinical pharmacology, clinical toxicity, and therapeutic response. Thus, as recommended by the comment, the warnings for the stimulant laxatives in the tentative final monograph are now limited to ingredient-specific warnings.

63. Numberous comments objected to the Panel's recommended warning for stimulant laxatives in § 334.60(a)(1), which states, "Caution: Prolonged or continued use of this product can lead to laxative dependency and loss of normal bowel function." They also objected to the following portion of the warning in recommended § 334.60(a)(2): "Serious side effects from prolonged use . . . can occur." Some of the comments argued that these warnings were unnecessary because the general warning for all OTC laxative drugs in recommended § 334.50(c)(3) already warns that OTC laxatives should not be used longer than 1 week excpet under the advice and supervision of a physician. Therefore, according to the comments, concerns about serious side effects, loss of normal bowel function, and laxative dependency from prolonged use are not an issue. Several of the comments argued that because the Panel could not define the term "dependency" (in recommended § 334.60(a)(1)), the warning should be deleted. Other comments argued that the warnings should not apply to specific stimulant laxatives. One comment cited 23 references (Ref. 1) in support of its argument that prolonged use of standardized senna during clinical studies did not cause serious side effects or lead to laxative dependency. One of the references, an article by Abraham (Ref. 2), describes a method for treating chronic constipation through the prolonged use of seena with gradually reduced doses given until regular bowel rhythm has been established and the need for a laxative is eliminated. The comment argued that this demonstrates that senna does not cause "dependency." Another comment cited an article by Dreiling, Fischl, and Fernandez (Ref. 3) in support of its contention that the prolonged use of bisacodyl does not cause serious side effects. The article reported a clinical trail in which bisacodyl was given for as long as 24 weeks and in doses as high as 20 mg per day without causing serious side effects "from prolonged use." The comments all recommended that § 334.60(a)(1) and the portion of § 334.60(a)(2) that concerns prolonged use, be deleted from the monograph.

The agency agrees with the comments that the warnings regarding prolonged use should be deleted from the monograph. The warning in recommended § 334.50(c)(3), which limits the use of laxative products to not longer than 1 week, is sufficient to warn consumers against the prolonged use of OTC laxatives. The agency has also reviewed the references cited by the comments and believes that standardized senna concentrate and bisacodyl used under professional supervision do not cause serious side effects from prolonged use or lead to laxative dependency. Thus, the warning in recommended § 334.60(a)(1), and that portion of the warning in recommended § 334.60(a)(2) concerning prolonged use, do not appear warranted for stimulant laxatives as a group and are not included in this tentative final monograph.

Reference

(1) Comment No. 37, Docket No. 78N-036L, Dockets Management Branch.

(2) Abrahams, A., "A Re-educative Regimen for Chronic (functional) Constipation," *The British Journal of Clinical Practice*, 18:1-5, 1964.

(3) Dreiling, D. A., R. A. Fischl, and O. Fernandez, "The Therapeutic Usefulness of Dulcolax (Bisacodyl), A New Nonpurgative Laxative," *American Journal of Digestive Disease*, 4:311-320, 1959.

64. Several comments objected to the portion of the warning in recommended § 334.60(a)(2) for stimulant laxatives which states that "Serious side effects from . . . overdose can occur." The comments recommended deleting this portion of the warning because it is repetitious of the general overdose warning for OTC drugs in § 330.1(g) which states, "In case of accidental overdosage, seek professional assistance or contact a poison control center immediately."

The agency agrees with the comments. Therefore, that portion of recommended § 334.60(a)(2) concerning overdose is not included in this tentative final monograph. In addition, the remainder of the warning in recommended § 334.60(a)(2) concerning prolonged use is also not included in this tentative final monograph. (See comment 63 above.)

65. Several comments argued that the Panel's recommended warning in § 334.60(a)(3) which states, "This product should be used only occasionally, but in any event no longer than daily for 1 week, except on the advice of a physician," is unnecessary. The comments pointed out that the warning in § 334.60(a)(3) is nearly identical to the general warning for all laxative drugs in recommended § 334.50(c)(3), which states "This product should not be used for a period of longer than 1 week except under the advice and supervision of a physician." The comments stated that the warning in § 334.60(a)(3) is repetitious and, therefore, should be deleted.

The agency agrees that the warnings in recommended §§ 334.60(a)(3) and 334.50(c)(3) provide similar information. To eliminate such redundancy, recommended § 334.60(a)(3) is not included in this tentative final monograph.

66. A comment asked whether danthron acts on the mucosa or the intramural nerve plexi and whether there is any possibility of nerve damage.

Although the precise mechanism of action of danthron is not known, the Panel discussed both theories of action—direct irritant effect on the

mucosa and stimulation of intramural nerve plexi. The Panel noted, however, that both theories lacked experimental confirmation. The agency is unaware of any data supporting the possibility of nerve damage when danthron is used as recommended for OTC use for no longer than 1 week.

67. One comment pointed out that the dosage statement for danthron in recommended § 334.18(e) does not contain a pediatric dosage and that the usual pediatric dosage for anthraquinone-type stimulant laxatives, such as danthron, is one-half the adult dosage for children 6 to 12 years of age and one-fourth the adult dosage for children 1 to 6 years of age. The comment recommended that the monograph be revised to include the following pediatric dosages for danthron:

Children 6 to 12 years of age: 37.5 mg daily
Children 1 to 6 years of age: 9.4 to 37.5 mg daily

The usual pediatric dosages that the comment recommends for danthron are limited to the senna-type anthraquinones. According to Godding (Refs. 1 and 2), Ewe (Ref. 3), Thompson (Ref. 4), and Breimer and Baars (Ref. 5), danthron differs from the senna-type anthraquinones in that the active components of the senna-type anthraquinones are rhein-glycosides containing a glucose molecule which "protects" the active components from systemic absorption. Thus the active components are not released from the glucose until they reach their active site in the colon. The active components of danthron, however, are "free anthraquinones," which lack the glucose molecule and are substantially absorbed systemically before reaching their active site in the colon. Because a considerable amount of danthron is absorbed before reaching its site of activity, it is less effective than the senna-type anthraquinones at a given dose. Also, because it is more readily absorbed into the system than the senna-type anthraquinones, danthron may be more systemically toxic. Therefore, the proportionate doses that apply to the senna-type anthraquinones cannot be applied to pediatric doses of danthron without scientific data to support the safety and effectiveness of a specific pediatric dose. The comment did not provide such data.

References

(1) Godding, E. W., "Hazards of Multilaxative Mixtures," *British Medical Journal*, 1:636, 1976.

(2) Godding, E. W., "Therapeutics of Laxative Agents with Special Reference to the Anthraquinones," *Pharmacology*, 14(Supplement 1):78–101, 1976.

(3) Ewe, K., "The Physiological Basis of Laxative Action," *Pharmacology*, 20(Supplement 1):2–20, 1980.

(4) Thompson, W. G., "Laxatives: Clinical Pharmacology and Rational Use," *Drugs*, 19:49–58, 1980.

(5) Breimer, D. D., and A. J. Baars, "Pharmacokinetics and Metabolism of Anthraquinone Laxatives," *Pharmacology*, 14(Supplement 1):30–47, 1976.

68. One comment pointed out that the professional labeling "for preparing the colon for x-ray or endoscopic examination" is provided for some of the anthraquinones, but not for danthron. The comment requested that this indication also apply to products containing danthron. No data were submitted to support this request.

The senna-type anthroaquinones are the only anthraquinone ingredients that contain professional labeling. As pointed out in comment 67 above, danthron reportedly is less effective than senna at a given dose because its active components are substantially absorbed into the system before reaching the active site in the colon. The active components of the senna-type anthraquinones appear to be "protected" from systemic absorption through their molecular structure which includes a glucose molescule. Data demonstrating that danthron is effective for use in "preparing of the colon for x-ray or endoscopic examination" are necessary before the agency can include this professional indication for danthron in the monograph. The comment did not provide any data; therefore, this indication is not included in this tentative final monograph.

69. Objecting to the classification of senna as a stimulant laxative, one comment argued that recent methods of investigation, described by Jones and Godding (Ref. 1), indicate that laxation resulting from senna is accompanied by the absence of interaluminal pressure and the rapid transport of colonic contents which, according to the comment, is almost the reverse action of stimulation. The comment stated that the Panel insisted on classifying senna as a "stimulant" as a matter of convenience. The comment contended that, although the exact mechanism of action for senna may not be known, the ingredient should not be classified "as a matter of convenience," but on the basis of scientific information.

The Panel reviewed the text cited by the comment (40 FR 12909) and considered the mechanism of action for senna discussed by the comment. The Panel pointed out that these mechanisms lack experimental confirmation. The comment provided no new data to show that these mechanisms are now accepted as scientifically sound.

Chemically, senna is identified as an anthraquinone as are the other "stimulant" laxatives such as cascara sagrada, danthron, etc. The major active components of the anthraquinone laxatives are anthraquinone glycosides (Ref. 2). Although the properties of the individual anthraquinone laxatives vary with the precise type of glycoside present and the ease with which the glycosides are released from the original molecule (Ref. 3), they are chemically related. Because this chemical relationship is known and the precise mechanism of action is unknown, the agency believes that there is little justification for abandoning the traditional "stimulant" classification as used by the Panel.

References

(1) "Management of Constipation," edited by Jones, F. A., and E. W. Godding, Blackwell Scientific Publications, London, p. 106, 1972.

(2) Godding, E. W., "Therapeutics of Laxative Agents with Special Reference to the Anthraquinones," *Pharmacology*, 14 (Supplement 1):78–101, 1976.

(3) Fingl, E., "Laxatives and Cathartics," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L. S. Goodman and A. Gilman, The Macmillan Co., New York, p. 977, 1975.

70. Serveral comments questioned the Panel's recommended dosages for senna preparations in § 334.18(h). The comment pointed out that 1 mL senna fluid extract is prepared from 1 g of senna leaf powder and requested that the dose for senna fluid extract be expanded from the 2 mL dose recommended by the Panel to 0.5 to 2 mL to correspond to the recommended dose for senna leaf powder (40 FR 12909). The comment also stated that senna syrup is prepared from a 1 to 4 dilution of senna fluid extract; therefore, the dose for senna syrup should be four times that allowed for senna fluid extract. The comment requested expanding the dosage for senna syrup from the 8 mL dose recommended by the Panel to provide for a range of 2 to 8 mL. The comment also stated that the parenthetical phrase "(single dose)" following the heading "Senna Preparations" in the Panel's anthraquinone dosage table at 40 FR 12909 was confusing and should be clarified. Another comment pointed out that the Panel did not provide for a rectal dose of senna, even though data on a suppository containing senna pod concentrate were submitted to the Panel. The comment requested that the

agency provide for a suppository dosage form in the monograph, with an adult dose of 0.6 to 1 g once or twice daily and a dose for children over 60 pounds that is one-half the adult dose.

The agency agrees that the Panel's recommended dosages for senna preparations are confusing and require clarification. The available data, including the submissions made to the Panel as well as additional references (Refs. 1 through 16), show that it is generally accepted that the active constituent in the various senna preparations is sennosides A and B. In many of the submissions to the Panel, the dose of the various senna preparations was standardized to the sennosides A and B content. Because the active constituent in the senna compounds is sennosides A and B, the agency is providing in the tentative final monograph a dosage for sennosides A and B only. The allowable sources of sennosides A and B, i.e., senna, senna pod concentrate, and senna fruit extract, are listed in the tentative final monograph, but specific dosages for each individual preparation (e.g., senna syrup, senna fluid extract, etc.,) are not provided as the Panel had recommended. Manufacturers may market their products in the formulation of their choice using any of the allowable sources of senna provided that the equivalent dosage conforms to the sennosides A and B dosage provided in the tentative final monograph.

In determining the dose of sennosides A and B to be included in the monograph, the agency found a wide variation in the single oral dose of the marketed products, from 12 mg up to 180 mg equivalent sennosides A and B. The single dose for most of the products ranged from 12 to 50 mg equivalent sennosides A and B with the provision of a repeat dose later in the day, resulting in a maximum total daily dose of 100 mg equivalent A and B. The dose for children 6 to 12 years of age was one-half the adult dose and for children 2 to 6 years of age the dose was one-quarter the adult dose. Because most of the marketed senna products fall within the above dosage schedule, the tentative final monograph reflects this dosage schedule.

The agency is aware of one product with a single adult dose of 160 mg equivalent sennosides A and B. However, this higher dose is not intended for general laxative purposes; it is used to cleanse te colon for x-ray or endoscopic examination. Although the agency believes this higher dose product may remain OTC, it is proposing that the indication be limited to the following: "For use as part of a bowel cleansing regimen in preparing the colon for x-ray or endoscopic examination." In addition, in the tentative final monograph the agency is proposing the following warning for these products in lieu of the general warnings in recommended § 334.50(c) (1) through (4): "Do not use this product unless directed by a doctor."

The agency has reviewed the data submitted on the suppository dosage form of senna containing 652 mg senna pod concentrate (equivalent to 30 mg sennosides A and B) and concludes that it is sufficient to establish general recognition of safety and effectiveness as an OTC laxative. Thirteen studies in 2,289 patients were presented to support the safety and effectiveness of this preparation. In 11 studies the senna suppositories were used alone, and in the other 2 studies they were used as part of a bowel cleansing regimen in preparing the bowel for sigmoidoscopy. The suppositories were usually inserted once or twice daily. The suppositories were shown to be effective in approximately 90 percent of the patients. Based on these data the agency has included in the tentative final monograph a suppository dosage form of 30 mg sennosides A and B to be used once or twice daily. Because none of the submitted studies were conducted in children, a children's dose is not included in the monograph at this time.

References

(1) OTC Volume 090029.
(2) OTC Volume 090058.
(3) OTC Volume 090064.
(4) OTC Volume 090077.
(5) OTC Volume 090078.
(6) OTC Volume 090080.
(7) OTC Volume 090081.
(8) OTC Volume 090082.
(9) OTC Volume 090083.
(10) OTC Volume 090084.
(11) OTC Volume 090085.
(12) OTC Volume 090086.
(13) OTC Volume 090087.
(14) OTC Volume 090088.
(15) "The Anthraquinone Laxatives," Proceedings of a Symposium, *Pharmacology*, 14 (Supplement 1):1–108, 1976.
(16) "Natural Anthraquinone Drugs," Proceedings of the 2nd Symposium on the Anthraquinone Laxatives, *Pharmacology*, 20 (Supplement 1):1–134, 1980.

71. One comment suggested that the adult oral dosage of cascara sagrada extract of 200 mg to 400 mg daily in recommended § 334.18(c)(4) be changed to permit a lower limit of 100 mg to conform with the dosage stated in the "British Pharmacopeia".

The comment did not submit any data to establish that 100 mg is an effective dose for cascara sagrada extract, nor does the "British Pharmacopeia" contain such data. Cascara sagrada extract was recognized in an official United States compendium (Ref. 1) at the time of the Panel's review, and the usual oral dosage was stated as 300 mg. The Panel expanded this dosage to permit a wider range of 200 to 400 mg based on the data it reviewed. The current official United States compendia do not state a usual dosage for cascara sagrada extract. Therefore, in the absence of additional data demonstrating that a dosage of 100 mg of cascara sagrada extract is effective, the dosage is not revised in the tentative final monograph.

Reference

(1) "The National Formulary", 14th Ed., American Pharmaceutical Association, Washington, p. 123, 1975.

72. One comment suggested that the phrase "or adjust to individual requirements" be added to the required dosage statements for senna. The comment stated that consumers should be allowed to adjust the dosage because variations in laxative responses from person to person and in the same person at different times are well known. The comment pointed out that the Panel recognized that the smallest dose of a laxative that is effective is the optimal dose to use (40 FR 12905) and that Jones and Godding (Ref. 1) recognized that sublaxative doses of senna pod give symptomatic relief from colonic pain. The comment concluded that, although a dosage range is given for some senna ingredients, individuals should be given latitude to adjust their own particular dose, even if it does not fall within the limits set by the Panel.

The dosage ranges and single doses provided in the monograph for senna ingredients are the minimum effective dose and the maximum safe dose for most consumers. This determination is based on a review of the scientific data, including the text cited by the comment, and marketing experience for the ingredients. A dose lower than that provided in the monograph may produce a laxative effective in some individuals and a dose above the maximum may be safe in some individuals. For most consumers, however, decreasing the dose below the minimum effective level may not result in effective laxation, and increasing the dose above the maximum safe dose may result in the consumer's ingesting more drug than is necessary to achieve laxation, thus creating a risk of side effects.

The labeling of senna products will contain directions for use that reflect a safe and effective dosage. The dosage range for senna already takes into

account the varying requirements of some individuals and reflects safe and effective upper and lower limits for a majority of consumers. Therefore, the agency does not believe that the phrase "or adjust to individual requirements" is necessary in the labeling.

Reference

(1) "Management of Constipation," edited by F. A. Jones and E. W. Godding, Blackwell Scientific Publications, London, p. 42, 1972.

73. One comment disagreed with the Panel's recommended oral dosage and directions for bisacodyl. The comment requested that the dose of 5 to 15 mg in recommended § 334.18(b) be followed by the phrase "(usually 10 mg) * * * ", which, according to the comment, is the labeled does on a currently marketed bisacodyl product and which is supported by the bulk of the existing clinical data. In further, support, the comment contended that an article by Wolcott (Ref. 1) reported that a dose of 5 mg of bisacodyl caused cramping and failed to produce an adequate laxative effect in some patients. One comment disagreed with the Panel's recommended directions for taking bisacodyl at bedtime. The comment contended that there is no clinically valid reason for such a restriction and that for some consumers, e.g., housewives, it may be more convenient to take bisacodyl in the morning. The comment recommended revising § 334.18(b) accordingly.

Although bisacodyl is most often used in a dose of 10 mg, there is no reason to add "(usually 10 mg)" to the dosage information contained in the monograph. The Panel reviewed data that supports the safety and effectiveness of the 5 to 15 mg dosage range, and the agency agrees with the Panel's recommendation.

The agency believes the comment has misunderstood the article by Wolcott (Ref. 1). Wolcott reported that only 25 of 150 patients required a dose of bisacodyl greater than 5 mg while only a "few of the patents experienced moderate cramping." Further, Wolcott studied chronically ill patients with severe elimination problems, and such patients do not represent a population who would normally take an OTC laxative drug product without professional supervision.

The agency agrees that there is no clinically valid reason for restricting the use of bisacodyl to any particular time of day and is not including any such reference in the tentative final monograph. Also, information on the labeling regarding expected time of action (see comment 23 above) will provide consumers with sufficient information to choose the time of day for taking bisacodyl that is best suited to their schedule.

Reference

(1) Wolcott, L.E., "Laxation in Patients with Cronic Disease Utilizing Bisacodyl," *Archives of Physical Medicine and Rehabilitation*, 44:375–377, 1963.

74. One comment suggested several revisions in the Panel's recommended warnings for bisacodyl in § 334.60(b). The comment pointed out that there are two dosage forms of bisacodyl, a rectal suppository and an oral enteric-coated tablet, and that some warnings apply only to the enteric-coated tablet and not the suppository. The comment recommended placing these warnings under a section specifically intended for bisacodyl enteric-coated tablets. One comment stated that the warning in recommended § 334.60(b)(2), which warns against the use of bisacodyl enteric-coated tablets in children under 3 years of age, should be revised to warn against use in children under 6 years of age except under the supervision of a doctor because many children between 3 and 6 years of age are not able to swallow an enteric-coated tablet without chewing it. The comment also pointed out that in the recommended warning in § 334.60(b)(4), "This product may cause abdominal discomfort, faintness, rectal burning, and mild cramps," "rectal burning" applies only to the suppository. The comment suggested including the complete warning for the bisacodyl suppository only and deleting the phrase "rectal burning" for the enteric-coated tablet.

The agency agrees with the comment. In the tentative final monograph the warnings are separated into one section for the enteric-coated tablets and another for the suppository. The tentative final monograph is also revised to warn against the use of bisacodyl enteric-coated tablets in children under 6 years of age, unless directed by a doctor, because children between 3 and 6 years of age may have difficulty swallowing the enteric-coated tablet without chewing it. These tablets should not be chewed because gastric irritation may occur if the enteric coated is destroyed (Ref. 1).

Reference

(1) Fingl, E., "Laxatives and Cathartics," *in* "The Pharmacological Basis of Therapeutics", 5th Ed., edited by L.S. Goodman and A. Gilman, Macmillan Publishing Co., New York, pp. 976–986, 1975.

75. One comment questioned the following language in recommended § 334.60(b)(5) for products containing bisacodyl: "Store in a cool place at temperatures not above 86 °F (30 °C)." The comment pointed out that FDA has long recognized the USP definition of "cool" as any temperature between 46 and 59 °F (8 and 15 °C). The comment stated that FDA should continue to use this definition and should delete the word "cool" from the statement in § 334.60(b)(5). The comment also suggested that the Centigrade equivalent required in this statement be optional because few people in the United States relate exclusively to Centigrade temperatures. The comment recommended revising § 334.60(b)(5) to read, "Store at temperatures not greater than 86 °F."

The agency agrees that in view of the USP definition of the word "cool" (Ref. 1), the word "cool" should be deleted from the statement in § 334.60(b)(5), but disagrees that the Centigrade equivalent should be optional in this statement. The agency, however, will depart from the USP format of using only Centigrade temperature by also requiring the Fahrenheit temperature to be stated, because consumers are more familiar with Fahrenheit temperatures. In the tentative final monograph the agency is revising this statement to read as follows: "Store at temperatures not above 86 °F (30 °C)."

Reference

(1) "The United States Pharmacopeia," 20th Revision, United States Pharmacopeial Convention, Inc., Rockville, MD, p. 8, 1980.

76. One comment requested that the professional labeling for bisacodyl in recommended § 334.80(f) be expanded to include its use in postoperative care, in colostomies, for chronic constipation and bowel retraining, in antepartum care, in preparation for delivery, and in postpartum care. The comment submitted date (Ref. 1) which, it claimed, demonstrates the safety and effectiveness of bisacodyl for these professional uses.

Based on its evaluation of the data submitted and the National Academy of Science/National Research Council's (NAS/NRC) drug efficacy study reports for bisacodyl, published in the **Federal Register** of May 24, 1972 (37 FR 10521), the agency tentatively concludes the following:

Postoperative care, antepartum care, preparation for delivery, and postpartum care are simply specific professional use indications for an effective laxative. As such, they are acceptable for bisacodyl professional labeling. The NAS/NRC reached the same conclusion with respect to these claims.

The data do not support the professional use of bisacodyl in colostomy care. In this regard, only one study (Ref. 2) was submitted. The study suggests that less irrigation was required with bisacodyl, but the study was conducted using an oral solution of bisacodyl rather than the currently marketed dosage forms of tablets and suppositories. In addition, the presentation of the data is rudimentary and the data are too seriously deficient in detail to permit a complete evaluation. This study was also reviewed by the NAS/NRC and found less than convincing.

The data do not support a claim for the use of bisacodyl in chronic constipation. The NAS/NRC appeared to consider bisacodyl effective for chronic constipation but felt that the full range of possible toxic effects from long continued use was not fully known. A study by Mandel and Silinsky (Ref. 3) showed bisacodyl more effective than glycerin suppositories in a group of elderly and chronically constipated people but did not address the question of chronic use of bisacodyl. Two additional studies (Refs. 4 and 5) tend to support the initial effectiveness of bisacodyl in chronic constipation; however, the data are insufficiently characterized to provide strong support for this claim. In two other studies (Refs. 6 and 7), the data are too seriously deficient in detail to permit any detailed evaluation. The remaining study (Ref. 8) is irrelevant because it compares only single doses of several agents. No study assesses the chronic (continued) use of bisacodyl in chronic constipation. As such, additional data are necessary before a professional use claim of chronic constipation may be made for bisacodyl.

The data do not support the professional use of bisacodyl in bowel retraining. The NAS/NRC appeared to consider bisacodyl effective for bowel retraining but felt that the full range of possible toxic effects from long continued use was not fully known. Four studies were submitted in support of the bowel retraining claim (Refs. 9 through 12). The studies submitted were generally open studies, which offered minimal to no data, or merely provided the opinion of the investigator. Essentially the studies provided no evidence to indicate the usefulness of bisacodyl in a program of bowel retraining.

The agency's comments and evaluations on the data and its recommendation for additional studies are on file in the Dockets Management Branch (Ref. 13).

References

(1) Comment No. C0041 and Amendment 002, Docket No. 78N-036L, Dockets Management Branch.

(2) Stevenson, T.B., and J.C. Hawk, "Use of a Contact Laxative Solution (Dulcolax) as an Adjunct in Colostomy Control," *American Surgeon*, 30:118–122, 1964.

(3) Mandel, L., and J. Silinsky, "Bisacodyl (Dulcolax): an Evacuant Suppository. A Controlled Therapeutic Trial in Chronically Ill and Geriatric Patients," *Canadian Medical Association Journal*, 83:384–387, 1960.

(4) Berk, M.S., "Comparative Study of Bowel Control in Nursing Home Patients," *Medical Times*, 97:106–112, 1969.

(5) Jackson, B., "Clinical Trial of a New Drug in Obstinate Constipation," *Canadian Nurse*, 54:1107–1109, 1958.

(6) Rider, J.A., "Treatment of Acute and Chronic Constipation With Bisoxatin Acetate and Bisacodyl: Double-Blind Crossover Study," *Current Therapeutic Research*, 13:386–392, 1971

(7) Broatch, D.L., A. Wilson, and J. Thompson, "The Treatment of Constipation in the Elderly," *Nursing Times*, November 29, 1968.

(8) Christopher, L.J., "A Controlled Trial of Laxatives in Geriatric Patients," *Practitioner*, 202:821–825, 1969.

(9) Happert, J.L., "Clinical Trials of a New Contact Laxative," *Gaz. Hop., 135:1145–1148, 1963.*

(10) Neff, F.M., "Some Problems in the Management of Constipation," *California Clinician*, November, 1961.

(11) Niswander, L.C., "Bowels Can Be Retrained and Controlled," *Hospital Management*, 93: 6, 8, and 10, 1962.

(12) Wolcott, L.E., "Laxation In Patients With Chronic Disease Utilizing Bisacodyl," *Archives of Physical Medicine and Rehabilitation*, 44:375–377, 1963

(13) Letter from William E. Gilbertson, FDA, to Pam C. Mead, Boehringer Ingelheim, Ltd., coded ANS LET 010, Docket No. 78N-036L, Dockets Management Branch.

77. One comment recommended that the daily dosage of 750 to 900 mg for dehydrocholic acid recommended by the Panel in § 334.18(f) be changed to 750 to 1,000 mg. The comment pointed out that the "National Formulary" (Ref. 1) provides a dosage of 500 mg three times daily, which gives a maximum daily dose of 1,500 mg. The comment stated that, in view of the low toxicity of dehydrocholic acid, an increase in the maximum daily dose from 900 mg to 1,000 mg should be acceptable. Lastly, the comment pointed out that the "Physicians' Desk Reference" (Ref. 2) and "Facts and Comparisons" (Ref. 3) list only a 250-mg tablet strength for dehydrocholic acid and, as such, the recommended 900 mg maximum daily dosage would be difficult to obtain.

The agency has reviewed the data submitted to the Panel for dehydrocholic acid (Refs. 4 and 5) and notes that they provide for a single ingredient product to be marketed as a 250-mg tablet with a dosage in multiples of 250 mg, i.e., one or two tablets three times a day. This dosage provides a maximum daily dose of 1,500 mg. Also, in the minutes of its November 16, 1973 meeting, the Panel found dehydrocholic acid to be safe and effective at a maximum daily dose of 1,500 mg. Therefore, the dosage for dehydrocholic acid provided in the Panel's report and recommended monograph is in error and the tentative final monograph is revised to provide for a daily dose of 750 to 1,500 mg.

References

(1) "The National Formulary," 14th Ed., American Pharmaceutical Association, Washington, pp. 171–172, 1975.

(2) "The Physicians' Desk Reference," 29th Ed., Medical Economics Co., Oradell, NJ, 1975.

(3) "Facts and Comparisons," Facts and Comparisons, Inc., St. Louis, 1975.

(4) OTC Volume 090079.

(5) OTC Volume 090097.

78. One comment pointed out that a harmless pink or orange discoloration may appear in alkaline urine when laxatives containing phenolphthalein are used and urged that an explanation statement to that effect be included in the labeling. Another comment suggested that such a statement might mislead the consumer into thinking that discolored urine was always to be disregarded, whereas discoloration may indicate the presence of glomerulonephritis, tumors, and other serious conditions.

The Panel was aware that up to 15 percent of a therapeutic dose of phenolphthalein may be absorbed and excreted by the kidney, giving a pink color to alkaline urine (40 FR 12910). However, the Panel apparently did not consider this discoloration to be of signification concern to require a warning. The agency concurs with the Panel's decision and agrees with the second comment that requiring a warning about pink or orange discoloration may mislead consumers. A warning would be more confusing than helpful and is not necessary for the short-term safe use of OTC laxatives containing phenolphthalein.

H. Comments on Stool Softener Laxatives

79. Several comments objected to the classification of "stool softeners" as "laxatives." The comments contended that it was incorrect and misleading to apply the term "laxative" to these agents when used alone because they do not increase peristaltic activity or act directly on the bowel, but merely penetrate and soften the stool to ease

passage. One comment argued that the use of the term "laxative" in connection with single-ingredient stool softeners would be misleading because it would imply to consumers that the product would promote a relatively quick laxative effect. One comment urged that single-ingredient stool softeners as labeled as a "a stool softener and aid in the relief of constipation." Another comment suggested that such products be labeled as "non-laxative constipation remedies" and/or "for the prevention and treatment of constipation."

The agency disagrees with these comments for several reasons. Stool softeners are chemically distinct from other classes of laxatives in that they are surface-active agents that lower surface tension. Mixed in the stool, they allow sufficient water and fat penetration to have a softening effect on the stool, thus permitting easier bowel movement (Ref. 1). Although stool softeners affect the stool rather than the bowel, their action is consistent with the broad definition of a laxative as being "any agent used for the relief of constipation." This definition of laxatives does not distinguish whether the agency acts on the bowel to increase peristaltic activity or on the stool itself, so long as it acts to relieve constipation. The mode of action of stool softeners is not sufficiently different from that of other laxative agents to warrant their differentiation from other types of laxatives, but these products should be labeled as "stool softener laxatives" in order to provide the best information to the consumer.

The agency is proposing in the tentative final monograph that a time frame for expected relief of constipation be included in the labeling of stool softener laxatives (see comment 23 above.) Therefore, it appears unlikely that the consumer will be misled into expecting "quick" laxation with a stool softener laxative.

Reference

(1) Fingl, E., "Laxatives and Cathartics" in "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A Gilman, Macmillian Publishing Co., Inc., New York, pp. 977–986, 1975.

80. Two comments argued that the warning in recommended § 334.50(c)(3) and § 334.62(a) limiting use to 1 week should not apply to single-ingredient stool softener laxatives. The comments argued that this limitation was inappropriate because stool softeners act on the stool and not on the bowel, thus their action does not affect bowel function. One of the comments suggested that the labeling restriction be revised to read, "Caution: Not for prolonged use unless directed by a physician." Several other comments contended that the general warning in recommended § 334.50(c)(3), "this product should not be used for a period of longer than 1 week except under the advice and supervision of a physician", and the specific ingredient warning for stool softeners in recommended § 334.62(a), "This product should be used only occasionally, but in any event no longer than daily for 1 week," are duplicative and that the specific warning in § 334.62(a) should be eliminated.

Although stool softeners do not act directly on the bowel, they do soften the stool and thereby aid in evacuating the stool, thus relieving constipation. As discussed by the Panel in its report (40 FR 12906), when it is necessary to use any laxative, including stool softeners, to facilitate the evacuation of the bowel for more than 1 week, the cause of the constipation should be investigated by a doctor because a sudden change in bowel habits may be an indication of serious disease.

However, the agency agrees that the general warning in recommended § 334.50(c)(3) is duplicative of recommended § 334.62(a) and therefore, the Panel's recommended warning in § 334.62(a) is not included in the tentative final monograph.

81. One comment requested that d-calcium pantothenate be classified as a Category I stool softener ingredient, contending that the Panel's classification of d-calcium pantothenate as a Category III stimulant laxative was incorrect. According to the comment, d-calcium pantothenate has been and is a stool softener, not a stimulant, laxative. The comment submitted one clinical study (Ref. 1), which, it claimed, demonstrates that this ingredient is a Category I stool softener laxative. The comment also stated that, to its knowledge, no untoward side effects have been experienced with a combination product containing d-calcium pantothenate.

The agency notes that "calcium pantothenate" is the USP and USAN name for "calcium D-pantothenate." The only study submitted in support of the classification of calcium pantothenate as a Category I stool softener was conducted using calcium pantothenate in combination with the Category I stimulant laxative danthron. The study is inadequate because no comparison was made between the combination and the two ingredients contained in the combination when used alone. No objective measurements or analysis were made, e.g. stool weight/volume, transit time, etc. The only data analysis that is provided with the study is an analysis of "panelist's preference", which is not a valid measurement of laxative effectiveness. Further, no data are provided that support the comment's claim that calcium pantothenate is a stool softener laxative as opposed to the Panel's classification as a stimulant laxative. Therefore, it will be necessary to provide additional effectiveness data before the agency may reclassify calcium pantothenate as a Category I stool softener laxative. Although the Panel also recommended at 40 FR 12918 that safety studies should be provided, the agency believes that further safety studies are unnecessary. Pantothenic acid, the active constituent of calcium pantothenate, is a common water-soluble vitamin that is present in all human tissues. It has no outstanding pharmacodynamic action and is essentially nontoxic.

The agency's comments and evaluation on the data are on file in the Dockets Management Branch (Ref. 2).

References

(1) Comment No. 23, Docket No. 78N–036L, Dockets Management Branch.

(2) Letter from William E. Gilbertson, FDA, to Raymond Spector, C.F. Kirk Laboratories, Inc., coded ANS LET 006, Docket No. 78N–036L, Dockets Management Branch.

I. Comment on Miscellaneous Laxatives

82. One comment requested that recommended § 334.22 be revised to provide for a carbon dioxide-releasing suppository consisting of 0.6 g sodium bicarbonate and 0.9 g potassium bitartrate, releasing approximately 90 mL carbon dioxide per suppository. The comment submitted two references in support of its request (Refs. 1 and 2). The comment stated that the directions for use are the same as for the product identified in recommended § 334.22(a).

The two studies submitted by the comment support the inclusion of the suppository in the monograph. The study be Bolton and Benson (Ref. 1) was an open trial in which 321 patients were given one rectal suppository on the morning of the second post-partum day to re-establish bowel function. The patients were questioned and 70.5 percent reported that they experienced effective bowel movements. In 61 percent the urge to evacuate occurred within 30 minutes after administering the suppository. Banner (Ref. 2) reported that use of a single suppository was successful in approximately 60 to 65 percent of patients. Use of a second suppository 30 minutes after the first one in some patients increased efficiency by 5 percent. He also concluded that the suppository is a

satisfactory substitute for enemas during the postpartum state. The Panel at 40 FR 12913 recognized the safety and effectiveness of carbon dioxide-releasing suppositories by including another carbon dioxide-releasing suppository in the monograph (containing sodium biphosphate, sodium acid pyrophosphate, and sodium bicarbonate). Although the tartrate/bicarbonate suppository releases less carbon dioxide than the one in the recommended monograph (90 mL as compared with 230 mL), experience with this suppository demonstrates its safety and effectiveness. Therefore, the tartrate suppository is included in this tentative final monograph.

References

(1) Bolton, R. N., and R. C. Benson, "A Unique Post Partum Rectal Suppository," *Obstetrics and Gynecology*, 13:501–503, 1959.

(2) Banner, E. A., "Rectal Suppositories as Substitutes for Enemas in the Post Partum Period," *Staff Meetings of the Mayo Clinic*, 28:567–568, 1953.

J. Comments on Laxative Combinations

83. Several comments objected to the Panel's recommendation to limit the number of laxative active ingredients allowed in a combination product (40 FR 12922). The comments criticized the Panel for seeking an absolute prohibition against combinations of three or more active ingredients based solely on what the comments characterized as subjective and arbitrary opinion. The comments stated that the Panel's recommendation was not founded upon scientific documentation and conflicts with both the Panel's and FDA's expressed willingness to permit manufacturers to show the rationality of a combination laxative product by demonstrating that each ingredient makes a therapeutic contribution to the overall effectiveness of the product. One comment stated that a prohibition against combining more than two ingredients required data establishing a possible risk of toxicity, synergistic effect, allergies, idiosyncratic reactions, or drug interactions.

The agency agrees with the comments that a fixed limit need not be set on the number of active ingredients a laxative drug product may contain. However, the agency believes the consumer is little served by a product containing multiple ingredients if laxation can be achieved safely and effectively by a smaller number of ingredients. Both the General Guidelines for OTC Drug Combination Products (Ref. 1) and the regulations at 21 CFR 330.10(a)(4)(iv) provide that an OTC drug product may combine two or more safe and effective active ingredients provided the product meets the combination policy in all respects.

If a manufacturer can show that a laxative combination meets the general guidelines for OTC combination drug products, the agency will have no objection to the product containing two or more Category I laxative ingredients. However, the comments did not submit any data to support specific combinations containing more than two laxative active ingredients. New data in support of such combinations may be submitted for up to 12 months following the publication of this document. Also, the agency has evaluated the Panel's combination formula in recommended § 334.31(b) in relation to marketed combination laxative products, the regulations (§ 330.10(a)(4)(iv)), and the combination guidelines (Ref. 1) and concludes that the formula allows those combinations of laxative ingredients identified in § 334.32 to meet these criteria for safe and effective OTC use. Combinations containing more than two laxative ingredients would also have to comply with the requirements of this formula. Any manufacturer wishing to market a product that is not within the specifications of the formula may submit data to support such a request.

Reference

(1) Food and Drug Administration, "General Guidelines for OTC Drug Combination Products, September 1978," Docket No. 78D–0322, Dockets Management Branch.

84. Several comments stated that the Panel failed to provide a mechanism for manufacturers to have Category II and Category III combination drug products reclassified to Category I status except through a citizen petition or a new drug application. Further, the comments argued that the Panel, by limiting the Category I combinations to those listed in recommended § 344.32, was denying manufacturers the opportunity to develop and submit data in the future for establishing additional combinations as Category I. The comments urged the agency to reject the Panel's recommendation.

The agency agrees that the Panel was in error in implying that the only mechanism for reclassifying Category II or Category III combinations was through a citizen petition or the new drug procedures. There are several mechanisms by which data can be submitted to reclassify Category II and III combinations to Category I. The OTC drug review regulations provide for new data to be submitted during the 90-day comment period following publication of the Panel's report. New data and information to support conditions excluded from the monograph may be filed for 12 months following the publication of this tentative final monograph in accordance with the revised Category III procedures published in the **Federal Register** on September 29, 1981 (46 FR 47730). In all cases, data demonstrating a combination to be generally recognized as safe and effective must be submitted before a new combination can be included in the monograph.

85. One comment expressed the opinion that one of the underlying policy reasons for the OTC drug review is to facilitate the reformulation of combination products. Specifically, the comment stated that where a combination contains a Category III ingredient, the manufacturer should be permitted to replace the Category III ingredient with a similar Category I ingredient, so long as the product is otherwise appropriately formulated and labeled.

The agency agrees with the concept expressed by the comment but points out that the combination product resulting from such a reformulation must be among the Category I combinations listed in this tentative final monograph.

86. One comment was concerned that the Panel made no judgments with respect to the rationality of the combinations it recommended for Category III status. The comment noted that, in approving Category I combinations, the Panel applied its criteria for determining Category I combinations (40 FR 12921), and in so doing actually expressed a judgment that only these combinations are rational concurrent therapy for a significant proportion of the target population. The comment concluded that it should not be "presumed" that all other combinations are irrational in the absence of an express judgment by the Panel.

The agency agrees. The Panel did not express an opinion regarding the rationality of every specific combination. Therefore, there may be rational combinations that are not specifically listed in Category I.

87. Two comments objected to the Panel restricting the allowable OTC laxative combination's to those listed in recommended § 334.32. One comment argued that specifying the ingredients allowed in a combination as is done in recommended § 334.32 (i.e., from individual products) is inappropriate. The comments suggested that any combination of Category I ingredients from a particular drug class such as laxatives, be permitted as long as the combination is in accord with the

general standards stated in § 330.10(a)(4) and the combination policy stated in § 330.10(a)(4)(iv).

These comments were submitted before the agency's guidelines for OTC combination products became available in 1978 (Ref. 1). Paragraph 6 of these guidelines states that final OTC drug monographs will list the specific ingredient combinations permitted for marketing under the monograph. Thus, the Panel's recommendations in § 334.32 are consistent with the current guidelines.

Reference

(1) Food and Drug Administration, "General Guidelines for OTC Drug Combination Products, September 1978," Docket No. 78D-0322, Dockets Management Branch.

88. Several comments recommended revising recommended § 334.32 to list permitted combinations by pharmacological class rather than by specific ingredient. The comments pointed out that the specified combinations of ingredients actually represent 10 types of combinations by pharmacological class, i.e., bulk/bulk, bulk/lubricant, bulk/stimulant, bulk/stool softener, lubricant/stimulant, lubricant/saline, saline/stimulant, stimulant/stimulant, stimulant/stool softener, and stool softener/hyperosmotic. The comments argued that because the Panel found the specific ingredients in each of these pharmacological classes to be safe and effective, every ingredient in each class should be safe and effective in a combination and should be interchangeable.

Criteria for establishing combinations as Category I are provided in the OTC Combination Guidelines (Ref. 1). Paragraph 6 of these guidelines states, "In those cases where the data are sufficient to support a finding by the agency that several ingredients in a therapeutic category can be considered interchangeable for purposes of formulating combinations, the monograph will so state and list those ingredients. This is the preferred approach and will be done whenever supported by data and the opinion of experts." Therefore, the agency agrees with the concept of listing combination drug products by pharmacological class, but does agree that sufficient data have been provided to allow all of the laxatives in each class to be interchanged randomly for the purpose of forming combinations. Further, as pointed out in comment 22 above, the precise mechanisms of action of laxative ingredients are not well known and insufficient data are available on their combined effects. Therefore, the combination section of the tentative final monograph is revised to group the Panel's recommended combinations by pharmacological class. However, it has not been revised to allow all of the ingredients in a class to be used interchangeably. Combinations for which adequate data exist have been included in the monograph. However, data are necessary to establish the safety and effectiveness of other specific combinations or to demonstrate that the specific ingredients in a pharmacological class are chemically and pharmacological interchangeable.

Reference

(1) Food and Drug Administration "General Guidelines for OTC Drug Combination Products, September 1978," Docket No. 78D-0322, Dockets Management Branch.

89. Two comments requested that the monograph be expanded to include "bowel cleansing systems," i.e., products containing several different laxative ingredients for sequential administration at specified intervals, for use in evacuating the bowel prior to surgery, colon x-ray, or endoscopic examination. The comments contended that this special use of laxatives is not covered by the Panel's recommended monograph even though such products are being sold OTC. The comments submitted studies (Refs. 1 and 2) on the use of two different bowel cleansing systems: (1) Magnesium citrate oral solution, bisacodyl tablets, and bisacodyl suppositories and (2) magnesium citrate oral solution, phenolphthalein, and sodium bicarbonate-sodium bitartrate (carbon-dioxide releasing) suppositories.

The agency reviewed the data submitted by the comments and Tentatively concludes that the two bowel cleansing systems are generally recognized as safe and effective for use in evacuating the bowel prior to surgery, colon x-ray, or endoscopic examination. The agency agrees with the comments that these bowel cleansing systems should be included in the OTC monograph and is proposing a statement of identity and a definition for these products in this tentative final monograph. However, the agency does not believe that bowel cleansing systems should be used for general laxative purposes and, therefore, is proposing to limit their indication to the following: "For use as part of a bowel cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination. In addition, the following warning is being proposed for these products in lieu of the general warnings in recommended § 334.50(c)(1) thru (4): "Do not use this product unless directed by a doctor." The agency also recognizes that in most of the submitted studies the bowel cleansing system was part of an overall regimen that included overhydration and certain dietary restrictions. Therefore, in addition to the appropriate directions for use for each laxative component of the bowel cleansing system, the agency is proposing to require manufacturers to supply information regarding fluid and dietary restrictions.

References

(1) Comment No. C00015, Docket No. 78N-0036L, Dockets Management Branch.

(2) Comment No. C00043, Docket No. 78N-0036L, Dockets Management Branch.

90. One comment argued that the Panel's restriction on the concurrent use of vitamins and minerals with a laxative should not apply to dietary bran products that are sold as cereals. The comment pointed out that FDA favors the fortification of cereals with vitamins and minerals (see the **Federal Register** of June 14, 1974; 39 FR 20989). The comment also disagreed with the Panel's position that a significant target population does not exist for concurrent use of laxatives with vitamins and minerals. The comment stated that people over 50 years of age often require vitamins and minerals concurrently with laxatives becuase if is well documented that the elderly are often on inadequate diets (Refs. 1 and 2). The Comment concluded that when the Panel stated that vitamins and minerals should not be added to laxative products, the Panel had drug type laxatives in mind and not cereals.

The agency agrees with the comment. As discussed in comment 38 above the agency does not intend to regulate in this monograph high fiber cereals that are offered only as foods.

References

(1) Rao, D. B., "Problems of Nutrition in the Aged," *Journal of the American Geriatrics Society*, 8:363-367, 1973.

(2) Smith, A. N. E., "Nutrition Survey and Problems of Detection of Malnutrition in the Elderly," *Nutrition*, 4:218-223, 1970.

91. One comment concurred with the Panel's finding at 40 FR 12916 that there is no evidence that the addition of vitamins and minerals to a laxative preparation contributes to a laxative effect and that constipation and vitamin needs ordinarily bear no relationship to each other. The comment noted, however, that the Panel apparently did not decide that minerals were unrelated to constipation. According to the comment, this fact constituted a silen'

recognition by the Panel of the constipating effect of iron. The comment pointed out that its combination vitamin and mineral products also contain a stool softener laxative. the comments stated that these products have never claimed a laxative effect and that the stool softener ingredient is included solely to overcome the constipating effect of iron.

There are two aspects to this comment: (1) The addition of vitamins/minerals to a laxative drug product intended primarily for laxative use and (2) the addition of an ingredient to a vitamin/mineral product for the purpose of alleviating the constipating effects of iron.

In the first case, the Panel concluded "that the addition of various vitamins and minerals, including trace elements, to laxative products is irrational concurrent thereapy and places such combinations in Category II." The agency concurs with this conclusion because a target population which could benefit from such combinations has not been adequately demonstrated. Vitamin/mineral deficiency and constipation do not routinely occur concurrently, thus the need for such a combination does not exist. In addition, OTC laxative drug products are intended only for occasional short-term use, whereas vitamins and minerals are normally taken daily for long-term dietary supplementation.

In the second case (the addition of an ingredient to a vitamin-mineral product to overcome the constipating effects of iron), the agency recognizes that iron may be constipating in some people. However, vitamin/mineral products that are intended for dietary supplementation are considered to be foods and ingredients added to them are also regulated under the food provisions of the Federal Food, Drug and Cosmetic Act.

92. One comment requested that 3 g psyllium seed (blond) and 30 mg casanthranol in combination be recognized as Category I. The comment argued that both ingredients were Category I laxatives and that a similar combination containing psyllium and senna concentrate was recognized as Category I. According to the comment, the Panel's only reason for failing to place the combination of psyllium seed (blond) and casanthranol in Category I was that it was unaware that a product, with only a slight difference in composition from the proposed Category I combination, had been marketed for 25 years with no known safety of effectiveness problems.

The Panel recognized the rationality of combining bulk laxatives with stimulant laxatives and included a combination containing psyllium and senna in the recommended monograph. Because senna and casanthranol are chemically and pharmacologically related anthraquinone laxatives, the agency believes it is rational to include in the monograph the combination mentioned in the comment. Accordingly, this combination is proposed as Category I in this tentative final monograph.

93. A comment requested that the combination of karaya gum and cascara sagrada be added to the list of Category I laxative combinations recommended § 334.32. The comment submitted data to establish that this combination of two Category I ingredients meets all criteria established by the Panel, as well as all criteria set forth in § 330.10(a)(4)(iv) (21 CFR 330.10(a)(4)(iv)) for Category I combination drug products.

The agency has reviewed the data submitted by the comment and has determined that the data provide support for the safety of the two ingredients when combined. The data consisted chiefly of acute oral toxicity and laxative effectiveness studies in Sprague-Dawley rats. Effectiveness studies in humans are needed. These studies should show that the conbination is, on a benefit-risk basis, equal to or better than each of the active ingredients used alone at its therapeutic dose. Therefore, the agency considers this combination a Category III combination and has not included it in the tentiative final monograph.

94. A comment, which was accompanied by a single supporting study (Ref. 1), requested that the combination of danthron (75 mg) and sodium lauryl sulfate (25 mg) be placed in Category I as a combination laxative product.

The study cited by the comment was designed to determine the adjuvant effect of sodium lauryl sulfate, at levels of 100 to 200 mg, in buffering or lowering the threshold of abdominal discomfort from high doses (300 to 600 mg) of danthron. No data were presented on the combination at the dosage levels proposed by the comment nor were data presented demonstrating any effect of sodium lauryl sulfate other than as a pharmaceutical adjuvant to lower the side effects of danthron. Therefore, the combination is classified as Category III and is not included in the tentative final monograph.

Reference

(1) Marks, M. M., "A Clinical Evaluation of a New Cathartic Compound," *Diseases of the Colon and Rectum*, 4:131–133, 1961.

95. A comment pointed out that data for the combination of magnesium hydroxide and simethicone labeled for the indication "lower abdominal distress as a concomitant of constipation" were submitted to the OTC Miscellaneous Internal Drug Products Panel, but not to the Laxative Panel. The comment noted that the Laxative Panel concluded at 40 FR 12921 that "products combining laxative ingredient(s) with other ingredients having nonlaxative pharmacologic effects are considered irrational unless it can be shown that there is a significant target population requiring concurrent treatment of symptoms that require laxative(s) and nonlaxative(s) in combination." Because data on the combination of magnesium hydroxide and simethicone were neither submitted to nor considered by the Laxative Panel, the comment requested that the agency not take any classification action regarding this combination until the OTC Miscellaneous Internal Drug Products Panel had completed its review of the combination.

The agency notes the Miscellaneous Internal Panel in its report on OTC Digestive Aid Drug Products published in the **Federal Register** of January 5, 1982 (47 FR 454), classified magnesium hydroxide and simethicone, both alone and in combination, in Category III for the treatment of the symptoms of immediate postprandial upper abdominal distress and the symptoms of intestinal distress (lower abdominal distress).

In addition, that Panel further concluded that the intestinal distress syndrome (lower abdominal distress) is self-limited, not attributable to any known organic disease, and is not accompanied by constipation or diarrhea.

The comment included no data to demonstrate the effectiveness of the combination of magnesium hydroxide and simethicone or to show that there is a significant target population requiring concurrent treatment of lower abdominal distress and constipation. Therefore, the agency is unaware of any data to establish that lower abdominal distress and constipation occur concomitantly or that the combination of magnesium hydroxide and simethicone is safe and effective for the idication proposed by the comment. Accordingly, the combination is Category II in this laxative tentative final monograph.

96. Two comments urged that recommended § 334.32(a) (10), (11), (12), and (14) be revised to permit the use of mineral oil emulsion as an alternative

ingredient for combinations of plain mineral oil with casanthranol, cascara sagrada, cascara sagrada fluid extract, and phenolphthalein, respectively. The comments pointed out that a number of the pertinent combination laxative drug products considered by the Panel in recommending these permitted combinations do in fact contain mineral oil in the form of mineral oil emulsion. The comments argued that it is inconsistent to classify plain mineral oil as an allowable ingredient in these combinations and to exclude mineral oil emulsion as an alternative ingredient in the same combination.

As discussed in comment 47 above, the agency has deleted reference to mineral oil emulsion from the monograph. Although manufacturers may choose to formulate the allowable mineral oil combination in an emulsion formulation, the monograph will list only mineral oil as the active ingredient in the allowable combinations.

97. One comment requested that the combination of calcium pantothenate and danthron be classified as Category I. The comment submitted data (Ref. 1) which, it claimed, demonstrate that the combination of calcium pantothenate and danthron is as effective as the Category I combination of docusate sodium and danthron.

The agency tentatively concludes that the data submitted are insufficient to support reclassifying the combination of danthron and calcium pantothenate into Category I. The same study was submitted to support calcium pantothenate as a single ingredient. (See comment 81 above.) Because no comparisons were made of the combination and the ingredient alone, the contribution of the ingredients to the combination has not been shown. In addition, the study had other problems that have already been discussed in comment 81 above. Therefore, the combination of danthron and calcium pantothenate remains in Catgeory III in this tentative final monograph.

Reference

(1) Comment No. 00023, Docket No. 78N-036L, Dockets Management Branch.

K. Comments on Data Pertinent for Laxative Ingredient Evaluation

98. Several comments addressed the testing guidelines recommended to move a laxative ingredient from Category III to Category I. Some comments were opposed to the guidelines, indicating that they were unclear, unnecessary, inconsistent, and possibly confusing. Other comments indicated that the testing guidelines provided inadequate time to complete the required testing. One comment stated that manufacturers should be allowed to use other well-controlled and well-designed studies to obtain necessary data and should not be restricted to using only the types of tests mentioned in the guidelines.

The agency has not addressed specific testing guidelines in this document. In revising the OTC drug review procedures relating to Category III, published in the **Federal Register** of September 29, 1981 (46 FR 47730), the agency advised that tentative final and final monographs will not include recommended testing guidelines for conditions that industry wishes to upgrade to monograph status. Instead, the agency will meet with industry representatives at their request to discuss testing protocols. The revised procedures also state the time in which test data must be submitted for consideration in developing the final monograph. (See also part III, paragraph A.2. below—Testing of Category II and Category III conditions.)

II. Agency Initiated Changes

1. The Panel recommended infant dosages for a number of laxative ingredients and comments were received recommending infant dosages for still more laxative ingredients. (See part I, comments 45 and 54 above.)

The agency is, however, concerned that constipation in infants may be a sign of a more serious condition that should be properly diagnosed by a doctor. Such conditions can include gastroenteritis, Hirschsprung's disease, congenital anal fissure, and anatomical abnormalities (Refs. 1 and 2).

In a study of constipation in 138 children, 14.5 percent (20) were found to have a disease that accounted for this symptom. Eight of these children, age 1 to 3½ years, were found to have anal fissures so severe as to require fairly vigorous medical or surgical treatment. The remaining 12 children were found to have a variety of problems including anatomical abnormalities of the anus and of the internal nervous system. The fact that 14.5 percent of the total group had diseases that accounted for the sympton of constipation empasizes the need for consulting a doctor in cases of infant constipation (Ref. 3).

Constipation is rare in breast-fed infants who receive an adequate amount of milk and in artificially fed infants who receive an adequate diet. The criterion for determining infant constipation is the nature for consistency of the stool and not its frequency. Most infants will have one or more stools daily, but some infants will pass a stool of normal consistency only at intervals of 36 to 48 hours (Ref. 4).

In view of the relative rarity of simple constipation in infancy and the high risk that it may be a sign of serious disease, anatomical abnormality, or an inadequate diet that should be properly diagnosed by a doctor, the agency is proposing that dosages for children under 2 years of age not appear in the OTC labeling. Dosages for children under 2 years of age are being included in the tentative final monograph only under professional labeling.

References

(1) Levine, M.D., "Children with Encopresis: A Descriptive Analysis," *Pediatrics*, 56:412–416, 1975.

(2) Bentley, J.F.R., "Progress Report: Constipation in Infants and Children," *GUT*, 12:85–90, 1971.

(3) Mercer, R.D., "Constipation," *The Pediatric Clinic of North America*, 14:175–185, 1967.

(4) "Textbook of Pediatrics," 11th Ed., edited by Wald E. Nelson, W.B. Saunders Co., Philadelphia, p. 208, 1979.

2. The agency concludes that the warning in recommended § 334.64(c), "Rectal bleeding or failure to evacuate may indicate a serious condition and a physician should be consulted", should apply to all laxative products and not just to one specific class of laxatives. Therefore, this warning is revised in this tentative final monograph to read: "Rectal bleeding or failure to have a bowel movement after use may indicate a serious condition. Discontinue use and consult your doctor." The agency is proposing that all laxative drug products be labeled with this warning as specified in this tentative final monograph at § 334.50(b)(4).

3. The Panel's recommended general warnings for sodium containing laxatives are not consistent with the sodium warnings required for antacid drug products (21 CFR 331.30(b)(5)). To resolve this inconsistency the agency proposes in this tentative final monograph that the sodium-restricted diet warning apply to all laxative products containing more than 5 mEq (115 mg) of sodium in the maximum recommended daily dose and that the kidney disease warning recommended by the panel be deleted. The agency proposes, however, to retain the Panel's recommended warning requiring a statement of sodium content per dosage unit for all laxative products containing more than 1 mEq (23 mg) of sodium per maximum daily dose because it is more informative than the one in the antacid monograph (21 CFR 331.30(e)). The agency invites comment on this proposal.

4. The agency has reviewed the warnings for phosphate-containing

laxatives and notes that one warning cautions against oral use of phosphate-containing laxatives by children under 6 years of age. The dosage and directions for use of such products in this tentative final monograph are for children 5 years of age and over because these products traditionally have been used in this age group. In order to eliminate the inconsistency the age limit in the warning in this tentative final monograph is revised to 5 years of age.

5. The agency has reviewed the Panel's definitions in recommended § 334.3 and has eliminated several terms from this section as unnecessary and redundant because their meaning is clear within the context of the monograph. However, two new terms, "carbon dioxide-releasing laxative" and "bowel cleansing system," have been added to the definitions in § 334.3 of this tentative final monograph because their meanings are not adequately clarified within the context of their use in the monograph.

6. The agency recognizes that saline laxatives may be irritating and cause nausea if taken with insufficient amounts of liquid (Refs. 1 and 2). In addition, saline laxatives are recommended to be taken with a full glass of water to achieve their maximum effect (Ref. 3). Therefore, in this tentative final monograph the agency proposes the direction to "drink a full glass (8 oz of liquid with each dose" for both bulk-forming and saline laxatives.

References

(1) Grollman, A., "Pharmacology and Therapeutics," Lea and Febiger, Philadelphia, p. 625, 1965.

(2) Bowman, W.C., and M.J. Rand, "Textbook of Pharmacology," Blackwell Scientific Publications, Oxford, England, p. 25.34, 1980.

(3) "United States Pharmacopeia Dispensing Information—1981," 2d Ed., United States Pharmacopeial Convention, Inc., Rockville, MD, p. 924.

7. It is unlcear whether the glycerin enema dosage in recommended § 334.12(a) refers to the total volume of enema solution or to the amount of glycerin in the enema solution. Because the data on safety and effectiveness of glycerin enema reviewed by the Panel was for an 80-percent solution of glycerin (Ref. 1), this tentative final monograph is revised to reflect that the dosage statement for glycerin enema is for an 80-percent glycerin solution.

Reference

(1) OTC Volume 090025, Docket No. 78N-036L, Dockets Management Branch.

8. The agency has reviewed the Panel's recommended warnings for castor oil-containing products advising against regular use (recommended § 334.60(c)). The agency believes that the revised indications and warnings proposed in this tentative final monograph for all laxative drug products sufficiently guard against regular use. Therefore, the agency is not including the Panel's recommended warnings for castor oil in this tentative final monograph.

9. The agency has reviewed the various studies submitted to support the professional use of laxative ingredients for use in preparing the colon for x-ray and endoscopic examination and/or for preparing the patient for surgery. In most of the studies submitted the laxative ingredients were not used alone, but were part of an overall regimen which included overhydration, dietary restrictions and/or other laxative agents. Therefore, in this tentative final monograph the agency proposes to modify the professional labeling indications for laxative ingredients used for bowel cleansing purpose to include the additional phrase, "for use as part of a bowel cleansing regimen."

III. The Agency's Tentative Adoption of the Panel's Report

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. *Summary of ingredient categories.* The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time, and concurs with the Panel's categorization of ingredients. For the convenience of the reader, the following table is included as a summary of the categorization of OTC laxative active ingredients.

Laxative active ingredients	Category
Bulk-forming laxatives:	
Agar	III.
Alpha cellulose	III.
Bran	I.
Calcium polycarbophil	I.
Carrageenan, degraded	II.
Carrageenan, native	III.
Guar gum	III.
Karaya	I.
Malt soup extract	I.
Methylcellulose	I.
Polycarbophil	I.
Psyllium ingredients	I.
Plantago ovata husks	
Plantago seeds	
Psyllium (hemicellulose)	
Psyllium, hydrophyllic mucilloid (psyllium hydrocolloid)	
Psyllium seed	
Psyllium seed (blond)	
Psyllium seed husks	
Sodium carboxymethylcellulose	I.
Hyperosmotic laxatives:	
Glycerin	I.
Sorbitol	I.
Lubricant laxative: Mineral oil	I.
Saline laxatives:	
Magnesium citrate oral solution, USP	I.
Magnesium hydroxide	I.
Magnesium sulfate	I.
Sodium biphosphate	I.
Sodium phosphate	I.
Tartaric acid and salts	III.
Stimulant laxatives:	
Aloe	I.
Aloin	III.
Bile salts (acid) and ox bile	III.
Bisacodyl	I.
Calcium pantothenate	III.
Calomel	III.
Cascara sagrada ingredients	I.
Casanthranol	
Cascara fluidextract, aromatic	
Cascara sagrada bark	
Cascara sagrada extract	
Cascare sagrada fluidextract	
Castor oil	I.
Colocynth resin	III.
Danthron	I.
Dehydrocholic acid	I.
Elaterin resin	III.
Frangula	III.
Gamboge resin	III.
Ipomea resin	III.
Jalap resin	III.
Phenolphthalein (white or yellow)	I.
Podophylum resin (podophyllin)	III.
Prune concentrate dehydrate and prune powder	III.
Rhubarb, Chinese	III.
Sennosides A and B	I.
Sodium oleate	III.
Stool Softener Laxatives:	
Docusate ingredients [1]	
Docusate calcium sulfosuccinate	
Docusate potassium sulfosuccinate	
Docusate sodium sulfosuccinate	
Poloxalkal (polykol)	III.
Carbon Dioxide-Releasing Laxatives:	
Released carbon dioxide from combined sodium biphosphate, anhydrous, sodium acid pyrophosphate, and sodium bicarbonate.	I.
Released carbon dioxide from combined, sodium biphosphate and sodium bitartrate.	I.

[1] To be discussed in a separate FEDERAL REGISTER publication.

2. *Testing of Category II and Category III conditions.* The Panel recommended testing guidelines for laxative drug products (40 FR 12922). The agency is offering these guidelines as the Panel's recommendations without adopting them or making any formal comment on them. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any laxative ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). That policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes in the Panel's Recommendations

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the Panel's report and recommended monograph with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made in the Panel's conclusions and recommendations follows.

1. Because of the number of changes that have been made, as summarized below, many of the section and paragraph numbers have been redesignated in this tentative final monograph. In addition, Subpart D has been redesignated as Subpart C, and the labeling sections of the monograph placed under Subpart C.

2. The following changes have been made to conform to the format and content of other recent OTC drug tentative final monographs:

a. A "statement of identity" section has been added for each laxative drug category.

b. The dosage information for each active ingredient has been moved to the directions section for the respective laxative drug category.

c. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments received to these proposals, the agency has determined that final monographs and any applicable OTC drug regulations will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option.

d. The signal word "warning" is being used in labeling instead of the signal word "caution." (See comment 27 above.)

3. Some of the Panel's recommended dosages did not specify the dosage interval but merely stated a daily dose. The tentative final monograph clarifies that the recommended dose is to be taken as a single daily dose. (See comment 12 above.)

4. The indication statement for laxative drug products has been revised to "For the relief of occasional constipation" [which may be followed by "(irregularity)."] (See comment 14 and 15 above.)

5. The professional labeling section has been revised to clarify that the required OTC labeling for a laxative drug product must be included in the labeling provided to health professionals. (See comment 21 above.)

6. The statement of identity for hyperosmotic laxatives is simply "laxative." (See comment 22 above.)

7. The tentative final monograph clarifies that the definitions of laxative drug categories need not appear in the labeling. However, the timeframes within which the different types of laxatives are expected to produce bowel movement are required in the labeling. (See comment 23 above.)

8. The definition of "short-term use" is not included in the tentative final monograph. (See comment 26 above.)

9. The phrase "this product" has been replaced with the phrase "laxative products" in those warning statements where the warning is applicable to all laxative products. (See comment 28 above.)

10. The drug interaction warning for cellulose derivatives is not included in the tentative final monograph. (See comment 35 above.)

11. The phrase "adequate liquid intake" in the directions of bulk-forming laxatives has been replaced with the phrase "Drink a full glass (8 oz) of liquid with each dose." The warnings recommended for bulk-forming laxatives that advised consumers to drink a full glass of liquid with each dose have been deleted because they are repetitious of the statements in the directions. In addition, the definition of "adequate liquid intake" is not included in the tentative final monograph. (See comment 36 above.)

12. The dosage of glycerin suppositories has been clarified to reflect the amount of glycerin per suppository. (See comment 45 above.)

13. The rectal use warning for glycerin products has been revised to read "For rectal use only." (See comment 46 above.)

14. Reference to mineral oil emulsion is not included in the tentative final monograph. The tentative final monograph includes warnings and directions for use for mineral oil only. (See comment 47 above.)

15. The warning for mineral oil products for persons who should not be administered mineral oil has been revised and does not contain a reference to "aged patients." (See comment 48 above.)

16. That portion of the warning for mineral oil products that warns not to administer mineral oil to persons having recent episodes of vomiting, regurgitation, or abdominal pain is not included in the tentative final monograph. (See comment 49 above.)

17. The drug interaction precaution for stool softener laxatives has been amended to include the phrase "unless directed by a doctor." (See comment 50 above.)

18. Specific sequestering agents for magnesium citrate in oral solution are not included in the tentative final monograph. (See comment 52 above.)

19. The dosage for magnesium citrate has been expanded to be compatible with USP requirements. (See comment 55 above.)

20. The professional labeling section of the tentative final monograph includes a professional indication for magnesium citrate and phosphate salts. (See comments 53 and 58 above.)

21. An infant dosage for magnesium hydroxide is included in the professional labeling section of the tentative final monograph. (See comment 54 above.)

22. The directions for the magnesium-containing saline laxatives have been amended to provide for a single daily dose. (See comment 56 above.)

23. The storage condition information for magnesium citrate oral solution has been revised to conform to the USP specifications. (See comment 57 above.)

24. The dosages for the phosphate salts have been revised. (See comment 58 above.)

25. The directions for saline laxatives in this tentative final monograph include the phrase "Drink a full glass (8 oz) of liquid with each dose." (See part II. paragraph 7 above.)

26. The general warnings for stimulant laxative drug products are not included in the tentative final monograph. (See comments 62 through 65 above.)

27. The dosages for the senna preparations have been revised to provide dosages for sennosides A and B only. (See comment 70 above.)

28. A suppository dose for sennosides A and B is included in the tentative final monograph. (See comment 70 above.)

29. The Panel's recommended monograph has been amended to include a bowel cleansing indication for a high dose of sennosides A and B. (See comment 70 above.)

30. The bisacodyl dosage have been revised to delete reference that the drug should be taken only at bedtime. (See comment 73 above.)

31. The warnings for bisacodyl products have been separated into two sections—one for enteric-coated tables, the other for the suppository. (See comment 74 above.)

32. The warning advising not to give bisacodyl enteric-coated tablets to children under 3 years of age has been revised to warn against the use of bisacodyl entreric-coated tablets in

children under 6 years of age. (See comment 74 above.)

33. The storage condition statement for bisacodyl products has been revised to delete reference to the word "cool." (See comment 75 above.)

34. The dosage for dehydrocholic acid has been revised to provide for a dose of 250 to 500 mg three times a day. (See comment 77 above.)

35. The specific 1-week use limitation for stool softener laxatives is not included in the tentative final monograph. (See comment 80 above.)

36. A carbon dioxide-releasing suppository consisting of sodium bicarbonate and potassium bitartrate is included in the tentative final monograph. (See comment 82 above.)

37. The tentative final monograph provides for bowel cleansing systems. (See comment 89 above.)

38. A combination containing psyllium seed (blond) and casanthranol is included in the tentative final monograph. (See comment 92 above.)

39. Dosages for children under 2 years of age are included only in the professional labeling section of the tentative final monograph. (See part II. paragraph 1 above.)

40. The rectal bleeding warning recommended by the Panel for the carbon dioxide-releasing suppositories has been revised and is being recommended for all laxative drug products. (See part II. paragraph 2 above.)

41. The sodium warnings for laxative drug products have been revised to conform to the sodium warnings required in the antacid monograph. (See part II. paragraph 3 above.)

42. The warning for orally-administrated phosphate-containing laxative drug products advising against use in children has been revised to be consistent with the directions for use. (See part II. paragraph 4 above.)

43. The agency has amended the definitions section of the monograph to delete unnecessary ones and to add new ones where necessary. (See part II. paragraph 5 above.)

44. The dosage for glycerin enema has been revised to reflect that the solution is an 80-percent concentration of glycerin. (See part II. paragraph 7 above.)

45. The agency has deleted the specific warnings recommended by the Panel for castor oil from the tentative final monograph. (See part II. paragraph 8 above.)

46. The agency has modified the professional labeling indications for laxative ingredients used in preparing the colon for x-ray and endoscopic examination and/or preparing the patient for surgery to reflect their actual use as part of bowel cleansing system. (See part II. paragraph 9 above.)

The agency proposes to revoke the existing warning and caution statements in § 369.20 for cathartics and laxatives and for mineral oil laxatives at the time this monograph becomes effective. The agency also proposes to revoke the existing regulations in § 201.302 for mineral oil at the time the final monograph becomes effective.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC laxative drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Pub. L. 96-354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC laxative drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC laxative drug products. Types of impact may include, but are not limited to, costs associated with products testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC laxative drug products should be accompanied by appropriate documentation. Because the agency has not previsously invited specific comment on the economic impact of the OTC drug review on laxative drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(a)(9) (propsoed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an enviornmental assessment nor an environmental impact statement is required.

Section 334.66(d)(3) of this proposed rule contains a collection of information requirement. As required by section 3504(h) of the Paperwork Reduction Act of 1980, FDA has submitted a copy of this proposed rule to the Office of Management and Budget (OMB) for its review of this collection of information requirement. Other organizations and individuals desiring to submit comments on this collection of information requirement should direct them to FDA's Dockets Management Branch (address above) and to the Office of Information and Regulatory Affairs, OMB, Rm. 3208, New Executive Office Bldg., Washington, DC 20503, Attn: Bruce Artim.

List of Subjects in 21 CFR Part 334

OTC drugs: Laxative drug products.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041-1042 as amended, 1050-1053 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is a proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended by adding new Part 334, to read as follows:

PART 334-LAXATIVE DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.

334.1 Scope.
334.3 Definitions.

Subpart B—Active Ingredients

334.10 Bulk-forming laxative active ingredients.
334.12 Hyperosmotic laxative active ingredients.
334.14 Lubricant laxative active ingredients.
334.16 Saline laxative active ingredients.
334.18 Stimulant laxative active ingredients.

Sec.

334.20 Stool softener laxative active ingredients [Reserved].
334.22 Carbon dioxide-releasing laxatives.
334.30 Permitted combinations of laxative active ingredients.
334.31 Laxative combination criteria.
334.32 Bowel cleansing systems.

Subpart C—Labeling

334.50 Labeling of laxative drug products.
334.52 Labeling of bulk-forming laxative drug products.
334.54 Labeling of hyperosmotic laxative drug products.
334.56 Labeling of lubricant laxative drug products.
334.58 Labeling of saline laxative drug products.
334.60 Labeling of stimulant laxative drug products.
334.62 Labeling of stool softener laxative drug products.
334.64 Labeling of carbon dioxide-releasing laxative drug products.
334.66 Labeling of bowel cleansing systems identified in § 334.32.
334.80 Professional labeling.

Authority: Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704).

Subpart A—General Provisions

§ 334.1 Scope.

(a) An over-the-counter laxative drug product in a form suitable for oral or rectal administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this part and each general condition established in § 330.1.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 334.3 Definitions.

As used in this part:

(a) *Laxative.* Any agent used for the relief of constipation.

(b) *Laxation.* To cause a bowel movement.

(c) *Constipation.* Infrequent or difficult bowel movement.

(d) *Bulk-forming laxative.* An agent that increases bulk volume and water content of the stool thereby promoting bowel movement.

(e) *Carbon dioxide-releasing laxative.* A suppository dosage form containing several ingredients that release cabon dioxide, thereby inducing gentle pressure in the rectum which promotes bowel movement.

(f) *Hyperosmotic laxative.* An agent that attracts water into the stool thereby promoting bowel movement.

(g) *Lubricant laxative.* An agent that lubricates the contents of the intestinal tract thereby promoting bowel movement.

(h) *Saline laxative.* An agent that increases water in the intestine thereby promoting bowel movement.

(i) *Stimulant laxative.* An agent that promotes bowel movement by one or more direct actions on the intestine.

(j) *Stool softener laxative.* An agent that penetrates and softens the stool thereby promoting bowel movement.

(k) *Bowel cleansing system.* A laxative drug product containing several different laxative ingredients for sequential administration at specified time intervals, for use in cleansing the bowel prior to surgery, colon x-ray, or endoscopic exmination.

Subpart B—Active Ingredients

§ 334.10 Bulk-forming laxative active ingredients.

The active ingredient of the product consists of any of the following when used within the dosage limits established for each ingredient in § 334.52(d):

(a) Bran.

(b) Cellulose (semisynthetic) ingredients.

(1) Methylcellulose.

(2) Sodium carboxymethylcellulose.

(c) Karaya.

(d) Malt soup extract.

(e) Polycarbophil.

(f) Psylllium ingredients.

(1) Plantago ovata husks.

(2) Plantago seed.

(3) Psyllium (hemicellulose).

(4) Psyllium hydrophyllic mucilloid.

(5) Psyllium seed.

(6) Psyllium seed (blond).

(7) Psyllium seed husks.

§ 334.12 Hyperosmotic laxative active ingredients.

The active ingredient of the product consists of any of the following when used within the dosage limits established for each ingredient in § 334.54(d):

(a) Glycerin.

(b) Sorbitol.

§ 334.14 Lubricant laxative active ingredients.

The active ingredient of the product consists of mineral oil when used within the dosage limit established in § 334.56(d).

§ 334.16 Saline laxative active ingredients.

The active ingredient of the product consists of any of the following when used within the dosage limits established for each ingredient in § 334.58(d):

(a) Magnesium citrate.

(b) Magnesium hydroxide.

(c) Magnesium sulfate.

(d) Sodium phosphate/sodium biphosphate marketed as a solution.

(e) Sodium phosphate.

(f) Sodium biphosphate.

§ 334.18 Stimulant laxative active ingredients.

The active ingredient of the product consists of any of the following when used within the dosage limits established for each ingredient in § 334.60 (d):

(a) Aloe.

(b) Bisacodyl.

(c) Cascara sagrada ingredients.

(1) Casanthranol.

(2) Cascara fluidextract, aromatic.

(3) Cascara sagrada bark.

(4) Cascara sagrada extract.

(5) Cascara sagrada fluidextract.

(d) Castor oil.

(e) Danthron.

(f) Dehydrocholic acid.

(g) Phenolphthalein.

(h) Sennosides A and B from any of the following sources: senna leaf powder, senna fluidextract, senna fruit extract, senna syrup, senna pod concentrate, or sennosides A and B crystalline.

§334.20 Stool softener laxative active ingredients [Reserved].

§ 334.22 Carbon dioxide-releasing laxatives.

The active ingredient of the product consists of the following when used within the dosage limits established in § 334.64(d):

(a) Carbon dioxide released from combined sodium biphosphate anhydrous, sodium acid pyrophosphate, and sodium bicarbonate.

(b) Carbon dioxide released from combined sodium bicarbonate and potassium bitartrate.

§ 334.30 Permitted combinations of active laxative ingredients.

The active laxative ingredients of the product consists of a combination of ingredients listed below provided the combination meets the laxative criteria established in § 334.31.

(a) The following bulk laxative ingredients may be combined provided the combination is labeled according to § 334.52:

(1) Malt soup extract identified in § 334.10(d) and psyllium seed (blond) identified in § 334.10(f)(6).

(2) Malt soup extract identified in § 334.10(d) and psyllium seed husks identified in § 334.10(f)(7).

(3) Methylcellulose identified in § 334.10(b)(1) and plantago ovata husks identified in § 334.10(f)(1).

(b) The following bulk laxative ingredient may be combined with the following lubricant laxative ingredient provided the combination is labeled according to §§ 334.52., and 334.56: Psyllium seed identified in § 334.10(f)(5) and mineral oil identified in § 334.14.

(c) The following bulk laxative ingredients may be combined with the following stimulant laxative ingredients provided the combination is labeled according to §§ 334.52 and 334.60:

(1) Psyllium (hemicellulose) identified in § 334.10(f)(3) and sennosides A and B identified in § 334.18(h).

(2) Psyllium seed (blond) identified in § 334.10(f)(6) and casanthranol identified in § 334.16(c)(1).

(d) [Reserved]

(e) the following lubricant laxative ingredient may be combined with the following stimulant laxative ingredients provided the combination is labeled according to §§ 334.56 and 334.60:

(1) Mineral oil identified in § 334.14 and casanthranol identified in § 334.18(c)(1).

(2) Mineral oil identified in § 334.14 and cascara sagradaextract identified in § 334.18(c)(4).

(3) Mineral oil identified in § 334.14 and cascara sagrada fluidextract identified in § 334.18(c)(5).

(4) Mineral oil identified in § 334.14 and phenolphthalein identified in § 334.18(g).

(f) The following lubricant laxative ingredient may be combined with the following saline laxative ingredient provided the combination is labeled according to §§ 334.56 and 334.58: Mineral oil identified in § 334.14 and magnesium hydroxide identified in § 334.16(b).

(g) The following saline laxative ingredient may be combined with the following stimulant laxative ingredient provided the combination is labeled according to §§ 334.58 and 334.60: Magnesium hydroxide identified in § 334.18(c)(4).

(h) The following stimulant laxative ingredients may be combined provided they are labeled according toi § 334.60:

(1) Aloe identified in § 334.18(a) and casanthranol identified in § 334.18(c)(1).

(2) Cascara sagrada extract identified in § 334.16(c)(4) and phenolphthalein identified in § 334.18(g).

§ 334.31 Laxative.

(a) The sum of the precentages of the effective dosage range (EDR) as determined in paragraph (b) of this section for each active ingredient in the combinations permitted in § 334.30 shall not exceed 100 percent.

(b) The method used for determining the EDR percentage value of each active ingredient is as follows:

$$\frac{\text{L max d} - \text{EDR (min)}}{\text{EDR (max)} - \text{EDR (min)}} \times 100 = \%\ \text{EDR of each ingredient where:}$$

(1) L max d is the labeled maximum daily dosage of the ingredient which must be within the effective daily dosage range for the ingredient established in §§ 334.52, 334.54, 334.56, 334.58, 334.60, or 334.62.

(2) EDR (min) is the effective daily dosage range (minimum) and EDR (max) is the effective daily dosage range (maximum) for the active ingredient established in §§ 334.52, 334.54, 334.56, 334.58, 334.60, or 334.62.

§ 334.32 Bowel cleansing systems.

(a) A kit containing the following 3 laxative drug products for sequential administration as specified in § 334.66(d)(3): magnesium citrate identified in § 334.16(a) and bisacodyl identified in § 334.18(b) in both an oral dosage form and a suppository dosage form.

(b) A kit containing the following 3 laxative drug products for sequential administration as specified in § 334.66(d)(6): magnesium citrate identified in § 334.16(a), phenolphthalein identified in § 334.18(g) in an oral dosage form, and carbon dioxide-releasing suppositories identified in § 334.22(b).

Subpart C—Labeling

§ 334.50 Labeling of laxative drug products.

In addition to the labeling described in §§ 334.52, 334.54, 334.56, 334.58, 334.60, 334.62, and 334.64, the labeling of laxative drug products contains the following statements unless otherwise specified.

(a) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the phrase "For relief of occasional constipation" [which may be followed by "(irregularity)."]

(b) *Warnings.* The labeling of the product contains the following information under the heading "Warnings." If applicable, the warnings in this section may be combined with the warnings in §§ 334.58 and 334.60 to eliminate duplicative words or phrases so the resulting warning is clear and understandable.

(1) "Do not use laxative products when abdominal pain, nausea, or vomiting are present unless directed by a doctor."

(2) "If you have noticed a sudden change in bowel habits that persists over a period of 2 weeks, consult a doctor before using a laxative."

(3) "Laxative products should not be used for a period longer than 1 week unless directed by a doctor."

(4) "Rectal bleeding or failure to have a bowel movement after use of a laxative may indicate a serious condition. Discontinue use and consult your doctor."

(5) *For products containing more than 5 milliequivalents (115 milligrams) sodium in the maximum recommended daily dose.* "Do not use this product if you are on a low salt diet unless directed by a doctor."

(6) *For products containing more than 25 milliequivalents (975 milligrams) potassium in the maximum recommended daily dose.* "Do not use this product if you have kidney disease unless directed by a doctor."

(7) *For products containing more than 50 milliequivalents (600 milligrams) magnesium in the maximum recommended daily dose.* "Do not use this product if you have kidney disease unless directed by a doctor."

(8) A product containing more than 1 milliequivalent (23 milligrams) sodium per maximum daily dose shall be labeled as to the sodium content per dosage unit.

(c) *Directions.* The labeling of the product contains the appropriate directions identified in §§ 334.52, 334.54, 334.56, 334.58, 334.60, 334.62, 334.64, and 334.66 under the heading "Directions" followed by "or as directed by a doctor."

(d) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this subpart.

§ 334.52 Labeling of bulk-forming laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.10 includes the established name of the drug, if any, and identifies the product as a "bulk-forming laxative."

(b) *Indications—Other required statement.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the phrase: "This product generally

produces bowel movement in 12 to 72 hours."

(c) *Warnings.* The labeling of the product contains the applicable warnings identified in § 334.50(b) under the heading "Warnings."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) *For products containing any ingredient identified in § 334.10.* "Drink a full glass (8 ounces) of liquid with each dose."

(2) *For products containing bran identified in § 334.10(a).* Adults and children 12 years of age and over: oral dosage is 6 to 14 grams. There is no maximum daily dose. Children under 12 years of age: consult a doctor.

(3) *For products containing methylcellulose and sodium carboxymethylcellulose identified in § 334.10(b) (1) and (2).* Adults and children 12 years of age and over: oral dosage is 4 to 6 grams in a single daily dose. Children 6 to under 12 years of age: oral dosage is 1 to 1.5 grams in a single daily dose. Children under 6 years of age: consult a doctor.

(4) *For products containing karaya identified in § 334.10(c).* Adults and children 12 years of age and over: oral dosage is 5 to 10 grams in a single daily dose. Children under 12 years of age: consult a doctor.

(5) *For products containing malt soup extract identified in § 334.10(d).* Adults and children 2 years of age and over: oral dosage is 12 to 64 grams in a single daily dose. Children under 2 years of age: consult a doctor.

(6) *For products containing polycarbophil identified in § 334.10(e).* Adults and children 12 years of age and over: oral dosage is 4 to 6 grams in a single daily dose. Children 6 to under 12 years of age: oral dosage is 1.5 to 3 grams in a single daily dose. Children 2 to under 6 years of age: oral dosage is 1 to 1.5 grams in a single daily dose. Children under 2 years of age: consult a doctor.

(7) *For products containing any psyllium ingredient identified in § 334.10(f).* Adults and children 12 years of age and over: oral dosage is 2.5 to 30 grams in a single daily dose. Children 6 to under 12 years of age: 1.25 to 15 grams in a single daily dose. Children under 6 years of age: consult a doctor.

§ 334.54 Labeling of hyperosmotic laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.12 includes the established name of the drug, if any, and identifies the product as a "laxative."

(b) *Indications—Other required statement.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the phrase: "This product generally produces bowel movement in ¼ to 1 hour."

(c) *Warnings.* In addition to the warnings identified in § 334.50(b), the labeling of the product contains the following statement under the heading "Warnings."

(1) *For products containing glycerin identified in § 334.12(a).* "May cause rectal discomfort or a burning sensation."

(2) *For products containing glycerin or sorbitol identified in § 334.12 (a) and (b).* "For rectal use only."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) *For products containing glycerin identified in § 334.12(a)*—(i) *Rectal suppository dosage.* Adults and children 6 years of age and over: rectal suppository dosage is 2 to 3 grams clycerin in a single daily dose. Children 2 to under 6 years of age: rectal suppository dosage is 1 to 1.7 grams glycerin in a single daily dose. Children under 2 years of age: consult a doctor.

(ii) *Rectal enema dosage.* Adults and children 6 years of age and over: rectal enema dosage is 5 to 15 milliliters of an 80 percent volume/volume solution in a single daily dose. Children 2 to under 6 years of age: rectal enema dosage is 2 to 5 milliliters as an 80 percent volume/volume solution in a single daily dose. Children under 2 years of age: consult a doctor.

(2) *For products containing sorbitol identified in § 334.12(b).* Adults and children 12 years of age and over: rectal enema dosage is 120 milliliters as a 25 to 30 percent weight/volume solution in a single daily dose. Children 2 to under 12 years of age: rectal enema dosage is 30 to 60 milliliters as a 25 to 30 percent weight/volume solution in a single daily dose. Children under 2 years of age: consult a doctor.

§ 334.56 Labeling of lubricant laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.14 includes the established name of the drug, if any, and identifies the product as a "lubricant laxative."

(b) *Indications—Other required statements.*

In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the following:

(1) *Oral dosage forms.* "This product generally produces bowel movement in 6 to 8 hours."

(2) *Rectal dosage forms.* "This product generally produces bowel movement in 2 to 15 minutes."

(c) *Warnings.* In addition to the warnings identified in § 334.50(b), the labeling of products containing mineral oil identified in § 334.14(a) for oral use contains the following statements under the heading "Warnings."

(1) "Do not administer to children under 6 years of age, to pregnant women, to bedridden patients, or to persons with difficulty swallowing."

(2) "As with any drug, if you are nursing a baby, seek the advice of a health professional before using this product."

(3) "*Drug interaction precaution:* Do not take this product if you are presently taking a stool softener laxative."

(4) "Do not take with meals."

(5) The warnings in paragraph (c)(1) and (2) of this section supersede the general warning required in § 201.63.

(d) *Directions.* The labeling of products containing mineral oil identified in § 334.14 contains the following information under the heading "Directions."

(1) *Oral dosage.* Adults and children over 12 years of age: oral dosage is a minimum single dose of 15 milliliters to a maximum daily dose of 45 milliliters. Children 6 to under 12 years of age: oral dosage is a minimum single dose of 5 milliliters to a maximum daily dose of 15 milliliters. The dose may be taken as a single daily dose or in divided doses. Children under 6 years of age: consult a doctor.

(2) *Rectal enema dosage.* Adults and children over 12 years of age and over: rectal enema dosage is 120 milliliters in a single daily dose. Children 2 to under 12 years of age: rectal enema dosage is 60 milliliters in a single daily dose. Children under 2 years of age: consult a doctor.

§ 334.58 Labeling of saline laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.15 includes the established name of the drug, if any, and identifies the product as a "saline laxative."

(b) *Indications—Other required statements.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the following:

(1) *Oral dosage forms.* "This product generally produces bowel movement in ½ to 6 hours."

(2) *Rectal dosage forms.* "This product generally produces bowel movement in 2 to 15 minutes."

(c) *Warnings.* In addition to the warnings identified in § 334.50(b), the labeling of the product contains the following statements under the heading "Warnings."

(1) *For products containing magnesium citrate identified in § 334.16(a) when formulated in oral solution.* "Store at temperatures between 46 and 86 °F (8 and 30 °C)."

(2) *For products containing phosphates identified in § 334.16 (d), (e), or (f).* (i) "Do not use this product if you have kidney disease unless directed by a doctor."

(ii) *Oral dosage forms.* "Do not give to children under 5 years of age unless directed by a doctor."

(iii) *Rectal dosage forms.* "Do not give to children under 2 years of age unless directed by a doctor."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) *Oral dosage forms.* "Drink a full glass (8 ounces) of liquid with each dose."

(2) *For products containing magnesium citrate identified in § 334.16(a).* Adults and children 12 years of age and over: oral dosage is 11 to 25 grams. Children 6 to under 12 years of age: oral dosage is 5.5 to 12.5 grams. Children 2 to under 6 years of age: oral dosage is 2.7 to 6.25 grams. The dose may be taken as a single daily dose or in divided doses. Children under 2 years of age: consult a doctor.

(3) *For products containing magnesium hydroxide identified in § 334.16(b).* Adults and children 12 years of age and over: oral dosage is 2.4 to 4.8 grams. Children 6 to under 12 years of age: oral dosage is 1.2 to 2.4 grams. Children 2 to under 6 years of age: oral dosage is 0.4 to 1.2 grams. The dose may be taken as a single daily dose or in divided doses. Children under 2 years of age: consult a doctor.

(4) *For products containing magnesium sulfate identified in § 334.16(c).* Adults and children 12 years of age and over: oral dosage is 10 to 30 grams. Children 6 to under 12 years of age: oral dosage is 5 to 10 grams. Children 2 to under 6 years of age: oral dosage is 2.5 to 5 grams. The dose may be taken as a single daily dose or in divided doses. Children under 2 years of age: consult a doctor.

(5) *For products containing sodium phosphate/sodium biphosphate identified in § 334.16(d) marketed as a solution*—(i) *Oral dosage.* Adults and children 12 years of age and over: oral dosage is sodium phosphate 3.42 to 7.56 grams, and sodium biphosphate 9.1 to 20.2 grams in a single daily dose. Children 10 to under 12 years of age: oral dosage is sodium phosphate 1.71 to 3.78 grams and sodium biphosphate 4.5 to 10.1 grams in a single daily dose. Children 5 to under 10 years of age: oral dosage is sodium phosphate 0.86 to 1.89 grams and sodium biphosphate 2.2 to 5.05 grams in a single daily dose. Children under 5 years of age: consult a doctor.

(ii) *Rectal enema dosage.* Adults and children 12 years of age and over: enema dosage is sodium phosphate 6.84 to 7.56 grams and sodium biphosphate 18.24 to 20.16 grams in a single daily dose. Children 2 to under 12 years of age: enema dosage is sodium phosphate 3.42 to 3.78 grams and sodium biphosphate 9.12 to 10.08 grams in a single daily dose. Children under 2 years of age: consult a doctor.

(6) *For products containing sodium phosphate identified in § 334.16(e).* Adults and children 12 years of age and over: oral dosage is 3.42 to 7.56 grams in a single daily dose. Children 10 to under 12 years of age: oral dosage is 1.71 to 3.78 grams in a single daily dose. Children 5 to under 10 years of age: oral dosage is 0.86 to 1.89 grams in a single daily dose. Children under 5 years of age: consult a doctor.

(7) *For products containing sodium biphosphate identified in § 334.16(f).* Adults and children 12 years of age and over: oral dosage is 4.5 to 20.2 grams in a single daily dose. Children 10 to under 12 years of age: oral dosage is 2.25 to 10.1 grams in a single daily dose. Children 5 to under 10 years of age: oral dosage is 1.12 to 5.05 grams in a single daily dose. Children under 5 years of age: consult a doctor.

§ 334.60 Labeling of stimulant laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.18 includes the established name of the drug, if any, and identifies the product as a "stimulant laxative."

(b) *Indications—Other required statement.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the following:

(1) *Oral dosage forms.* "This product generally produces bowel movement in 6 to 12 hours."

(2) *Rectal dosage forms.* "This product generally produces bowel movement in ¼ to 1 hour."

(3) *For products containing sennosides A and B in the dosage specified in § 334.60(d)(13).* The product should contain the following statement under the heading "Indications" instead of the statements required in §§ 334.50(a) and 334.60(b) (1) and (2): "For use as part of a bowel cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination."

(c) *Warnings.* In addition to the warnings identified in § 334.50(b), the labeling of the product contains the following statements under the heading "Warnings."

(1) *For products containing bisacodyl identified in § 334.18(b).* "Store at temperatures not above 86° F (30° C)."

(i) *Enteric-coated tablet dosage forms.* (*a*) "Do not chew tablets."

(*b*) "Do not give to children under 6 years of age, or to persons who cannot swallow without chewing, unless directed by a doctor."

(*c*) "Do not take this product within 1 hour after taking an antacid or milk."

(*d*) "This product may cause abdominal discomfort, faintness, and cramps."

(ii) *Rectal suppository dosage forms.* "This product may cause abdominal discomfort, faintness, rectal burning, and mild cramps."

(2) *For products containing phenolphthalein identified in § 334.18(g).* "If skin rash appears, do not use this product or any other preparation containing phenolphthalein."

(3) *For products containing sennosides A and B in the dosage specified in § 334.60(d)(13).* The product should contain the following statement under the heading "Warnings" instead of the statements required in § 334.50(b): "Do not use this product unless directed by a doctor."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) *For products containing aloe identified in § 334.18(a).* Adults and children over 15 years of age: oral dosage is 120 to 250 milligrams in a single daily dose. Children 8 to under 15 years of age: oral dosage is 80 to 120 milligrams in a single daily dose. Children 6 to under 8 years of age: oral dosage is 40 to 80 milligrams in a single daily dose. Children under 6 years of age: consult a doctor.

(2) *For products containing bisacodyl identified in § 334.18(b)*—(i) *Oral dosage.* Adults and children 12 years of

age and over: oral dosage is 5 to 15 milligrams in a single daily dose. Children 6 to under 12 years of age: oral dosage is 5 milligrams in a single daily dose. Children under 6 years of age: consult a doctor.

(ii) *Rectal suppository dosage.* Adults and children 12 years of age and over: rectal suppository dosage is 10 milligrams in a single daily dose. Children 6 to under 12 years of age: rectal suppository dose is 5 milligrams in a single daily dose. Children under 6 years of age: consult a doctor.

(3) *For products containing casanthranol identified in § 334.18(c)(1).* Adults and children 12 years of age and over: oral dosage is 30 to 90 milligrams in a single daily dose. Children 2 to under 12 years of age: oral dosage is 15 to 45 milligrams in a single daily dose. Children under 2 years of age: consult a doctor.

(4) *For products containing aromatic cascara fluidextract identified in § 334.18(c)(2)* Adults and children 12 years of age and over: oral dosage is 2 to 6 milliliters in a single daily dose. Children 2 to under 12 years of age: oral dosage is 1 to 3 milliliters in a single daily dose. Children under 2 years of age: consult a doctor.

(5) *For products containing cascara sagrada bark identified in § 334.18(c)(3).* Adults and children 12 years of age and over: oral dosage is 300 to 1000 milligrams in a single daily dose. Children 2 to under 12 years of age: oral dosage is 150 to 500 milligrams in a single daily dose. Children under 2 years of age: consult a doctor.

(6) *For products containing cascara sagrada extract identified in § 334.18(c)(4).* Adults and children 12 years of age and over: oral dosage is 200 to 400 milligrams in a single daily dose. Children 2 to under 12 years of age: oral dosage is 100 to 200 milligrams in a single daily dose. Children under 2 years of age: consult a doctor.

(7) *For products containing cascara sagrada fluidextract identified in § 334.18(c)(5).* Adults and children 12 years of age and over: oral dosage is 0.5 to 1.5 milliliters in a single daily dose. Children 2 to under 12 years of age: oral dosage is 0.25 to 0.75 milligrams in a single daily dose. Children under 2 years of age: consult a doctor.

(8) *For products containing castor oil identified in § 334.18(d).* Adults and children 12 years of age and over: oral dosage is 15 to 60 milliliters in a single daily dose. Children 2 to under 12 years of age: oral dosage is 5 to 15 milliliters in a single daily dose. Children under 2 years of age: consult a doctor.

(9) *For products containing danthron identified in § 334.18(e).* Adults and children 12 years of age and over: oral dosage is 75 to 150 milligrams in a single daily dose. Children under 12 years of age: consult a doctor.

(10) *For products containing dehydrocholic acid identified in § 334.18(f).* Adults and children 12 years of age and over: oral dosage is 250 to 500 milligrams three times a day, not to exceed 1500 milligrams in 24 hours. Children under 12 years of age: consult a doctor.

(11) *For products containing phenolphthalein identified in § 334.18(g).* Adults and children 12 years of age and over: oral dosage is 30 to 270 milligrams daily in a single or divided daily dose. Children 6 to under 12 years of age: oral dosage is 30 to 60 milligrams in a single or divided daily dose. Children 2 to under 6 years of age: oral dosage is 15 to 30 milligrams in a single or divided daily dose. Children under 2 years of age: consult a doctor.

(12) *For products containing sennosides A and B identified in § 334.18(h)*—(i) *Oral dosage.* Adults and children 12 years of age and over: oral dosage is 12 to 50 milligrams once or twice daily. Children 6 to under 12 years of age: oral dosage is 6 to 25 milligrams once or twice daily. Children 2 to under 6 years of age: oral dosage is 3 to 12.5 milligrams once or twice daily. Children under 2 years of age: consult a doctor.

(ii) *Rectal suppository dosage.* Adults and children 12 years of age and over: rectal suppository dosage is 30 milligrams once or twice daily. Children under 12 years of age: consult a doctor.

(13) *For products containing sennosides A and B identified in § 334.18(h) and labeled for use only as specified in paragraphs (b)(3) and (c)(3) of the section.* Adults and children 12 years of age and over: oral dosage is 160 milligrams in a single daily dose. Children under 12 years of age: consult a doctor.

§ 344.62 Labeling of stool softener laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.20 includes the established name of the drug, if any, and identifies the product as a "stool softener laxative."

(b) *Indications—Other required statements.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the following:

(1) *Oral dosage forms.* "This product generally produces bowel movement in 12 to 72 hours."

(2) *Rectal dosage forms.* "This product generally produces bowel movement in 2 to 15 minutes."

(c) *Warnings.* [Reserved]

(d) *Directions.* [Reserved]

§ 334.64 Labeling of carbon dioxide-releasing laxative drug products.

(a) *Statement of identity.* The labeling of the product containing any ingredient identified in § 334.22 includes the established name of the drug, if any, and identifies the product as a "laxative."

(b) *Indications—Other required statement.* In addition to the indication identified in § 334.50(a), the product also contains a statement under the heading "Indications" that is limited to the phrase: "This product generally produces bowel movement in 5 to 30 minutes."

(c) *Warnings.* In addition to the warnings identified in § 334.50(b), the product also contains the following information under the heading "Warnings."

(1) "For rectal use only."

(2) "Do not lubricate with mineral oil or petrolatum prior to rectal insertion."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) *For products containing the carbon dioxide-releasing ingredients identified in § 334.22(a).* Adults and children 12 years of age and over: rectal dosage is one suppository containing 1.2 to 1.5 grams of sodium biphosphate anhydrous, 0.04 to 0.05 gram of sodium acid pyrophosphate and 1 to 1.5 grams of sodium bicarbonate in a single daily dose. Children under 12 years of age: consult a doctor.

(2) *For products containing the carbon dioxide-releasing ingredients identified in § 334.22(b).* Adults and children 12 years of age and over: rectal dosage is one suppository containing 0.6 gram of sodium bicarbonate and 0.9 gram of potassium bitartrate in a single daily dose. Children under 12 years of age: consult a doctor.

(3) *For products containing the carbon dioxide-releasing ingredients identified in § 334.22(a) and (b).* "Moisten suppository by placing it under a water tap for 30 seconds or in a cup of water for at least 10 seconds before insertion."

§ 334.66 Labeling of bowel cleansing systems identified in § 334.32.

(a) *Statement of identity.* The labeling of the product containing the bowel cleansing systems identified in § 334.32(a) and (b) contains the established names of the drugs, if any.

and identifies the product as a "bowel cleansing system."

(b) *Indications.* The labeling of the product contains a statement of the indication under the heading "Indications" that is limited to the phrase: "For use as part of a bowel cleansing regimen in preparing patients for surgery or for preparing the colon for x-ray or endoscopic examination."

(c) *Warnings.* The labeling of the product contains the following statements instead of the warnings in § 334.50(b) under the heading "Warnings": "Do not use this product unless directed by a doctor."

(1) *For products containing the bowel cleansing system identified in § 334.32(a).* The labeling of the product also contains the warnings identified in §§ 334.50(b) (5), (6), (7), and (8); 334.58(c); and 334.60(c) as applicable.

(2) *For products containing the bowel cleansing system identified in § 334.32(b).* The labeling of the product also contains the warnings identified in §§ 334.50(b) (5), (6), (7), and (8); 334.58(c); 334.60(c); and 334.64(c) as applicable.

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions."

(1) "Open and read the enclosed directions and labels at least 24 hours in advance of examination."

(2) "Follow each step and complete all instructions or the entire x-ray or endoscopic examination may have to be repeated."

(3) *Package insert.* The following information may be in the form of a package insert. (i) The manufacturer should include a detailed description of the diet to be followed as part of the bowel cleansing regimen, i.e., a clear liquid diet, together with a commentary on the importance of these dietary restrictions.

(ii) The manufacturer should include a detailed set of instructions for the intake of at least 40 ounces of clear fluid including black coffee, plain tea, strained fruit juice, soft drinks, or water, but not milk or cream, during the course of the bowel cleansing regimen. This shall include commentary on the importance of a high fluid intake to the success of the bowel cleansing regimen.

(iii) Detailed directions should be provided specifying the following dosages, time intervals, routes of administration, and sequence for the administration of the individual single entity laxative products included in the bowel cleansing system. This may specify exact times of day for administration of each laxative to insure proper time intervals and should be integrated with instructions regarding dietary restrictions and fluid intake to provide a detailed set of directions for the complete bowel cleansing regimen.

(*a*) *For the bowel cleansing system identified in § 334.32(a).* Twenty five grams magnesium citrate in oral solution; 15 to 20 milligrams bisacodyl administered orally 2 hours after administration of magnesium citrate in oral solution; 10 milligrams of bisacodyl administered by suppository 9 hours after the administration of the oral bisacodyl and at least 2 hours before the scheduled examination or x-ray.

(*b*) *For the bowel cleansing system identified in § 334.32(b).* Twenty five grams of magnesium citrate in oral solution; 270 milligrams phenolphthalein administered orally 2½ hours after administration of the magnesium citrate in oral solution; 1 carbon dioxide-releasing suppository of the type identified in § 334.22(b) administered 7 hours after administration of the phenolphthalein; 1 carbon dioxide-releasing suppository of the type identified in § 334.22(b) administered 8 hours after the first suppository and at least 2 hours before the scheduled examination or x-ray.

§ 334.80 Professional labeling.

The labeling of the product provided to health professionals (but not to the general public) contains the following information in addition to the labeling identified in §§ 334.50, 334.52, 334.54, 334.56, 334.58 and 334.60.

(a) *Indications.*—(1) *For products containing mineral oil identified in § 334.14.* "For preparing the colon for x-ray or endoscopic examination."

(2) *For products containing magnesium citrate in oral solution identified in § 334.16(a), sodium phosphate/sodium biphosphate identified in § 334.16(d), or bisacodyl identified in § 334.18(b).* "For use as part of a bowel cleansing regimen in preparing the patient for surgery or for preparing the colon for x-ray endoscopic examination."

(3) *For products containing castor oil identified in § 334.334.18(d).* "For preparing the colon for x-ray or endoscopic examination."

(4) *For products containing bisacodyl identified in § 334.18(b).* "For use as a laxative in postoperative care, antepartum care, postpartum care, and in preparation for delivery."

(b) *Warnings.* The labeling of the product contains the following information under the heading "Warnings."

(1) *For products containing karaya identified in § 334.10(c).* (i) "Rare cases of allergic reactions and urticaria caused by karaya have been reported."

(ii) "Inadequate fluid intake may cause obstructions of the large bowel."

(2) *For products containing sodium biphosphate or sodium phosphate identified in § 334.16 (d), (e), and (f).* "Do not use in patients with megacolon, as hypernatremic dehydration may occur. Use with caution in patients with impaired renal functions."

(3) *For products containing mineral oil identified in § 334.14.* "Side effects with the proper use of mineral oil are few. However, laxation, anal leakage, and dermatologic reactions may occur with chronic use and particularly with excess dosage. Owing to its property as a lipid solvent, mineral oil may interfere with the absorption of provitamin A, vitamin A, and vitamin D, leading to impairment of calcium and phosphorus metabolism. This occurs only under conditions of chronic usage. Administration of mineral oil may lower prothrombin levels, probably secondary to imparied vitamin K absorption, and regular use in pregnancy may predispose to hemorrhagic disease of the newborn. Because of possible interference with nutrition, mineral oil should not be ingested in close proximity to meals. These side effects occur very rarely and then only with chronic and abusive use."

(c) *Directions.* The labeling of the product may contain the following additional information under the heading "Directions."

(1) *For products containing malt soup extract identified in § 334.10(d).* Children under 2 years of age: oral dosage is 6 to 32 grams in a single daily dose.

(2) *For products containing polycarbophil identified in § 334.10(e).* Children under 2 years of age: oral dosage is 0.5 to 1 gram in a single daily dose.

(3) *For products containing glycerin identified in § 334.12(a).* Children under 2 years of age: (i) rectal suppository dosage is 1 to 1.7 grams of glycerin, in a single daily dose. (ii) rectal enema dosage is 2 to 5 milliliters of glycerin, as an 80 percent solution, in a single daily dose.

(4) *For products containing magnesium hydroxide identified in § 334.16(b).* Children under 2 years of age: oral dosage is 0.035 to 0.043 gram per kilogram per dose.

(5) *For products containing bisacodyl identified in § 334.18(b).* Children under 2 years of age: rectal suppository dosage is 5 milligrams in a single daily dose.

(6) *For products containing casanthranol identified in § 334.18(c)(1).*

Children under 2 years of age: oral dosage is 7.5 to 22.5 milligrams in a single daily dose.

(7) *For products containing aromatic cascara fluidextract identified in § 334.18(c)(2).* Children under 2 years of age: oral dosage is 0.5 to 1.5 milliliters in a single daily dose.

(8) *For products containing cascara sagrada bark identified in § 334.18(c)(3).* Children under 2 years of age: oral dosage is 75 to 250 milligrams in a single daily dose.

(9) *For products containing cascara sagrada extract identified in § 334.18(c)(4).* Children under 2 years of age: oral dosage is 50 to 200 milligrams in a single daily dose.

(10) *For products containing cascara sagrada fluidextract identified in § 334.18(c)(5).* Children under 2 years of age: oral dosage is 0.125 to 0.375 milligram in a single daily dose.

(11) *For products containing castor oil identified in § 334.18(d).* Children under 2 years of age: oral dosage is 1 to 5 milliliters in a single daily dose.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register.**

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA–305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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Part III

Department of Health and Human Services

Food and Drug Administration

21 CFR Parts 310 and 331

Hypophosphatemia and Hyperphosphatemia Drug Products for Over-the-Counter Human Use

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310 and 331

[Docket No. 80N-0395]

Hypophosphatemia and Hyperphosphatemia Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that would amend the professional labeling section of the monograph for over-the-counter (OTC) antacid drug products to include additional warnings for the professional labeling of aluminum-containing antacid drug products and a hyperphosphatemia claim for products containing aluminum carbonate, and that would establish that drug products labeled for OTC use in treating hypophosphatemia (abnormally low plasma level of phosphate in the blood) or hyperphosphatemia (abnormally high plasma level of phosphate in the blood) are not generally recognized as safe and effective and are misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of December 9, 1980 (45 FR 81154) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC hypophosphatemia and hyperphosphatemia drug products as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based on the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. Interested persons were invited to submit comments by March 9, 1981. Reply comments in response to comments filed in the initial comment period could be submitted by April 8, 1981.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, two pharmaceutical manufacturers, one State government, one health professional organization, and two health professionals submitted comments. In response to the comments submitted, one reply comment was received from a health professional organization. These comments are also on public display in the Dockets Management Branch.

In this proposed rule, FDA states for the first time its position on OTC hypophosphatemia and hyperphosphatemia drug products. Final agency action on this matter will occur with the publication at a future date of a final rule relating to OTC hypophosphatemia and hyperphosphatemia drug products.

This proposed rule would amend Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations by adding to Subpart E of Part 310 new §§ 310.541 and 310.542, and to Subpart D of Part 331 new § 331.31(a) (3) and (4). This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC hypophosphatemia and hyperphosphatemia drug products, based on the comments received and the agency's independent evaluation of the Panel's report. As discussed in the final rule revising the procedural regulations for reviewing and classifying OTC drugs, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Category II and III). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) This document retains the concepts of Category I, II, and III at the proposed rule stage.

The agency recognizes that the Panel considered two ingredients, aluminum phosphate gel and aluminum carbonate gel, for use in hypophosphatemia and hyperphosphatemia, respectively. However, in the final monograph for OTC antacid drug products these compounds are designated as aluminum phosphate and aluminum carbonate. Therefore, throughout this document these ingredients will be referred to by the names used in the antacid final monograph.

The agency advises that the effective date of the final rule will be 12 months after the date of publication in the **Federal Register**. Manufacturers are encouraged to comply voluntarily with the rule at the earliest possible date.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

I. The Agency's Tentative Conclusions on the Comments

1. One comment requested that the agency eliminate all aluminum-containing drug products from the OTC market because recent experimental and clinical data implicate aluminum as the causative agent in some presenile and senile dementia of the Alzheimer's type. The comment pointed out numerous studies which indicate that aluminum plays a role in Alzheimer's disease, an organic brain syndrome (Ref. 1). In several of the studies, aluminum was observed in the tangled neurofilaments of Alzheimer's patients. Other studies suggested that aluminum accumulations in the brain have been correlated with

the oral ingestion of aluminum-containing antacids. The comment argued that these clinical findings are collaborated by animal data in which encephalopathies have been induced in rabbits and rats given toxic doses of aluminum. The comment also pointed out that significant elevations of aluminum have been reported in the parathyroid glands of patients taking aluminum-containing drugs as concurrent therapy during dialysis and speculated that parathyroid function may be affected by these elevations. The comment concluded by suggesting that more research is needed to define the safe use of aluminum salts in chronic therapy for hyperphosphatemia, and suggesting that physicians should be advised to monitor the renal function of those patients taking chronic dosages of aluminum-containing antacids.

A second comment submitted several literature reports regarding the role of aluminum-containing antacids in clacium and fluoride metabolism in man (Ref. 2). The comment noted that urine and stool excretion of calcium apparently increased with small doses of aluminum-containing antacids and concluded that long-term use of such products may lead to substantial clacium loss. The comment also stated that the data demonstrate that aluminum-containing antacids inhibit the intestinal absorption of fluoride.

The agency has evaluated the data submitted by the comments as well as available data reported in the literature in determining the toxicity of aluminum-containing drug products. There is some evidence that ingestion of large amounts of aluminum-containing products for prolonged periods may lead to adverse effects, but there is also considerable speculation in the literature with little supporting data.

Aluminum and Alzheimer's disease. Crapper and colleagues (Refs. 3 through 8) have been the major proponents of a role for aluminum as a causative factor of Alzheimer's disease. They have reported elevated aluminum levels in the brains of persons with Alzheimer's disease. They hypothesized that aluminum may interfere with the transcription of genetic information and may lead to altered protein synthesis within the neuron (Ref. 8). Trapp et al. (Ref. 9) have also reported a higher concentration of brain aluminum contents in a small number of persons with Alzheimer's disease although the difference in aluminum levels between Alzheimer's and control patients was considerably lower than that reported by Crapper. Perl and Brody (Ref. 10) studied the aluminum content within individual neurons of brain tissue from three cases of Alzheimer's disease and three nondemented controls. They found that aluminum is frequently present in the nuclei of neurons with neurofibrillary tangles both in the presence and absence of Alzheimer's disease, although neurons with neurofibrillary tangles were found more often in the Alzheimer patients. McDermott et al. (Ref. 11) measured brain aluminum levels in 10 patients with Alzheimer's disease and in 9 control patients. Aluminum concentrations in individual samples were highly variable, and no significant differences were observed between the two groups. There was also no correlation between mean aluminum concentrations and the degree of neurofibrillary degeneration in each brain. Markesbery et al. (Ref. 12) examined 74 specimens of tissue from 12 Alzheimer's patients and 166 specimens from 28 nondemented individuals. Their data showed no significant difference in aluminum content of Alzheimer's patients and normal controls. No correlation between neurofibrillary tangle formations and aluminum content was established.

Aluminum can produce some of the histopathlogical and clinical features of Alzheimer's disease in certain animal species. Petit, Biederman, and McMullen (Ref. 13) have demonstrated that an infusion of aluminum tartrate into the lateral ventricles of rabbits decreased learning and retention of an avoidance task compared to saline-infused controls. Crapper and Dalton (Refs. 4 and 5) reported that subarachnoid injection of aluminum chloride into cats induced neurofibrillary degeneration and impaired the acquisition and short-term retention of a conditioned avoidance response. The relationship of changes induced in these animals to the human disease is not at all clear, particularly in view of the unphysiological route of administration of the aluminum in these studies. On the other hand, Crapper and De Boni (Ref. 14) have noted that not all species are as affected by such infusions as the cat and rabbit. Aluminum concentrations 4 to 10 times those employed in cats did not induce a progressive encephalopathy or neurofibrillary degeneration in two strains of rats.

Recently, Crapper and De Boni stated that the presence of increased amounts of aluminum in the brain of Alzheimer patients may simply indicate the absorption of aluminum by a deteriorating system. They state that the cause of Alzheimer's disease is unknown and there is no evidence to support the possibility that aluminum initiates the Alzheimer process (Ref. 15).

In an editorial on Alzheimer's disease in the British Medical Journal (Ref. 16), it was stated that "Despite the plethora of hypotheses, however, objective analysis of all the data—immunological, genetic, virological, pathological, and biochemical—shows that we still have no idea of the aetiology of Alzheimer's disease."

Aluminum and the parathyroid glands. Although the comment suggests that aluminum may have an effect on parathyroid function, the agency has reviewed the available literature and found no data to support this hypothesis (Refs. 17 through 22). Some studies in rats suggest that elevated parathyroid hormone levels may increase the absorption of aluminum from the gastrointestinal tract (Ref. 17). There is little evidence, however, that this is of clinical importance.

Aluminum and phosphate/calcium/fluoride metabolism. Several studies have been conducted which imply that aluminum may detrimentally affect phosphate, calcium, and flouride balance. It is known that aluminum forms insoluble complexes with phosphate in the gastrointestinal tract and decreases phosphate absorption. Prolonged use of aluminum-containing antacids by normophosphatemic patients may result in hypophosphatemia which may lead to adverse reactions. Studies by Lotz, Zisman, and Bartter (Ref. 23); Cooke, Teitelbaum, and Avioli (Ref. 24); and Spencer et al. (Refs. 25 and 26) indicate that an increase in calcium excretion may occur with the ingestion of aluminum antacids. These reports are contradicted in a report by Cann, Prussin, and Gordan (Ref. 17) who report that the calcium balance is unchanged. The precise results of any calcium loss related to aluminum ingestion have not been defined.

Spencer et al. (Refs 27 and 28) have conducted studies that apparently show that aluminum forms insoluble complexes with fluoride ions in the gastrointestinal tract, thereby decreasing fluoride absorption. Although the authors have suggested that this decrease in fluoride absorption may contribute to skeletal demineralization, the suggestion is speculative because the fasting plasma fluoride levels did not change and because the role of normal dietary fluoride in maintaining skeletal bone has not been defined. Although there is evidence that oral aluminum antacids can lead to decreased fluoride absorption, the physiological

significance of this finding in adults is unclear.

Aluminum and renal dialysis. Evidence of neurotoxicity associated with aluminum is strongest for encephalopathy that occurs in renal failure patients undergoing dialysis (Refs. 29 through 42). Although aluminum has not been proven to be a causative factor, there is considerable indirect evidence that it has a role in development of the syndrome. The evidence appears to be stronger that high dialysate aluminum levels have contributed to the development of dialysis encephalopathy. It is also considered likely that high doses of oral aluminum compounds may contribute to total body aluminum. Studies have also been reviewed that indicate that bone aluminum levels are significantly elevated in chronic renal failure patients (Refs. 19, 20, 35, and 43 through 46). The level appears to be highest in patients on dialysis, related to the duration of dialysis, and has been correlated with the incidence of osteomalacic renal osteodystrophy in these patients.

In conclusion, the agency believes that a role for aluminum in the pathogenesis of Alzheimer's disease cannot be ruled out, but the evidence supporting such a rule is very weak. No data were found to indicate that parathyroid function is affected by aluminum. There are conflicting reports on the effect of aluminum antacids on calcium balance, but there is little evidence to support an etiologic role for aluminum antacids in osteoporosis. There is evidence that oral aluminum compounds can lead to reduced fluoride absorption, but the significance of this finding in adults is unclear at this time. In view of these findings, the agency does not believe the availability of OTC aluminum-containing antacids presents a significant hazard and thus will not require that they be removed from the OTC market. However, because of the potential role of aluminum in the development of dialysis encephalopathy syndrome, osteomalacic renal osteodystrophy, and hypophosphatemia, the agency believes it is appropriate to provide additional information in the professional labeling section of the antacid monograph (21 CFR 331.31) for aluminum-containing antacids as follows:

(1) Evidence suggests that elevated tissue aluminum levels have a role in development of the dialysis encephalopathy syndrome. A number of cases have been associated with elevated aluminum levels in the dialysate water. There is also evidence that small amounts of ingested aluminum are absorbed from the gastrointestinal tract, and it is likely that renal excretion of absorbed aluminum is impaired in renal failure. Prolonged use of aluminum-containing antacids in such patients may contribute to increased tissue levels of aluminum.

(2) Aluminum forms insoluble complexes with phosphate in the gastrointestinal tract, thus decreasing phosphate absorption. Prolonged use of aluminum-containing antacids by normophosphatemic patients may result in hypophosphatemia if phosphate intake is not adequate. In its more severe forms, hypophosphatemia can lead to anorexia, malaise, muscle weakness, and osteomalacia.

References

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2. One comment disagreed with the Panel's recommendation to include in the OTC labeling of aluminum-containing antacids a warning advising consumers against the use of such products if they have kidney disease except under the advice and supervision of a physician. The comment noted that the Panel cited only one report as evidence supporting this proposed warning (Ref. 1). Although the report suggests that the oral ingestion of aluminum may play a role in the development of dialysis encephalopathy in patients with severe kidney disease, the comment argued that the cause of dialysis encephalopathy in patients with severe kidney disease is complex and that there is disagreement about the toxicity or lack of toxicity of aluminum. In support of its argument, the comment cited a survey conducted by the European Dialysis and Transplant Association (Ref. 2), which showed no correlation between the ingestion of aluminum hydroxide and dialysis encephalopathy. The comment concluded that, although a warning concerning the risk potential in dialysis patients may be appropriate for professional labeling, such a warning was unwarranted on the OTC labeling of aluminum-containing antacid products. A second comment disagreed and cited a number of references in support of its opinion that there is a causative relationship between orally consumed aluminum-contalning drugs and dialysis encephalopathy. (Ref. 3).

The agency has thoroughly reviewed all of the available data concerning aluminum toxicity. (See comment 1 above.) In view of the evidence available at this time, the agency does not believe that the kidney-disease warning recommended by the Panel is warranted on the OTC labeling of aluminum-containing antacid products. No data could be found on the effects of mild or moderate impairment of renal function on the absorption, urinary excretion, or overall balance of oral aluminum. While there is evidence that ingestion of large amounts of aluminum-containing products for prolonged periods may lead to adverse effects, the labeling for OTC aluminum-containing antacids already includes a warning advising against the use of these products for more than 2 weeks. In addition, the strongest evidence for toxicity of aluminum is the encephalopathy that occurs in renal failure patients undergoing dialysis. While the evidence appears to be stronger that high aluminum levels of the dialysate have contributed to the development of dialysis encephalopathy, oral ingestion of aluminum compounds may contribute to total body aluminum. However, because there are no data on the effects of mild or moderate impairment of renal function on the absorption, urinary excretion, or overall balance of oral aluminum, and because persons at highest risk are those with severe renal failure who are generally under the care of a physician, the agency believes it is more prudent to inform the health professional of the potential risks involved rather than to require the kidney-disease warning recommended by the Panel. (See comment 1 above.)

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(3) Comment No. C0006, Docket No. 80N–0395, Dockets Management Branch.

3. One comment was concerned that the commercial availability of aluminum phosphate may be interrupted if the Panel's recommendation to eliminate the drug as an OTC antacid product is adopted. It was the comment's understanding that during the change from OTC to prescription status aluminum phosphate would be unavailable to physicians for use by kidney transplant patients who depend on the drug for postoperative management. A second comment, from a manufacutuer of aluminum phosphate, advised the agency of its intent to change the claims on its product from antiacid to hypophosphatemia and to switch the product from OTC to prescription status within the time period established for the implementation of the final monograph.

The agency appreciates the comment's concern regarding the continued availability of aluminum phosphate; however, it is unlikely that the marketplace will be interrupted in switching the product from OTC to prescription status. As discussed below, the agency believes that claims for the treatment of hypophosphatemia should not be permitted in the labeling of OTC drug products. Between publication of this tentative final regulation and the final regulation on hypophosphatemia and hyperphosphatemia drug products, manufacturers will have sufficient time to submit and have approved a new drug application for the prescription use of aluminum phosphate in treating hypophosphatemia. If a new drug application (NDA) is approved before the regulation becomes effective, the product may be switched to prescription status at that time. As noted above, the manufacturer of one aluminum phosphate product has advised the agency of its intention to change the marketing status of its product from OTC to prescription within the specified time period.

4. One comment suggested that the Panel's recommended regulation in § 310.542, which describes hyperphosphatemia and sets conditions that restrict the marketing of products containing aluminum carbonate labeled to treat hyperphosphatemia, would not serve any useful purpose because the marketing of OTC drug products containing aluminum carbonate would be regulated by professional labeling appearing in the monograph for OTC

antacid drug products. The comment added that a petition had been submitted to amend the professional labeling for antacid drug products (21 CFR 331.31) to include the use of aluminum carbonate for the treatment of hyperphosphatemia, and that this amendment will ensure that this indication will be included only in the professional labeling of antacid drug products containing aluminum carbonate.

The Panel recognized in its report (45 FR 81157) that aluminum carbonate can be marketed OTC as an antacid drug product and recommended that any labeling claims for hyperphosphatemia be limited to professional labeling only. The citizen petition (Docket No. 81P-0091/CP) requesting that the professional labeling of the monograph for OTC antacid drug products (21 CFR 331.31) be amended to include the hyperphosphatemia indication for aluminum carbonate was responded to by the agency on October 23, 1981 (Ref. 1). The agency stated that aluminum carbonate is safe and effective for the treatment, control, and management of hyperphosphatemia under medical supervision and that information distributed to medical professionals may include this indication. Because aluminum carbonate may be marketed OTC as an antacid without an NDA, the agency believes that the hyperphosphatemia claim may be considered as professional labeling for this ingredient. Therefore, the agency is proposing in this document to amend the professional labeling section of the antacid monograph (§ 331.31) to include the hyperphosphatemia claim. However, proposed § 310.542 states that the hyperphosphatemia claim is not acceptable for OTC labeling and that any drug product promoting this claim for OTC use is regarded as a new drug.

Reference

(1) Letter from W. F. Randolph, FDA, to J. N. Bathish, Wyeth Laboratories, Inc., October 23, 1981, Item Code PAV, Docket No. 81P-0091/CP, Dockets Management Branch.

II. The Agency's Tentative Adoption of the Panel's Report

FDA has considered the comments and other relevant data and information available and concurs with the Panel that, because the conditions of hypophosphatemia and hyperphosphatemia are not amenable to self-treatment, claims for the treatment of hypophosphatemia or hyperphosphatemia should not be permitted in the labeling of OTC drug products. However, the agency only concurs in part with the Panel's recommended rule that manufacturers wishing to make such claims for their products need to proceed through the new drug route. As discussed in comment number 4 above, the agency believes it is reasonable for hyperphosphatemia claims for aluminum carbonate to be included in the professional labeling section of the monograph for OTC antacid drug products because aluminum carbonate can be marketed OTC as a single ingredient antacid product.

However, a similar approach is not viable for aluminum phosphate. Although aluminum phosphate historically has been promoted as an OTC antacid, the Panel expressed concern that products containing this ingredient would not meet the acid neutralizing requirements of the antacid monograph (21 CFR Part 331, Subpart C). In fact, the manufacturer of one such product pointed out in its submission to the Panel that its product would not meet the acid neutralizing requirements of the antacid monograph (Ref. 1). The agency conducted the acid neutralizing capacity test on the manufacturer's aluminum phosphate product and found that the labeled minimum antacid dose of 15 milliliters (mL) neutralized only 4.38 milliequivalents (mEq) of acid, while a stable pH of 3.5 could not be established for the maximum dose of 30 mL (Ref. 2). Therefore, aluminum phosphate does not meet the acid neutralizing requirements of the antacid monograph and cannot be marketed as a single ingredient antacid drug product. Because the available data indicate that aluminum phosphate cannot be marketed OTC as a single ingredient antacid product, the professional labeling approach is not an appropriate mechanism with respect to this ingredient and an approved NDA would be required for marketing of the product.

The Panel recommended that if aluminum phosphate does not conform to the acid neutralizing requirement of the antacid monograph that it be removed from the list of antacid ingredients generally recognized as safe and effective (§ 331.11). Although aluminum phosphate as a single ingredient does not meet the requirements of the antacid monograph, it could potentially meet the requirements of that portion of § 331.10(a) that each ingredient of a combination product be included at a level that contributes at least 25 percent of the total acid neutralizing capacity of a combination antacid product, calculated on the basis of the procedures in § 331.21. Because aluminum phosphate does have some acid neutralizing capacity, it could be utilized as one component of a combination antacid drug product. Therefore, the agency will not adopt the Panel's recommendation to remove aluminum phosphate from the antacid monograph, but is proposing to amend the antacid monograph to clarify that aluminum phosphate is acceptable for use only in combination.

The agency is revising § 310.541(b) and § 310.542(b) to clarify that a product covered by the regulation is a new drug for which an approved NDA is required for marketing, and in the absence of an approved NDA the product would also be misbranded under section 502 of the act.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC hypophosphatemia and hyperphosphatemia drug products, is a major rule.

For purposes of the Regulatory Flexibility Act, the economic assessment concluded that, while the average economic impact of the overall OTC drug review on small entities will not be significant, the possibility of larger-than-average impacts on some small firms in some years might exist. Therefore, the assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose a significant impact on a substantial number of small entities. The analysis identified the possibilities of reducing burdens on small firms through the use of (a) relaxed safety and efficacy standards or (b) labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act. Nevertheless, to avoid overlooking any problems or feasible possibilities of relief peculiar to this group of products, the agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have

on OTC hypophosphatemia and hyperphosphatemia drug products. Comments regarding the economic impact of this rulemaking should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on hypophosphatemia and hypophosphatemia drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

References

(1) OTC Volume No. 170043, Docket No. 80N–0395, Dockets Management Branch.

(2) Memorandum from Director, Division of Drug Chemistry (HFN–420) to Director, Division of OTC Drug Evaluation (HFN–510), FDA, December 28, 1982, OTC Volume 17HTFM, Docket No. 80N–0395, Dockets Management Branch.

List of Subjects

21 CFR Part 310

New drugs.

21 CFR Part 331

OTC drugs, Antacids.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended, by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Parts 310 and 331 to read as follows:

PART 310—NEW DRUGS

1. Part 310 is amended by adding new §§ 310.541 and 310.542, to read as follows:

§ 310.541 Over-the-counter (OTC) drug products containing active ingredients offered for use in the treatment of hypophosphatemia.

(a) Hypophosphatemia is a condition in which an abnormally low plasma level of phosphate occurs in the blood. This condition is not amenable to self-diagnosis or self-treatment. Treatment of this condition should be restricted to the supervision of a physician. For this reason, any drug product containing ingredients offered for OTC use in the treatment of hypophosphatemia cannot be considered generally recognized as safe and effective.

(b) Any drug product that is labeled, represented, or promoted for OTC use in the treatment of hypophosphatemia is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption For a New Drug" (Form FDA–1571) (OMB Approval No. 0910–0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for use in the treatment of hypophosphatemia is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

§ 310.542 Over-the-counter (OTC) drug products containing active ingredients offered for use in the treatment of hyperphosphatemia.

(a) Hyperphosphatemia is a condition in which an abnormally high plasma level of phosphate occurs in the blood. This condition is not amenable to self-diagnosis or self-treatment. Treatment of this condition should be restricted to the supervision of a physician. For this reason, any drug product containing ingredients offered for OTC use in the treatment of hyperphosphatemia cannot be considered generally recognized as safe and effective.

(b) Any drug product that is labeled, represented, or promoted for OTC use in the treatment of hyperphosphatemia is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption For a New Drug" (Form FDA–1571) (OMB Approval No. 0910–0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for use in the treatment of hyperphosphatemia is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

PART 331—ANTACID PRODUCTS FOR OVER-THE-COUNTER (OTC) HUMAN USE

2. Part 331 is amended by revising § 331.11(a)(4) to read as follows:

§ 331.11 Listing of specific antacid ingredients.

(a) * * *

(4) Aluminum phosphate when used as part of an antacid combination product and contributing at least 25 percent of the total acid neutralizing capacity. Maximum daily dosage limit is 8 grams.

3. Part 331 is amended in § 331.31 by adding new paragraphs (a)(3) and (4) to read as follows:

§ 331.31 Professional labeling.

(a) * * *

(3) *For products containing aluminum identified in § 331.11(a)—Warnings.* (i) Evidence suggests that elevated tissue aluminum levels have a role in development of the dialysis encephalopathy syndrome. A number of cases have been associated with elevated aluminum levels in the dialysate water. There is also evidence that small amounts of ingested aluminum are absorbed from the gastrointestinal tract, and it is likely that renal excretion of absorbed aluminum is impaired in renal failure. Prolonged use of aluminum-containing antacids in such patients may contribute to increased tissue levels of aluminum.

(ii) Aluminum forms insoluble complexes with phosphate in the gastrointestinal tract, thus decreasing phosphate absorption. Prolonged use of aluminum-containing antacids by

normophosphatemic patients may result in hypophosphatemia if phosphate intake is not adequate. In its more severe forms, hypophosphatemia can lead to anorexia, malaise, muscle weakness, and osteomalacia.

(4)— *For products containing aluminum carbonate identified in § 331.11(a)(1)—Indication.* "For the treatment, control, or management of hyperphosphatemia, or for use with a low phosphate diet to prevent formation of phosphate urinary stones, through the reduction of phosphates in the serum and urine."

* * * * *

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompained by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730).Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record in March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final rule is published in the **Federal Register** unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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federal register

Tuesday
January 15, 1985

Part IV

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 310

Aphrodisiac Drug Products for Over-the-Counter Human Use

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 80N-0419]

Aphrodisiac Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administation (FDA) is issuing a notice of proposed rulemaking that would establish that aphrodisiac drug products for over-the-counter (OTC) human use are not generally recognized as safe and effective and are misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products and the public comment on an advance notice of proposed rulmaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food Drug Administation, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 1, 1982 (47 FR 43572) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify aphrodisiac drug products for OTC oral use as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based on the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. Interested persons were invited to submit comments by December 30, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by January 31, 1983.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above) after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, one consumer submitted a comment. This comment is on public display in the Dockets Management Branch.

In this proposed rule to amend Part 310 by adding to Subpart E new § 310.528 (21 CFR 310.528), FDA states for the first time its position on aphrodisiac drug products for OTC use. Final agency action on this matter will occur with the publication at a future date of a final rule relating to aphrodisiac drug products for OTC use.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC aphrodisiac drug products, based on the comment received and the agency's independent evaluation of the Panel's report. As discussed in the final rule revising the procedural regulations for reviewing and classifying OTC drugs, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final rule stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). (See the **Federal Register** of September 29, 1981; 46 FR 47730). This document retains the concepts of Categories I, II, and III at the proposed rule stage.

In the advance notice of proposed rulemaking, the agency stated that if it proposed to adopt the Panel's recommendation it would propose that aphrodisiac drug products for OTC oral use be eliminated from the OTC market effective 6 months after the date of publication of a final rule in the **Federal Register**, regardless of whether further testing was undertaken to justify their future use. Based on all information available to date, the agency has broadened the scope of this rulemaking and is proposing that any aphrodisiac drug product for OTC use be found not to be generally recognized as safe and effective. If the proposed finding is adopted in the final rule, the agency advises that the conditions under which the drug products that are subject to this rule are not generally recognized as safe and effective and are misbranded (nonmonograph conditions) will be effective 6 months after the date of publication of the final rule in the **Federal Register**. Upon the effective date of the final rule, OTC aphrodisiac drug products in interstate commerce will be regarded as unapproved new drugs and subject to regulatory action. Manufacturers are encouraged to comply voluntarily with the proposed rule at the earliest possible date.

I. The Agency's Tentative Conclusions on the Comment

The comment stated that yohimbine is known to be a workable aphrodisiac and that it has been tested at the Queens University in Canada as well as elsewhere. The comment contained a copy of a syndicated column that appeared in an unnamed newspaper (Ref. 1). The column responded to a reader who wrote that yohimbine, obtained in Mexico, had returned his potency to normal but that his doctor doubted that yohimbine was effective. The columnist stated that researchers at Queens University in Canada have reported that yohimbine may help some men who suffer from impotence, but the columnist did not provide any details of the study.

The agency telephoned the columnist and obtained the name of the publication that cited the Queens University study (Ref. 2). Subsequently, the agency obtained a copy of the journal in which the study was discussed.

The Queens University researchers reported on a number of studies, conducted during the late 1960's and mid 1970's using yohimbine in the treatment of impotence. The researchers stated that because of the variety of methodological problems the results are far from convincing and that the technologies used in the earlier studies did not provide for an accurate etiological diagnosis and for an objective assessment of therapeutic response. Accordingly, because of advances in diagnostic procedures and objective assessment, these researchers decided to reassess the value of yohimbine in a pilot study using 6 milligrams of yohimbine three times

daily in 23 highly selected patients in whom a firm diagnosis of primarily organic dysfunction was made. The researchers concluded that the results suggest that yohimbine may be beneficial in selected cases but that the number of satisfactory results is lower than the number given in previous reports. In addition, the researchers stated that, before pharmacological manipulation becomes established as an alternative to current surgical procedures for the treatment of erectile failure, controlled trials must be conducted to rule out a placebo effect.

The agency is aware that a 3-year study is being conducted at Queens University with the support of the Medical Research Council of Canada to determine the effectiveness of yohimbine as an aphrodisiac in highly selected cases and to resolve the question of diagnostic accuracy and objectivity frequently detracting from previous studies on the nonsurgical treatment or erectile dysfunction. Even if yohimbine were shown to be effective, the agency would concur with the Panel that individuals suffering from decreased libido and impaired sexual performance should not self-medicate, but should seek treatment under professional guidance. Therefore, at this time, the agency concludes that all aphrodisiac drug products, including yohimbine, are not appropriate for OTC use.

References

(1) Graedon, Joe, "Aphrodisiac May Really Work," *in* "The People's Pharmacy" (syndicated newspaper column, undated), Comment No. C–00001, Docket No. 80N–0419, Dockets Management Branch.

(2) Morales, A. et al., "Nonhormonal Pharmacological Treatment of Organic Impotence," abstract, *The Journal of Urology*, 128:45–47, The Williams and Wilkins Co., July 1982.

II. The Agency's Tentative Adoption of the Panel's Report

The Panel discussed the use of cantharides, don qual, estrogens, ginseng, golden seal, gotu kola, Korean ginseng, licorice, sarsaparilla, methyltestosterone, nux vomica, Pega Palo, sytrychnine, testosterone, yohimbine, and yohimbine hydrochloride as aphrodisiacs for OTC oral human use. FDA has considered the comment and other relevant data and information available at this time and concludes that it will tentatively adopt the Panel's report and recommendation.

The agency is tentatively adopting the following conclusions set forth by the Panel (45 FR 43574–43575): (1) that testosterone and methyltestosterone have a recognized influence on libido and sexual performance, but that these drugs are powerful hormones with potentially serious untoward effects and must be used only under the supervision of a physician; (2) that serious health risks are associated with alleged aphrodisiacs such as cantharides; (3) that there is no conclusive scientific evidence demonstrating the safety or effectiveness of any of the plant materials that have been used historically for aphrodisiac purposes; (4) and that individuals suffering from decreased libido and impaired sexual performance should not self-medicate, but should seek treatment under professional guidance.

In addition, the agency is aware that there are currently marketed products labeled as vitamins and minerals for OTC use as aphrodisiacs. Although the Panel did not address the use of vitamins and minerals as aphrodisiacs, the agency is aware of no data or information to support the safety and effectiveness of any vitamin or mineral for this use. Therefore, § 310.528(a) of the proposed rule includes vitamins and minerals among the ingredients that are not generally recognized as safe and effective for use as aphrodisiacs.

Whereas the Panel (the Advisory review Panel on OTC Miscellaneous Internal Drug Products) limited its deliberation to oral products, the agency believes that this rulemaking appropriately should apply to any ingredient labeled for use as an OTC aphrodisiac (any drug which is claimed to arouse or increase sexual desire or improve sexual performance). The agency is unaware of any data to support the oral or topical use of any OTC aphrodisiac drug product. Therefore, the agency tentatively concludes that any aphrodisiac for OTC use is classified as Category II.

The agency is also revising § 310.528(b) to clarify that a product covered by the regulation is a new drug for which an approved NDA is required for marketing, and that in the absence of an approved NDA the product would also be misbranded under section 502 of the act.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for aphrodisiac drug products for OTC use, is a major rule.

For purposes of the Regulatory Flexibility Act, the economic assessment concluded that, while the average economic impact of the overall OTC drug review on small entities will not be significant, the possibility of larger-than-average impacts on some small firms in some years might exist. Therefore, the assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose a significant impact on a substantial number of small entities. The analysis identified the possibilities of reducing burdens on small firms through the use of (a) relaxed safety and efficacy standards or (b) labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act. Nevertheless, to avoid overlooking any problems or feasible possibilities of relief peculiar to this group of products, the agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC aphrodisiac drug products. Comments regarding the economic impact of this rulemaking should be accompanied by appropriate documentation. The agency previously invited public comment in the advance notice of proposed rulemaking regarding any impact that this rulemaking would have on aphrodisiac drug products for OTC oral use. No comments on economic impacts were received. Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by May 15, 1985. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

New drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)) and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)) and under 21 CFR 5.11 it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 310 by adding to Subpart E new § 310.528, to read as follows:

PART 310—NEW DRUGS

§ 310.528 Drug products containing active ingredients offered over-the-counter (OTC) for human use as an aphrodisiac.

(a) Cantharides, don qual, estrogens, ginseng, golden seal, gotu kola ginseng, licorice, sarsaparilla, methyltestosterone, minerals, nux vomica, Pega Palo, strychnine, testosterone, vitamins, yohimbine, and yohimbine hydrochloride have been present as ingredients in drug products for use as an aphrodisiac. Androgens (e.g., testosterone and methyltestosterone) and estrogens are powerful hormones when administered internally and are not safe for use except under the supervision of a physician. There is a lack of adequate data to establish general recognition of the safety and effectiveness of any of these ingredients, or any other ingredient, for OTC use as an aphrodisiac. Labeling claims for aphrodisiacs for OTC use (any drug which is claimed to arouse or increase sexual desire or improve sexual performance) are either false, misleading, or unsupported by scientific data. The following claims are examples of some that have been made for aphrodisiac drug products for OTC use: "acts as an aphrodisiac;" "arouses or increases sexual desire and improves sexual performance;" "helps restore sexual vigor, potency, and performance;" "improves performance, staying power, and sexual potency;" "builds virility and sexual potency;" "creates an uncontrollable desire for immediate sexual gratification;" and "expands nature's gift of love." Based on evidence presently available, there is no ingredient that can be generally recognized as safe and effective for OTC use as an aphrodisiac.

(b) Any OTC drug product that is labeled, represented, or promoted for use as an aphrodisiac is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FDA –1571) (OMB Approval No. 0910-0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted OTC as an aphrodisiac is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such OTC drug product in interstate commerce that is not in compliance with this section is subject to regulatory action.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA–305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final rule is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

[FR Doc. 85–676 Filed 1–14–85; 8:45 am]

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federal register

Tuesday
January 15, 1985

Part V

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 333

Topical Acne Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 333

[Docket No. 81N-0114]

Topical Acne Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Adminstration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) topical acne drug products are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Antimicrobial (II) Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10).

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 23, 1982 (47 FR 12430) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC topical acne drug products, together with the recommendations of the Advisory Review Panel on OTC Antimicrobial (II) Drug Products, which was the advisory review panel responsible for evaluating date on the active ingredients in this drug class. Interested persons were invited to submit comments by June 21, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by July 21, 1982.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, eight drug manufacturers, one drug manufacturer association, one counsulting firm, three physicians, and one consumer submitted comments. Copies of the comments received are on public display in the Dockets Management Branch.

The advance notice of proposed rulemaking, which was published in the **Federal Register** on March 23, 1982 (47 FR 12430), was designated as a "proposed monograph" in order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10). Similarly, the present document is designated in the OTC drug review regulations as a "tenative final monograph." Its legal status, however, is that of a proposed rule. In this tenative final monograph (proposed rule) to establish Part 333, Subpart D, FDA states for the first time its position on the establishment of a monograph for OTC topical acné drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC topical acne drug products.

This proposal constitutes FDA's tenative adoption of the Panel's conclusions and recommendations on OTC topical acne drug products as modified on the basis of the comments received and the agency's independent evaluation of the Panels report. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). (See the **Federal Register** of September 29, 1981; 46 FR 47730). The Court in *Cutler* held that the OTC drug review regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Acccordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register**. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the advance notice of proposed rulemaking for OTC topical acne drug products (published in the **Federal Register** of March 23, 1982 (47 FR 12430)), the agency suggested that the conditions included in the monograph (Category I) be effective 30 days after the date of publication of the final monograph in the **Federal Register** and that the conditions excluded from the

monograph (Category II) be eliminated from OTC drug products effective 6 months after the date of publication of the final monograph, regardless of whether further testing was undertaken to justify their future use. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The Agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and reformulate their products and have them in compliance in the marketplace. However, if the agency determines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

All "OTC Volumes" cited through this document refer to the submissions made by interested persons pursuant to the call-for-data notice published in the **Federal Register** of December 16, 1972 (37 FR 26842) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

I. The Agency's Tentative Conclusions on the Comments

A. General Comments

1. One comment contended that OTC drug monographs are interpretive, as opposed to substantive, regulations. The comment referred to statements on this issue submitted earlier to other OTC drug rulemaking proceedings.

The agency addressed this issue in paragraph 85 through 91 of the preamble to the procedures for classification of OTC drug products, published in the **Federal Register** of May 11, 1972 (37 FR 9464) and in paragraph 3 of the preamble to the tentative final monograph for antacid drug products, published in the **Federal Register** of November 12, 1973 (38 FR 31260). FDA reaffirms the conclusions stated there. Subsequent court decisions have confirmed the agency's authority to issue substantive regulations by rulemaking. See, e.g., *National Nutritional Foods Association* v. *Weinberger*, 512 F. 2d 688, 696–98 (2d Cir. 1975) and *National Association of Pharmaceutical Manufacturers* v. *FDA*, 487 F. Supp. 412 (S.D.N.Y. 1980), *aff'd* 637 F. 2d 887 (2d Cir. 1981).

2. One comment pointed out an error in the Panel's report under part II. paragraph A.1.b.(2) regarding the statement that "Clinical response was evaluated after 2 weeks by lesion counts. . . ." (See 47 FR 12448.) The comment believed that it should read 12 weeks instead of 2 weeks.

This was a printing error; the sentence should have read "Clinical response was evaluated after 12 weeks. . . ."

3. Noting the statement under part II. paragraph I.2., Criteria for Evaluating Effectiveness, that "studies in induced or experimental acne were similarly not considered as proof of effectiveness" (47 FR 12442), one comment stated that comedolytic studies are important in making a preliminary determination of effectiveness of some active ingredients and urged the agency to add the following sentence: "However, animal and human comedolytic studies can be used as corroborative and supporting evidence of effectiveness."

The agency agrees with the comment that animal and human comedolytic studies can be useful as supporting evidence of effectiveness. Even though the Panel did not consider studies in induced acne as sole proof of effectiveness, FDA does not believe that the Panel's statement precludes manufacturers from using this type of study as preliminary or supporting evidence of effectiveness.

4. One comment stated that acne responds favorably to the application of mouthwash to the infected area once or twice daily. The comment specifically mentioned a mouthwash containing thymol, eucalyptol, methyl salicylate, and menthol in alcohol as an effective acne remedy. The comment suggested that mouthwashes be considered as the initial treatment for acne because they are less expensive and "just as effective" as OTC acne drug products.

Because the comment did not submit any data to support its contention that mouthwashes are effective acne treatments, the agency cannot agree with the comment's conclusion. Thymol, one of the ingredients in the mouthwash mentioned by the comment, was classified Category II as an active acne ingredient by the Panel and has been reclassified Category III by the agency. (See comment 7 below.) No data were submitted on eucalyptol, and it was not contained in any acne drug products. Therefore, this ingredient was not reviewed by the Panel. The Panel identified methyl salicylate, menthol, and alcohol as inactive ingredients.

It appears that the effectiveness of mouthwashes as acne remedies would likely be due to the alcohol present in the products. The product mentioned by the comment contains 26.9 percent alcohol. Alcohol was classified as an antiseptic at a concentration of 60 to 95 percent by the Advisory Review Panel on OTC Miscellaneous External Drug Products in its report published in the **Federal Register** of May 21, 1982 (47 FR 22324). However, the Advisory Review Panel on OTC Antimicrobial (II) Drug Products did not review alcohol as an active ingredient for the treatment of acne, and the agency is not aware of adequate data that support the use of alcohol as an acne drug product.

B. Comments on Active Ingredients

5. One comment submitted data (Ref. 1) addressing two of the Panel's concerns on povidone-iodine: availability of elemental iodine from the complex and the stability of povidone-iodine (47 FR 12465). The comment stated that substantial data were submitted to the OTC Antimicrobial (I) Panel and other panels showing that iodine is freely released from the complex and the rate of iodine release is controlled by tissue demand. The comment contended that at equilibrium any iodine that is removed from the complex is replaced within less than 25 milliseconds (Refs. 2 and 3). The comment pointed out that chemical titration studies were submitted to the antimicrobial rulemaking, and these

studies show that povidone-iodine provides the same amount of available iodine as tincture of iodine (Ref. 4). Regarding the stability of the complex, the comment contended that even if a stability issue existed, it would be outside the scope of the review, as stability is covered by the current good manufacturing practice regulations (CGMP) (21 CFR Parts 210 and 211). The comment stated that, under the CGMP regulations, minimum standards have been set to ensure product stability for finished drug products (21 CFR 211.166), and the manufacturer of the finished dosage form is responsible for complying with these stability standards. The comment added that expiration dating as well as appropriate storage conditions are determined through required written testing programs.

The Panel considered povidone-iodine to be safe. However, it believed that further studies were needed on availability and stability and to determine effectiveness of the drug in the treatment of acne (47 FR 12465). The agency has reviewed the data submitted regarding availability (Refs. 2 and 3) and agrees with the comment that iodine is rapidly released from the povidone-iodine complex. According to the references that were submitted, a povidone-iodine solution at a concentration of 1 to 10 percent contains over 99 percent complexed iodine (Ref. 2). The concentration of free iodine in the solution reaches a maximum of 8×10^{-5} moles/liter. At equilibrium, the povidone-iodine complex is self-monitoring. Based on an iodine-starch reaction as a biological model, it has been shown that any iodine that is removed from the complex would be replaced within less than 25 milliseconds (Ref. 3). In addition, povidone-iodine is recognized in the United States Pharmacopeia/National Formulary (USPXXI/NFXVI) and subject to the requirements contained therein.

The agency also agrees with the comment that issues regarding stability can be resolved by the CGMP regulations (21 CFR Parts 210 and 211). These regulations require a written testing program to assess the stability of finished products and to determine appropriate storage conditions and an expiration date. Section 211.137(a) requires that drug products bear an expiration date supported by appropriate stability testing. Where an expiration date is not necessary under the provisions of § 211.137(g), manufacturers must have appropriate data to show that the drug products are stable for at least 3 years. Therefore, FDA concludes that further submissions of data on the stability of povidone-iodine are not needed for purposes of this rulemaking proceeding.

The agency believes that the issues of availability of iodine from the povidone-iodine complex and stability of the complex have been resolved for this ingredient. However, the agency believes that a double-blind, vehicle-controlled study is still needed to resolve the Panel's concerns regarding povidone-iodine's effectiveness in the treatment of acne. Thus, povidone-iodine remains in Category III for use in the treatment of acne.

References

(1) Comment No. C00012, Docket No. 81N-0114, Dockets Management Branch.

(2) Schenck, H. U., et al., "Structure of Povidone-Iodine," *in* "Current Chemotherapy and Infectious Disease," Volume I, American Society for Microbiology, Washington, pp. 477–478, 1980.

(3) Ditter, W., D. Horn, and E. Luedekke, "Thermodynamic and Kinetic Examinations Concerning the Complex Binding State and the Rate of Liberation of Iodine from Aqueous Iodine-PVP-Solutions," included in Comment No. C00012, Docket No. 81N-0114, Dockets Management Branch.

(4) Comment No. C00108, Docket No. 75N-0183, Dockets Management Branch.

6. Several comments requested that the agency reclassify salicylic acid 0.5 to 5 percent from Category III to Category I. The comments pointed out that the Panel reviewed several well-designed studies supporting the effectiveness of salicylic acid (47 FR 12466), but none of these studies used the vehicle as the control as was required by the Panel. One comment submitted two vehicle-controlled studies (Refs. 1 and 2) which it believed met the Panel's criteria and demonstrated the effectiveness of salicylic acid in the treatment of acne. In one study, 2 percent salicyclic acid was tested against the vehicle and an active control (5 percent benzoyl peroxide) in 180 subjects (Ref. 1). In the second study, salicylic acid 0.5 and 2 percent were compared to the vehicle control in 187 subjects (Ref. 2).

The agency has reviewed the submitted studies (Refs. 1 and 2) and concludes that they meet the Panel's criteria for well-designed studies (47 FR 12472) and demonstrate the effectiveness of salicylic acid in the treatment of acne. In a 12-week study of 180 subjects, good or excellent results (for total lesions) were obtained by 40 percent of the subjects using 2 percent salicylic acid. Such results were obtained for only 5 percent of the subjects using the vehicle and 2 percent of the subjects using benzoyl peroxide (Ref. 1). Salicylic acid was particularly effective on inflammatory lesions (papules and pustules), where 86 percent of the subjects treated with salicylic acid had good or excellent results, compared with 11 percent for the vehicle and 15 percent for benzoyl peroxide. Although there was no statistically significant difference between the three treatments in their effect on closed comedones, salicylic acid was significantly more effective than the vehicle or benzoyl peroxide in the reduction of total lesions, inflammatory lesions, and open comedones ($p < 0.001$).

In the second study, in which 0.5 and 2 percent salicylic acid were tested against the vehicle in 187 subjects, both concentrations of salicylic acid were found to be superior to the vehicle control in reducing inflammatory lesions, open and closed comedones, and total lesion count ($p < 0.001$) (Ref. 2). At the end of the treatment, 98 percent of the subjects using 2 percent salicylic acid showed good or excellent results compared with 91 percent using 0.5 percent salicylic acid and 11 to 12 percent of the subjects in the two control groups. Based on these studies and the data cited by the Panel (47 FR 12466), the agency is proposing to classify salicylic acid 0.5 to 2 percent in Category I for the treatment of acne.

Although the Panel considered salicylic acid to be safe in concentrations up to 5 percent, the agency is proposing to limit the upper concentration to 2 percent. The only safety data discussed by the Panel were on the 0.5- to 2-percent concentration, which was judged to be a mild irritant when applied to either normal or abraded skin of rabbits. The Panel also reported results of the application of a lotion containing 2 percent salicylic acid to normal and abraded rabbit skin and to the eyes of rabbits (47 FR 12465–6). In part, the Panel based its acceptance of the 5-percent concentration as safe on a theoretical calculation of systemic absorption (47 FR 12466). The studies submitted to the agency following publication of the advance notice of proposed rulemaking used 2 percent salicylic acid, and adverse reactions reported were minimal (Refs. 1 and 2). The agency is concerned that there is an increased potential for irritation from concentrations greater than 2 percent and that adequate data have not been submitted to establish general recognition of the safety of concentrations above 2 percent in treating acne. In its topical antifungal report, the Panel had recommended a safe concentration of 3 percent for topical antifungal use, but stated that

this ingredient should be restricted to "relatively small body areas" (47 FR 12549). As the Panel pointed out, "the major difference in the use of salicylic acid in acne as opposed to its use in fungal infections of the foot and groin is the very large surface area over which acne may be involved" (47 FR 12465). Letters from Dr. Leyden (Ref. 3) and Dr. Shalita (Ref. 4) submitted as comments to the advance notice of proposed rulemaking support general recognition of this 0.5- to 2-percent concentration, but do not indicate general recognition of higher concentrations. As another comment pointed out (Ref. 5), many of the studies reviewed by the Panel utilized salicylic acid at a 0.5-percent concentration. Based on the submitted data, the agency proposes that salicylic acid 0.5 to 2 percent be classifed in Category I but that concentrations greater than 2 percent up to 5 percent remain in Category III pending receipt of data to establish general recognition of safety at these concentrations.

The agency's detailed comments and evaluation of the data are on file in the Dockets Management Branch (Ref. 6).

References

(1) Shalita, A. R., "Double-blind Investigation of 2% Salicylic Acid Solution Versus Vehicle Solution and Active Control (Benzoyl Peroxide 5%) in the Treatment of Acne Vulgaris Pillsbury Grades I to III," included in Comment No. C00002, Docket No. 81N-0114, Dockets Management Branch.

(2) Leyden, J., "Double-blind Investigation of 0.5% and 2% Salicylic Acid Solutions (Medicated Pads) Versus Vehicle Solutions (Pads) in the Treatment of Acne Vulgaris Pillsbury Grades I to III," included in Comment No. SUP, Docket No. 81N-0014, Dockets Management Branch.

(3) Comment No. C00009, Docket No. 81N-0114, Dockets Management Branch.

(4) Comment No. C00004, Docket No. 81N-0114, Dockets Management Branch.

(5) Comment No. C00011, Docket No. 81N-0114, Dockets Management Branch.

(6) Letter from W. E. Gilbertson, FDA, to E. J. Hiross, Sterling Drug Inc., coded LET002, Docket No. 81N-0114, Dockets Management Branch.

7. One comment objected to the Panel's Category II classification of thymol, specifically disagreeing with the Panel's assessment that there are insufficient data available to determine safety. The comment requested that the views of other panels be considered, noting that thymol was found by the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (TOPICAL Analgesic Panel) to be safe as an external analgesic at a concentration of 1 to 2 percent, not irritating when applied to the skin, and virtually unabsorbed topically (44 FR 69855). The comment added that the Advisory Review Panel on OTC Oral Cavity Drug Products found thymol (0.006 to 0.1 percent) safe for topical use on mucous membranes of the mouth and throat (47 FR 22888); and that the Antimicrobial II Panel, which evaluated antifungal drug products in addition to acne drug products, found that thymol, up to and including 0.2 percent, is safe as an inactive ingredient for use in topical antifungal formulations (47 FR 12522). The comment stated that numerous safety studies were submitted to the Panel, including clinical trials in which thymol was used on about 600 humans for up to 6½ months, and that no significant adverse effects were seen.

The comment contended that the Panel's reason for placing thymol in Category II for effectiveness, i.e., the absence of data evaluating the effectiveness of thymol in a vehicle-controlled study for the treatment of acne (47 FR 12462), was inconsistent with other Panel statements, specifically "ingredients were placed in Category II if there was no rational explanation of their mode of action, no substantial scientific evidence to suggest effectiveness, no general acceptance by consultant 'acne experts' and no supportive evidence of effectiveness in the medical literature on acne." Stating its belief that Category II should be reserved for cases where no data have been presented or where the data presented show that an ingredient has no effect, the comment maintained that placing an ingredient in Category II merely because of the absence of a vehicle-controlled study was an inappropriate course of action. The comment added that it had submitted to the Panel five clinical studies on thymol that demonstrated a statistical and clinical improvement in acne (Ref. 1). The comment also objected to the Panel's statement that thymol has questionable antibacterial activity at 0.16 to 0.5 percent concentration (47 FR 12462) and submitted new in vitro data to support antibacterial activity (Ref. 2).

The agency has reviewed the data submitted (Refs. 1, 2, and 3) and proposes to reclassify thymol from Category II to Category III. Regarding safety, the Panel stated that data are needed on absorption from small areas of application to intact and broken skin, effect on wound healing, and irritation potential (47 FR 12462). As the comment noted, the same Panel considered thymol at concentrations of 0.2 percent or less to be safe as an inactive ingredient in topical antifungal formulations (47 FR 12523), even though the Panel stated that more data were needed to determine the safety at higher concentrations. Based on the lack of adverse effects from the use of thymol (0.0162 percent) in clinical trials (Ref. 1), the lack of irritation or sensitization on animals and humans (Refs. 1 and 3), and the Panel's view that 0.2 percent (or less) thymol is safe for topical antifungal use, the agency believes that thymol in concentrations up to 0.2 percent can be considered safe for topical use in the treatment of acne. However, more data are needed on the safety of concentrations greater than 0.2 percent for the treatment of acne.

Although the agency believes that the conclusions of panels other than the initial reviewing panel should be considered when making a safety determination, a safety determination by a panel for a use other than topical application in acne cannot necessarily be applied to the topical treatment of acne. The Topical Analgesic Panel based its approval of the safety of thymol at a concentration of 1 to 2 percent on clinical use. Topical application to acne differs from topical analgesic use because a larger surface area is involved and duration of treatment is longer, usually involving several months of use. The agency does not believe that concentrations of thymol greater than 0.2 percent have been widely used in the treatment of acne to allow general recognition of safety. Thus the agency proposes that thymol only in a concentration of 0.2 percent or less be considered safe for the treatment of acne.

Regarding effectiveness, the Panel reviewed the clinical studies mentioned by the comment in which thymol 0.0162 percent was tested (Ref. 1) and stated that none of the studies tested thymol against a vehicle control (47 FR 12462). The Panel recommended, and the agency concurs, that thymol should be evaluated by a double-blind, vehicle-controlled clinical trial. The comment submitted data on antibacterial activity in which the minimal inhibitory concentration of thymol against one strain of *Corynebacterium acnes* was found to be between 62.5 micrograms/milliliter (μg/ml) and 125 μg/mL (Ref. 2). Although this study indicates that thymol has antibacterial activity in vitro, it is not adequate evidence to move thymol to Category I or to allow the antibacterial labeling recommended by the Panel. The Panel recommended that in vivo testing is necessary in order for a Category I ingredient to use antibacterial labeling (47 FR 12473).

The agency believes that even though the data do not meet the Panel's criteria, they are supportive evidence that thymol may have an effect on acne.

Thus, the agency proposes that thymol in a concentration of 0.2 percent or less be considered safe for the treatment of acne, but that further data are needed on effectiveness (Category III). For concentrations greater than 0.2 percent up to 0.5 percent, data are needed on both safety and effectiveness (Category III).

The agency's detailed comments and evaluation of the submissions and the references cited by the comment are on file in the Dockets Management Branch (Ref. 4).

References

(1) OTC Volume 070156.
(2) Comment No. C00010, Docket No. 81N-01114, Dockets Management Branch.
(3) OTC Volume 070155.
(4) Letter from W. E. Gilbertson, FDA, to J. D. Clark, Warner-Lambert Co., coded LET003, Docket No. 81N-0114, Dockets Management Branch.

C. Comments on Combination Products

8. One comment urged the agency to place the combination of sulfur and salicylic acid in Category I without requiring additional testing. The comment compared this combination to the combination of sulfur and resorcinol, which the Panel had placed in Category I. Although not submitting any data, the comment stated that salicylic acid is superior to resorcinol as a keratolytic agent. In addition, the comment pointed out that salicylic acid is less likely to be systemically absorbed than resorcinol because it is less soluble and that the occasional pigmemtation problems that may occur with topical use of resorcinol are not seen with salicylic acid.

The Panel concluded that data on the effectiveness of sulfur-salicylic acid combinations were inadequate (47 FR 12471). The agency has reviewed the data submitted to the Panel (Refs. 1 through 4) and agrees with the Panel's assessment. The agency is aware of two clinical studies on the combination (Refs. 5 and 6) that were reviewed by the Panel (47 FR 12466), but neither study met the Panel's criteria. No new data on this combination have come to the agency's attention. As discussed in comment 6 above, the agency proposes to classify salicylic acid 0.5 to 2 percent as Category I as a single ingredient. Sulfur 3 to 10 percent is also in Category I as a single ingredient (47 FR 12447). However, the Panel did not provide for a combination of two Category I acne ingredients, stating that each ingredient's contribution to the efficacy of the combination should be demonstrated in a clinical trial (47 FR 12468).

The combination policy in § 330.10(a)(4)(iv), as supplemented by the agency's general guidelines for OTC drug combination products (Ref. 7), specifies the criteria for OTC combination drug products. The agency's guidelines state that ingredients from the same therapeutic category that have different mechanisms of action may be combined to treat the same symptoms or conditions if the combination meets the OTC combination policy in 21 CFR 330.10(a)(4)(iv) in all respects and the combination is, on a benefit-to-risk basis, equal to or better than each of the active ingredients used alone at its therapeutic dose. The guidelines also state that Category I active ingredients from the same therapeutic category that have the same mechanism of action should not ordinarily be combined unless there is some advantage over the single ingredient in terms of enhancing effectiveness, safety, patient acceptance, or quality of formulation.

According to the Panel, the exact mechanisms of action for salicylic acid and sulfur are unknown, although both ingredients have keratolytic activity (47 FR 12447 and 12466). Although the mechanisms of action are unknown, under either aspect of the combination policy described above, data must be submitted demonstrating that the combination of ingredients is equal to or better than the individual ingredients alone. For the sulfur-resorcinol combination, the Panel discussed a study in which the combination was found to be superior to sulfur and placebo in the reduction of papules and whiteheads (47 FR 12469). The combination was not compared with resorcinol; however, the Panel had concluded that resorcinol is not effective as a single ingredient (47 FR 12459). In addition, the Panel cited several other studies that support the effectiveness of the sulfur-resorcinol combination (47 FR 12468). Because sulfur and salicylic acid are both considered effective as single ingredients, data are needed showing that the combination is equal to or better than the single ingredients. The comment, however, did not submit any such data for the sulfur-salicylic acid combination. Combinations containing ingredients from the same therapeutic category, such as sulfur and salicylic acid, will be permitted if adequate data are presented to the agency.

References

(1) OTC Volume 070090.
(2) OTC Volume 070092.
(3) OTC Volume 070261.
(4) OTC Volume 070268.
(5) Riley, K. A., "Therapeutic Skin Washing in Seborrhea and Acne Vulgaris," *Medical Times*, 86:973–977, 1958.
(6) Baird, J. W., "Acne. A New Approach to an Old Problem," *Journal of Pediatrics*, 52:152–157, 1958.
(7) Food and Drug Administration, "General Guidelines for OTC Drug Combination Products," September 1978, Docket No. 78D-0322, Dockets Management Branch.

9. Several comments urged the agency to broaden the range of acceptable concentrations for sulfur-resorcinol combinations beyond the Panel's recommendation of 8 percent sulfur combined with either 2 percent resorcinol or 3 percent resorcinol monoacetate. One comment, noting that the Panel had placed 3 to 10 percent sulfur in Category I as a single ingredient (47 FR 12447), requested that 3 to 10 percent sulfur be allowed in combination with 2 percent resorcinol or 3 percent resorcinol monoacetate. Noting the Panel's statement that resorcinol enhances the activity of sulfur (47 FR 12469), the comment asserted that "There simply is no basis for assuming that resorcinol enhances the activity of eight percent sulfur, but not of other concentrations of sulfur within the Category I range."

Other comments requested that 2 percent sulfur be allowed in combination with 1 percent resorcinol to make available the widest possible choice of safe and effective medications. One of the comments stated that there should be no question about safety as the Panel judged the combination to be safe at the highest concentrations. Pointing out the Panel's statement that "consumer interests are best served by exposure to the fewest ingredients possible at the lowest possible dosage regimen that is consistent with a satisfactory level of effectiveness" (47 FR 12468), another argued that lowering the concentration of this combination would be consistent with the Panel's statement. Both comments mentioned a study that was reviewed by the Panel (47 FR 12469), comparing the effectiveness of a combination containing 2.66 percent colloidal sulfur (equivalent to 2 percent sulfur) and 1 percent resorcinol with a combination of 8 percent sulfur and 2 percent resorcinol, sulfur alone, and placebo (Ref. 1). The comments contended that this study met the Panel's criteria and showed that the combination of 2 percent sulfur and 1 percent resorcinol was "equivalent" to the combination of 8 percent sulfur and 2 percent resorcinol and was superior to the placebo and to sulfur alone in reducing papules and whiteheads.

The agency is proposing to allow a combination of 3 to 8 percent sulfur with either 2 percent resorcinol or 3 percent

resorcinol monoacetate. The Panel concluded that 3 to 10 percent sulfur is safe and effective in the treatment of acne (47 FR 12447) and that resorcinol enhances the activity of sulfur (47 FR 12469). Because the Panel approved a combination of 8 percent sulfur and 2 percent resorcinol, the agency believes it would be reasonable to allow lower concentrations of sulfur (3 to 8 percent) that safe and effective to be combined with resorcinol. As both sulfur and resorcinol have keratolytic activity and may prove to be too irritating to the skin when combined in higher concentrations and because resorcinol enhances the activity of sulfur, the agency would require safety studies prior to allowing a combination of sulfur greater than 8 percent with resorcinol.

FDA agrees with the comments that there would be no safety problems for sulfur-resorcinol combinations in lower concentrations that proposed above, but the agency does not agree that data are adequate to determine effectiveness. The agency has reviewed the study cited by the comments (Ref. 1) and the Panel's criteria for evaluating effectiveness (47 FR 12442). The study did not meet the criteria of being a multi-center study involving more than one investigator, and it did not use the vehicle as the control. The Panel stated that although a clinical trial did not meet all of its criteria, an ingredient could still be considered for Category I provided there is supporting evidence of effectiveness. The agency is not aware of any other data supporting the effectiveness of a sulfur-resorcinol combination at the low concentrations requested by the comment; nor is the agency aware of any marketed products at this concentration. As discussed by the Panel, the two sulfur-resorcinol creams were superior to placebo and sulfur alone in the reduction of papules and whiteheads. However, no difference was found between the four treatment groups in overall complexion, pustules, blackheads, and oiliness (47 FR 12469). While the study is supportive of effectiveness, and the agency is aware that resorcinol enhances the activity of sulfur, the agency believes that further study is needed to establish the effectiveness of the combination of sulfur 2 percent and resorcinol 1 percent.

Reference

(1) OTC Volume 070250.

D. Comments on Labeling

10. Noting its continuing opposition to the exclusivity policy, one comment stated that FDA should not prohibit the use of alternative OTC labeling terminology to describe indications, if that terminology is truthful, not misleading, and intelligible to the consumer. The comment stated that existing statutory provisions (15 U.S.C. 1453(a) and sections 502(e) and 508 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(e) and 358)) and 21 CFR 201.61 do not show a congressional intent to authorize FDA to legislate the exact wording of OTC drug claims to the exclusion of other equally accurate and truthful claims for these products, and that section 502(c) (21 U.S.C. 352(c)) of the act demonstrates a congressional intent to the contrary.

During the course of the OTC drug review, the agency has maintained that the terms that may be used in an OTC drug product's labeling are limited to those terms included in a final OTC drug monograph. (This policy has become known as the "exclusivity rule.") The agency's position has been that it is necessary to limit the acceptable labeling language to that developed and approved through the OTC drug review process in order to ensure the proper and safe use of OTC drugs. The agency has never contended, however, that any list of terms developed during the course of the review exhausts all the possibilities of terms that appropriately can be used in OTC drug labeling. Suggestions for additional terms or for other labeling changes may be submitted as comments to proposed or tentative final monographs within the specified time periods or through petitions to amend monographs under § 330.10(a)(12). For example, the labeling proposed in this tentative final monograph has been expanded and revised in response to comments received.

During the course of the review, FDA's position on the "exclusivity rule" has been questioned many times in comments and objections filed in response to particular proceedings and in correspondence with the agency. The agency has also been asked by The Proprietary Association to reconsider its position. In a notice published in the **Federal Register** of July 2, 1982 (47 FR 29002), FDA announced that a hearing would be held to asist the agency in resolving this issue. On September 29, 1982, FDA conducted an open public forum at which interested parties presented their views. The forum was a legislative type administrative hearing under 21 CFR Part 15 that was held in response to a request for a hearing on the tentative final monographs for nighttime sleep-aids and stimulants (published in the **Federal Register** of June 13, 1978; 43 FR 25544). The agency's decision on this matter will be announced in the **Federal Register** following conclusion of its review of the material presented at the hearing.

11. One comment requested that the agency add the following two labeling statements, which the comment contended are truthful and not misleading, to the Panel's recommended § 333.350(b)(1): "Dermatologist tested" and "One of the most effective acne pimple medications you can buy without a prescription." The comment also requested the addition of the claim "Antibacterial (or antimicrobial) action against *P. acnes*, the organism commonly associated with acne" to the Panel's recommended § 333.350(b)(3).

The OTC drug review program establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. Two principal conditions examined during the review are allowable ingredients and allowable labeling. FDA has determined that it is not practical—in terms of time, resources, and other considerations—to set standards for all labeling found in OTC drug products. Accordingly, OTC drug monographs regulate only labeling related in a significant way to the safe and effective use of covered products by lay persons. OTC drug monographs establish allowable labeling for the following items: product statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action.

Because the first two claims suggested by the comment, "Dermatologist tested" and "One of the most effective acne pimple medications you can buy without a prescription," are not directly to the safe and effective use of acne drug products, the agency considers these claims to be outside the scope of the monograph. Such statements or terms will be evaluated by the agency on a product-by-product basis, unde the provisions of section 502 of the act (21 U.S.C. 352) relating to labeling that is false and misleading. Moreover, any term that is outside the scope of the monograph, even though it is truthful and not misleading, may not appear in any portion of the labeling required by the monograph and may not detract from such required information. However, statements and terms outside the scope of the monograph may be included elsewhere in the labeling provided they are not false or misleading.

Although the Panel recommended labeling for antibacterial activity (47 FR 12476), none of the Category I

ingredients met the Panel's in vivo criteria for antibacterial activity (47 FR 12473). Thus, no ingredients were recommended to use the antibacterial claims. None of the comments received following publication of the Panel's report submitted in vivo data relating to antibacterial activity. Therefore, because there are no ingredients that can use the antibacterial labeling, the agency is not proposing antibacterial labeling claims, including the claim suggested by the comment, in this tentative final monograph.

12. Several comments objected to the warning recommended by the Panel for all acne products in § 333.350(c)(1)(ii), "Other topical acne medications should not be used at the same time as this medication." The comments noted that dermatologists frequently prescribe the concomitant or sequential use of benzoyl peroxide with retinoic acid or salicylic acid, and one comment cited a reference to this effect (Ref. 1). One comment stated that the combined use of a comedolytic agent with an antimicrobial or antibiotic is rational, safe, and routine therapy; while other comments were concerned that the warning would preclude the use of non-drug acne cleansers and medicated soaps. According to one comment, market research has shown that many consumers think of non-drug cleansers as "medications," and therefore the warning could cause confusion. Another comment believed the warning would prevent consumers from using a medicated acne wash product containing a Category I ingredient before applying an acne product intended to remain on the skin.

The comments either suggested deleting the warning or provided alternate warnings. One comment recommended the following warning: "Do not use other topical medications at the same time or immediately following application of this medicine." Another comment believed it would be more appropriate to warn the consumer about the potential for increased dryness and irritation when more than one acne medication is used. Two comments believed that specific safety concerns should be addressed only in the warnings for the ingredients in question. One of these comments pointed out that the Panel's real concern was that the use of sulfur with benzoyl peroxide would enhance the sensitization potential of benzoyl peroxide (47 FR 12469). This comment suggested deleting the general warning at § 333.350(c)(1)(ii) and revising the warning for sulfur in § 333.350(c)(3) to include the statement "Topical acne medications containing benzoyl peroxide should not be used at the same time as this medication" or a similarly worded warning.

The agency agrees with the comments that the warning proposed in § 333.350(c)(1)(ii) could be confusing to consumers who use a medicated or nonmedicated acne cleanser prior to applying an acne medication intended to remain on the skin. As pointed out by the comments, the warning also contradicts the common practice among dermatologists of prescribing more than one acne medication for a patient. The Panel's original concern was that using benzoyl peroxide and sulfur at the same time could increase irritation or cause a sensitization problem. However, the Panel expanded this concept into a broad warning that would cover all ingredients because it believed that the use of any two keratolytic agents may result in an adverse effect (Ref. 2).

All of the Category I acne ingredients are keratolytic and tend to dry out the skin. The agency believes that some type of warning is necessary to alert consumers using more than one acne product about the increased potential for dryness and irritation. Thus, the agency is proposing, instead of the warning recommended by the Panel, the following warning for all acne drug products in § 333.350(c)(1)(ii): "Using other topical acne medications at the same time or immediately following use of this product may increase dryness or irritation of the skin. If this occurs, only one medication should be used unless directed by a doctor."

References

(1) Frank, S.B., "Acne-Update for the Practitioner," Yorke Medical Books, New York, pp. 141, 145, 150–158, 250, and 253–254, 1979.

(2) Summary Minutes of the 54th Meeting of the Advisory Review Panel on OTC Antimicrobial (II) Drug Products, November 14 and 15, 1980, p. 10, included in OTC Volume 07BPA2.

13. One comment requested that the words "pharmacist" and "sensitive areas of the neck" be deleted from the warning for benzoyl peroxide recommended by the Panel in § 333.350(c)(2), which reads as follows:

Do not use this medication if you have very sensitive skin or if you are sensitive to benzoyl peroxide. This product may cause irritation, characterized by redness, burning, itching, peeling, or possibly swelling. More frequent use or higher concentrations may aggravate such irritation. Mild irritation may be reduced by using the product less frequently or in a lower concentration. If irritation becomes severe, discontinue use; if irritation still continues, consult a doctor or pharmacist. Keep away from eyes, lips, mouth, and sensitive areas of the neck. This product may bleach hair or dyed fabrics.

The comment objected to the word "pharmacist" because the training and experience of most pharmacists does not qualify them to diagnose or treat dermatological conditions. The comment believed that in the situation described in the warning most pharmacists would refer the consumer to a physician.

The comment objected to the phrase "sensitive areas of the neck" stating it would be confusing to the consumer because it implies that a "greater sensitivity exists in certain unspecified areas of the neck." The comment noted that the consumer is already forewarned about using the product on very sensitive skin and thus the warning regarding the neck is redundant. The agency agrees with the comment. Although the pharmacist is an important member of the health care team, FDA believes that the situation covered by the warning, where the patient may have an allergic reaction to benzoyl peroxide, is more appropriately handled by the physician. It is likely in such a case that the physician will treat the patient with a prescription medication, particularly if the reaction is severe. Thus, the agency is not including the word "pharmacist" in the warning proposed in this tentative final monograph. The agency also agrees with the reasons cited by the comment for not including the phrase "sensitive areas of the neck" in the warning. Thus, the benzoyl peroxide warning proposed in § 333.350(c)(2) of this tentative final monograph reads as follows: "* * * If irritation becomes severe, discontinue use; if irritation still continues, consult a doctor. Keep away from eyes, lips, and mouth. This product may bleach hair or dyed fabrics.

E. Comments on Testing Procedures

14. Several comments suggested revision or requested clarification of the Category III testing guidelines. One comment stated that the safety guidelines are too detailed and are more appropriate for new chemical entities than for ingredients that have a long history of use, but are in Category III because of specific safety questions. Another comment recommended deleting the safety guidelines because there are no ingredients in Category III for safety reasons.

The agency has not addressed specific testing guidelines in this document. In revising the OTC drug review procedures relating to Category III, published in the **Federal Register** of September 29, 1981 (46 FR 47730), the agency advised that tentative final and

final monographs will not include recommended testing guidelines for conditions that industry wishes to upgrade to monograph status. Instead, the agency will meet with industry representatives at their request to discuss testing protocols. The revised procedures also state the time in which test data must be submitted for consideration in developing the final monograph. (See also part II. paragraph A.2. below—Testing of Category II and Category III conditions.)

15. Two comments disagreed over how to interpret the criterion of a 0.75 log reduction of *P. acnes* that the Panel recommended in the in vivo test to determine antibacterial activity (47 FR 12474). One comment urged the agency to make the testing for the reduction of free fatty acids a mandatory rather than an optional confirmatory test. The comment contended that the free fatty acid determination should be required to ensure that the antibacterial agent has penetrated and is acting at the follicular level. The comment stated that it is possible for a drug to reduce a number of *P. acnes* on the surface of the skin but be ineffective in the treatment of acne.

None of the ingredients reviewed by the Panel met the requirement for antibacterial labeling, and no new antibacterial data have been submitted to FDA. Therefore, any questions regarding antibacterial testing will be addressed when in vivo test data are submitted to the agency. In addition, the testing procedures to determine antibacterial activity recommended by the Panel in § 333.340 have not been included in the proposed monograph.

II. The Agency's Tentative Adoption of the Panel's Report

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. *Summary of ingredient categories.* The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time, and is proposing to reclassify salicylic acid (0.5 to 2 percent) from Category III to Category I and thymol (up to 0.2 percent) from Category II to Category III. For the convenience of the reader, the following table is included as a summary of the categorization of topical acne active ingredients by the Panel and the proposed classification by the agency.

Topical acne active ingredients	Panel	Agency
Alkyl isoquinolinium bromide	II	II
Aluminum salts (alcloxa, aluminum chlorohydrox, aluminum hydroxide, and magnesium aluminum silicate)	III	III
Benzocaine	III	III
Benzoic acid	III	III
Benzoyl peroxide	I	I
Borates (boric acid and sodium borate)	III	III
Calcium polysulfide	III	III
Calcium thiosulfate	III	III
Camphor	III	III
Chlorhydroxyquinoline	III	III
Chloroxylenol	III	III
Coal tar	III	III
Dibenzothiophene	III	III
Estrone	III	III
Magnesium sulfate	III	III
Phenolates (phenol and phenolate sodium)	III	III
Phenyl salicylate	III	III
Povidone-iodine	III	III
Pyridoxine malsate	III	III
Resorcinol and resorcinol monoacetate (as single ingredients)	III	III
Salicylic acid (0.5 to 2 percent)	III	I
Salicylic acid (over 2 up to 5 percent)	III	III
Sodium thiosulfate	III	III
Sulfur	I	I
Tetracaine hydrochloride	III	III
Thymol	II	III
Vitamin E	III	III
Zinc salts (zinc oxide, zinc stearate, and zinc sulfide)	III	III

2. *Testing of Category II and Category III conditions.* The Panel recommended testing guidelines for topical acne drug products at 47 FR 12471. The agency's position regarding the Panel's testing guidelines is discussed in comment 14 above. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any topical acne ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). That policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the Panel's report and recommended monograph with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made by the agency follows.

1. The agency is proposing to classify salicylic acid 0.5 to 2 percent in Category I. Concentrations of salicylic acid greater than 2 percent up to 5 percent remain in Category III pending receipt of data to establish general recognition of safety. (See comment 6 above.)

2. The agency is proposing to reclassify thymol from Category II to Category III. (See comment 7 above.)

3. The agency is proposing to broaden the range of acceptable concentrations of sulfur-resorcinol combinations. The Panel recommended that 8 percent sulfur can be combined with 2 percent resorcinol or 3 percent resorcinol monoacetate, and the agency is proposing to allow 3 to 8 percent sulfur to be combined with 2 percent resorcinol or 3 percent resorcinol monoacetate. (See comment 9 above.)

4. The definitions proposed in § 333.303 include only those definitions considered necessary for this tentative final monograph. The Panel's recommended definitions for "follicle" and "lesion" have been deleted because they are not used in the labeling proposed in the tentative final monograph. Also, as discussed in paragraph 5 below, these words are not widely understood by consumers.

5. The agency has reviewed the indications statements recommended by the Panel in § 333.350(b)(1) and (2) and does not believe that some of the words or phrases are appropriate for consumer labeling. The agency has not included the words "lesion" or "follicle" in the proposed labeling because it does not believe that most consumers would understand these words. Other phrases recommended by the Panel that the agency believes are not clear or would be misleading to the consumer include "Reduces blackheads," "Loosens blackheads," "Helps remove blackheads," "Helps remove acne pimples," "Unclogs pores to help clear acne," and "Unplugs pores to help clear acne." The agency believes that the phrase "Reduces blackheads" is more clearly and accurately stated as "Reduces the number of blackheads" and has included the latter in the labeling proposed below. "Loosens blackheads" would not be helpful to consumers because it does not meaningfully describe the action of acne drug products. The agency also believes that the phrase "Helps remove" does not accurately describe the action of these drug products and could be misleading to consumers. Although acne drug products work by penetrating pores, and

this fact is indicated in the proposed labeling, phrases such as "Unclogs pores" and "Unplugs pores" do not provide accurate descriptions of the drugs' activity.

Other terms recommended by the Panel, such as "Anti-acne formula," "Anti-acne medication," and "Anti-acne formulation," are not indications for use, but would be more appropriately considered statements of identity. The statement of identity recommended by the Panel in § 333.350(a) for acne drug products is "acne medication," which the agency is adopting and proposing in this tentative final monograph. The agency finds no reason to retain the other three terms identified above.

FDA believes that the remainder of the statements in § 333.350(b)(1) and (2) accurately express the action of acne drug products. To improve clarity and reduce repetition, the agency has consolidated the numerous claims recommended by the Panel into a few concise statements. The agency is proposing the following indications for acne drug products under § 333.350(b):

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the following:

(1) "For the" (select one of the following: "treatment" or "management") "of acne."

(2) *Other allowable indications.* In addition to the required indication identified in paragraph (b)(1) of this section, the labeling of the product may contain additional indication statements that are limited to one or more of the following:

(i) (Select one of the following: "Dries," "Dries up," "Dries and clears," "Clears," "Clears up," "Clears up most," "Helps clear," "Helps clear up," "Reduces the number of," or "Reduces the severity of") (select one or more of the following: "blackheads," "acne pimples," or "acne blemishes") which may be followed by "and allows skin to heal."

(ii) "Penetrates pores to" (select one of the following: "eliminate most," "control," "clear most," or "reduce the number of") (select one or both of the following: "blackheads" or "acne pimples").

(iii) "Helps keep skin clear of new acne pimples."

(iv) "Helps prevent new" (select one or more of the following: "blackheads," "acne pimples," or "acne blemishes") which may be followed by "from forming."

(v) "Helps prevent the development of new acne pimples."

6. The agency is not proposing the antibacterial labeling recommended by the Panel in § 333.350(b)(3) because none of the Category I ingredients were recommended to use antibacterial labeling and no in vivo data relating to antibacterial activity were submitted following publication of the Panel's report. (See comment 11 above.) In addition, the agency is not proposing the testing procedures to determine antibacterial activity recommended by the Panel in § 333.340. (See comment 15 above.)

7. The agency is not proposing the labeling for product attributes recommended by the Panel in § 333.350(b)(4). The Panel recommended that terms used to describe certain physical and chemical qualities of a drug product may be used in the labeling as long as these terms do not imply any therapeutic effect and are distinctly separated from the indications statements. These terms, such as "greaseless" or "nonstaining," are intended to provide consumer information and relate to a product's color, odor, or feel. As stated in comment 11 above, OTC drug monographs regulate only labeling information related in a significant way to those therapeutic properties of covered products having a direct bearing on their safe and effective use by lay persons. Claims concerning nontherapeutic characteristics of drugs, such as product attributes, are not dealt with in OTC drug monographs. Such terms may not appear in any portion of the labeling that is required by the monograph, but may appear elsewhere in the labeling. Labeling claims of this type are, however, subject to the drug misbranding provisions of the act.

8. The warning recommended by the Panel regarding the use of more than one topical acne medication at the same time in § 333.350(c)(1)(ii) has been revised and is being proposed as follows: "Using other topical acne medications at the same time or immediately following use of this product may increase dryness or irritation of the skin. If this occurs, only one medication should be used unless directed by a doctor." (See comment 12 above.)

9. The benzoyl peroxide warning recommended by the Panel in § 333.350(c)(2) has been revised and is being proposed as follows: ". . . If irritation becomes severe, discontinue use; if irritation still continues, consult a doctor. Keep away from eyes, lips and mouth. This product may bleach hair or dyed fabrics." (See comment 13 above.)

10. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments received to these proposals, the agency has determined that final monographs and any applicable OTC drug regulation will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option.

The agency advises that those parts of § 369.20 applicable to topical acne drug products will be revoked at the time that this monograph becomes effective.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC topical acne drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Pub. L. 96–354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC topical acne drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invited public comment in the advance notice of proposed rulemaking regarding any impact that this rulemaking would have on OTC topical acne drug products. No comments were received. Any comments on the agency's initial determination of the economic consequences of this proposed rulemaking should be submitted by May 15, 1985. The agency will evaluate any comments and supporting data that are received and will reassess the economic

impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the Federal Register of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 333

OTC drugs; Topical acne drug products.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)) and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)) and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 333 (which was proposed to be added in the Federal Register of January 6, 1978 (42 FR 1210)) by revising proposed Subpart D, to read as follows:

PART 333—TOPICAL ANTIMICROBIAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart D—Topical Acne Drug Products

Sec.

333.301 Scope.
333.303 Definitions.
333.310 Acne active ingredients.
333.320 Permitted combinations of active ingredients.
333.350 Labeling of acne drug products.

Authority: Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704).

Subpart D—Topical Acne Drug Products

§ 333.301 Scope.

(a) An over-the-counter acne drug product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this subpart and each general condition established in § 330.1.

(b) References in this subpart to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 333.303 Definitions.

As used in this subpart:

(a) *Acne.* An inflammatory skin disease involving the oil glands and hair follicles of the skin.

(b) *Acne drug product.* A drug product used to reduce the number of acne lesions.

(c) *Blackhead.* An acne lesion characterized by a black tip.

(d) *Pimple.* A small, prominent, inflamed elevation of the skin.

§ 333.310 Acne active ingredients.

The active ingredient of the product consists of any of the following when labeled according to § 333.350.

(a) Benzoyl peroxide 2.5 to 10 percent.

(b) Resorcinol 2 percent when combined in accordance with § 333.320(a).

(c) Resorcinol monoacetate 3 percent when combined in accordance with § 333.320(b)

(d) Salicylic acid 0.5 to 2 percent.

(e) Sulfur 3 to 10 percent.

(f) Sulfur 3 to 8 percent when combined in accordance with § 333.320.

§ 333.320 Permitted combinations of active ingredients.

(a) Resorcinol identified in § 333.310(b) when combined with sulfur identified in § 333.310(f) provided the product is labeled according to § 333.350.

(b) Resorcinol monoacetate identified in § 333.310(c) when combined with sulfur identified in § 333.310(f) provided the product is labeled according to § 333.350.

§ 333.350 Labeling of acne drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an "acne medication."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the following:

(1) "For the" (select one of the following: "treatment" or "management") "of acne."

(2) *Other allowable indications.* In addition to the required indication identified in paragraph (b)(1) of this section, the labeling of the product may contain additional indication statements that are limited to one or more of the following:

(i) (Select one of the following: "Dries," "Dries up," "Dries and clears," "Clears," "Clears up," "Clears up most," "Helps clear," "Helps clear up," "Reduces the number of," or "Reduces the severity of") (select one or more of the following: "blackheads," "acne pimples," or "acne blemishes") which may be followed by "and allows skin to heal."

(ii) "Penetrates pores to" (select one of the following: "eliminate most," "control," "clear most," or "reduce the number of") (select one or both of the following: "blackheads" or "acne pimples").

(iii) "Helps keep skin clear and new acne pimples."

(iv) "Helps prevent new" (select one or more of the following: "blackheads," "acne pimples," or "acne blemishes") which may be followed by "from forming."

(v) "Helps prevent the development of new acne pimples."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) *For products containing any ingredient identified in § 333.310.* (i) "For external use only."

(ii) "Using other topical acne medications at the same time or immediately following use of this product may increase dryness or irritation of the skin. If this occurs, only one medication should be used unless directed by a doctor."

(2) *For products containing benzoyl peroxide identified in § 333.310(a).* "Do not use this medication if you have very sensitive skin or if you are sensitive to benzoyl peroxide. This product may cause irritation, characterized by redness, burning, itching, peeling, or possibly swelling. More frequent use or higher concentrations may aggravate such irritation. Mild irritation may be reduced by using the product less frequently or in a lower concentration. If irritation becomes severe, discontinue use; if irritation still continues, consult a doctor. Keep away from eyes, lips, and mouth. This product may bleach hair or dyed fabrics."

(3) *For products containing sulfur identified in § 333.310(e) and (f).* "Do not get into eyes. If excessive skin irritation develops or increases, discontinue use and consult a doctor."

(4) *For products containing any combination identified in § 333.320.* "Apply to affected areas only. Do not use on broken skin or apply to large areas of the body."

(d) *Directions.* The labeling of the product containing any ingredient identified in § 333.310 contains the following statements under the heading "Directions":

(1) "Cleanse the skin thoroughly before applying medication. Cover the entire affected area with a thin layer one to three times daily. Because excessive drying of the skin may occur,

start with one application daily, then gradually increase to two or three times daily if needed or as directed by a doctor."

(2) The directions described in paragraph (d)(1) of this section are intended for products that are applied and left on the skin. Other products, such as soaps or masks, may be applied and removed and should have appropriate directions.

(e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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January 15, 1985

Part VI

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 310

Stomach Acidifier Drug Products for Over-the-Counter Human Use

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 79N-0176]

Stomach Acidifier Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that would establish that over-the-counter (OTC) stomach acidifier drug products are not generally recognized as safe and effective and are misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Willaim E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of October 19, 1979 (44 FR 60316), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC stomach acidifier drug products as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based on the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluation data on the active ingredients in this drug class. Interested persons were invited to submit comments by January 17, 1980. Reply comments in response to comments filed in the initial comment period could be submitted by February 18, 1980.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, two drug manufacturers and one college of pharmacy submitted comments. These comments received are on public display in the Dockets Management Branch.

In this proposed rule to amend Part 310 by adding to Subpart E new § 310.540 (21 CFR 310.540), FDA states for the first time its position on OTC stomach acidifier drug products. Final agency action on this matter will occur with the publication at a future date of a final rule relating to OTC stomach acidifier drug products.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC stomach acidifier drug products, based on the comments received and the agency's independent evaluation of the Panel's report. As discussed in the final rule revising the procedural regulations for reviewing and classifying OTC drugs, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final rule, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) This document retains the concepts of Categories I, II, and III at the proposed rule stage.

In the advance notice of proposed rulemaking, the agency stated that if it proposed to adopt the Panel's recommendation it would propose that stomach acidifier drug products be eliminated from the OTC market effective 6 months after the date of publication of a final rule in the **Federal Register**, regardless of whether further testing was undertaken to justify their future use. Based on all information available to date, the agency is proposing that stomach acidifiers as a class of drugs be found to be ineffective. If this proposed finding is adopted in the final rule, the agency advises that the conditions under which the drug products that are subject to this rule are not generally recognized as safe and effective and are misbranded (nonmonograph conditions) will be effective 6 months after the date of publication of the final rule in the **Federal Register.** On or after that date, no OTC drug products that are subject to the rule may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Manufacturers are encouraged to comply voluntarily with the proposed rule at the earliest possible date.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notices published in the **Federal Register** of November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179). The volumes are on public display in the Dockets Management Branch.

I. The Agency's Tentative Conclusions on the Comments

1. One comment requested that the statement "the basal rate is almost 30 milliliters (mL) of a dilute solution of hydrochloric acid per hour," in the Panel's discussion of stomach physiology (44 FR 60318), be clarified to read "30 mL of gastric fluid." The comment contended that the phrase "dilute solution of hydrochloric acid" could be mistaken to mean "diluted hydrochloric acid, USP," which would contain more pure hydrochloric acid than that which is available from the same amount of gastric fluid.

The agency agrees that the statement referred to by the comment could be misinterpreted. The agency believes that a less ambiguous statement reflecting the Panel's intended meaning would be as follows: "the basal rate is almost 30 mL of gastric fluid per hour."

2. Two comments disagreed with the Panel's conclusions that the conditions of achlorhydria and hypochlorhydria are asymptomatic and not amenable to self-diagnosis, and that no OTC stomach acidifier active ingredient is generally recognized as effective in treating these conditions. The comments asserted that submitted data showed that achlorhydria is accompanied by recognizable symptoms such as gas, diarrhea, abdominal distention, nausea,

and vomiting. The comments added that even if this condition is asymptomatic, the Panel's concern about self-diagnosis is unwarranted because OTC stomach acidifiers are generally used only after consultation with a doctor. The comments proposed that stomach acidifiers be available OTC with labeling recommending their use only on the advice of a doctor or other health professional. The comments pointed out that such an approach was recommended by the same Panel in the advance notice of proposed rulemaking for OTC exocrine pancreatic insufficiency drug products (44 FR 75669). To support the effectiveness of stomach acidifiers, one of the comments discussed several published studies and other information previously submitted to the Panel (Refs. 1 through 12). Similarly, the other comment argued that the Panel did not adequately consider or respond to the submitted data, specifically citing published studies, extracts from medical texts, and affidavits from five gastroenterologists and two hematologists (Refs. 13, 14, and 15).

The comments predicted that diluted hydrochloric acid, USP, will continue to be used by doctors to treat achlorhydria and hypochlorhydria even if OTC stomach acidifier drug products are removed from the market, and added that removal of these stomach acidifier drug products will eliminate a form of therapy that is safer than the use of diluted hydrochloric acid, USP.

After evaluating the data reviewed by the Panel and the additional information presented in the comments, FDA concludes that achlorhydria and hypochlorhydria are not established medical conditions causing any specific symptoms that require treatment. The data and information cited by the comments were also considered by the Panel. The Panel determined, and the agency concurs, that the data and information do not provide sufficient evidence that these conditions require treatment. Although hydrochloric acid replacement therapy has traditionally been used in the conditions of achlorhydria and hypochlorhydria, there are no adequate and well-controlled studies to demonstrate that administration of hydrochloric acid has any therapeutic value in either condition. This same conclusion was reached by the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for drugs containing glutamic acid hydrochloride (Ref. 16). Moreover, recent evaluations of hydrochloric acid therapy in recognized pharmacology texts also concur with the Panel's findings. For example, in the sixth edition of the Pharmacological Basis of Therapeutics, Harvey indicates that definitive clinical evidence of hydrochloric acid's effectiveness is lacking and reports of positive results may be based upon a placebo effect (Ref. 17). The fourth edition of AMA Drug Evaluations concludes that there are no established indications for hydrochloric acid, and the fifth edition of the Review of Medical Pharmacology likewise notes that the consensus now is that the use of hydrochloric acid as a replacement therapy in patients with achlorhydria or hypochlorhydria is not an accepted indication (Refs. 18 and 19). Therefore, the agency concludes that any ingredient recommended for stomach acidifier use is Category II.

The comments' recommendation to label the products for use only upon the advice of a doctor does not remedy the failure to have adequate evidence of safety and effectiveness. No stomach acidifier active ingredient has been shown to be generally recognized as safe and effective in treating achlorhydria and hypochlorhydria. Nor are there recognizable symptoms of these conditions that may properly be treated with an OTC drug product. Although such an approach was used in the advance notice of proposed rulemaking for OTC exocrine pancreatic insufficiency drug products, in that case the Panel classified two active ingredients as generally recognized as safe and effective and the Panel believed that the condition of exocrine pancreatic insufficiency could be self-treated because of recognizable sysptoms.

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(12) Wintrobe, M.M., "Clinical Hematology," 4th Ed., Lea and Febiger, Philadelphia, p. 134, 1956.

(13) OTC Volume 170103.

(14) OTC Volume 170104.

(15) OTC Volume 170124.

(16) NAS–NRC Report on Aclor Capsules (NDA 4–484), copy included in OTC Volume 17ATFM.

(17) Harvey, S. C., "Gastric Antacids and Digestants," *in* "The Pharmaceutical Basis of Therapeutics," edited by L. S. Goodman and A. Gilman, the Macmillan Co., New York, p. 970, 1980.

(18) "AMA Drug Evaluations," 4th Ed., Publishing Sciences Group, Inc., Littleton, MA, p. 1008, 1980.

(19) Meyers, F. H., E. Jawetz, and A. Goldfien, "Review of Medical Pharmacology," 5th Ed., Lange Medica; Publication, Los Altos, CA, p. 322, 1976.

3. One comment stated that a combination stomach acidifier drug product containing betaine hydrochloride and pepsin, which was reviewed by the Panel, is useful in replenishing pepsin in cases of gastric achylia, a condition in which the stomach fails to secrete hydrochloric acid and pepsin. Gastric achylia is often found in patients with pernicious anemia or gastric carcinoma. The comment requested that the combination product be classified in Category I, but added that "at a minimum, the final monograph should be deferred and acidifiers at least allowed to remain on the market pending an opportunity to conduct and complete further studies to evaluate their effectiveness."

The agency agrees with the Panel that the combination of betaine hydrochloride and pepsin is not generally recognized as effective in treating achlorhydria and hypochlorhydria. As discussed in comment 2 above, the agency concludes

that no ingredient is generally recognized as safe and effective for treating these conditions. Pepsin replacement therapy is not within the scope of this document. Pepsin was reviewed by the Advisory Review Panel on OTC Miscellaneous Internal Drug Products for use as an OTC digestive aid and judged to be not generally recognized as effective for the treatment of symptoms of either immediate postprandial upper abdominal distress or intestinal distress. (See the **Federal Register** of January 5, 1982; 47 FR 467 and 479.) The agency's position on the status of pepsin for use as a digestive aid will be initially stated when the tentative final monograph on OTC digestive aid drug products is published in a future issue of the **Federal Register.**

The comment's request that the final rule be deferred to permit additional studies to be conducted is unjustified. In the **Federal Register** of September 29, 1981 (46 FR 47730), FDA set forth revised procedural regulations for reviewing and classifying OTC drugs. This final rule revised the time period during which new data may be submitted without petition to FDA to support the inclusion in a final monograph of a condition not classified in Category I in a proposed monograph or tentative final monograph. Submission of data without petition is permitted until 12 months after publication of a tentative final monograph (21 CFR 330.10(a)(7)(iv)). New data submitted after that time will be considered only after the final monograph has been published unless the Commissioner finds that good cause warrants earlier consideration (21 CFR 330.10(a)(7)(v)). The agency will not delay a rulemaking proceeding so that additional studies may be conducted. In the case of stomach acidifier drug products, manufacturers have been aware of the Panel's recommendations at least since October 1979. Therefore, manufacturers have had ample opportunity to conduct studies and to submit new data.

4. One comment, referring to a product containing glutamic acid hydrochloride, and another comment, referring to a product containing betaine hydrochloride and pepsin, claimed that these products were exempt from the "new drug" provisions of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) under the "grandfather" provisions of the 1938 act and the 1962 amendments to the act. The comments stated that each product was marketed prior to 1938, that only insubstantial changes have been made in formulation and labeling since that time, and that the products' current labeling contains the same representations for use that were contained in the labeling used before 1938. The comments concluded that each product was a "grandfathered" product not subject to this regulation.

To qualify for exemption from the "new drug" definition under the 1938 grandfather clause, the drug product must have been subject to the Food and Drug Act of 1906, prior to June 25, 1938, and at such time its labeling must have contained the same representations concerning the conditions of its use (21 U.S.C. 321(p)(1)). Under the 1962 grandfather clause, a drug product which preceding October 9, 1962, (1) was commercially used or sold in the United States, (2) was not a "new drug" as defined in the 1938 act, and (3) was not covered by an approved NDA under the 1938 act, would not be subject to the added requirement of effectiveness "when intended solely for use under conditions prescribed, recommended, or suggested in the labeling with respect to such drugs." Pub. L. 87–781, section 701(c)(4), 76 Stat. 788, note following 21 U.S.C. 321.

The person seeking to show that a drug comes within a grandfather exemption must prove every essential fact necessary for invocation of the exemption. See *United States* v. *An Article of Drug * * * "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied,* 412 U.S. 938 (1973). Furthermore, the grandfather clause will be strictly construed against one who invokes it. See id.; *United States* v. *Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir.), *cert. denied,* 385 U.S. 899 (1966).

A change in composition or labeling precludes the applicability of the grandfather exemption. *See USV Pharmaceutical Corp. v. Weinberger,* 412 U.S. 655, 663 (1973). The firm concedes that minor changes have been made in the labeling and formulation of the glutamic acid hydrochloride product since it was first marketed, prior to 1938. In any event, the evidence shows that both the labeling and the composition of the product have changed since passage of the 1938 act. Therefore, the product fails to qualify for the 1938 grandfather exemption.

In order to qualify for the 1962 grandfather exemption, it must be proven, among other things, that the product was generally recognized among qualified experts as safe for its intended uses (i.e., it was not a "new drug" under the 1938 act) and that the product was not covered by an approved NDA. The glutamic acid hydrochloride product was labeled for the treatment of achlorhydria, pernicious anemia, and gastric carcinoma. There are no adequate and well-controlled studies showing that the glutamic acid hydrochloride product is safe for use in pernicious anemia or gastric carcinoma. The product is not now, and never has been, generally recognized by qualified experts as safe for these recommended uses. Furthermore, the product (as a "me-too" product) was covered by an effective NDA as of October 9, 1962, within the meaning of the grandfather clause. *See USV Pharmaceutical Corp.* v. *Weinberger,* 412 U.S. 655 (1973). Therefore, the glutamic acid hydrochloride product fails on at least two grounds to qualify for the 1962 grandfather exemption.

No evidence was submitted to the agency to show that the labeling and composition of the betaine hydrochloride product have remained unchanged since either 1938 or 1962. Without such evidence, the product cannot qualify for either grandfather exemption. The manufacturer has suggested that FDA should search for evidence to support the company's grandfather claim. However, the burden of proof with respect to the grandfather exemption is not on FDA, but on the person seeking the exemption. *See An Article of Drug * * * "Bentex Ulcerine," supra; Upjohn* v. *Finch, supra.*

In any event, the 1938 and 1962 grandfather clauses apply only to the new drug provisions of the act and not to the adulteration and misbranding provisions. The OTC drug review was designed to implement both the misbranding and the new drug provisions of the act. (See 21 CFR 330.10; 37 FR 9466 (May 11, 1972) (comment 23).) The grandfather clauses do not preclude the agency from reviewing any currently marketed OTC drug, regardless of whether it has grandfather protection from the new drug provisions, in order to ensure that the drug is not misbranded. The agency concludes that the product referred to by the comments are subject to this proposed rulemaking.

II. The Agency's Tentative Adoption of the Panel's Report

FDA has considered the comments and other relevant data and information available at this time and concludes that it will tentatively adopt the Panel's report and recommendation that betaine hydrochloride, glutamic acid hydrochloride, diluted hydrochloric acid, and pepsin labeled for use as OTC stomach acidifiers are classified Category II.

The agency is also revising § 310.540 to clarify that a product covered by the

regulation is a new drug for which an approved NDA is required for marketing, and in the absence of an approved NDA the product would also be misbranded under section 502 of the act.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC stomach acidifier drug products, is a major rule.

For purposes of the Regulatory Flexiblity Act, the economic assessment concluded that, while the average economic impact of the overall OTC drug review on small entities will not be significant, the possibility of larger-than-average impacts some small firms in some years might exist. Therefore, the assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose a significant impact on a substantial number of small entities. The analysis identified the possibilities of reducing burdens on small firms through the use of (a) relaxed safety and efficacy standards or (b) labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act. Nevertheless, to avoid overlooking any problems or feasible possibilities of relief peculiar to this group of products, the agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC stomach acidifier drug products. Comments regarding the economic impact of this rulemaking should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on OTC stomach acidifier drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

New drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p) 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 310 by adding to Subpart E new § 310.540, to read as follows:

PART 310—[AMENDED]

§ 310.540 Drug products containing active ingredients offered over-the-counter (OTC) for use as stomach acidifiers.

(a) Betaine hydrochloride, glutamic acid hydrochloride, diluted hydrochloride acid, and pepsin have been present as ingredients in over-the-counter (OTC) drug products for use as stomach acidifiers. Because of the lack of adequate data to establish the effectiveness of these or any other ingredients for use in treating achlorhydria and hypochlorhydria, and because such conditions are asymptomatic, any OTC drug product containing ingredients offered for use as a stomach acidifer cannot be considered generally recognized as safe and effective.

(b) Any OTC drug product that is labeled, represented, or promoted for use as a stomach acidifier is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FDA–1571) (OMB Approval No. 0910–0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted as a stomach acidifier for OTC use is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA–305) (address above). Received data and

comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final rule is published in the Federal Register unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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Tuesday
January 15, 1985

Part VII

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 310

Hair Grower and Hair Loss Prevention Drug Products for Over-the-Counter Human Use

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 310

[Docket No. 80N-0357]

Hair Grower and Hair Loss Prevention Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking that would establish that over-the-counter (OTC) hair grower and hair loss prevention drug products for external use are not generally recognized as safe and effective and are misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Managment Branch (HFA-305), Food and Drug Administration, Rm., 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTRY INFORMATION: In the **Federal Register** of November 7, 1980 (45 FR 73955) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking that would classify OTC hair grower and hair loss prevention drug products for external use as not generally recognized as safe and effective and as being misbranded and would declare these products to be new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)). The notice was based on the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in this drug class. Interested persons were invited to submit comments by February 5, 1981. Reply comments in response to comments filed in the initial comment period could be submitted by March 9, 1981.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. In response to the advance notice of proposed rulemaking, 1 research laboratory, 6 drug marketing firms, 2 drug manufacturers, 3 physicians, 12 consumers, 2 United States Senators, and the U.S. Postal Service submittted comments. These comments are on public display in the Dockets Management Branch.

In this proposed rule to amend Part 310 by adding to Subpart E new § 310.527 (21 CFR 310.527), FDA states for the first time its position on OTC hair grower and hair loss prevention drug products for external use. Final agency action on this matter will occur with the publication at a future date of a final rule relating to OTC hair grower and hair loss prevention drug products for external use.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC hair grower and hair loss prevention drug products for external use, based on the comments received and the agency's independent evaluation of the Panel's report. As discussed in the final rule revising the procedural regulations for reviewing and classifying OTC drugs, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final rule stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) This document retains the concepts of Categories I, II, and III at the proposed rule stage.

In the advance notice of proposed rulemaking, the agency stated that if it proposed to adopt the Panel's recommendation it would propose that hair grower and hair loss prevention drug products for external use be eliminated from the OCT market effective 6 months after the date of publication of a final rule in the **Federal Register**, regardless of whether further testing was undertaken to justify their future use. Based on all information available to date, the agency is proposing that hair grower and hair loss prevention drug products for external use as a class of drugs be found to be ineffective. If this proposed finding is adopted in the final rule, the agency advises that the conditions under which the drug products that are subject to this rule are not generally recognized as safe and effective and are misbranded (nonmonograph conditions) will be effective 6 months after the date of publication of the final rule in the **Federal Register**. On or after that date, no OTC drug products that are subject to the rule may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Manufacturers are encouraged to comply voluntarily with the proposed rule at the earliest possible date.

I. The Agency's Tentative Conclusions on the Comments

A. General Comments on Hair Grower and Hair Loss Prevention Drug Products.

1. Two comments agreed with the Panel's conclusion that all OTC hair grower and hair loss prevention drug products are not effective and that they should be classified as Category II. The comments stated that these products are worthless and that their sale bilks the public of large sums of money each year, and one comment added that the proposed regulation should be enacted promptly.

2. Several comments objected to the Panel's recommendation that all OTC hair grower and hair loss prevention drug products be classified as Category II. The comments contended that banning such products from OTC use is an infringement of consumers' freedom of choice by medical experts and the government. Some of the comments expressed concern that the ban will interrupt ongoing hair grower treatment programs which consumers are satisfied with. The comments urged that, because hair grower ingredients are not harmful, consumers should be allowed to decide

whether they want to use these products.

FDA's statutory mandate includes protection and promotion of the public health by ensuring that drugs are not only safe but also effective for their intended use. The Commissioner's Decision on the Status of Laetrile, published in the **Federal Register** of August 5, 1977 (42 FR 39768), expresses the agency's position on freedom of choice with respect to ensuring that drugs are not only safe, but also effective. That statement reads in part as follows:

> In passing the 1962 Amendments to the act—the amendments that require that a drug be proved effective before it may be marketed—Congress indicated its conclusions that the absolute freedom to choose an ineffective drug was properly surrendered in exchange for the freedom from the danger to each person's health and well-being from the sale and use of worthless drugs * * *. To the extent that any freedom has been surrendered by the passage of the legislation which bans from the marketplace drugs that have not been proven to be effective, that surrender was a rational decision which has resulted in the achievement of a greater freedom from the dangers to health and welfare represented by such drugs.

Hair grower treatment programs will not be interrupted pursuant to publication of this proposed rule; however, OTC drug products that are subject to this rulemaking, and that are not the subject of an approved NDA, will have to comply with the final rule. In the absence of data demonstrating that the ingredients present in OTC hair grower and hair loss prevention drug products are generally recognized as safe and effective, these ingredients cannot be included in an OTC drug monograph. After the effective date of the final regulation, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this regulation will be subject to regulatory action.

3. While supporting the prosecution of those parties who mislead the public with allegedly outrageous claims such as those made by some mail order houses, one comment opposed the Panel's recommendation for Category II classification of OTC hair grower and hair loss prevention drug products, stating that such a classification would impose an economic hardship on legitimate businesses and suppliers. The comment further stated that the company submitting the comment does not have the resources to conduct a double-blind study on the effectiveness of its drug products, which have "properties" similar to the ingredients reviewed by the Panel, and that even if double-blind studies were to prove that its products were no more effective than a placebo, it can point to hundreds of heads of healthier, fuller hair and a large number of satisfied customers. The comment stated that it believed that the burden of proof for safety and effectiveness should be borne by FDA, rather than businesses, and requested FDA to examine closely the need for and the equity of a proposed rule.

Under the statutory scheme established by Congress, an OTC drug may not legally be marketed unless it is generally recognized as safe and effective by qualified experts and has been marketed to a material extent and for a material time (21 U.S.C. 321(p)), or is the subject of an approved new drug application (21 U.S.C. 355), and is not adulterated or misbranded (21 U.S.C. 351, 352). Those persons marketing OTC drugs have an obligation to comply with the law.

In order to ensure that only safe and effective OTC drugs are marketed, FDA began this ongoing review of OTC drug ingredients in 1972. Under the regulations establishing the procedures for classifying OTC drugs as generally recognized as safe and effective and not misbranded, the agency has requested interested persons to submit data and information pertinent to the designated categories of OTC drugs (21 CFR 330.10a(a)(2)). Calls for data on hair grower products were published in the **Federal Register** of November 16, 1973 (38 FR 31697) and August 27, 1975 (40 FR 38179). Interested persons had an opportunity to submit data and information after publication of the advance notice of proposed rulemaking and again have such an opportunity after publication of this proposed rule (21 CFR 330.10(a) (6) and (7)). The agency makes its determinations with respect to ingredients in each OTC drug rulemaking proceeding on the basis of the data and information in the administrative record for that rulemaking (21 CFR 330.10(a)(10)). Standards for effectiveness are detailed in § 330.10(a)(4)(ii), and include a requirement for controlled clinical investigations. Isolated case reports, random experience, and reports lacking the details that permit scientific evaluation are not considered adequate to establish effectiveness. General recognition of effectiveness is ordinarily based upon published studies which may be corroborated by unpublished studies and other data. If there are no controlled studies, an explanation as to why such studies are not considered necessary must be provided. Anecdotal evidence is not sufficient to demonstrate general recognition among experts of a drug's safety and effectiveness. See, e.g., *Weinberger* v. *Hynson, Westcott and Dunning, Inc.*, 412 U.S. 609, 629 (1973).

The comment has failed to provide any data in accordance with the procedures described above, and its anecdotal evidence of "hundreds of heads of healthier, fuller hair and a large number of satisfied customers" is insufficient to meet the burden of proof established by law to demonstrate that the products at issue are generally recognized as safe and effective hair grower of hair loss prevention drug products for OTC use.

FDA has closely examined the need for and equity of the proposed rule. The need for the OTC drug review proceedings was described in detail in the **Federal Register** notices establishing the applicable procedures. (See the **Federal Register** of January 5, 1972 (37 FR 85) and of May 11, 1972 (37 FR 9464).) Although the comment argued that similar ingredients were reviewed by the Panel and that its firm does not have the resources to conduct a double-blind study for effectiveness, the agency cannot accept the comment's argument as a valid reason to waive standard procedures. FDA has a statutory mandate to assure that all OTC drug products are safe and effective for their intended use. Special economic concerns of individual firms cannot override the agency's charge to carry out the public health requirements of the statute.

4. One comment, which cited several references, urged that FDA postpone indefinitely any action on the recommended Category II classification of hair grower and hair loss prevention drug products until current products and techniques have been thoroughly researched and investigated (Refs. 1 through 9). Urging that FDA abandon its current data base on hair grower drug products on the basis that it is "outdated and insufficient," the comment recommended that FDA reclassify only those active ingredients that have been researched, and allow the free enterprise system to promote further research and development of hair grower products. The comment discussed what it considered to be the seven most important causes of hair depletion and the six principal methods of treating male pattern baldness: massage, vitamins, hormones, high frequency electrical units, cosmetics, and galvanic stimulation. The comment stated that a system that combines current techniques with biotin therapy will have the best success rate in treating hair loss and stimulating hair

regrowth. Another comment contained a consumer's testimonial on the use of hot water packs applied to the scalp to stop the balding process.

The references cited by one comment included general descriptions of the hair growth process, possible causes of hair loss, the use of electricity to stimulate the scalp and also bone growth, and the processes of hair transplanting, implanting, and weaving (Refs. 1 through 8). The references also contained general descriptions of the use of germicides to arrest male pattern baldness, topical and oral estrogen therapy for hair loss in women, and the use of oral ferrous gluconate in iron-deficient persons with hair loss (Refs. 1 and 7). Another article dealt with the possible role of alcohol ingestion in promoting hair growth (Ref. 9).

This rulemaking proceeding addresses OTC drug products for external use as hair growers or for hair loss prevention. Thus, the following products or methods discussed by the comments are not included in this rulemaking: oral estrogen therapy, oral ferrous gluconate, alcohol ingestion, cosmetics, hot water packs, massage, high-frequency electrical units, galvanic stimulation, hair transplanting, hair weaving, and hair implanting.

None of the references provided data to show that germicides or topical estrogens are effective as hair growers or for hair loss prevention. The use of biotin as an OTC hair grower is discussed in comment 12 below, and topical estrogen use is further discussed in comment 10 below.

The agency will not delay its OTC drug rulemaking proceedings to allow additional time for further research. In accordance with agency regulations, additional information or data on OTC hair grower or hair loss prevention drug ingredients may be submitted following the publication of this proposed rule (21 CFR 330.10(a)(7)) or in accordance with the NDA procedures (21 CFR Part. 314).

References

(1) Zizmor, J., and J. Foreman, "Hang On To Your Hair," *Working Woman*, 3:58–59 and 82–83, 1978.

(2) "Disprove Theory on Cause of Baldness," *Science News Letter*, 76:289, 1959.

(3) Cohn, N., "Hairsapoppin'," *New York*, 11:57–64, 1978.

(4) "Electric Healing," *Time*, 113:139, 1979.

(5) Elliott, J., "Electrical Stimulation of Bone Growth Wins Clinical Acceptance," *Journal of the American Medical Association*, 243:1401–1403, 1980.

(6) "'Muscle Heads' Don't Get Bald," *Science Digest*, 42: (inside cover) 1957.

(7) Benezra, N., "A Hair-Raising Tale," *Family Health*, 9:25–29, 1977.

(8) Crawford, A., and R. Fettiplace, "Reversal of Hair Cell Responses by Current," *Journal of Physiology*, 295:66P, 1979.

(9) DeLeon, G., "The Baldness Experiment," *Psychology Today*, 11:62–66, 1977.

5. One comment reserved the right to contest the legality of any rulemaking as applicable to its biotin-containing hair preparations, which are available only to consumers enrolled in a professional treatment program for the control and prevention of hair loss. The comment contended that these preprations are not subject to classification under the OTC drug review program.

This rulemaking applies to all drug products offered OTC, i.e., without prescription, for external use as hair growers or for hair loss prevention. Criteria for limitation to prescription use are set forth in 21 U.S.C. 353. By law, prescription drug product labels must bear the statement, "Caution: Federal law prohibits dispensing without prescription" (21 U.S.C. 353(b)(4)) prior to dispensing.

The comment submitted no evidence to show that the firm's product is available by prescription only. Nor is there evidence that this product appropriately would be limited to prescription use. The comment submitted a product brochure containing guidelines for the proper utilization of its preparations: a cream, a lotion, and a shampoo. The brochure states that the preparations are primarily directed toward the control of excessive hair loss and the stimulation of regrowth of hair where the follicles are still viable. The brochure also states that all dispensers of the preparations have been trained in the parent clinic, and that no person may avail himself of the treatment without first being examined by a trained doctor or technician thoroughly indoctrinated in the fundamental concepts of using the preparations. However, the comment did not submit any labels for the preparations. At this time the agency is unable to determine whether the proposed regulation is or is not applicable to the preparations referred to by the comment. Further discussion of biotin as an OTC hair grower drug ingredient appears in comment 12 below.

6. One comment contended that the advance notice of proposed rulemaking on OTC hair grower and hair loss prevention drug products went beyond its intended scope in recommending Category II status for *all* OTC drug products offered for use as hair growers or for hair loss prevention, including ingredients of products that were not submitted to the OTC drug review. For this reason, the comment argued that the procedural requirements of section 553 of the Administrative Procedure Act (APA) were violated.

The APA, in 5 U.S.C. 553, requires that a published notice of proposed rulemaking include the terms or substance of the proposed rule or a description of the subjects and issues involved. Interested persons must then be given an opportunity to comment on the proposal. The rulemaking on OTC hair grower and hair loss prevention drug products not only meets the APA requirements, but affords interested persons more notice and a greater opportunity to participate in the rulemaking process than the APA requires.

There has been clear public notice that the OTC hair grower and hair loss prevention drug products rulemaking will apply to each product within the drug category, whether or not a submission has been made for each product. The original notice requesting data and information for all miscellaneous external OTC drugs (specifically including hair growers) pointed out that the submission of data was entirely voluntary. However, the notice also stated that "the monographs resulting from the OTC drug review will, pursuant to [§ 330.10], be regarded by the Food and Drug Administration as fully applicable to every OTC drug regardless whether any such submission has been made for a particular product. See *Weinberger* v. *Bentex Pharmaceuticals, Inc.*, 412 U.S. 645 (1973); *Warner-Lambert Company* v. *Federal Trade Commission*, 361 F. Supp. 948 (D.D.C. 1973); and *United States* v. *Coli-Trol 80 Medicated*, CCH F.D. Cosm. L. Rep., Para. 40,837 (N.D. Ga. 1973)." (See the **Federal Register** of November 16, 1973; 38 FR 31697.) A subsequent call for data, giving interested persons another opportunity to submit information on miscellaneous external OTC drug products, including hair growers, was published in the **Federal Register** of August 27, 1975 (40 FR 38179). That notice repeated the statement describing the scope of the monographs and provided another opportunity to submit data to the panel "because any OTC drug product containing an active ingredient not listed in the appropriate monograph will be considered misbranded or a new drug requiring a new drug application."

As the comment observed, the advance notice of proposed rulemaking published in the **Federal Register** of November 7, 1980 (45 FR 73960) stated that the rule under consideration would apply to any OTC drug product labeled, represented, or promoted for external use as a hair grower or hair loss

prevention agent. Under § 330.10(a)(6) any interested person was given 90 days to comment on the advance notice. This tentative final order is a proposed rule, which again makes it clear that the final rule would cover all OTC hair grower or hair loss prevention drug products for external use (see proposed § 310.527 below). Under § 330.10(a)(7) interested persons may file comments or objections and hearing requests on this proposal within 60 days. Within 12 months after publication of this proposed rule, interested persons may file new data; comments on the new data may be filed within 60 days after that 12 month period.

Thus, any interested person will have had several notices of the scope of the final rule and will have had several opportunities to submit data and information on any hair grower or hair loss prevention ingredient. There is no violation of the APA's procedural requirements in this rulemaking.

B. Comments on Hair Grower and Hair Loss Prevention Ingredients

7. One comment described a proposed pilot study of the effectiveness of an undisclosed ingredient derived from plant sources as a hair grower and requested that the ingredient be placed in Category III pending the outcome of this study. The comment provided general information about studies on the safety of the ingredient in animals and human subjects and concluded that no safety problems were observed.

Because the name of the ingredient was not provided, the agency is unable to fully assess it or to determine whether or not it is a new drug as defined in section 201(p) of the act (21 U.S.C. 321(p)). The comment did not provide adequate data for FDA to reach any conclusion on the safety of the ingredient to be studied. Data on the number of test animals used and their body weight, and the oral LD_{50} levels, as well as raw data, were lacking. Before proceeding to a limited human trial or pilot study, further animal toxicity studies should be conducted. Tests on the ingredient's topical irritancy and topical and systemic sensitivity in humans (e.g., the Draize test) then need to be conducted. Although the comment described use of the ingredient by subjects in many countries, no specific information on its use was provided. For example, data were lacking on the frequency of topical application and duration of use of the ingredient in human subjects, as well as on the method and frequency of observation of the subjects after testing was begun. If the duration of use of the ingredient is not short-term, chronic toxicity data also need to be obtained. The number of subjects—three—in the proposed pilot study is not sufficient to demonstrate statistically significant results.

The agency's detailed comments and evaluations on the information submitted are on file with the Dockets Management Branch (Ref. 1). Because the data and information provided by the comment were inadequate, and the ingredient is unknown, the agency cannot classify it at this time. Further, the agency's letter to the commenter seeking additional information (Ref. 1) was returned to FDA, marked "moved left no address." The undisclosed ingredient would be considered a "nonmonograph condition" at the time that the final regulation becomes effective.

Reference

(1) Letter from W. E. Gilbertson, FDA, to L. Imhotep, Imhotep Hair and Scalp Research Laboratories, coded LET010 to C00014, Docket No. 80N-0357, Dockets Management Branch.

8. Two comments advocated the use of orally ingested vitamin and mineral supplements to produce hair growth. One comment submitted information on a hair grower program that includes the use of oral vitamin and mineral supplements with the topical application of products containing certain B-vitamins (biotin, inositol, choline, pyridoxine, and niacin); amino acids (cystine, cysteine, and methionine); nucleic acids; jojoba oil; and aminobenzoic acid (formerly *para*-aminobenzoic acid).

The Panel's recommendations on OTC hair grower and hair loss prevention drug products addressed only active ingredients for external use (topical application). The Panel classified the topical use of vitamins and amino acids as Category II (45 FR 73957). The comments did not submit any data on the safe and effective use of B-vitamins, amino acids, jojoba oil, aminobenzoic acid, or nucleic acids for topical use as OTC hair growers or for hair loss prevention. The agency is not aware of any data that demonstrate the safety and effectiveness of any of these ingredients for topical hair grower or hair loss prevention use; therefore, the agency is proposing these ingredients as Category II.

Orally ingested vitamins and minerals are not considered within the purview of this rulemaking, which covers only products for external use. Although orally ingested vitamins and minerals are normally considered foods subject to the misbranding provisions of section 403 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343), the intended use of a product determines whether it is a "drug," a "food," or both. This intended use may be inferred from the product's labeling, promotional material, advertising, and any other relevant factor. See, e.g., *National Nutritional Foods Ass'n* v. *Mathews*, 557 F. 2d 325, 334 (2d Cir. 1977). An orally ingested product intended for drug use must be either generally recognized as safe and effective (21 U.S.C. 321(p)) or the subject of an approved new drug application (21 U.S.C. 355) and may not be misbranded (21 U.S.C. 352). Because no data were submitted regarding the use of orally ingested vitamins and minerals as hair growers or for hair loss prevention, the agency is unable to address this matter further at this time.

9. One comment noted that, at the dosage necessary to produce significant hair growth, the topical use of the female hormone estrogen produced female characteristics in males. These included breast enlargement, diminished growth of body and facial hair, and the appearance of a subcutaneous layer of fat. The comment concluded that treatments involving the use of topical hormones for hair growth necessitate a doctor's supervision and are not a viable alternative for the general public.

The agency agrees with the comment. The Panel discussed the side effects of topical estrogens and recommended a limit on the daily dosage of estradiol that would be safe for OTC use (45 FR 73958). The agency acknowledges that female characteristics have been produced in males using topical estrogens and finds that a product causing the side effects described by the comment is not suitable for OTC use. Further discussion of the use of topical estrogens as OTC hair growers is presented in comment 10 below.

10. One comment noted that the dose of estradiol classified by the Panel as ineffective was not specified in the listing of Category II active ingredients at 45 FR 73958. The comment requested that the dose be included in the listing to avoid confusion with larger doses that are used by clinicians and medical investigators and that may have an effect on hair growth.

The list of Category II ingredients at 45 FR 73958 is only a summary list. The paragraph preceding the list states that the Panel classified these hair grower and hair loss prevention ingredients as not generally recognized as effective for OTC use. The Panel subsequently discussed the topical use of estrogens and estradiol as hair growers and determined that the maximum daily dose of estradiol that is safe for OTC use is 5.5 micrograms per day (μg/day)

(i.e., 666 International Units per day (IU/day)). (See 45 FR 73958 and 73959.) However, doses of estradiol that are safe for OTC use were not found by the Panel to be effective. Although higher doses of estradiol are reported to have been used by clinicians and medical investigators, no data were presented to establish general recognition of safety or effectiveness for *OTC use*. The agency finds no reason to state a concentration for estradiol in the summary list because estradiol is not considered as safe and effective for OTC use at any concentration.

11. One comment complained that data and information on a hair grower drug product that had been submitted to the agency as part of the Drug Efficacy Study Implementation (DESI) review were not made available to the Panel, and therefore that the following statement in recommended § 310.527 is untrue: "Data or any other ingredient intended for use as a hair grower or for hair loss prevention in OTC drug products have not been submitted to the Food and Drug Administration for review for safety and effectiveness." The comment also expressed concern that, if the agency adopted the Panel's recommendation for Category II status of all OTC hair grower drug products, the approved NDA for this hair grower drug product would be revoked, thereby denying the manufacturer the right to a hearing under the DESI proceedings.

The drug product referred to by the comment consists of two topically applied preparations: an aqueous solution of sulfanilamide 0.25 percent (Formula A) and an aqueous solution of lanolin 1.5 percent (Formula B). This product has been the subject of an NDA that was approved for safety on February 26, 1948. It was reviewed for effectiveness by the National Academy of Sciences-National Research Council (NAS–NRC) under FDA's DESI review and was subsequently classified by FDA as "possibly effective." (See the **Federal Register** announcement, "Certain Sulfonamide-Containing Preparations for Topical, Ophthalmic, or Otic Use," published on September 25, 1970; 35 FR 14954.) The agency later issued a notice of opportunity for hearing in which the "possibly effective" indications were reclassified to "lacking substantial evidence of effectiveness" because no new data on effectiveness had been submitted within the period provided. (See the **Federal Register** of February 12, 1972; 37 FR 3196.)

The call for data for OTC miscellaneous external drug products (including hair grower and hair loss prevention drug products) was published in the **Federal Register** of November 16, 1973 (38 FR 31697), after the agency had announced in the **Federal Register** that the preparations containing sulfanilamide and lanolin, respectively, lacked substantial evidence of effectiveness. In response to the call for data, informationi on lanolin was submitted; the Panel concluded that there is no evidence to show that lanolin has an effect on hair growth (45 FR 73958).

In the **Federal Register** of April 28, 1981 (46 FR 23811), the agency announced a denial of hearing and withdrawal of approval of the NDA for the preparations in the DESI review proceeding. In that announcement, the agency extensively discussed the submitted data and information on the two preparations and concluded that there was a lack of substantial evidence that they have the effect represented under the conditions of use prescribed, recommended, or suggested in the labeling. The labeling contains the claims that the product softens the scalp, removes dandruff scales, and aids the scalp and hair. It is implied in advertisements for the product that it offers the user the expectation of diminished hair loss, hair regrowth in cases of baldness, and alleviation of dandruff. After considering all of the material submitted, the agency concluded that there was no genuine and substantial issue of fact requiring a hearing, and that the legal objections raised were without merit.

The comment submitted to this rulemaking provided no new data or information for the agency to consider with respect to the Panel's conclusion on lanolin or the agency's conclusion previously reached through the DESI review on the two preparations. Based on the Panel's recommendation and on the agency's analysis set forth in the **Federal Register** at April 28, 1981 (46 FR 23811), the agency proposes that sulfanilamide and lanolin be classified in this tentative final regulation as Category II for use as OTC hair growers or for hair loss prevention.

The concerns expressed by the comment (i.e., denying the right to a hearing and possible revocation of the product's NDA) have already been addressed by the agency in the DESI review proceeding and need not be addressed in this rulemaking. The agency points out that the comment to this rulemaking was submitted before the April 28, 1981 **Federal Register** announcement was published.

The statement in § 310.527, "Data on any other ingredient intended for use as a hair grower * * * have not been submitted to the Food and Drug Administration for review * * *," was intended by the Panel to refer to data submitted to the agency's OTC drug review, pursuant to the call-for-data notice for OTC miscellaneous external drug products. Because this statement is not a necessary part of the regulation, it is not being included in this tentative final regulation.

12. Four comments submitted data and information to support their contention that topically applied biotin, a B-vitamin, is an effective OTC hair grower and hair loss prevention ingredient. One comment opposed the marketing of biotin-containing products as hair growers and described them as frauds, stating that these products were the subject of an April 1980 Florida court case involving the U.S. Postal Service. Of the comments supporting Category I status of biotin, one comment requested that further action on the advance notice of proposed rulemaking be delayed until the results of a double-blind study have been submitted. One comment submitted 10 volumes of data and information from a "retrospective" study in support of the safety and effectiveness of biotin 0.005 to 0.1 percent, which included log books, records on patients, photographs, and data summaries (Ref. 1) and a supplement to the data (Ref. 2). Another comment suggested that a prospective controlled study be conducted to show whether biotin-containing products are effective for this use because the quality of the photographs in the data submitted prevented any conclusions from being reached.

The agency is aware that the mail-order sale of a biotin hair grower product was halted as the outcome of an administrative proceeding completed in 1980 by the U.S. Postal Service. Actions taken by the U.S. Postal Service, however, are separate from actions taken under the Federal Food, Drug, and Cosmetic Act. In addition, data and information not available in 1980 may now be available for submission to FDA.

The comments provided information that included brochures on biotin products, a description and a copy of an article by Settel (Ref. 3), and a statement from a consumer on the effectiveness of biotin as a hair grower. A reference on dihydrotestosterone-A, cited by one comment, could not be obtained either from libraries or from the comment source (Ref. 4). The product brochure and the article by Settel provided no data for the agency to review on biotin's safety and effectiveness. In addition, statements from consumers cannot be

considered as adequate proof of effectiveness or safety.

The submitted study (Ref. 1) was not controlled and therefore is inadequate. The agency agrees with the comment that the photographs included in these data prevent any conclusions from being reached; the photographs display such variability in technique that they provide inadequate data for assessment. Other data were also inadequate: questionable methods of evaluating hair root viability, the use of untrained observers, and the use of drugs in addition to biotin in the course of treatment preclude reliance on those studies.

The agency agrees with the coment that a prospective controlled study on biotin is the preferred approach to study design. The agency's detailed comments and evaluations on the data submitted are on file in the Dockets Management Branch (Ref. 5).

The comment's request to delay action on the advance notice of proposed rulemaking was made in December 1980. Since that time the person who made the comment has submitted no new data or information. The agency will not delay its OTC drug rulemaking proceedings to allow additional time for further research. In accordance with agency regulations, new data may be submitted within 12 months following publication of this proposed rule (21 CFR 330.10(a)(7)).

After reviewing the data and information submitted by the comments, the agency is proposing that biotin be classified in Category II because the data are inadequate to demonstrate this ingredient's safety or effectiveness as an OTC hair grower and hair loss prevention drug ingredient.

References

(1) Comment No. C00022, Volume I through Volume X, Docket No. 80N-0357, Dockets Management Branch.

(2) Comment No. SUP002, Docket No. 80N-0357, Dockets Management Branch.

(3) Settel, E., "Control of Excessive Hair Loss Through Topical Enzyme Therapy," *Drug and Cosmetic Industry*, 121:34-37 and 156-158, 1977.

(4) Comment No. C00013, Docket No. 80N-0357, Dockets Management Branch.

(5) Letter from W. E. Gilbertson, FDA, to E. Settel, coded LET012 to C00022, Docket No. 80N-0357, Dockets Management Branch.

13. Several comments defended the use of topical preparations that are used to treat hair loss attributed to accumulation of sebum, the secretion of the sebaceous glands. One comment stated that sebum collects around the hair shaft at the follicle and hardens, choking off the follicle, and that topical preparations are especially effective in dissolving sebaceous accumulations. The comments provided statements from consumers on the effectiveness and safety of these products. One comment, from a hair grower consultant firm, stated that the firm's submission to the Panel was mistakenly reviewed for the claim of treating male pattern baldness, rather than for sebum hair loss. The comment argued that the ingredients in its products (i.e., estradiol, isopropanol, methyl ethyl ketone, sufonated vegetable and mineral oils, ammonium lauryl sulfate, and benzethonium chloride) should at least have been classified as Category III by the Panel and requested that FDA delay final classification of the ingredients in its products for not less than 18 months to allow time to submit "confirmatory efficacy data." One comment described as "successful" a hair loss prevention product containing the chemical dinitrochlorobenzene.

The Panel noted that the theory that sebum can cause hair loss is not generally accepted by the medical profession today and that studies have shown no quantitative difference in the amount of sebum present on the bald scalp, the hairy scalp of balding men, and the scalp of men who showed no baldness (45 FR 73958). The agency agrees with the Panel that hair loss has not been shown to be related to the production of sebum. No data have been submitted by the comments to show that sebum causes hair loss.

With regard to the statement made in one comment, that a company's submission was not reviewed for a claim for sebum hair loss, the agency notes that the Panel thoroughly discussed this submission and claim in its report, prefacing its discussion with the following statement: "A third manufacturer submitted both safety and effectiveness data for a variety of products used for sebum hair loss" (45 FR 73958). The comment submitted information on a variety of products used to treat sebum hair loss and identified several ingredients in the product as active ingredients: estradiol 0.011 milligram per fluid ounce (mg/fl oz), isopropanol, methyl ethyl ketone, sulfonated vegetable and mineral oils, ammonium lauryl sulfate, and benzethonium chloride. The agency tentatively concurs with the Panel that these ingredients are safe when used as labeled in the submission, but that the data fail to demonstrate the effectiveness of these ingredients for hair loss prevention. As stated in comment 12 above, statements from consumers cannot be regarded as adequate proof of safety and effectiveness of these products. Furthermore, the agency concurs with the Panel's classification of estradiol 0.011 mg/fl oz as the only active ingredient among these ingredients, when used in OTC hair grower and hair loss prevention drug products. The product containing benzethonium chloride is labeled as an "antiseptic dressing for the hair and scalp" that "helps to destroy and control bacteria * * * and aids in combing or 'setting' the hair." The Panel classified benzethonium chloride as an inactive ingredient. The comment did not present any evidence that the product has any effect on hair growth or hair loss prevention; thus, there is no basis to consider benzethonium chloride an active ingredient for these uses.

The firm's request for an 18-month delay was dated February 5, 1981. The firm has submitted no new data subsequent to its request. As discussed in comments 4 and 12 above, action on the advance notice of proposed rulemaking is not being delayed; data may be submitted following the publication of this proposed rule (21 CFR 330.10(a)(7)) or in accordance with the NDA procedures (21 CFR Part 314).

No data were submitted on the safety and effectiveness of dinitrochlorobenzene. One company commenting on this ingredient described its use by West German researchers in treating alopecia areata, a type of baldness that is unrelated to male pattern baldness (Ref. 1). The company also stated that dinitrochlorobenzene produces contact dermatitis, which can be severe enough to warrant discontinuation of treatment. Thus, the agency concludes the information is inadequate to consider dinitrochlorobenzene as generally recognized as safe and effective for OTC use as a hair grower or for hair loss prevention.

Reference

(1) "Checkup on Medicine: Elaboration on a Baldness Cure," *Science Digest*, 85:83, February 1979.

14. One comment included data and information on a product containing "sulfur at 1 percent on carbon in a fraction of paraffinic hydrocarbons" (Refs. 1 and 2) and requested that FDA consider the entire formula of the product as active and classify it as safe and effective for OTC use for the prevention of hair loss.

FDA has reviewed the data and information and determined that the comment did not provide adequate data to establish the safety and effectiveness of the active ingredients. The description of the active ingredients as

"sulfur at 1 percent on carbon in a fraction of paraffinic hydrocarbons" is inadequate for the agency to fully assess the ingredients or to determine whether any of the ingredients is a new drug as defined in section 201(p) of the act (21 U.S.C. 321(p)). The agency has requested that the firm submit the chemical names and descriptions of the active ingredients as well as their concentrations, and also requested clarification of the confidentiality status of a section of the safety data (Ref. 3). To date, no reply has been received from the firm.

The safety data submitted with the comment included photographs of histologic examinations in animals; however, these photographs were poorly reproduced and could not be evaluated. Although the data contained an evaluation of carcinogenicity, the Ames test for mutagenicity was not conducted. The agency notes that a number of the study subjects stated that the test preparation and the placebo lotion caused stinging and burning. However, in the absence of details on the product's formulation, the agency is unable to assess the significance of this information in relation to the overall safety of the ingredients. The data also included an effectiveness study; however, the efficacy criteria were arbitrarily defined and difficult to interpret. The statistical methodologies used to evaluate hair loss were not appropriate and there were various numerical inconsistencies in the sponsor's tables. The efficacy end-points used to evaluate hair growth were not based on objective criteria, and the significance level for multiple comparisons was not adjusted when subjective responses were evaluated. In addition, the length of time that the study was conducted was not adequate to show persistence of results. In view of these inadequacies, the agency cannot consider the data submitted by the comment as adequate to establish safety or effectiveness. Thus, the agency proposes to classify sulfur 1 percent on carbon in a fraction of paraffinic hydrocarbons as Category II for OTC use for the prevention of hair loss.

The agency's detailed comments and evaluations on the data and information submitted are on file with the Dockets Management Branch (Ref. 4).

References

(1) Comment No. RPT, Volume I through Volume IV, Docket No. 80N-0357, Dockets Management Branch.

(2) Comment No. SUP, Docket No. 80N-0357, Dockets Management Branch.

(3) Comment No. LET005, Docket No. 80N-0357, Dockets Management Branch.

(4) Letter from W.E. Gilbertson, FDA, to W. Pendergast, attorney for Fortkan International, Inc., coded LET015, Docket No. 80N-0357, Dockets Management Branch.

15. Four comments included data and information, which included a copy of a product brochure and statements by a consumer and a physician, to show that effectiveness of certain hair grower products that appear to contain polysorbate 20 or polysorbate 60 (a nonionic surface active ingredient), urea, biotin, and pantothenol. Two of the comments each included seven volumes of data and information on the product's safety and effectiveness (Refs. 1 and 2). Another comment cited a report on a hair preparation that included information on studies conducted on the safety and effectiveness of "certain non-ionic surface-active agents" when applied to the human scalp and skin (Ref. 3).

The data and information submitted with two comments (Refs. 1 and 2) contained histograms, pictures, and tables that were not readily discernible. In particular, the reproduced photographs were of such poor quality that an assessment of hair regeneration could not be made. The agency subsequently requested that the firms that filed the comments submit original versions of these data and that the names of the active incredients and the confidentiality status of the product formulations be clarified (Refs. 4 and 5). No communications have been received from the firms; thus, the agency is unable to consider further the data and information provided by the comments. The agency's detailed comments and evaluations on the information submitted are on file with the Dockets Management Branch (Refs. 6 and 7).

The report cited by one comment (Ref. 3) described only the results of studies; data from observations were not presented. In addition, the formulation (including identification of the active ingredients) of the hair preparation used in the studies was not revealed. The brochure provided by one comment provided no data for evaluation, and, as stated in comments 12 and 13 above, statements from consumers do not constitute adequate evidence of safety or effectiveness.

The agency concludes that the data and information submitted with the comments are inadequate for the agency to classify the ingredients in the products discussed above as generally recognized as safe and effective for use as OTC hair growers or for hair loss prevention. The agency's conclusions on biotin are presented in comment 12 above.

References

(1) Comment No. C00015, Volume I through Volume VII, Docket No. 80N-0357, Dockets Management Branch.

(2) Comment No. C00016, Volume I through Volume VII, Docket No. 80N-0357, Dockets Management Branch.

(3) Setalla, K., and I. Schreck-Purola, "Baldness and Its Cure: Safety and Mode of Effect of Hair Preparation," The First Department of Pathology, University of Helsinki, Finland, 1977.

(4) Letters from W.E. Gilbertson, FDA, to K. Cox, Florida Nutrition Center, Inc., coded LET007 and LET008, Docket No. 80N-0357, Dockets Managment Branch.

(5) Letters from W.E. Gilbertson, FDA, to C. Richardson, Standard Research Laboratories, coded LET006 and LET009, Docket No. 80N-0357, Dockets Management Branch

(6) Letter from W.E. Gilbertson, FDA, to K. Cox, Florida Nutrition Center, Inc., coded LET011, Docket No. 80N-0357, Dockets Management Branch.

(7) Letter from W. E. Gilbertson, FDA, to C. Richardson, Standard Research Laboratories, coded LET013, Docket No. 80N-0357, Dockets Management Branch.

II. The Agency's Tentative Adoption of the Panel's Report

The Panel discussed the use of ascorbic acid, benzoic acid, estradiol, lanolin, tetracaine hydrochloride, and wheat germ oil for OTC use as hair growers or for hair loss prevention. Based on the comments, the agency has also considered the ingredients amino acids, aminobenzoic acid, biotin and all other B-vitamins, topical hormones, jojoba oil, nucleic acids, pantothenol, polysorbate 20, polysorbate 60, sulfanilamide, sulfur 1 percent on carbon in a fraction of paraffinic hydrocarbons, and urea for these uses. FDA has considered the Panel's recommendations, the comments, and other data and information available at this time and concludes that it will tentatively adopt the Panel's report and recommendation that all OTC drug products labeled for external use as hair growers or for hair loss prevention be classified Category II.

The agency is also revising § 310.527(b) to clarify that a product covered by the regulation is a new drug for which an approved NDA is required for marketing, and in the absence of an approved NDA the product would also be misbranded under section 502 of the act.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these

economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for ORC hair grower and hair loss prevention drug products for external use, is a major rule.

For purposes of the regulatory Flexibility Act, the economic assessment concluded that, while the average economic impact of the overall OTC drug review on small entities will not be significant, the possibility of larger-than-average impacts on some small firms in some years might exist. Therefore, the assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose a significant impact on a substantial number of small entities. The analysis identified the possibilities of reducing burdens on small firms through the use of (a) relaxed safety and efficacy standards or (b) labels acknowledging unproven safety or efficacy. However, the analysis concluded that there is no legal basis for any preferential waiver, exemption, or tiering strategy for small firms compatible with the public health requirements of the Federal Food, Drug, and Cosmetic Act. Nevertheless, to avoid overlooking any problems or feasible possibilities of relief peculiar to this group of products, the agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC hair grower and hair loss prevention drug products for external use. Comments regarding the economic impact of this rulemaking should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on hair grower and hair loss prevention drug products for external use, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979; 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 310

New drugs.

PART 310—[AMENDED]

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended in Part 310 by adding to Subpart E new § 310.527, to read as follows:

§ 310.527 Drug products containing active ingredients offered over-the-counter (OTC) for external use as hair growers or for hair loss pervention.

(a) Amino acids, aminobenzoic acid, ascorbic acid, benzoic acid, biotin and all other B-vitamins, estradiol and other topical hormones, jojoba oil, lanolin, nucleic acids, pantothenol, polysorbate 20, polysorbate 60, sulfanilamide, sulfur 1 percent on carbon in a fraction of paraffinic hydrocarbons, tetracaine hydrochloride, urea, and wheat germ oil have been marketed as ingredients in over-the-counter (OTC) drug products for external use as hair growers or for hair loss prevention. There is a lack of adequate data to establish the effectiveness of these or any other ingredients intended for external use as OTC hair growers or for hair loss prevention. Based on evidence presently available, labeling claims for OTC hair grower and hair loss prevention drug products for external use are either false, misleading, or unsupported by scientific data. Therefore, any OTC drug product for external use containing an ingredient offered for use as a hair grower or for hair loss prevention cannot be considered generally recognized as safe and effective for its intended use.

(b) Any OTC drug product that is labeled, represented, or promoted for external use as a hair grower or for hair loss prevention is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act, for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing. In the absence of an approved new drug application, such product is also misbranded under section 502 of the act.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FDA–1571) (OMB Approval No. 0910–0014), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that any drug product labeled, represented, or promoted for external use as a hair grower or for hair loss prevention is safe and effective for the purpose intended.

(d) After the effective date of the final regulation, any such OTC drug product initially introduced or initially delivered for introduction into interstate commerce that is not in compliance with this section is subject to regulatory action.

Interested persons may, on or before May 15, 1985, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and

comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final rule, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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Part VIII

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 341

Cold, Cough Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for OTC Antihistamine Drug Products

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 341

[Docket No. 76N-052H]

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for OTC Antihistamine Drug Products

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) antihistamine drug products (drug products used for the relief of the symptoms of hay fever and upper respiratory allergies (allergic rhinitis) and the symptoms of sneezing and runny nose associated with the common cold) are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal deals only with antihistamine drug products and is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 9, 1976 (41 FR 38312) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products, together with the recommendations of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. Interested persons were invited to submit comments by December 8, 1976. Reply comments in response to comments filed in the initial comment period could be submitted by January 7, 1977.

In a notice published in the **Federal Register** of March 21, 1980 (45 FR 18400), the agency advised that it had reopened the administrative record for OTC cold, cough, allergy, bronchodilator, and antiasthamtic drug products to allow for consideration of data and information that had been filed in the Dockets Management Branch after the date the administrative record previously had officially closed. The agency concluded that any new data and information filed prior to March 21, 1980 should be availaable to the agency in developing a proposed regulation in the form of a tentative final monograph.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. Data and information received after the administrative record was reopended have also been put on display in the Dockets Management Branch. In response to the advance notice of proposed rulemaking, 12 manufacturers, 2 manufacturers' associations, 16 health care professionals, and 6 health care professional societies submitted comments on antihistamine drug products. Copies of the comments received are on public display in the Dockets Management Branch.

FDA is issuing the tentative final monograph for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products in segments. This document on antihistamine drug products is the fifth segment to be published. The first segment, on anticholinergic drug products and expectorant drug products, was published in the **Federal Register** of July 9, 1982 (47 FR 30002). The second segment, on bronchodilator drug productss, was published in the **Federal Register** of October 26, 1982 (47 FR 47520). The third segment, on antitussive drug products, was published in the **Federal Register** of October 19, 1983 (48 FR 48576). The fourth segment, on nasal decongestant drug products, is being published elsewhere in this issue of the **Federal Register**. A subsequent segment on combination drug products and general comments will be published in a future issue of the **Federal Register**.

The advance notice of proposed rulemaking, which was published in the **Federal Register** on September 9, 1976 (41 FR 38312), was designated as a "proposed monograph" in order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10). Similarly, the present document is designated in the OTC drug review regulations as a "tentative final monograph." Its legal status, however, is that of a proposed rule. In this tentative final monograph (proposed rule), FDA states for the first time its position on the establishment of a monograph for OTC antihistamine drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC antihistamine drug products.

This tentative final monograph would amend Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations in Part 341 (as set forth in the tentative final monograph on anticholinergic durg products and expectorant drug products that was published in the **Federal Register** of July 9, 1982 (47 FR 30002)) in Subpart A, by adding in § 341.3, new paragraph (d); in Subpart B, by adding new § 341.12; and in Subpart C, by adding new § 341.72, and by adding in § 341.90, new paragraphs (b), (c), (d), (e), (f), (g), (h), (i), (j), and (k). This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC antihistamine drug products, as modified on the basis of the comments received and the agency's independent evaluation of the Panel's report. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979).

(See the Federal Register of September 29, 1981; 46 FR 47730.) The Court in *Cutler* held that the OTC drug regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process, before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the Federal Register. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions that would cause the durg to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the advance notice of proposed rulemaking for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products (published in the Federal Register of September 9, 1976 (41 FR 38312)), the agency suggested that the conditions included in the monograph (Category I) be effective 30 days after the date of publication of the final monograph in the Federal Register and that the conditions excluded from the monograph (Category II) be eliminated from OTC drug products effective 6 months after the date of publication of the final monograph, regardless of whether further testing was undertaken to justify their future use. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the Federal Register. The agency believes that within 12 months after the date of publication most manufacturers can show new labeling and have their products in compliance in the marketplace. However, if the agency detemines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notice published in the Federal Register of August 9, 1972 (37 FR 16029) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

The Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products recommended that doxylamine succinate be classified in Category I as an antihistamine at adult oral dosages of 7.5 to 12.5 milligrams (mg) every 4 to 6 hours, not to exceed 75 mg in 24 hours (see 41 FR 38419). However, since the Panel's report was published, controversy has arisen concerning whether or not there is an association of a prescription drug product containing doxylamine succinate with birth defects. This drug product is prescribed as an antinauseant for use during pregnancy. In 1982, Eskenazi and Bracken (Ref. 1) reported the results of a case control study of 1747 women, which suggests that a child born to a mother who used the doxylamine containing product was at an approximately four fold increased risk for developing pyloric stenosis. The Boston Collaborative Drug Surveillance Program recently reported to the agency preliminary results of a cohort study that also found an association between exposure to a product containing doxylamine succinate during pregnancy and the occurence of pyloric stenosis in infants. The reported increase in risk was 2.7 fold, a finding consistent with the Eskenazi and Bracken study. Preliminary results from this study suggest risk increasing with increasing numbers of prescriptions. These reports, however, do not establish that the association is causal. Other factors, in particular, the nausea and vomiting, may account for the observed association. Mitchell et al. (Ref. 2) recently presented the findings of a case-control study conducted by the Drug Epidemiology Unit of Boston University. This study, representing by far the largest available data base, compared the use of a product containing doxylamine succinate among the mothers of 325 infants with pyloric stenosis to its use in mothers of 3,153 infants with other malformations. No association between the use of a product containing doxylamine succinate during pregnancy and the development of pyloric stenosis was found. In addition, the agency has examined Medicaid data to determine whether in this data base there is an association between the use of a doxylamine succinate containing drug

product by women during pregnancy and the occurrence of pyloric stenosis in infants (Ref. 3). Based on an analysis of these data, the agency has concluded that the Medicaid data do not support such an association.

The agency is aware that at this time the scientific and medical communities are actively discussing and debating whether or not doxylamine succinate, in fact, plays a causal role in reported birth defects. This subject has been discussed and debated without resolution at several scientific meetings such as the Teratology Society meeting and the Society for Epidemiologic Research meeting that were held in June 1984. The possible association of doxylamine succinate with birth defects continues to be disputed.

The time necessary to complete a full review and evaluation of the new studies concerning the use of a product containing doxylamine succinate and birth defects could result in a considerable delay in the publication of the tentative final monograph for OTC antihistamine drug products. Accordingly, the agency has decided to remove all discussion of the safety and effectiveness of doxylamine succinate from this document.

The agency intends to review and evaluate the new data and information concerning the relationship between doxylamine succinate and birth defects that is currently being generated in as expeditious a manner as possible. Based on its review and evaluation of the data and information, the agency will publish a separate document in the **Federal Register** addressing the status of this ingredient.

At this time, drug products containing doxylamine succinate as an OTC antihistamine will remain in the marketplace with the warning required for all OTC drug products, as follows: "As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product."

References

(1) Eskenazi, B., and M. Bracken, "Bendectin (Debenox) as a Risk Factor for Pyloric Stenosis," *American Journal of Obstetrics and Gynecology*, 144:919–924, 1982.

(2) Mitchell, A. A., et al., "Birth Defects in Relation to Bendectin Use in Pregnancy II. Pyloric Stenosis," *American Journal of Obstetrics and Gynecology*, 147:737–742, 1983.

(3) Rosa, F.W., draft of unpublished study, OTC volume 04HTFM, Docket No. 76N–052H, Dockets Management Branch.

I. The Agency's Tentative Conclusions on the Comments

A. General Comments on Antihistamine Drug Products

1. One comment stated that the Panel gave certain antihistamines (i.e., diphenhydramine, methapyrilene, phenindamine, pheniramine, promethazine, pyrilamine, and thonzylamine) Category I status on the basis of low-quality evidence. The comment stated that the Panel recognized that there were no controlled clinical trials for these drugs, that chronic toxicity studies in animals had not been performed, and that there was no evidence that systematic literature searches were conducted or that FDA adverse reaction files were studied. The comment concluded that these drugs have been adjudged "safe" on the basis of superficial information. The comment contended that controlled clinical trials are required for general recognition of safety and effectiveness. The comment recommended that a complete new review of cough and cold ingredients be conducted by FDA and that FDA impose an immediate ban of all ingredients that are not proven safe and effective by scientific studies equivalent to those required for prescription drugs.

In determining that certain antihistamines should be generally recognized as safe and effective for OTC use, the Panel followed applicable regulations relating to the OTC drug review. The regulations, at 21 CFR 330.10(a)(4)(i), state: "Proof of safety shall consist of adequate tests by methods reasonably applicable to show the drug is safe under the prescribed, recommended, or suggested conditions of use. This proof shall include results of significant human experience during marketing. General recognition of safety shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data."

The Panel's conclusions as to the safety of the aforementioned antihistamine drugs were arrived at in accordance with the above regulation. For the determination of safety, the Panel reviewed published and unpublished studies, Poison Control Center statistics, FDA adverse reaction reports, and other data in the literature, and it used clinical and marketing experience to corroborate these data.

Subsequent to the Panel's determinations, new data were developed concerning some of these ingredients. On the basis of these data, the agency has taken appropriate regulatory action and in this tentative final monograph is making necessary changes to the Panel's recommendation. For example, the Panel recommended classification of methapyrilene hydrochloride and methapyrilene fumarate in Category I as antihistamines. Subsequent to this recommendation, a National Cancer Institute (NCI) study, not available to the Panel, provided data from which the agency concluded that methapyrilene is a potent carcinogen in animals and must be considered a potential carcinogen in man. These data are on file in the Dockets Management Branch (address above) under Docket No. 75N–0244 and have been published (Ref. 1).

In June 1979, the agency initiated a recall of all oral and topical products containing methapyrilene. Manufacturers have voluntarily recalled all methapyrilene-containing products from the market, and FDA has withdrawn all NDAs for products containing methapyrilene. Products containing methapyrilene are considered misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352) and "new drugs" under section 201(p) of the act (21 U.S.C. 321(p)). The agency has therefore placed methapyrilene fumarate and methapyrilene hydrochloride in Category II in this document.

The Panel recommended a Category I classification for promethazine hydrochloride. However, the agency has concerns regarding the safe use of promethazine hydrochloride as an OTC antihistamine and has determined that although promethazine hydrochloride has been widely used as a prescription drug product with a relatively low incidence of serious adverse reactions, at this time general recognition of the safety of this ingredient for long-term use as an OTC antihistamine has not been adequately established. (See comment 9 below.) Therefore, the agency is proposing that promethazine hydrochloride be Category III at this time as an OTC antihistamine.

For the determination of effectiveness, the agency agrees that the studies on which the Panel based its conclusions concerning diphenhydramine hydrochloride, phenindamine tartrate, pyrilamine maleate, and thonzylamine hydrochloride were not well-controlled. However, the Panel reviewed published studies, as cited in its report, and used clinical and marketing experience to corroborate these studies. The agency concludes that the evidence in these studies and the Panel's expertise in evaluating the clinical and marketing experience are sufficient to establish

general recognition of effectivenes of these ingredients as antihistamines.

The agency has reviewed the Panel's recommendations and all of the supporting data and concludes that there is a sufficient basis to determine that brompheniramine maleate, chlorpheniramine maleate, diphenhydramine hydrochloride, phenindamine tartrate, pheniramine maleate, pyrilamine maleate, and thonzylamine hydrochloride are generally recognized as safe and effective when used as ingredients in antihistamine drug products intended for OTC use.

Reference

(1) Lijinsky, W., M. D. Reuber, and B. N. Blackwell, "Liver Tumors Induced in Rats by Chronic Oral Administration of the Common Antihistamine Methapyrilene Hydrochloride," *Science*, 209:817–819, 1980.

2. Several comments pointed out that the table of symptoms and pharmacological groups in part II. paragraph B. of the Panel's report (41 FR 38320) omitted antihistamines as a pharmacological group for treating runny nose. The comments stated that both the report and the Panel's recommended monograph contain "running nose" as a Category I claim for antihistamines. Several of the comments also criticized the Panel's omission from the table, the report, and the monograph of antihistamines as a pharmacological group for treating "sinus congestion." These comments argued that because "congestion" is a symptom of allergic rhinitis, and the Panel has placed antihistamines in Category I for the alleviation of the symptoms of allergic rhinitis, "sinus congestion" should be included as a symptom to be treated with antihistamines.

The agency agrees the antihistamines were inadvertently omitted from the table of symptoms and pharmacological groups as a treatment for runny nose. Runny nose as may occur in allergic rhinitis is listed as a Category I claim for antihistamines in the Panel's report and in § 341.72(a) (1), (2), and (6) of its recommended monograph. Therefore, the table of symptoms and pharmocological groups in part II. paragraph B. is amended by the publication of this document.

The agency does not agree that antihistamines should be included in the table, report, or recommended monograph for the treatment of "sinus congestion." The Panel recommended antihistamines only for the treatment of specific symptoms, i.e., runny nose, sneezing, itching of the nose or throat, and itchy, watery eyes associated with allergic rhinitis, and did not recommended antihistamines for the alleviation of all symptoms associated with allergic rhinitis, as stated by the comment. Sinus congestion may result in impaired sinus drainage due to nasal obstruction caused by allergic rhinitis or the "common cold." The Panel reviewed studies that measured the effects of antihistamines or nasal obstructions (Refs. 1, 2, and 3). These studies demonstrated that antihistamines did not reduce nasal obstruction and therefore did not aid in sinus drainage. To the contrary, the studies indicated that antihistamines may sometimes further aggravate nasal obstruction (Refs. 2 and 3). For that reason, the Panel placed antihistamines in Category II for claims for the relief of symptoms such as nasal obstructions, nasal stuffiness, etc. The Comments did not provide any data that demonstrate that antihistamines are effective in the treatment of "sinus congestion." The agency concurs in the Panel's Category II classification.

References

(1) OTC Volume 040306.
(2) OTC Volume 040114.
(3) OTC Volume 040123.

3. One comment stated that two antihistamines should not be taken simultaneously and recommended that the labeling should be clear on this matter. The comment did not further elaborate on its statement.

The comment did not provide any information or examples. It is not clear whether there was concern about the simultaneous ingestion of two drug products each containing antihistamines ingredients that are specifically labeled as "antihistamines" or the simultaneous ingestion of two different drug products both containing antihistamines ingredients but for different use, e.g., one product labeled for "nighttime sleep-aid use" with no labeling as an antihistamine and another product labeled for "antihistamines use."

The agency recognizes that such products are currently available in the OTC drug marketplace but is unaware of any information that would raise health concerns. It is unlikely that a consumer would concurrently take two different OTC drug products both containing antihistamines. The proposed labeling for antihistamines in this tentative final monograph specifically requires that the product's principal intended use, i.e., "antihistamines," be stated in the labeling. By reading the labels, a consumer is made aware that different drug products contain antihistamine intended to treat the same symptoms. Therefore it is unlikely that two such products would be taken simultaneously.

The agency recognizes that at least one antihistamine ingredient, diphenhydramine hydrochloride, because of its numerous pharmacologic properties, is marketed as an "antihistamines," "antitussive," and "nighttime sleep-aid" drug product. A consumer could simultaneously ingest two such products to alleviate concurrent symptoms. However, the agency is unaware of any information that this does occur. In addition, the agency is unaware of any data demonstrating that the simultaneous ingestion of two antihistamines labled for different uses would result in a significant safety problem.

Therefore, the agency believes that the proposed labeling for antihistamines drug products in this tentative final monograph is adequate and that at this time there is no justification for expanding the labeling to include specific warnings regarding the simultaneous ingestion of two antihistamines. The agency invites specific comments on this issue.

4. Several comments requested that antihistamines, such as chlorpheniramine maleate, be allowed to make claims for the treatment of symptoms of the common cold. Symptoms for which Category I labeling claims were requested included the relief of runny nose, sneezing, itching of the nose or throat, and itchy, watery eyes when associated with the common cold. Two comments provided new data describing the results of clinical studies in which chlorpheniramine maleate was evaluated for treating symptoms of the common cold (Ref. 1). Another comment stated that there was little evidence to substantiate the usefulness of antihistamines for treating symptoms of the common cold and that, in fact, there are studies that demonstrate a lack of effectiveness for the use of antihistamines in treating symptoms of the common cold. The comment did not identify these studies.

The agency has reviewed the new data submitted in support of the use of chlorpheniramine maleate in treating the symptoms of the common cold enumerated above. The data submitted included independently conducted, multicenter, double-blind studies in which chlorpheniramine maleate was compared with a placebo in patients with the common cold over a 7-day period. In design and overall methodology, these studies follow the guidelines recommended by the Panel for studying antihistamines in the treatment of symptoms associated with

the common cold. An additional study conducted by a single investigator included 196 patients with the common cold who were followed for a 2-day period. This study was similar to the multicentered studies except for the length of time the patients were studied. The studies provide evidence that chlorpheniramine is significantly more effective than a placebo in alleviating the symptoms of runny nose and sneezing associated with the common cold. However, the data do not provide statistical evidence to show that chlorpheniramine is effective in relieving itching of the nose or throat, or itchy, watery eyes associated with the common cold. The agency has, therefore, concluded that chlorpheniramine is effective in treating runny nose and sneezing associated with the common cold. Because the pharmacologic actions of the various Category I antihistamines are similar, the agency believes that the data submitted for chlorpheniramine allow Category I status for these claims to be extended to all Category I antihistamine active ingredients. Accordingly, an indication for the temporary relief of runny nose and sneezing associated with the common cold has been added to proposed § 341.72(b) of this tentative final monograph.

Reference

(1) Comment Nos. SUP004 and SUP005, Docket No. 76N-0052, Dockets Management Branch.

5. One comment recommended that, in view of the reported toxicity of brompheniramine maleate and chlorpheniramine maleate, the quantity of these antihistamines contained in OTC packages should be limited. For example, the comment recommended limiting brompheniramine and chlorpheniramine products to 24 foil-wrapped tablets for the 4-mg strength tablets and to 12 tablets for the 8- and 12-mg strength tablets. The comment also recommended that containers of larger quantities of these antihistamines have child-resistant closures. The comment did not provide any data to support its recommendations.

FDA has established quantity limitations for certain OTC drugs in order to limit the possibility of accidental poisoning of children. See, for example, 21 CFR 201.308 (ipecac syrup) and 21 CFR 201.314 (children's aspirin). The Consumer Product Safety Commission (CPSC), however, has the authority to require child resistant closures for OTC drug containers. FDA is aware that CPSC has reviewed the available data on antihistamines to determine if child-resistant closures are warranted for OTC drug products containing these ingredients. CPSC has published a final rule that drug products containing more than 75 mg diphenhydramine hydrochloride in a single package and in a dosage form intended for oral administration be required to have child-resistant packaging. (See CPSC Requirements for Child-Resistant Packaging: Diphenhydramine Hydrochloride published in the Federal Register on February 15, 1984; 46 FR 5337.) CPSC found that serious toxic effects can be produced with doses of diphenhydramine hydrochloride as low as 100 mg.

CPSC reviewed the toxicity of antihistamines other than diphenhydramine. However, it did not propose that any antihistamine other than diphenhydramine be required to be packaged with child-resistant closures. Because of the lack of significant toxicity data for antihistamines other than diphenhydramine, CPSC concluded that child-resistant closures were not necessary for these drugs, regardless of the amount of drug contained in each package.

The comment did not submit any data demonstrating a need to limit the package size of non-diphenhydramine antihistamine drug products. Moreover, FDA does not have other data or information showing that limiting the package size for these antihistamines is necessary. In the case of diphenhydramine, CPSC is requiring that child-resistant closures be used for packages of drug products containing greater than 75 mg diphenhydramine. If the agency proposed limiting the package size of such drug products to 75 mg diphenhydramine or less, each package would contain only six children's doses of 12.5 mg or one and one-half adult doses of 50 mg. Limiting the package size to such low numbers of dosages would be impractical. The agency believes that CPSC's requirement for child-resistant closures for drug products containing diphenhydramine provides a sufficient safeguard against accidental overdose in children, and that package size limitations are therefore unnecessary for such drug products.

B. Comments on Switching Prescription Antihistamine Active Ingredients to OTC Status

6. Several comments agreed and others disagreed with the Panel's recommendation to allow the OTC marketing of certain antihistamines which were previously available only by prescription or at higher dosage levels than those currently permitted for OTC use. The comments which disagreed with the Panel unanimously recommended that those antihistamines which were previously available by prescription only, i.e., promethazine hydrochloride, diphenhydramine hydrochloride, brompheniramine maleate, chlorpheniramine maleate at a dosage of 4 mg, should remain prescription products. In general, the comments expressed opinions, without supporting data, that the benefits obtained from allowing these antihistamines to become available OTC would not outweigh the risks to which consumers would be exposed. Among the risks mentioned were (1) toxic effects from overdosage, (2) varying degrees of drowsiness and different adverse reactions in different patients, (3) a potential for becoming dependent on the sedative effect of antihistamines, (4) the development of a tolerance to antihistamines, and (5) confusion among consumers from too many antihistamines on the market. The comments also expressed concern that asthmatics with severe bronchitis would suffer from a thickening of secretions due to the anticholinergic effect of antihistamines.

In the preamble to the Panel's report at 41 FR 38313, the agency disagreed with the Panel's classification of diphenhydramine hydrochloride as a Category I antihistamine. The agency's objection to the Panel's recommendation to place these ingredients in Category I was based on the degree of drowsiness produced as a side effect. Subsequently, in a final decision concerning the OTC marketing of diphenhydramine hydrochloride as an OTC antitussive drug product, published in the Federal Register of August 31, 1979 (44 FR 51512), the Commissioner found that the risk of drowsiness in itself does not justify restricting a drug to prescription use if "the manufacturer provides essential information in the labeling and packages the drug in child-resistant containers." The requirement of child-resistant closures has been addressed in comment 5 above. The agency, therefore, is proposing in this tentative final monograph that diphenhydramine hydrochloride at an adult dosage of 25 to 50 mg and doxylamine succinate at an adult dosage of 7.5 to 12.5 mg every 4 to 6 hours be Category I as OTC antihistamine drug products. (See comments 8 and 15 below.)

The agency disagrees with a comment that contended that higher doses of chlorpheniramine maleate should not be allowed OTC. Chlorpheniramine maleate has been available by prescription at the 4-mg dosage level

and OTC at the 2-mg and the 4-mg dosage levels; however, data reviewed by the Panel shows that chlorpheniramine maleate at a dosage of 4 mg every 4 to 6 hours is the minimum effective dosage for adults. Therefore, the agency is proposing that chlorpheniramine maleate be available OTC at the 4-mg dosage. The warning statements proposed in § 341.72 of this tentative final monograph will advise consumers of the appropriate use of antihistamines and of the risks associated with them. (See comment 12 below.)

The agency agrees with the Panel's classification of brompheniramine maleate and is proposing that this ingredient be Category I.

Issues regarding the safety of promethazine hydrochloride have not yet been resolved. The agency is proposing a Category III classification of this ingredient at this time. (See comment 9 below.)

7. One comment contended that the antihistamine dexchlorpheniramine maleate should be made available OTC. The comment explained that chlorpheniramine maleate, which the Panel classified as a Category I antihistamine, is a mixture of dextro- and levo-optical forms in which most of the activity of the antihistamine results from the dextro-optical form. The comment pointed out that dexchlorpheniramine maleate is composed of the dextro-optical form. The comment argued that a small dose of the more active dexchlorpheniramine would give the same effectiveness as a larger dose of chlorpheniramine and would, therefore, be safer because patients would be exposed to a small amount of active ingredient. The comment cited "The United States Dispensatory" (Ref. 1) in support of its argument, as follows: "* * * it would appear that administration of the dextro isomer in half the dose of the racemic compound would provide practically the same antihistaminic activity as the latter (i.e., chlorpheniramine) and but half of its toxic effects; the expectation has been confirmed clinically." The comment recommended that the agency classify dexchlorpheniramine maleate as a Category I antihistamine in doses of 2, 4, and 6 mg.

Dexchlorpheniramine maleate is currently marketed under an approved abbreviated new drug application (ANDA) as a prescription drug at a dose of 2 mg every 4 to 6 hours for adults, a dose of 1 mg every 4 to 6 hours for children 6 to under 12 years of age, and a dose of 0.5 mg every 4 to 6 hours for children 2 to under 6 years of age (Refs. 2 and 3). Chlorpheniramine maleate is currently marketed as an OTC antihistamine drug, and the agency is proposing to place chlorpheniramine maleate in Category I at a dose of 4 mg every 4 to 6 hours for adults and a dose of 2 mg every 4 to 6 hours for children 6 to under 12 years of age. (See comment 12 below.)

An in vitro and an in vivo study of dexchlorpheniramine maleate, chlorpheniramine maleate (racemic mixture), and the levo-optical form of chlorpheniramine maleate in guinea pigs and dogs has demonstrated that the dextro-optical form (dexchlorpheniramine maleate) of chlorpheniramine maleate is the active moiety in the racemic mixture (Ref. 4). The data from this study demonstrate that dexchlorpheniramine maleate has approximately twice the antihistaminic activity of chlorpheniramine maleate (racemic mixture). Therefore, the appropriate OTC dosages for dexchlorpheniramine maleate are half the proposed dosages for chlorpheniramine maleate.

A review of FDA adverse reaction reports since 1976 (Ref. 5) indicates that only one adverse reaction (a patient fainting) has been reported in cases where dexchlorpheniramine maleate was the only drug given.

Based on the safe and effective use of dexchlorpheniramine maleate under an approved ANDA, the safe and effective use of chlorpheniramine maleate for many years as an OTC antihistamine, and a review of FDA adverse reaction reports, the agency believes that dexchlorpheniramine maleate can be generally recognized as safe and effective for OTC use. The agency is therefore proposing that dexchlorpheniramine maleate be classified as Category I as an OTC antihistamine at a dose of 2 mg every 4 to 6 hours, not to exceed 12 mg in 24 hours, for adults and a dose of 1 mg every 4 to 6 hours, not to exceed 6 mg in 24 hours, for children 6 to under 12 years of age. The agency also proposes a dose of 0.5 mg every 4 to 6 hours, not to exceed 3 mg in 24 hours, for children 2 to under 6 years of age under professional labeling in the tentative final monograph. The labeling warnings are identical to those being proposed for chlorpheniramine maleate.

Only timed-release dosage forms are currently approved for adult doses greater than 2 mg every 4 to 6 hours. An approved NDA is required for such products. (See comment 13 below.) Therefore, dosages of 4 to 6 mg will not be included in this tentative final monograph.

Although the agency is proposing in this tentative final monograph to switch dexchlorpheniramine maleate to OTC use from its present status as a prescription drug, OTC marketing may not begin at this time. In the **Federal Register** of June 3, 1983 (48 FR 24925), FDA explained the enforcement policy for drugs that were originally on prescription status but which were being proposed for OTC marketing under the OTC drug review. As noted there, 21 CFR 330.13 permits OTC marketing of a drug previously limited to prescription use prior to publication of a final monograph provided that certain conditions are met. To qualify for such treatment, the drug must, at a minimum, have been considered by an OTC drug advisory review panel and either recommended for OTC marketing by the panel or subsequently determined by FDA to be suitable for OTC marketing. Dexchlorpheniramine maleate was not considered by a panel and, therefore, does not qualify for early OTC marketing under the terms of the enforcement policy set out in § 330.13. Moreover, FDA believes that the drug is not appropriate for OTC marketing at this time. FDA believes that public comments submitted in response to the proposed switch in status should be evaluated before OTC marketing is begun. Accordingly, until such comments are reviewed, dexchlorpheniramine maleate remains a prescription drug subject to the terms and conditions specified in its approved ANDA.

References

(1) Osol, A., R. Pratt, and A.R. Gennaro, "The United States Dispensatory," 27th Ed., J.B. Lippincott Co., Philadelphia, p. 302, 1973.

(2) Letter from M. Seife, FDA, to Schering Corporation, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(3) Copy of FDA-approved labeling from ANDA 86-835, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(4) Roth, F. E., and W. M. Govier, "Comparative Pharmacology of Chlorpheniramine (Chlor-trimeton) and It's Optical Isomers," *Journal of Pharmacology and Experimental Therapeutics*, 124:347-349, 1958.

(5) Department of Health and Human Services, Food and Drug Administration, "Annual Adverse Reaction Summary Listing," pertinent pages for the years 1976-1982, included in OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

8. A number of comments discussed the Panel's recommendation to allow diphenhydramine hydrochloride to be marketed OTC for use as an antihistamine. The comments varied from complete disagreement with the Panel's recommendation to suggestions that the agency place limitations on the

strength of the tablets and/or the size of the packages and that child-resistant closures be required for all OTC products containing this ingredient. One comment suggested that diphenhydramine hydrochloride be available OTC only after consultation with a pharmacist or "prescriber." All of the comments were concerned about diphenhydramine hydrochloride's pronounced tendency for causing drowsiness.

In the preamble to the Panel's report at 41 FR 38313, the agency dissented from the Panel's Category I classification of diphenhydramine hydrochloride as an OTC antihistamine ingredient. It was pointed out that at that time no product containing diphenhydramine hydrochloride was marketed OTC as an antihistamine at any dosage level. In the preamble to the Panel's report, the agency also deferred a decision on the Panel's recommendation to place diphenhydramine hydrochloride in Category I as an antitussive ingredient until the agency made a decision concerning a pending supplemental NDA for OTC status of diphenhydramine hydrochloride as an antitussive. Subsequently, in a final decision concerning the OTC marketing of diphenhydramine hydrochloride as an antitussive drug product published in the **Federal Register** of August 31, 1979 (44 FR 51512), the Commissioner found that the risk of drowsiness in itself does not justify restricting a drug to prescription use if "the manufacturer provides essential information in the labeling and packages the drug in child-resistant containers." Diphenhydramine presently is marketed OTC as an antitussive under an approved supplemental NDA.

The agency believes that the proposed warning in this tentative final monograph that reads "May cause marked drowsiness; alcohol may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Use caution when driving a motor vehicle or operating machinery" and the warning for products labeled for children under 12 years of age that reads "May cause marked drowsiness" are adequate to allow OTC marketing of diphenhydramine hydrochloride. These warnings are similar to those required under the approved supplemental NDA for the antitussive drug product containing diphenhydramine.

The agency, therefore, is proposing diphenhydramine hydrochloride as Category I in this tentative final monograph for use as an OTC antihistamine at an adult dosage of 25 to 50 mg every 4 to 6 hours, not to exceed 300 mg in 24 hours, and for children 6 to 12 years of age at a dosage of 12.5 to 25 mg every 4 to 6 hours, not to exceed 150 mg in 24 hours.

9. Many comments were opposed to the Panel's classification of promethazine hydrochloride as a Category I antihistamine for relieving the symptoms of allergic rhinitis. These comments agreed with the agency's decision (as stated in the preamble of the Panel's advance notice of proposed rulemaking) to limit promethazine hydrochloride to its present status as a prescription drug. The comments asserted that promethazine should not be available on an OTC basis because of (1) its adverse side effects (especially sedation and blood dyscrasias), (2) the potential for abuse and overdosage, (3) the risk in children, and (4) the possibility of increased development of promethazine-induced dyskineasias. The comments concluded that the risk of adverse effects from the OTC availability of promethazine hydrochloride is not justified in the absence of an offsetting benefit in the form of therapeutic superiority in comparison with antihistamine ingredients already marketed OTC.

Only one comment (a reply comment) agreed with the Panel's Category I classification, contending that promethazine has an outstanding safety record based on its long history of use, that there was no basis for implicating promethazine hydrochloride as the cause for blood dyscrasias, and that promethazine hydrochloride cannot be distinguished from other OTC antihistamines in terms of its sedative and other adverse effects on the central nervous system.

After reviewing these comments, the Center for Drugs and Biologics (CDB) expressed its concerns regarding the effect of promethazine hydrochloride on the central nervous system in a feedback letter to a manufacturer (Ref. 1). Based on an incidence of 1 in 2,468 (0.04 percent) of extrapyramidal syndrome associated with the use of promethazine hydrochloride that was cited by the Panel (41 FR 38390) and a report of four cases of choreoathetosis that were related to the use of promethazine at dosages comparable to those recommended by the Panel (Ref. 2), the CDB questioned whether a drug with the side effect of choreoathetosis and a known incidence of extrapyramidal side effects has an acceptable benefit-to-risk ratio for OTC use. The agency had previously stated in the preamble of the Panel's report (41 FR 38312) that children seem particularly liable to develop adverse central nervous system reactions, such as extrapyramidal disturbances from the use of promethazine, CDB added that it does not consider the rare drug-related cases of blood dyscrasias an issue that would preclude OTC use of this ingredient inasmuch as other OTC antihistamines also can be associated with such reactions, but because of its other concerns was proposing that promethazine hydrochloride be placed in Category III.

In response to this letter, the manufacturer petitioned the agency to reopen the administrative record for the OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products rulemaking to include new data and information regarding the safety of promethazine hydrochloride (Refs. 3 and 4). The new data and information submitted by the manufacturer clarify the data regarding the incidence of extrapyramidal effects associated with the use of promethazine in both adults and children and point out errors in the data cited by CDB regarding the association between the use of promethazine and the occurrence of choreoathetosis. The agency has included these data and information in the administrative record for this rulemaking in reaching its decision on the status of promethazine in this tentative final monograph (Ref. 5).

The manufacturer noted that the CDB's information on the 0.04 percent incidence rate of extrapyramidal syndrome was based on only one case in 2, 468 patients, as cited by the Panel at 41 FR 38390. The manufacturer stated that its review of the single case report disclosed that it involved the injectable dosage form of promethazine and not the oral dosage form. The agency has confirmed that this is correct. The 0.04 percent incidence rate was derived from the Panel's review of adverse reaction reports from the Boston Coillaborative Drug Surveillance Program (BCDSP) and the University of Florida Adverse Reaction Study. The manufacturer included in its petition a statement from Jick, a recognized epidemiologist of the BCDSP, that the one case cited by the Panel is the only United States case of extrapyramidal syndrome reported through the BCDSP program (Ref. 4). Jick added that the data in BCDSP were updated through the end of 1981, and four additional cases of extrapyramidal symptoms, all of which were from Western Europe, were identified. Of the four cases, three involved injectable promethazine in relatively high doses, and only one case involved a patient who received oral promethazine. Jick

stated that the patients were elderly, had chronic pulmonary problems and other serious disorders, and received other medications that are likely to have influenced what occurred. Jick concluded that the data do not indicate that promethazine at the suggested OTC oral dosages would present any important risk of the occurrence of extrapyramidal symptoms.

The manufacturer added that the only other reference cited in the agency's letter that describes cases of extrapyramidal effects associated with promethazine was the ADR Highlights (Ref. 2). Fourteen cases are described, of which four purportedly involved promethazine. The manufacturer stated that the ADR Highlights omitted information on the route of administration of the drug in addition to containing other errors on the drugs involved and the doses administered.

The agency acknowledges that inaccuracies existed in the data base and that correction of these errors leads FDA to conclude that the possibility of choreoathetosis occurring with OTC oral doses of promethazine is unlikely. This conclusion is supported by a review of FDA adverse reaction data for the period 1970–1981 and a review of the published literature. These sources reveal only a few cases of extrapyramidal effects possibly associated with dosages of promethazine that would be available OTC. Also, based on the above data, there is no evidence to indicate that these effects would be more likely to occur in children. Based upon the available data, the agency's concerns regarding the occurrence of extrapyramidal effects and choreoathetosis and the concern that children seem particularly liable to develop adverse central nervous system reactions to promethazine have been adequately addressed. Thus, these are no longer issues that would preclude use of this ingredient at proposed OTC oral dosages.

The agency has also reviewed additional information on promethazine obtained from the National Prescription Audit (NPA) and the National Disease and Therapeutic Index (NDTI) data systems (Ref. 6). The data show that promethazine hydrochloride has been widely used as a prescription drug product, primarily in combination with other active ingredients, with a relatively low incidence of serious adverse reactions. The agency has further concerns regarding the safe use of this ingredient solely as an OTC antihistamine drug product, particularly for extended periods of time as for allergy treatment. Promethazine hydrochloride is a phenothiazine, and long-term phenothiazine therapy has been associated with the occurrence of tardive dyskinesia (Ref. 7), a serious central nervous system syndrome that may persist indefinitely after discontinuation of the medication. Some of the comments also expressed concern about the possibility of increased development of promethazine-induced dyskinesias; however, specific cases of the occurrence of tardive dyskinesia with the use of promethazine hydrochloride have not been reported.

Based on data available to the agency (Ref. 6), FDA finds that promethazine hydrochloride has not been used extensively as an antihistamine on a long-term basis. A review of NPA and NDTI data for the period 1975 to 1981–1982 (Ref. 6) shows that the majcr use of the manufacturer's promethazine hyrochloride as a prescription drug is in combination products for acute cough/cold therapy. Single entity promethazine hydrochloride tablets are most frequently used for antiemetic actions and have the highest percentage of continued use. The data show that virtually all of the manufacturer's promethazine combination drug products are used for "cough/cold" indications while their use as an "antihistamine/anti-allergy" drug is virtually nil. The data also show that the single-ingredient promethazine drug products (i.e., tablets and syrup) are used as an antihistamine/antiallergy" drug to a limited degree (i.e., average of 12 percent of the NDTI mentions for the period 1975 to 1981–1982). In addition, the NDTI data indicate that these promethazine products are used mostly on a short-term rather than on a long-term basis, with the exception of single ingredient tablets (Ref. 6). The high ratios of new to refill prescriptions in the NPA data also demonstrate that these products are not used on a long-term basis with the exception of single ingredient tablets (Ref. 6). Long-term use of the single ingredient tablets most frequently represents its use as an antiemetic in chronic illnesses, such as cancer, and not as an antihistamine in patients with allergic rhinitis. The conclusion that promethazine hydrochloride has not been used extensively as an antihistamine on a long-term basis is further supported by the manufacturer's statement in its submission that "the average course of therapy under a prescription for an oral promethazine product is about 6–9 days" (Ref. 3).

The agency believes that many consumers who use OTC antihistamines to treat the symptoms of allergic rhinitis use these products on a long-term basis because the symptoms of allergic rhinitis usually occur for extended periods of time. However, promethazine hydrochloride has not been used extensively as an antihistamine on a long-term basis in the OTC target population, i.e., patients with allergic rhinitis. Therefore, there is no assurance that long-term use of promethaine hydrochloride as an OTC antihistamine will not cause the serious side effect tardive dyskinesia.

Accordingly, the agency remains unpersuaded that promethazine, as a phenothiazine, can be generally recognized as safe for OTC use. Many of the comments received in response to the Panel's Category I recommendation for promethazine hydrochloride were from health professionals who opposed OTC status for this drug. The CDB raised the concern in its May 7, 1982 letter that promethazine, as a phenothiazine, is distinct from other antihistamines in terms of its chemical structure and its adverse effects on the central nervous system (Ref. 1). In its petition (Ref. 4), the manufacturer acknowledged that promethazine is chemically related to phenothiazines, but that it is widely recognized that differences in chemical structures and pharmacology substantially lessen the possibility that promethazine could cause the range of side effects associated with other phenothiazines (Ref. 8). The manufacturer also stated that the Panel concluded, after analysis of published reference studies and adverse experience reports on promethazine, that this drug does not cause the wide range of serious or potentially toxic effects that characterize other members of the chemical class of phenothiazines (41 FR 38390). Despite the Panel's recommendation, at this time, FDA is not assured that general recognition of the safety of promethazine hydrochloride for OTC use has been adequately established. The agency is therefore proposing that promethazine hydrochloride as a single ingredient be Category III in this tentative final monograph. The agency specifically invites public comment on the issues discussed above and on the suitability of promethazine hydrochloride for OTC use as a single entity antihistamine drug. Combination drug products containing promethazine hydrochloride will be discussed in the combinations segment of the cough-cold tentative final monograph, in a future issue of the **Federal Register.**

References

(1) Letter from W.E. Gilbertson, FDA, to D.L. Shaw, Wyeth Laboratories, coded LET074, Docket No. 76N-052H, Dockets Management Branch.

(2) Mendelis, P.S., "Antipsychotic Drugs and Choreoathetosis," Adverse Drug Reaction Highlights, Division of Drug Experience, Center for Drugs and Biologics, FDA, Rockville, MD, January 25, 1982.

(3) Comment No. C00188, Docket No. 76N-052H, Dockets Management Branch.

(4) Comment No. CP0002, Docket No. 76N-052H, Dockets Management Branch.

(5) Letter from W.F. Randolph, FDA, to S.J. Land and W.W. Vodra, Arnold & Porter, coded PAV, Docket No. 76N-052H, Dockets Management Branch.

(6) Unpublished data obtained from the National Prescription Audit and the National Disease and Therapeutic Index data systems, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(7) Baldessarini, R.J., "Drugs and the Treatment of Psychiatric Disorders," *in* "The Pharmacologic Basis of Therapeutics," 6th Ed., edited by A.G. Gilman, L.S. Goodman, and A. Gilman, Macmillian Publishing Co., New York, pp. 391-447, 1980.

(8) Domino, E.F., "Antipsychotics: phenothiazines, Thioxamthines, Butyrophiones, and Rawolfia Alkaloids," *in* "Drill's Pharmacology in Medicine," 4th Ed., edited by J.R. DiPalma, McGraw-Hill Book Co., New York, p. 471, 1971.

C. Comments on Specific Antihistamine Active Ingredients

10. One comment submitted a study of the effectiveness of phenyltoloxamine citrate to support its reclassification from Category III to Category I as an OTC antihistamine active ingredient (Ref. 1).

The agency has reviewed the study and concludes that this study alone is inadequate to reclassify phenyltoloxamine citrate as a category I antihistamine active ingredient. After a statistical analysis of the data, the agency recognizes that the study demonstrates that there is a statistically significant difference between the pharmacologic action of the placebo and phenyltoloxamine in favor of the active ingredient at 1- and 2-hour intervals after a single dose has been given. However, the study does not demonstrate the effectiveness of phenyltoloxamine over a long enough period of time when given on a dosage schedule that would be representative of the actual conditions under which the drug would be used. The single-dose study can be characterized as a clinical pharmacology study and does not demonstrate that phenyltoloxamine citrate is clinically effective.

Additional data from multiple-dose clinical studies carried out over a period of at least 1 week, and including an adequate number of patients per dose level as well as placebo, demonstrating the effectiveness of phenyltoloxamine are necessary to reclassify this active ingredient in Category I. There may be a problem of carry-over effect in a crossover study in which each patient is on a drug for a week or more. Therefore, a sufficient washout period should be allowed if a crossover design is used. Phenyltoloxamine citrate will remain in Category III as an OTC antihistamine active ingredient until additional data are received, reviewed, and accepted by the agency.

The agency's detailed comments and evaluations of the data are on file in the Dockets Management Branch (Ref. 2).

References

(1) Comment Nos. C00168, LET003, and SUP007, Docket No. 76N-0052, Dockets Management Branch

(2) Letter from W.E. Gilbertson, FDA, to A.D. Flanagan, Warner/Chilcott, coded C00168/ANS, Docket No. 76N-052H, Dockets Management Branch.

D. Comments on Dosages for Antihistamine Active Ingredients

11. Several comments disagreed with the Panel's recommendation to increase the currently available OTC dosage of chlorpheniramine maleate from 2 mg every 4 to 6 hours to 4 mg every 4 to 6 hours with a maximum daily dose of 24 mg. The comments stated that chlorpheniramine maleate has been previously available only by prescription at the 4-mg dosage level and that the increase in dosage from 2 to 4 mg will lead to undersirable side effects, especially excessive drownsiness and overdosage. One comment recommended that chlorpheniramine maleate should continue to be sold OTC in its present dosage form. Another comment stated that the data on which the Panel based its decision to increase the maximum daily dose from 16 to 24 mg were inadequate. The comment explained that the majority of patients treated at the 24-mg daily dosage level were reported in a single uncontrolled study and were selected from a population of patients with a long history of allergy. Many patients had previously received antihistamine therapy. The comment questioned whether this group of patients is appropriate to assess the need for the higher OTC dose of chlorpheniramine maleate. The comment recommended that the maximum daily dose of chlorphenirame maleate for OTC use the 16 mg since there are adequate data to support this dosage.

The agency has reviewed these comments and the data evaluated by the Panel and notes the Panel's conclusion that chlorpeniramine maleate has not been shown to be effective for adults at a dose less than 4 mg. In addition, chlorpheniramine maleate has been marketed first as a prescription drug product and then as an OTC drug product for many years at the Panel's recommended adult dose of 4 mg every 4 to 6 hours, not to exceed 24 mg in 24 hours. The safety and effectiveness of chlorpheniramine maleate at this dosage have been widely recognized. The agency concludes that chlorpheniramine maleate is safe and effective for OTC use at the Panel's recommended 4-mg dosage level. Therefore, it is unnecessary to change the Panel's recommended dosage in this tentative final monograph by restricting the dosage to 16 mg in 24 hours.

13. One comment expressed concern that certain time-release dosage forms containing chlorpheniramine maleate appear to release all of the ingredient in a short period of time. The comment argued that such dumping causes marked drowsiness in some patients. The comment, however, did not make any specific recommendation to the agency.

Timed-release formulations are considered new drugs within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(p)). Timed-release formulations are so complex that the state of the art does not permit standardization to the point of inclusion in an OTC drug monograph as a Category I condition. (See 42 FR 56736.) In order to market these drug products, an approved NDA, containing appropriate bioavailability data, is required under section 505 of the act (21 U.S.C. 355) and FDA regulations at Part 314 (21 CFR 314). This requirement is based on the agency's recognition that there is a possibility of overdosage if products that are designed to release the active ingredients over a prolonged period are improperly manufactured, and the active ingredients are released all at once or over too short a time interval.

Chlorpheniramine maleate is generally recognized as safe at an adult oral dosage of 4 mg every 4 to 6 hours, not to exceed 24 mg in 24 hours. An NDA is required for any timed-release product containing chlorpheniramine maleate.

E. Comments on Labeling of Antihistamine Drug Product

13. Several comments stressed the importance of making consumers aware through appropriate label warnings that drowsiness is a potential side effect of the use of antihistamines. One comment

specifically recommended that the warning state "Caution: May cause drowsiness. Alcohol may intensify this effect. Use care when operating a car or dangerous machinery."

The agency agrees with the comments that consumers should be warned that drowsiness is a potential side effect of antihistamine active ingredients. In fact, the Panel recommended the warnings "May cause drowsiness" or "May cause marked drowsiness" in § 341.72(b) (6) and (7) of its monograph. The degree and the frequency of the drowsiness produced by a specific antihistamine active ingredient determines which one of the above warnings is required.

The specific warning suggested by one comment would combine the drowsiness warning with related warnings concerning the use of alcohol or operating a motor vehicle or dangerous equipment when taking antihistamines. Combining these related warnings would be beneficial to consumers. However, the agency does not believe that all of the specific language suggested by the comment should be used in the warnings. The comment suggests that the warning "Alcohol may intensify this effect" be substituted for the Panel's recommended warning "Avoid alcoholic beverages while taking this product." The agency has determined that the consumer must be warned to avoid alcohol to ensure the safe use of antihistamines on an OTC basis. Moreover, adding the phrase "alcohol may increase the drowsiness effect" to the warning provides more information to the consumer as to why alcohol should be avoided while taking an antihistamine. The agency has, therefore, included this phrase in the warning.

In addition, the agency believes that revising the Panel's recommended wording "* * * operating heavy machinery" to the wording "* * * operating machinery" better conveys the intent of the Panel. Some equipment that requires mental alertness to operate safely is not "heavy." In addition, warning consumers to use care when operating "dangerous" machinery, as the comment suggests, may not be adequate. Consumers may not consider some machinery dangerous when operated by an alert individual. However, virtually all machinery is potentially dangerous if operated by a person who is drowsy and not alert.

The agency concludes that combining the specific laberling suggested by the comment with the warnings recommended by the Panel, with some modifications, will provide more informative labeling for the consumer. Therefore, the warnings concerning drowsiness, the use of alcohol, and driving a motor vehicle or operating machinery have been revised in this tentative final monograph. Section 341.72(c)(3) reads as follows: "May cause drowsiness; alcohol may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Use caution when driving a motor vehicle or operating machinery." Section 341.72(c)(4) reads as follows: "May cause marked drowsiness; alcohol may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Use caution when driving a motor vehicle or operating machinery."

14. One comment suggested that antihistamines should be labeled to inform consumers that these drugs are useful in treating allergic rhinitis and hives, but should not be labeled for treating the symptons of asthma.

The Panel recommended that antihistamines be lebeled for use in treating symptoms of allergic rhinitis. The agency agrees with the comment and the Panel's recommendations regarding this use.

The Panel recommended as part of § 341.72(b)(2), which has been redesignated § 341.72(c)(2) in the tentative final monograph, that antihistamines be labeled with a warning that persons with asthma should not take them except under the advice and supervision of a physician. The Panel pointed out in its report that many physicians consider the drying side effect of antihistamines to be undesirable in patients with bronchial asthma, and some doctors maintain that such drugs should be contraindicated in patients with this disease. The agency concurs with this recommendation and the warning proposed by the Panel.

Hives as a symptom of an allergic reaction was not included in the Panel's report. No data were submitted to the Panel concerning the use of antihistamines for hives, nor were any data reviewed by the Panel concerning this use of antihistamines. The comment also did not provide any data to substantiate its recommendation. Accordingly, an indication for the use of antihistamines in the treatment of hives as a symptom of an allergic reaction is not being proposed in this tentative final monograph.

15. Several comments pointed out that some OTC products containing antihistamines may be labeled and marketed for use only in pediatric populations. The comments argued that certain warnings and caution statements in the Panel's recommended monograph, i.e., "Do not take this product if you have glaucoma or difficulty in urination due to enlargement of the prostate gland, avoid driving a motor vehicle or operating heavy machinery, and avoid alcoholic beverages while taking this product," apply only to adults and should not be required on products labeled strictly for use in children. The comments recommended that an exemptiong statement should be added to the monograph under § 341.50(c) stating, "Warnings which are inappropriate for children's products may be eliminated in the labeling of products containing dosage instructions for children only."

The agency agrees that the warnings recommended by the Panel in § 341.72(b)(2), (3), and (4), which have been redesignated as § 341.72(c)(2), (3), and (4) in this tentative final monograph, concerning operating a motor vehicle or machinery, avoiding alcoholic beverages, and the part of the warning statements concerning "difficulty in urination due to enlargement of the prostate gland" are not necessary in the labeling of products intended only for pediatric use. These warnings are not applicable to children and their presence in the labeling would tend to distract parents from label warnings which are important. However, the agency does not agree that the part of the warning about glaucoma in § 341.72(b)(2) should be deleted from the labeling of pediatric products in this tentative final monograph because glaucoma does occur in children [Refs. 1 and 2]. In addition, the agency is proposing that the warnings be reworded to reflect the administration of the product by adults rather than self-administration. Accordingly, the tentative final monograph is amended by adding the following to new § 341.72(c):

(6) *For products labeled for children under 12 years of age.* The labeling of the product contains only the warnings identified in paragraphs (c) (1) and (5) of this section as well as the following:

(i) "Do not give this product to children who have asthma or glaucoma unless directed by a doctor."

(ii) *For products containing brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, dexchlorpheniramine maleate, phenindamine tartrate, pheniramine maleate, pyrilamine maleate, thonzylamine hydrochloride, or triprolidine hydrochloride identified in § 341.12(a), (b), (c), (d), (g), (h), (i), (j), and (k).* "May cause drowsiness."

(iii) *For products containing diphenhydramine hydrochloride and doxylamine succinate identified in*

§ 341.12(e) and (f). "May cause marked drowsiness."

References

(1) Scheie, H.G., and D.M. Albert, "Textbook of Ophthalmology," 9th Ed., W.B. Saunders Co., Philadelphia, pp. 542–547, 1977.

(2) Ellis, P.P., and D.L. Smith, "Handbook of Ocular Therapeutics and Pharmacology," 4th Ed., the C.V. Mosby Co., St. Louis, p. 108, 1973.

16. One comment disagreed with the Panel's recommended label warning for pheniramine maleate that states "May cause marked drowsiness." The comment pointed out that pheniramine maleate is in the same chemical class of antihistamines as chlorpheniramine and brompheniramine, i.e., the alkylamines, that this class of antihistamines causes the least amount of drowsiness, and that the Panel recommended the less severe warning "May cause drowsiness" for chlorpheniramine and brompheniramine maleate. The comment urged the agency to require the same label warning, "May cause drowsiness", for pheniramine maleate as allowed for chlorpheniramine and brompheniramine maleate.

The agency has reviewed the data cited in the Panel's report concerning the sedative effects of pheniramine maleate as compared with brompheniramine maleate and chlorpheniramine maleate. In one study reviewed by the Panel, 20, percent of 171 patients receiving a 25-mg dose of pheniramine maleate experienced sedation as a side effect (Ref. 1). In comparison, the Panel states at 41 FR 38382 that brompheniramine maleate produced sedation in 20 percent of less of the individuals taking the ingredient and at 41 FR 38383 that chlorpheniramine maleate produced sedation in 10 to 20 percent of the individuals taking the ingredient. In another study reviewed by the Panel, the frequency of side effects, chiefly drowsiness, seen in 184 subjects receiving 10 mg pheniramine did not exceed the number of side effects in an equal number of subjects receiving a placebo (Ref. 2). Roth and Tabachnick (Ref. 3) have classified the sedative effect of pheniramine maleate as "moderate," compared to a classification of "slight sedation" for brompheniramine maleate and chlorpheniramine maleate. However, Roth and Tabachnick (Ref. 3) did not classify the sedative effect of pheniramine as "marked sedation." The agency agrees with the comment that the warning regarding drowsiness for pheniramine should be the same as that required for chlorpheniramine and brompheniranine. The agency concludes that the data reviewed by the Panel do not support the need for a stronger warning regarding drowsiness for drug products containing pheniramine maleate. Therefore, the agency proposes to change the warning statement for pheniramine maleate to "May cause drowsiness."

References

(1) Loveless, M.H., and M. Dworin, "Allergy and Antihistamine Therapy: A Review," *The Bulletin of the New York Academy of Medicine*, 25:473–487, 1949.

(2) Lowell, F.C., et al., "The Antihistamine Drugs in the Treatment of the Common Cold," *New England Journal of Medicine*, 244:132, 1951.

(3) Roth, F.E., and I.I.A. Tabachnick, "Histamine and Antihistamine," *in* "Drill's Pharmacology in Medicine," 4th Ed., edited by J.R. DiPalma, McGraw-Hill Book Co., New York, p. 1009, 1971.

17. One comment stated that the Panel's recommended warning in § 341.72(b)(8), "*Caution*: May cause nervousness and insomnia in some individuals," is unnecessary for phenindamine tartrate. The comment cited OTC Volume 040126 (Ref. 1) for review with respect to the necessity for the above warning.

The agency has reviewed six references contained in OTC Volume 040126 that were reviewed and cited by the Panel in its report and finds that insomnia and nervousness are dominant side effects which may occur with the use of phenindamine tartrate. Paul et al. (Ref. 2) evaluated phenindamine tartrate in 280 patients. Sleeplessness occurred in 6.4 percent and nervousness in 5.4 percent. In this study, the total daily dosage ranged from 25 to 150 mg, with most adults taking 25 mg three times a day. McGavack et al. (Ref. 3) found that dryness of the mouth, insomnia, and constipation were the major symptoms in patients receiving a total daily dose of 75 to 600 mg of phenindamine tartrate. Boyd, Weissberg, and McGavack (Ref. 4) found that 24 percent of patients who received a total daily dose of 150 mg experienced insomnia and dryness of the mouth. Criep and Aaron (Ref. 5) evaluated 389 patients who received a dosage of 25 mg of phenindamine tartrate every 4 hours and found that 89 (23 percent) experienced side reactions. Of the 89 patients who had side reactions, 22 percent experienced nervousness and palpitations, 22 percent had nausea, and 10 percent had insomnia.

Pennypacker and Sharpless (Ref. 6) gave patients 25 to 50 mg of phenindamine tartrate daily and found that of 40 patients, 35 percent (14) experienced insomnia and 22.5 percent (9) tenseness. Cohen, Davis, and Mowry (Ref. 7) studied 292 patients who received a total daily dose of 50 to 200 mg of phenindamine tartrate; 54 of the patients (18 percent) experienced side effects. Of these 54 patients, 33 experienced nervous side reactions.

In other unpublished studies contained in OTC Volume 040126, the recommended effective adult oral dosage of 25 mg of phenindamine tartrate was not used. The evaluations were done with tablets which contained only 10 mg of phenindamine tartrate. For this reason, the data on side effects reported in these studies cannot be used to support the comment's request to eliminate the warning.

Because the data reviewed by the Panel (Refs. 1 through 7) show that phenindamine tartrate may cause insomnia and nervousness, the agency agrees with the Panel's recommendation that the warning, "May cause nervousness and insomnia in some individuals," be required for phenindamine tartrate.

References

(1) OTC Volume 040126.

(2) Paul, A.B., et al., Clinical Evaluation of a New Antihistaminic Compound," *The Laryngoscope*, 58:1044–1054, 1948.

(3) McGavack, T.H., et al., "Clinical Evaluation of Phenindamine (2-Methyl-9-phenyl-2, 3, 4, 9-Tetra-hydro-1-Pyridindene Hydrogen Tartrate) as an Antihistamine Agent," *American Journal of the Medical Sciences*, 216:437–475, 1948.

(4) Boyd, L.J., J. Weissberg, and T.H. McGavack, "Tolerance Studies of the Antihistamine Drug Thephorin," *New York State Journal of Medicine*, 48:1596–1598, 1948.

(5) Criep, L.H., and T.H. Aaron, "Thephorin: An Experimental and Clinical Evaluation in Allergic States," *Journal of Allergy*, 19:304–312, 1948.

(6) Pennypacker, C.S., and I. Sharpless, "Clinical Study of a New Antihistaminic Drug—Thephorin," *Pennsylvania Medical Journal*, 51:1407–1411, 1948.

(7) Cohen, E.B., H.P. Davis, and W.A. Mowry, "Thephorin in Allergy," *American Journal of Medicine*, 5:44–47, 1948.

18. One comment stated that the Panel used an inappropriate standard in categorizing some Category II claims and that the claims "fast" and "prompt" were rejected by the Panel for antihistamine labeling because the time is indeterminate. The comment stated that if the drug provides fast or prompt relief, as these terms are understood by consumers, then these claims are not misleading and should be permitted.

The OTC drug review program establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. Two principal conditions examined during the review are allowable ingredients

and allowable labeling. The FDA has determined that it is not practical—in terms of time, resources, and other considerations—to set standards for all labeling found in drug products. Accordingly, OTC drug monographs regulate only labeling related in a significant way to the safe and effective use of covered products by lay persons. OTC drug monographs establish allowable labeling for the following items: products statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action.

As with all OTC drug products, antihistamines are expected to achieve their intended results within a reasonable period of time. However, the specific period of time within which antihistamines achieve these results is not related in a significant way to the safe and effective use of the products. Therefore, terms such as "fast" or "prompt" are outside the scope of the OTC drug review. For other classes of products in the OTC drug review, however, statements; relating to time of action may properly fall within the list of terms covered by the monograph

The agency emphasize that even though terms such as "fast" or "prompt" are outside the scope of the OTC drug review for this class of products, they are subject to the prohibitions in section 502 of the act (21 U.S.C. 352) relating to labeling that is false or misleading. Such statements or terms will be evaluated by the agency on a product-by-product basis, under the provisions of section 502 of the act (21 U.S.C. 352) relating to labeling that is false or misleading.

Moreover, any statement or term that is outside the scope of the monograph, even though it is truthful and not misleading, may not appear in any portion of the labeling required by the monograph and may not detract from such required information. However, statements and terms outside the Scope of the monograph may be included elsewhere in the labeling, provided the are not false or misleading.

F. Comments on Testing Guidelines

19. Two comments disagreed with the Panel's recommended Category III testing criteria for the evaluation of antihistamines in treating the symptoms of the common cold. (See part VII. paragraph C.2.d. of the Panel's report—Methods of study (41 FR 38396).) The comments argued that it was unreasonable to give the antihistamine throughout the entire course of the cold if the specific symptom being treated, e.g., runny nose, is no longer in evidence. The comments recommended that the testing criteria be changed so that the study need only be of sufficient length to distinguish clearly between the effect of the drug and the placebo. One of the comments argued that requiring three positive studies from three different investigators, as the Panel recommended, was unnecessary and contended that because two studies were considered adequate in other Category III testing recommended by the Panel, the same requirement should apply in this case.

The other comment argued that the criteria for stratifying patients according to age, sex, and severity of symptoms were unnecessary. The comment contended that stratifying by sex and age would be insignificant as a factor in patients' response to medication and that in view of other strict criteria, which would eliminate potential patients, stratifying by sex and age would result in an additional loss of qualified patients for investigation. The comment believe that stratifying by symptom severity would be too prone to subject interpretation because one could not specify when peak severity would occur in the course of the illness. Both comments recommended that the agency reject the specified panel testing criteria.

The agency has reviewed data in studies designed to demonstrate the effectiveness of the antihistamine chlorpheniramine maleate in treating the symptoms of the common cold that were submitted in response to the advance notice of proposed rulemaking (Ref. 1). Although they do not meet all of the criteria of the Panel's testing guidelines, they have been accepted by the agency as demonstrating the effectiveness of chlorpheniramine for use in treating the symptoms of runny nose and sneezing when associated with the common cold. (See comment 4 above.) One of the acceptable studies did not follow the patients for the entire course of the illness. The study covered the time period over which the symptoms studied were in evidence. Therefore, studies which are of sufficient length to distinguish between the effectiveness of the drug and the placebo in treating a particular symptom are acceptable. In addition, because the pharmacologic actions of the various Category I antihistamines are similar, the agency believes that the data submitted for chlorpheniramine maleate allow Category I status for treating the symptoms of runny nose and sneezing when associated with the common cold to be extended to all Category I antihistamine active ingredients. (See comment 4 above.)

In summary, the agency concludes that adequate data demonstrating the safety and/or effectiveness of a Category III condition are necessary to reclassify that condition to Category I status but that this does not necessarily require that the guidelines recommended by the Panel be followed. The Panel's testing criteria are considered to be recommendations to the agency. Although the submitted chlorpheniramine studies did not stratify patients according to age, sex, severity, and duration of illness, they have been accepted by the agency. Stratification of patients by the above criteria is not a necessary requirement for studies designed to demonstrate the effectiveness of antihistamines in treating symptoms associated with the common cold. Studies submitted in support of the effectiveness and safety of a Category III condition are evaluated on the basis of their own merits rather than on how well they meet the Panel's requirements. However, the agency emphasizes that each study submitted to support a request for the reclassification of a Category III condition to Category I status must substantiate the reclassification whether or not the Panel's recommended guidelines are followed.

Reference

(1) Comment Nos. SUP004 and SUP005, Docket No. 76N-0052, Dockets Management Branch.

II. The Agency's Tentative Adoption of the Panel's Report

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. *Summary of ingredient categories.* The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time, and has made some changes in the categorization of antihistamine active ingredients recommended by the Panel. As a convenience to the reader, the following list is included as a summary of the categorization of antihistamine active ingredients recommended by the Panel and the proposed categorization by the agency.

Antihistamine active ingredients	Panel	Agency
Brompheniramine maleate	I	I
Chlorpheniramine maleate	I	I
Dexbrompheniramine maleate	(*)	I
Dexchlorpheniramine maleate	(*)	I
Diphenhydramine hydrochloride	I	I
Methapyrilene fumarate	I	II
Methapyrilene hydrochloride	I	II
Phenindamine tartrate	I	I
Phenindamine tartrate	I	I

Antihistamine active ingredients	Panel	Agency
Phenyltoloxamine citrate	III	III
Pyrrobutamine hydrochloride	I	III
Pyrilamine maleate	I	I
Thenyldiamine hydrochloride	III	III
Thonzylamine hydrochloride	I	I
Triprolidine hydrochloride	(*)	I

*Not reviewed.

The agency points out that any of the antihistamines proposed as Category I in this tentative final monograph, except dexchlorpheniramine (see comment 7 above), may be marketed OTC in a combination drug product in accord with the Panel's permitted combinations of Category I active ingredients in the analgesic, antitussive, and decongestant categories recommend in § 341.40 of the advance notice of proposed rulemaking (41 FR 38420). The tentative final monograph on cough-cold combination drug products will be published in a future issue of the Federal Register and will discuss the combinations proposed by the agency. Any interim marketing that is permitted is subject to the agency's conclusions in the final monograph.

2. *Testing of Category II and Category III conditions.* The Panel recommended testing guidelines for antihistamine drug products (41 FR 38329 and 38394). The agency's position regarding the Panel's testing guidelines is discussed in comment 23 above. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any antihistamine ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the Federal Register of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). This policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes in the Panel's Recommendations

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the antihistamine section of the Panel's report and recommended monograph with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made by the agency follows.

1. The agency has modified § 341.3(d) and § 341.72(a) (redesignated § 341.72(b) in the tentative final monograph) to include the use of antihistamines for the temporary relief of runny nose and sneezing associated with the common cold. The agency has reviewed and accepted data which demonstrate the effectiveness of chlorpheniramine maleate in treating these symptoms when associated with the common cold. In addition, because the pharmacologic actions of the various Category I antihistamines are similar, the agency believes that the data submitted on chlorpheniramine allow an indication for treating the symptoms of runny nose and sneezing when associated with the common cold to be extended to all Category I antihistamine active ingredients. The agency proposes to substitute the term "runny" for the term "running" which was used by the Panel. The agency recognizes that the term "runny" is grammatically correct, particulary when it is used in reference to a condition of the nose. The agency believes the term "runny" is more commonly used than the term "running" and is, therefore, better understood by consumers. (See comment 4 above.)

2. Dexbrompheniramine maleate has been marketed as a single ingredient prescription drug product under an approved NDA for 23 years (Ref. 1). It has also been marketed in combination with pseudoephedrine sulfate under an approved NDA for 19 years as a prescription drug product that delivers an adult dose of 2 mg of dexbrompheniramine every 4 hours using a sustained release delivery from a 6-mg tablet taken every 12 hours (Ref. 2). This product has been approved for OTC marketing under an NDA (Ref. 3). The agency has reviewed the literature concerning the safety and effectiveness of dexbrompheniramine maleate as an antihistamine. Based on this literature, and the review by the Drug Efficacy Study Group (DESI) published in the Federal Register of March 19, 1973 (38 FR 7265), the agency believes that the drug can be generally recognized as safe and effective for OTC use.

Dexbrompheniramine maleate is the dextrorotatory isomer (d-isomer) of brompheniramine maleate, which is a racemic histamine antagonist composed of d- and l-isomers. Pharmacological studies have shown that the antihistaminic activity resides almost exclusively in the d-isomer, and that there is very little difference in the toxicities of the d-isomer and the d,l mixture in experimental animals (Ref. 4). Because dexbrompheniramine maleate is about twice as potent as brompheniramine maleate, it is used in clinical practice at one-half the does of brompheniramine maleate.

The agency has reviewed studies by Frank (Ref. 5), Olansky and Olansky (Ref. 6), and Romanoff and Guidatti (Ref. 7) concerning the safety and effectiveness of dexbrompheniramine maleate alone. The studies showed the drug to be an effective antihistamine, at a dosage of 2 mg, with a low incidence of side effects (drowsiness, slight dizziness). One of the studies, using a double-blind design, showed a significant response to dexbrompheniramine, compared to a placebo, among ptients with respiratory symptoms due to allergic rhinitis and pollinosis. Symptoms such as itching, sneezing, and watery eyes were relieved in the patients receiving the drug (Ref. 7).

In addition, the agency has reviewed studies by Mayer and Savitt (Ref. 8), Kapstad and Warland (Ref. 9) Lofkvist and Svenson (Ref. 10), and Fierburg (Ref. 11) concerning the safety and effectiveness of dexbrompheniramine meleate in combination with pseudoephedrine sulfate. All of these studies were double-blinded and evaluated combination drug products that are marketed under the approved NDA (Refs. 8 through 11). The studies were performed in patients with perennial allergic rhinitis or vasomotor rhinitis. A crossover design was used in three of the studies (Refs. 8, 10 and 11). All of these studies demonstrated that dexbrompheniramine maleate in combination with pseudoephedrine sulfate is effective in relieving symptons when compared to several different reference drugs or placebos. Patients receiving the dexbrompheniramine-pseudoephedrine combination experienced a lessening of sinus congestion and of runny nose. Three other studies, which were not double-blind but controlled clinical comparisons, showed similar results (Refs. 12, 13, and 14).

Side effects reported in these studies were similar to those reported for other antihistamine-nasal decongestant drugs and included drowsiness, dry mouth and dry throat, dizziness, nausea, swelling in the face, headache, restlessness, tachycardia, and constipation. There were relatively few side-effects reported in all, and in only one case did a patient reduce the medication to one tablet a day because of drowsiness and dry mouth (Ref. 5).

A review of FDA adverse reaction reports since 1970 indicates that conditions such as rash, hypertension, transient myopia, nervousness, and insomnia have been reported in cases where the combination drug dexbrompheniramine-pseudophedrine

was taken (Ref. 15). In these cases, overdose was not indicated, nor was enough information available to indicate a possible cause-and-effect relationship between the use of dexbrompheniramine maleate and the reaction.

Based on the above data and information, the agency believes that dexbrompheniramine maleate can be generally recognized as safe and effective for OTC use. The agency is therefore proposing that dexbrompheniramine maleate be classified as Category I as an OTC antihistamine at a dose of 2 mg every 4 to 6 hours, not to exceed 12 mg in 24 hours, for adults and a dose of 1 mg every 4 to 6 hours, not to exceed 6 mg in 24 hours, for children 6 to under 12 years of age. The agency also proposes a dose of 0.5 mg every 4 to 6 hours, not to exceed 3 mg in 24 hours, for children 2 to under 6 years of age under professional labeling in the tentative final monograph. The labeling warnings are identical to those being proposed for brompheniramine maleate.

Dexbrompheniramine maleate was not considered by an OTC advisory review panel and, therefore, does not meet the terms of the enforcement policy in § 330.13. The agency has approved an NDA that currently allows the OTC marketing of products containing dexbrompheniramine. Thus, FDA does not believe it is necessary to prohibit OTC marketing of dexbrompheniramine under this proposal while public comments to its proposed monograph status are being evaluated. OTC marketing may be initiated subject to the terms and conditions specified in this tentative final monograph and subject to the risk that FDA may adopt a different position in the final monograph that may require relabeling, recall, or other regulatory action.

References

(1) Letter from I. Siegel, FDA, to White Laboratories, Inc., OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(2) Letter from J.W. Winkler, FDA, to White Laboratories, Inc., OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(3) Letter from J.P. Mann, FDA, to Schering Corporation, OTC Volume 04HTFM, Docket No. 76N-052H, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(4) Roth, F.E., "Antihistimine Activity of the Optical Isomers of Pheniramine and its Chlor- and Brom-Substituted Derivatives," *Chemotherapia*, 3:120–127, 1961.

(5) Frank, D.I., "Clinical Evaluation of Dexbrompheniramine Maleate (Disomer) in Ear, Nose and Throat Allergies," *Current Therapeutic Research*, 1:115–121, 1959.

(6) Olansky, M., and S. Olansky, "Antihistaminic Activity of Dexbrompheniramine (Disomer). Appraisal in Pediatric Allergies," *Annals of Allergy*, 18:415–419, 1960.

(7) Romanoff, A., and F.P. Guidotti, "Evaluation of Dexbrompheniramine Maleate in Allergy by Double-Blind Procedure. Preliminary Report," *New York State Journal of Medicine*, 60:3800–3803, 1960.

(8) Mayer, P.S., and A.E. Savitt, "Allergic Rhinitis and Air Pollution: A Double-Blind Crossover Analysis," *The Eye, Ear, Nose and Throat Monthly*, 51:9–12, 1972.

(9) Kapstad, B., and A. Warland, "Therapeutic Effectiveness of an Oral Anti-Histamine Combination (Dexbrompheniramine Maleate/D-Isoephedrine Sulfate) in the Treatment of Patients with Allergic Rhinitis," *Acta Allergologica*, 31:233–226, 1976.

(10) Lofkvist, T., and G. Svensson, "A Comparative Evaluation of Oral Decongestants in the Treatment of Vasomotor Rhinitis," *The Journal of International Medical Research*, 6:56–60, 1978.

(11) Fierberg, A.A., "Allergic Nasal Congestion, Effects of Oral Treatment with a Combination of Dexbrompheniramine and D-Isoephedrine," *Annals of Allergy*, 22:324–328, 1964.

(12) Frank, D.I., "Evaluation of Two Sustained-Action Oral Decongestants: A Controlled Study," *Current Therapeutic Research*, 6:158–161, 1964.

(13) Pullen, F.W., and W.W. Montgomery, "Comparative Evaluation of Oral Decongestants," *Archives of Otolaryngology*, 77:10–12, 1963.

(14) Jungert, S., "A Comparison of the Efficacy and Safety of Two Preparations in the Treatment of Allergic and Vasomotor Rhinitis, Disophrol Chronosule Capsules and Tavegyl Tablets," *Current Therapeutic Research*, 24:269–273, 1978.

(15) Department of Health and Human Services, Food and Drug Administration, Adverse Reaction Summary Listings, pertinent pages for 1970–82, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

3. The agency has proposed placing dexchlorpheniramine maleate in Category I based on the safe and effective use of this drug product as a prescription drug under an approved ANDA, a review of FDA adverse reaction reports, and the safe and effective use of the racemic mixture, chlorpheniramine maleate, as an OTC drug product for many years. However, it may not be marketed OTC at this time. (See comment 7 above.)

4. The agency has deleted the reference to methapyrilene in § 341.12(e), the reference to § 341.12(e) in § 341.72(b)(7), and the reference to methapyrilene in § 341.90(f) of the Panel's recommended monograph. These sections provided dosages, a warning, and professional labeling for methapyrilene preparations, which are no longer marketed because of the NCI study showing that these drugs are associated with the development of tumors in laboratory animals. The agency has reclassified methapyrilene preparations in Category II. (See comments 1 and 6 above.)

5. The agency has deleted the reference to promethazine hydrochloride in § 341.12(h), the reference to § 341.12(h) in § 341.72(b)(7), and the reference to promethazine hydrochloride in § 341.90(i) of the Panel's recommended monograph. These sections provided dosages, a warning, and professional labeling for promethazine hydrochloride. In the agency's preamble to the Panel's report and recommended monograph (41 FR 38312), the agency disagreed with the Panel's Category I classification of promethazine hydrochloride. The agency concludes that general recognition of the safety of this ingredient for OTC use has not been adequately established. Consequently, the agency has reclassified promethazine hydrochloride in Category III. (See comment 9 above.)

6. Triprolidine hydrochloride has been marketed under an approved NDA for 24 years as a prescription drug product at a dose of 2.5 mg every 6 to 8 hours for adults, a dose of 1.25 mg every 6 to 8 hours for children 6 to 12 years of age, a dose of 0.938 mg every 6 to 8 hours for children 4 to under 6 years of age, a dose of 0.625 mg every 6 to 8 hours for children 2 to under 4 years of age, and a dose of 0.313 mg every 6 to 8 hours for infants 4 months to under 2 years of age (Refs. 1 and 2). In addition, drug products containing triprolidine hydrochloride as a single ingredient and in combination with pseudoephedrine hydrochloride have been approved for OTC marketing under NDAs (Ref. 3). In a 1973 Drug Efficacy Study Implementation (DESI) notice (38 FR 9339), the agency concluded that this drug is effective. FDA has reviewed the literature and marketing history of triprolidine hydrochloride as an antihistamine and believes that this drug can be generally recognized as safe and effective for OTC use.

Studies by Fruchard and Fruchard (Ref. 4); Britton et al. (Ref. 5); Wolfromm and Liacopoulos (Ref. 6); Bye et al. (Ref. 7); Nicholson (Ref. 8); Bye et al. (Ref. 9); and Peck, Fowle, and Bye (Ref. 10) were reviewed for the safety and effectiveness of triprolidine hydrochloride. Most of the studies were double-blind (Refs. 5, 7, 8, and 9). In 27 out of 36 vasomotor rhinitis cases, triprolidine hydrochloride promptly relieved the symptoms (within 15

minutes), had a long duration of action (about 5 to 6 hours), and was well tolerated (Ref. 6). In another study (Ref. 4), good results were reported in all patients with symptoms of spasmodic rhinitis. These authors also reported that triprolidine hydrochloride acts rapidly and is well tolerated. Both studies (Refs. 4 and 6) indicated that triprolidine is a powerful antihistamine and antianaphylactic agent with mild side effects and rapid action. Studies by Nicholson (Ref. 8) and Peck, Fowle, and Bye (Ref. 10) showed that the effect of triprolidine hydrochloride was immediate and lasts for about 7 hours wiht a maximum effect at the third hour. The double-blind studies of this drug indicated that, after repeated doses of the drug in a 24-hour period, the degree of drowsiness tended to decrease (Refs. 5, 7, and 9). No evidence of an increased drug effect due to accumulation was reported (Ref. 9). The reported side effects were drowsiness (Refs. 4, 5, 6, 7, and 9) and digestive disturbance (Refs. 4 and 6). FDA adverse reaction reports for triprolidine hydrochloride since 1969 show only two reports of rash (Ref. 11).

Based on the above data and information, the agency is proposing that triprolidine hydrochloride be classified as Category I as an OTC antihistamine at a dose of 2.5 mg every 6 to 8 hours, not to exceed 10 mg in 24 hours, for adults, and a dose of 1.25 mg every 6 to 8 hours, not to exceed 5 mg in 24 hours, for children 6 to under 12 years of age. The agency also proposes to place in professional labeling a dose of 0.938 mg every 6 to 8 hours, not to exceed 3.75 mg in 24 hours, for children 4 to under 6 years of age; a dose of 0.625 mg every 6 to 8 hours, not to exceed 2.5 mg in 24 hours, for children 2 to under 4 years of age; and a dose of 0.313 mg every 6 to 8 hours, not to exceed 1.25 mg in 24 hours, for infants 4 months to under 2 years of age. The agency is proposing that the general labeling recommended by the Panel for OTC antihistamine drugs be used for triprolidine hydrochloride.

Triprolidine was not considered by an OTC advisory review panel and, therefore, does not meet the terms of the enforcement policy in § 330.13. The agency has approved several NDAs that currently allow the OTC marketing of products containing triprolidine. Thus, FDA does not believe it is necessary to prohibit OTC marketing of triprolidine under this proposal while public comments to its proposed monograph status are being evaluated. OTC marketing may be initiated subject to the terms and conditions specified in this tentative final monograph and subject to the risk that FDA may adopt a different position in the final monograph that may require relabeling, recall, or other regulatory action.

References

(1) Letters from P. DeFelice, FDA, to Burroughs-Wellcome Co., Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(2) Copies of FDA-approved labeling from NDA 11-110 and NDA 11-496, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

(3) Letters from J.P. Mann, FDA, to Burroughs-Wellcome Co., OTC Volume 04HTFM, Docket No. 76N-052H, Docket Management Branch.

(4) Fruchard, J., and J. Fruchard, "Un Nouval Antihistaminique: Actidil," *Journal de Medecine de Bordeaux et du Sud-Quest, 134:1356-1358, 1957.*

(5) Britton, M.G., et al., "Two Doses of Triprolidine for Treatment of Allergic Rhinitis," *Annals of Allergy*, 4(5):330-332, 1979.

(6) Wolfromm, R., and P. Liacopoulos, "Clinical Trial of a New Synthetic Antihistamine-Trans-1 (4 methylephenyl)-1-(2-pyridyl)-3-pyrrolidinoprop-ene Hydrochloride," Extract from *La Semaine des Hopitaux de Paris (La Semaine Medicale Professionelle et Medico-Sociale)* 13, 1957.

(7) Bye, C., et al., "The Effects of Repeated Doses of Triprolidine on Subjective Drownsiness and Peformance Tests in Man," *British Journal of Clinical Pharmacology*, 2(4):379p-380p, 1975.

(8) Nicholson, A.N., "Effect of the Antihistamines Brompheniramine Maleate and Triprolidine Hydrochloride on Performance in Man," *British Journal of Clinical Pharmacology*, 8:321-324, 1979.

(9) Bye, C.E., et al., "Evidence for Tolerance to the Central Nervous Effects of the Histamine Antagonist, Triprolidine, in Man," *European Journal of Clinical Pharocology*, 12:181-186, 1977.

(10) Peck W., A. S. E. Fowle, and C. Bye, "A comparison of triprolidine and Clemastine on Histamine Antagonism and Performance Tests in Man: Implications for the Mechanism of Drug Induced Drowsiness," *European Journal of Clinical Pharmacology*, 8:455-463, 1975.

(11) Department of health and Human Services, Food and Drug Administration, "Annual Adverse Reaction Summary Listing," pertinent pages for the years 1969-1982, OTC Volume 04HTFM, Docket No. 76N-052H, Dockets Management Branch.

7. The agency has added to § 341.72 a "Statement of identity" paragraph (designated as § 341.72(a)) and a "Directions" paragraph (designated as § 341.72(d)) to conform with the format of other recently published advance notices of proposed rulemaking and tentative final monographs. Inclusion of the "Statement of identity" paragraph has necessitated a redesignation of § 341.72(a) to § 341.72(b), and § 341.72(b) to § 341.72(c). The agency is also redesignating Subpart D as Subpart C and placing the labeling sections of the monograph in Subpart C.

8. The agency has proposed a new indication for the use of antihistamines for the temporary relief of runny nose and sneezing associated with the common cold in paragraph (2) of new § 341.72(b). (See comment 4 and part II, paragraph B. 1. above.) The agency has also combined serveral required indications under new § 341.72(b)(1). The agency has replaced the Panel's wording "Alleviates, decreases, or temporarily relieves" with the option to select the word "relieves," "alleviates, "decreases," "reduces," or "dries" for the symptom "runny nose" and the option to select the word "relieves," "alleviates," "decreases," or "reduces" for the Symptoms "Sneezing, itching of the nose or throat, and itchy, watery eyes" in the combined indications for antihistamines. These options provide manufacturers the flexiblity to select different terms for labeling. Manfacturers are encouraged to submit additional words for possible inclusion as selection options in the "Indications" section of the final monograph for antihistamines drug products. Therefore, indications in § 341.72(a), which has been redesignated § 341.72(b) have been revised as follows: Paragraphs (2), (3), (4), (5), and (6), of § 341.72(a) have been revised and combined in paragraph (1) of new § 341.72(b). The new indication for the use of antihistamines for symptoms associated with the common cold has been added in paragraph (2) of new § 341.72(b). New § 341.72(b) (1) and (2) reflect the combining of indications for the temporary relief of runny nose, sneezing, itching of the nose or throat, and itchy, watery eyes due to allergic rhinitis and for the temporary relief of runny nose and sneezing associated with the common cold.

9. The agency has deleted § 341.72(b)(5) of the Panel's recommended monograph. This section provided the warning "Do not give this product to children under 6 years except under advise and supervision of a physician," for all antihistamine drug products. The directions provided under new § 341.72(d) state clearly that a doctor should be consulted for the use of anthistamine drug products in children under 6 years of age. The agency believes that the warning is therefore repetitious and unnecessary.

10. In § 341.72(b) (3), (4), and (8) the Panel recommended the use of the signal word "Caution" in a section of the labeling where the heading *"Warnings"* is also recommended. The agency notes that historically there has not been a consistent usage for the signal words "warning" and "caution" in OTC drug labeling. For example, in §§ 369.20 and

369.21 (21 CFR 396.20 and 396.21), which list "warning" and "caution" statements for drugs, the signal words "warning" and "caution" are both used. In some instances either of these signal words is used to convey the same or smiliar precautionary information.

FDA has considered which of these signal words would be most likely to attract consumers' attention to that information describing conditions under which the drug product should not be used or its use should be discontinued. The agency concludes that the signal word "warning" is more likely to flag potential danges so that consumers will read the information being conveyed. Therefore, FDA has determined that the signal word "warning," rather than the word "caution," will be used routinely in OTC drug labeling that is intended to alert consumers to potential safety problems. Accordingly, the signal word "Caution" has deleted from this tentative final monograph.

11. The agency has added to § 341.72(b) (redesignated as § 341.72(c)) a paragraph on warnings that are appropriate for products that are labeled for children under 12 years of age. The agency acknowledges that some warnings which the Panel recommended for all antihistamine drug products are inappropriate for products which are labeled for children under 12 years of age. In addition, the warnings for products labeled for children under 12 years of age have been worded to reflect the administration of the product by adults rather than self-administration. (See comment 15 above.)

12. The agency has combined several warnings under new § 341.72(c) and believes that combining the drowsiness warning with related warnings concerning the use of alcohol or operating a motor vehicle or machinery while taking antihistamines will provide more informative labeling for the consumer. Therefore, the warnings (in § 341.72(b), which has been redesignated § 341.72(c)), have been revised as follows: Paragraphs (6), (7), and (8) have been redesignated as (3), (4), and (5). Paragraphs (3) and (4) of § 341.72(b) have been revised, combined, and added to paragraphs (3) and (4) of new § 341.72(c). New § 341.72(c) (3) and (4) reflect a combining of warnings concerning drowsiness and the use of alcohol or operating a motor vehicle or machinery while taking antihistamines. (See comment 13 above.)

13. Because antihistamines have an anticholinergic effect which can reduce the volume of bronchial secretions and cause thickening of these secretions, the Panel recommended that antihistamines bear a warning that people with asthma not take these drugs unless directed by a doctor, and the agency is proposing such a warning in this tentative final monograph. The agency believes that in addition to this warning, the labeling of antihistamine drug products should inlcude a warning against use of antihistamines in patients with any obstructive pulmonary disease in which clearance of secretions is a problem. The Panel stated that it is important to avoid anticholinergics in the presence of bronchial asthma or chronic obstructive pulmonary disease because of the possibility that anticholinergics may cause secretions to become less fluid and difficult to remove, and thus cause obstruction of the respiratory passages (41 FR 38377). The Panel's recommended warning in § 341.72(b)(2) of the advance notice of proposed rulemaking included asthma, but did not include chronic obstructive pulmonary disease as a contraindication for the use of antihistamines. The agency believes that this warning should be expanded to include all types of chronic obstructive pulmonary disease. This term applies to patients with clinically significant, irreversible, generalized airways obstruction associated with varying degrees of chronic bronchitis, abnormalities in small airways, and/or emphysema (Ref. 1). Because respiratory distress symptoms such as difficulty in beathing and shortness of breath are characteristic of chronic obstructive pulmonary disease, the agency believes that such descriptive terms should also be included in the warning in order to provide more information to the consumer. Therefore, the agency is proposing to amend the Panel's recommended warning to read, "Do not take this product if you have asthma, glaucoma, emphysema, chronic pulmonary disease, shortness of breath, difficulty in breathing, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor." The agency is proposing the term chronic pulmonary disease rather than chronic obstructive pulmonary disease in this warning because it believes that the shorter term will be more understandable to consumers.

Reference

(1) Berkow, R., editor, "The Merck Manual," 14th Ed., Merck Sharp & Dohme Research Laboratories, Rahway, NJ, pp. 628–635, 1982.

14. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments received to these proposals, the agency has determined that final monographs and any applicable OTC drug regulations will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option.

The agency proposes to revoke the existing warning and caution statements in §§ 369.20 and 369.21, and exemptions for certain drugs limited by NDAs to prescription sale in § 310.201(a)(13), for oral antihistamine drug products at the time that this monograph becomes effective. The agency proposes to revoke § 310.201(a)(4) and to delete phenyltoloxamine citrate from bearing the warning and caution statements required by § 369.21 at the time that this monograph becomes effective if this ingredient is reclassified in Category I as an OTC antihistamine in the final monograph.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** on February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that no one of these rules, including this proposed rule for OTC antihistamine drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Public Law 96–354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC antihistamine drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC antihistamine drug products. Types of impact may include,

but are not limited to, costs associated with product testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC antihistamine drug products should be accompanied by appropriate documentation. Because the agency has not previously invited specific coment on the economic impact of the OTC drug review on antihistamine drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has carefully consídered the potential environmental effects of this proposal and has concluded that the action will not have a significant impact on the human environment and that an environmental impact statement therefore will not be prepared. The agency's finding of no significant impact, and the evidence supporting this finding, contained in an environmental assessment (under 21 CFR 25.31, proposed in the **Federal Register** of December 11, 1979; 44 FR 71742), which may be seen in the Dockets Management Branch, Food and Drug Administration.

List of Subjects in 21 CFR Part 341

OTC drugs: Anticholinergics, Expectorants, Bronchodilators, Antitussives, Nasal decongestants, Antihistamines.

On July 9, 1982 at 47 FR 40002, FDA proposed to amend 21 CFR Subchapter D by adding a new Part 341. Proposed Part 341, as amended on October 26, 1982 (47 FR 47520) and October 19, 1983 (48 FR 48576) would be further amended as follows:

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11, it is proposed to make the following amendments:

PART 341—[AMENDED]

1. In proposed Subpart A, § 341.3 is amended by adding new paragraph (d) to read as folows:

§ 341.3 Definitions.

* * * * *

(d) *Antihistamine drug.* A drug used for the relief of the symptoms of hay fever and upper respiratory allergies (allergic rhinitis) and the symptoms of sneezing and runny nose associated with the common cold.

2. In proposed Subpart B, new § 341.12 is added to read as follows:

§ 341.12 Antihistamine active ingredients.

The active ingredients of the product consist of any of the following when used within the dosage limits established for each ingredient:

(a) Brompheniramine maleate.
(b) Chlorpheniramine maleate.
(c) Dexbrompheniramine maleate.
(d) Dexchlorpheniramine maleate.
(e) Diphenhydramine hydrochloride.
(f) Phenindamine tartrate.
(g) Pheniramine maleate.
(h) Pyrilamine maleate.
(i) Thonzylamine hydrochloride.
(j) Triprolidine hydrochloride.

3. In proposed Subpart C, new § 341.72 is added and § 341.90 is amended by adding new paragraphs (b), (c), (d), (e), (f), (g), (h), (i), (j), and (k) to read as follows:

§ 341.72 Labeling of antihistamine drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as an "antihistamine."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to both of the following phrases: (1) "Temporarily" (select one of the following: "relieves," "alleviates," "decreases," "reduces," or "dries") "runny nose and" (select one of the following: "relieves," "alleviates," "decreases," or "reduces") "sneezing, itching of the nose or throat, and itchy, watery eyes due to hay fever" (which may be followed by one or both of the following: "or other upper respiratory allergies" or "(allergic rhinitis)")."

(2) "Temporarily" (select one of the following: "relieves," "alleviates," "decreases," "reduces," or "dries") "runny nose and" (select one of the following: "relieves," "alleviates," "decreases," or "reduces") "sneezing associated with the common cold."

(c) *Warnings.* The labeling of the product contains the following warnings, under the heading "Warnings":

(1) "May cause excitability especially in children."

(2) "Do not take this product if you have asthma, glaucoma, emphysema, chronic pulmonary disease, shortness of breath, difficulty in breathing, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor."

(3) *For products containing brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, dexchlorpheniramine maleate, phenindamine tartrate, pheniramine maleate, pyrilamine maleate, thonzylamine hydrochloride, or triprolidine hydrochloride identified in § 341.12 (a), (b), (c), (d), (f), (g), (h), (i), and (j).* "May cause drowsiness; alcohol may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Use caution when driving a motor vehicle or operating machinery."

(4) *For products containing diphenhydramine hydrochloride identified in § 341.12(e).* "May cause marked drowsiness; alcohol may increase the drowsiness effect. Avoid alcoholic beverages while taking this product. Use caution when driving a motor vehicle or operating machinery."

(5) *For products containing phenindamine tartrate identified in § 341.12(f).* "May cause nervousness and insomnia in some individuals."

(6) *For products that are labeled only for use by children under 12 years of age.* The labeling of the product contains only the warnings identified in paragraphs (c) (1) and (5) of this section as well as the following:

(i) "Do not give this product to children who have asthma or glaucoma unless directed by a doctor."

(ii) *For products containing brompheniramine maleate, chlorpheniramine maleate, dexbrompheniramine maleate, dexchlorpheniramine maleate, phenindamine tartrate, pheniramine maleate, pyrilamine maleate, thonzylamine hydrochloride, or triprolidine hyrochloride identified in § 341.12(a), (b), (c), (d), (f), (g), (h), (i), and (j).* "May cause drowsiness."

(iii) *For products containing diphenhydramine hydrochloride identified in § 341.12(e).* "May cause marked drowsiness."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *For products containing brompheniramine maleate identified in § 341.12(a).* Adults: oral dosage is 4 milligrams every 4 to 6 hours, not to exceed 24 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 2 milligrams every 4 to 6 hours, not to exceed 12 milligrams in 24 hours, or as

directed by a doctor. Children under 6 years of age: consult a doctor.

(2) *For products containing chlorpheniramine maleate identified in § 341.12(b).* Adults: oral dosage is 4 milligrams every 4 to 6 hours, not to exceed 24 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 2 milligrams every 4 to 6 hours, not to exceed 12 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(3) *For products containing dexbrompheniramine maleate identified in § 341.12(c).* Adults: oral dosage is 2 milligrams every 4 to 6 hours, not to exceed 12 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 1 milligram every 4 to 6 hours, not to exceed 6 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(4) *For products containing dexchlorpheniramine maleate identified in § 341.12(c).* Adults: oral dosage is 2 milligrams every 4 to 6 hours, not to exceed 12 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 1 milligram every 4 to 6 hours, not to exceed 6 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(5) *For products containing diphenhydramine hydrochloride identified in § 341.12(e).* Adults: oral dosage is 25 to 50 milligrams every 4 to 6 hours, not to exceed 300 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 12.5 to 25 milligrams every 4 to 6 hours, not to exceed 150 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(6) *For products containing phenindamine tartrate identified in § 341.12(f).* Adults: oral Dosage is 25 milligrams every 4 to 6 hours, not to exceed 150 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 12.5 milligrams every 4 to 6 hours, not to exceed 75 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(7) *For products containing pheniramine maleate identified in § 341.12(g).* Adults: oral dosage is 12.5 to 25 milligrams every 4 to 6 hours, not to exceed 150 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 6.25 to 12.5 milligrams every 4 to 6 hours, not to exceed 75 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(8) *For products containing pyrilamine maleate identified in § 341.12(h).* Adults: oral dosage is 25 to 50 milligrams every 6 to 8 hours, not to exceed 200 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 12.5 to 25 milligrams every 6 to 8 hours, not to exceed 100 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(9) *For products containing thonzylamine hydrochloride identified in § 341.12(i).* Adults: oral dosage is 50 to 100 milligrams every 4 to 6 hours, not to exceed 600 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 25 to 50 milligrams every 4 to 6 hours, not to exceed 300 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor.

(10) *For products containing tripolidine hydrochloride identified in § 341.12(j).* Adults: oral dosage is 2.5 to 6 milligrams every 8 to 8 hours, not to exceed 10 milligrams in 24 hours, or as directed by a doctor. Children 6 to under 12 years of age: oral dosage is 1.25 milligrams every 6 to 8 hours, not to exceed 5 milligrams in 24 hours, or as directed by a doctor. Children under 6 years of age: consult a doctor. (e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements in this section.

§ 341.90 Professional labeling.

* * * * *

(b) *For products containing brompheniramine maleate identified in § 341.12(a).* Children 2 to under 6 years of age: oral dosage is 1 milligram every 4 to 6 hours, not to exceed 6 milligrams in 24 hours.

(c) *For products containing chlorpheniramine maleate identified in § 341.12(b).* Children 2 to under 6 years of age: oral dosage is 1 milligram every 4 to 6 hours, not to exceed 6 milligrams in 24 hours.

(d) *For products containing dexbrompheniramine maleate identified in § 341.12(c).* Children 2 to under 6 years of age: oral dosage is 0.5 milligram every 4 to 6 hours, not to exceed 3 milligrams in 24 hours.

(e) *For products containing dexchlorpheniramine maleate identified in § 341.12(d).* Children 2 to under 6 years: oral dosage is 0.5 milligram every 4 to 6 hours, not to exceed 3 milligrams in 24 hours.

(f) *For products containing diphenhydramine hydrochloride identified in § 341.12(e).* Children 2 to under 6 years of age: oral dosage is 6.25 milligrams every 4 to 6 hours, not to exceed 37.5 mg in 24 hours.

(g) *For products containing phenindamine tartrate identified in § 341.12(f).* Children 2 to under 6 years of age: oral dosage is 6.25 milligrams every 4 to 6 hours, not to exceed 37.5 milligrams in 24 hours.

(h) *For products containing pheniramine maleate identified in § 341.12(g).* Children 2 to under 6 years of age: oral dose is 3.125 to 6.25 milligrams every 4 to 6 hours, not to exceed 37.5 milligrams in 24 hours.

(i) *For products containing pyrilamine maleate identified in § 341.12(h).* Children 2 to under 6 years of age: oral dosage is 6.25 to 12.5 milligrams every 4 to 6 hours, not to exceed 50 milligrams in 24 hours.

(j) *For products containing thonzylamine hydrochloride identified in § 341.12(i).* Children 2 to under 6 years of age: oral dosage is 12.5 to 25 milligrams every 4 to 6 hours, not to exceed 150 milligrams in 24 hours.

(k) *For products containing triprolidine hydrochloride identified in § 341.12(j).* Children 2 to under 6 years of age: oral dosage is 0.938 milligram every 4 to 6 hours, not to exceed 3.744 milligrams in 24 hours. Children 2 to under 4 years of age: oral dosage is 0.625 milligram every 6 to 8 hours, not to exceed 2.5 milligrams in 24 hours. Infants 4 months to under 2 years of age: oral dosage is 0.313 milligram every 6 to 8 hours, not to exceed 1.252 milligrams in 24 hours.

Interested persons may, on or before May 15, 1985 submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through

Friday. Any scheduled oral hearing will be announced in the **Federal Register.**

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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Tuesday
January 15, 1985

Part IX

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 341

Cold, Cough Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Over-the-Counter Nasal Decongestant Drug Products

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 76N-052N]

21 CFR Part 341

Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products for Over-the-Counter Human Use; Tentative Final Monograph for Over-the-Counter Nasal Decongestant Drug Products

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) nasal decongestant drug products (drug products used for relieving the symptom of nasal congestion caused by acute or chronic rhinitis) are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the report and recommendations of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products and public comments on an advance notice of proposed rulemaking that was based on those recommendations. This proposal deals only with nasal decongestant drug products and is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs on the proposed regulation by May 15, 1985. New data by January 15, 1986. Comments on the new data by March 17, 1986. These dates are consistent with the time periods specified in the agency's revised procedural regulations for reviewing and classifying OTC drugs (21 CFR 330.10). Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of September 9, 1976 (41 FR 38312), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products, together with the recommendations of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthamatic Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. Interested persons were invited to submit comments by December 8, 1976. Reply comments in response to comments filed in the initial comment period could be submitted by January 7, 1977.

In a notice published in the **Federal Register** of March 21, 1980 (45 FR 18400), the agency advised that it had reopened the administrative record for OTC cold, cough, allergy, bronchodilator, and antiasthamatic drug products to allow for consideration of data and information that had been filed in the Dockets Management Branch after the date the administrative record previously had officially closed. The agency concluded that any new data and information filed prior to March 21, 1980 should be available to the agency in developing a proposed regulation in the form of a tentative final monograph.

In accordance with § 330.10(a)(10), the data and information considered by the Panel were put on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above), after deletion of a small amount of trade secret information. Data and information received after the administrative record was reopened have also been put on display in the Dockets Management Branch. In response to the advance notice of proposed rulemaking, 16 manufacturers, 2 manufacturers' associations, 4 consumers, the staff members of one bureau of a government agency, 19 health care professionals, and 5 health care professional societies submitted comments on nasal decongestants. One manufacturer submitted a reply comment. Copies of the comments received are on public display in the Dockets Management Branch.

FDA is issuing the tentative final monograph for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products in segments. This document on nasal decongestant drug products is the fourth segment to be published. The first segment, on anticholinergic drug products and expectorant drug products, was published in the **Federal Register** of July 9, 1982 (47 FR 30002). The second segment, on bronchodilator drug products, was published in the **Federal Register** of October 26, 1982 (47 FR 47520). The third segment, on antitussive drug products, was published in the **Federal Register** of October 19, 1983; 48 FR 48576). The fifth segment, on antihistamine drug products, is being published elsewhere in this issue of the **Federal Register**. A subsequent segment on combination drug products and general comments will be published in a future issue of the **Federal Register**.

The advance notice of proposed rulemaking, which was published in the **Federal Register** on September 9, 1976 (41 FR 38312), was designated as a "proposed monograph" in order to conform to terminology used in the OTC drug review regulations (21 CFR 330.10). Similarly, the present document is designated in the OTC drug review regulations as a "tentative final monograph." Its legal status, however, is that of a proposed rule. In this tentative final monograph (proposed rule) the FDA states for the first time its position on the establishment of a monograph for OTC nasal decongestant drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC nasal decongestant drug products.

This tentative final monograph would amend Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations in Part 341 (as set forth in the tentative final monograph on anticholinergic drug products and expectorant drug products that was published in the **Federal Register** of July 9, 1982 (47 FR 30002)) in Subpart A, by adding in § 341.3, new paragraphs (h) and (i); in Subpart B, by adding new § 341.20; and in Subpart C, by adding new § 341.80, and by adding in § 341.90, new paragraphs (m) and (n). This proposal constitutes FDA's tentative adoption of the Panel's conclusion and recommendations on OTC nasal decongestant drug products, as modified on the basis of the comments received and the agency's independent evaluation of the Panel's report. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). (See the **Federal Register** of September

29, 1981; 46 FR 47730.) The Court in *Cutler* held that the OTC drug review regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OTC drug rulemaking process, before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register**. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced into interstate commerce unless they are the subject of an approved new drug application (NDA). Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the advance notice of proposed rulemaking for OTC cold, cough, allergy, bronchodilator, and antiasthmatic drug products (published in the **Federal Register** of September 9, 1976 (41 FR 38312)), the agency suggested that the conditions included in the monograph (Category I) be effective 30 days after the date of publication of the final monograph in the **Federal Register** and that the conditions excluded from the monograph (Category II) be eliminated from OTC drug products effective 6 months after the date of publication of the final monograph, regardless of whether further testing was undertaken to justify their future use. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products will have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and have their products in compliance in the marketplace. However, if the agency determines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

All "OTC Volumes" cited throughout this document refer to the submissions made by interested persons pursuant to the call-for-data notice published in the **Federal Register** of August 9, 1972 (37 FR 16029) or to additional information that has come to the agency's attention since publication of the advance notice of proposed rulemaking. The volumes are on public display in the Dockets Management Branch.

The Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products recommended that phenylpropanolamine preparations be classified in Category I for nasal decongestant use at adult oral dosages equivalent to these phenylpropanolamine hydrochloride dosages: 25 milligrams (mg) every 4 hours or 50 mg every 8 hours not to exceed 150 mg in 24 hours (see 41 FR 38420; September 9, 1976). Similarly, the Advisory Review Panel on OTC Miscellaneous Internal Drug Products recommended that phenylpropanolamine hydrochloride be classified as Category I for appetite control use in adult oral dosages of 25 to 50 mg, not exceeding 150 mg daily. (See 47 FR 8484; February 26, 1982.) However, FDA became aware of reports of studies, made available after the Panels' reports had been submitted, indicating that certain dosages of phenylpropanolamine cause blood pressure elevation. These studies were discussed in the preamble to the advance notice of proposed rulemaking for OTC weight control drug products (47 FR 8466–8468). At that time, the agency specifically requested comments and information on the extent to which phenylpropanolamine induces or aggravates hypertension and interacts with medications that inhibit prostaglandin synthesis.

Numerous comments on the recommended phenylpropanolamine dosage levels and related issues have been submitted to FDA in both the OTC weight control and the OTC nasal decongestant rulemakings. Because the issues concerning the safety of phenylpropanolamine for weight control use and for nasal decongestant use are closely related, the agency has decided to address these issues in the **Federal Register** publication to be published in the near future. Therefore, phenylpropanolamine preparations will not be categorized or further discussed in this tentative final monograph for OTC nasal decongestant drug products.

I. The Agency's Tentative Conclusions on the Comments

A. General Comments on Nasal Decongestant Drug Products

1. One comment stated that there is no evidence that "so-called nasal

decongestants" are of any clinical value. No data or published references were submitted or cited to support this statement.

The Panel reviewed the scientific literature and data submissions, listened to testimony from interested parties, and considered all other available data and information before categorizing OTC nasal decongestant active ingredients. The Panel classified in Category I those active ingredients for which it had appropriate supportive data to establish general recognition of safety and effectiveness. In addition, the Panel placed in Category III those active ingredients for which it did not have sufficient data to establish safety and effectiveness. Additional data must be submitted on these Category III ingredients before they can be generally recognized as safe and effective. The agency believes that those ingredients which have been categorized as safe and effective do have clinical value for the indications listed in this tentative final monograph.

2. One comment disagreed with the Panel's recommendation that claims such as "most recommended by doctors" be placed in Category II because such claims are difficult to substantiate. The comment contended that "difficulty in substantiating does not imply inability to substantiate." Thus, according to the comment, the Panel's reasoning justifies placing this type of claim in Category III. More importantly, the comment argued, this type of claim is not specifically related to safety or effectiveness. If this type of statement were true, the comment contended, banning its use is an inappropriate prior restraint and in violation of the First Amendment to the Constitution.

The OTC drug review program establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. Two principal conditions examined during the review are allowable ingredients and allowable labeling. The FDA has determined that it is not practical—in terms of time, resources, and other considerations—to set standards for all labeling found in OTC drug products. Accordingly, OTC drug monographs regulate only labeling related in a significant way to the safe and effective use of covered products by lay persons. OTC drug monographs establish allowable labeling for the following items: product statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action.

The agency believes terms such as "most recommended by doctors" are unrelated to the characteristics of the drugs in question and, therefore, do not relate in a significant way to the drugs' safe and effective use. Accordingly, the term "most recommended by doctors" is outside the scope of the OTC drug review. The agency emphasizes that even though terms such as "most recommended by doctors" are outside the scope of the OTC drug review, they are subject to the prohibitions in section 502 of the act (21 U.S.C. 352) relating to labeling that is false of misleading. Such statements or terms will be evaluated by the agency on a product-by-product basis, under the provisions of section 502 of the act (21 U.S.C. 352) relating to labeling that is false or misleading.

Moreover, any statement or term that is outside the scope of the monograph, even though it is truthful and not misleading, may not appear in any portion of the labeling required by the monograph and may not detract from such required information. However, statements and terms outside the scope of the monograph may be included elsewhere in the labeling, provided they are not false or misleading.

3. One comment stated that two nasal decongestants should not be taken simultaneously and recommended that the labeling should be clear on this matter. The comment did not further elaborate on its statement.

The agency believes that the comment is referring to two different drug products, each containing a nasal decongestant, for similar uses. The proposed labeling for nasal decongestants in this tentative final monograph specifically requires that the product's principal intended use, i.e., "nasal decongestant" be stated in the labeling. Further, all products containing a nasal decongestant will bear similar indications for use. By reading the label, the consumer should understand that two different drug products containing nasal decongestants are intended to treat the same symptoms and should not be taken simultaneously. The agency, therefore, believes that two nasal decongestants contained in different products will not inadvertently be taken simultaneously because the proposed labeling for nasal decongestants is explicit enough to inform the consumer of the proper use of these drugs. In addition, the agency is unaware of any data that indicate that the proposed labeling for nasal decongestants is inadequate to prevent the inadvertent use of two nasal decongestants simultaneously. (Note: the combination of two nasal decongestants in the same product will be discussed in the combinations segment of the tentative final monograph in a future issue of the Federal Register.)

B. Comments on the Switch of Prescription Nasal Decongestants to OTC Status

4. Several comments agreed with the Panel's classification of oxymetazoline hydrochloride and xylometazoline hydrochloride as Category I OTC topical nasal decongestants. Other comments were opposed to the OTC availability of these ingredients for various reasons. Several comments stated that the habituation and rebound congestion caused by these drugs contraindicated their OTC availability. One comment petitioned the FDA to remove oxymetazoline hydrochloride nasal spray and nasal solution from the OTC market because it is a new drug and the subject of a new drug application which limits its introduction into interstate commerce as a prescription only product. Another comment stated that the use of a xylometazoline hydrochloride nasal spray was the probable cause of a specific incident of severe cardiac upset.

The agency's position regarding the marketing status of ingredients recommended for OTC use which had previously been limited to prescription use is contained in the Code of Federal Regulations at 21 CFR 330.13(b)(2). This regulation explains that such ingredients placed in Category I by a Panel may be marketed OTC following publication of the Panel's proposed monograph subject to the risk that the Commissioner may not accept the Panel's recommendation and may instead adopt a different position that may require relabeling, recall, or other regulatory action. Because the Panel considered oxymetazoline hydrochloride safe, it recommended that this drug, previously available only by prescription prior to publication of the Panel's report in the Federal Register, be reclassified to permit OTC use. Because oxymetazoline has been placed in Category I and the Panel's report has been published without an agency dissent, a manufacturer may market the drug OTC, prior to promulgation of a final monograph, subject to the risk that the Commissioner may subsequently adopt a position different from the Panel's recommendation.

The agency recognizes the problem of rebound congestion associated with the use of topical nasal decongestants. Rebound congestion occurs when

topical nasal decongestants are used too frequently and for too long a period of time. The nasal mucous membranes become more congested and edematous as the drug's vasoconstrictor effect subsides. This effect leads to continued use of the drug and perpetuation of the rebound phenomenon. The Panel also addressed this problem and recommended that all nasal drops and sprays be labeled to limit use to not more than 3 days so as to discourage prolonged use. The Panel also recommended labeling that advised the consumer to consult a doctor if symptoms persisted after 3 days of use. (See § 341.80(b)(1)(ii), 41 FR 38423.) Although aware that continued use of these drugs might result in rebound congestion, the Panel thought that the clinical and marketing data it reviewed showed these drugs to be safe and effective when used according to label directions. Therefore, the Panel concluded that the drug should be available for OTC use.

From the information available, the agency cannot determine the cause of the cardiac upset reported in one of the comments. However, it is reported in the literature that the imidazolines (a class of drugs which includes naphazoline hydrochloride, oxymetazoline hydrochloride, and xylometazoline hydrochloride) may cause arrhythmias, presumably due to coronary vasoconstriction (Ref. 1). Because of these effects, the imidazolines should be used sparingly and with caution in infants, young children, and patients with cardiovascular disease (Refs. 1 and 2).

Studies of the effect of the imidazolines on the intestinal smooth muscle of the rabbit and on the cardiovascular system of the cat showed that the pharmacological action of these drugs, particularly oxymetazoline, is strong (Ref. 3). Nasal decongestants that are administered orally are known to be capable of producing systemic effects. Consequently, the Panel recommended a warning to persons with high blood pressure, heart disease, diabetes, or thyroid disease not to take the drug except under the advice and supervision of a physican. (See § 341.80(b)(2)(iii), 41 FR 38423.) A warning that the product should be used very cautiously in patients with hyperthyroidism, coronary artery disease, hypertension, and diabetes mellitus has also been required for prescription topical nasal decongestants containing oxymetazoline and xylometazoline for over 10 years (Refs. 4 and 5). Because the Panel believed that absorption of the drug into the general circulation was negligible following topical use, the Panel did not recommend a similar warning statement; therefore, the above warning was not required for these products marketed on an OTC basis pursuant to § 330.13 following publication of the Panel's report.

The agency believes that use of these drugs in a generally healthy person is safe, but is concerned that systemic effects can occur in small children or in persons with cardiovascular disease as a result of absorption from the gastrointestinal tract if an excessive amount of the drug is swallowed. Because some of the drug is often swallowed when nose drops and sprays are administered, systemic effects such as those occurring from an orally administered dose can occur. Because of the possibility of generalized vasoconstriction and tachycardia, persons with hypertension, heart disease, diabetes, or hyperthyroidism should only use nasal decongestants as directed by a doctor (Refs. 1, 2, 4, 5, and 6).

Use of these drugs can also produce effects which could alter the balance of insulin and glucose in a diabetic patient (Refs. 6 and 7). Additionally, because of the vascular problems which frequently accompany diabetes, diabetic patients should consult a doctor before using topical nasal decongestants.

Because of the potential side effects that topical nasal decongestants can produce, the agency believes that, in the interest of safety, the warning proposed by the Panel in § 341.80(b)(2)(iii) for oral nasal decongestants shoul also apply to all topical nasal decongestants (except topical inhalants). Based on the Panel's review of data showing that the topical inhalants (propylhexedrine and l-desoxyephedrine) produce little or no significant vasopressor side effects (41 FR 38402 and 38407), the agency proposes to exclude topical inhalants from this warning requirement. Therefore, in this tentative final monograph, the warning as stated in § 341.80(c)(1)(i)(c) "Do not take this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor," will be applicable to all oral nasal decongestants, and a similar warning in § 341.80(c)(2)(iii)(*b*) "Do not use this product if you have heart disease, high blood pressure * * *" will be applicable to all topical nasal decongestants except topical inhalants. The agency also proposes to restrict the use of oxymetazoline hydrochloride and xylometazoline hydrochloride in children under 6 years of age. (See comment 28 below.)

The agency believes that the above warning and limitation of the product to 3 days use will provide for the safe use of these ingredients as OTC topical nasal decongestants.

References

(1) "AMA Drug Evaluations," 4th Ed., American Medical Association, New York, p. 454, 1980.

(2) Harvey, S.C., "Sympathomimetic Drugs," *in* "Remington's Pharmaceutical Sciences," 16th Ed., edited by A. Osol, et al., Mack Publishing Co., Easton, PA pp. 818–819, 1980.

(3) Mujic, M., and J.M. Van Rossum, "Comparative Pharmacodynamics of Sympathomimetic Imidazolines; Studies on Intestinal Smooth Muscle of the Rabbit and the Cardiovascular System of the Cat," *Archives Internationales de Pharmacodynamie et de Therapie*, 155:432–449, 1965.

(4) Copy of FDA approved labeling from NDA 11–919, in OTC Volume 04NTFM, Docket No. 76N–052N, Dockets Management Branch.

(5) Copy of FDA approved labeling from NDA 14–717, in OTC Volume 04NTFM, Docket No. 76N–052N, Dockets Management Branch.

(6) "New Drugs," American Medical Association, Chicago, pp. 211–212, 1965.

(7) "Clinical Pharmacology; Basic Principles in Therapeutics, 2d Ed., Macmillan Publishing Co., Inc., New York, p. 192, 1978.

C. Comments on Specific OTC Nasal Decongestant Active Ingredients

5. One comment stated that there is concern about camphor poisoning in children (Refs. 1 and 2) and recommended that the camphor content of OTC nasal decongestant products (topical inhalants) be limited to less than 0.75 gram (g)/30 grams (g) or to less than 2.5 percent (weight/volume). The comment stated that there is no evidence that warning statements deter childhood poisoning, but concluded that this lower concentration would reduce the risk of serious accidental poisoning while still permitting an adequate concentration of camphor.

The Panel concluded that camphor is safe when applied topically or as an inhalant at specific concentrations, but that there were insufficient data to permit final classification of its effectiveness when labeled for use as a nasal decongestant (41 FR 38406). For adults and children 2 to under 12 years of age, the Panel recommended that camphor should be used in the form of a 5-percent ointment preparation, a 7-percent solution for steam inhalation, or a lozenge containing 0.02 to 15 mg camphor. Following publication of this Panel's recommendations on camphor,

the Advisory Review Panel on OTC Miscellaneous External Drug Products (Miscellaneous External Panel) also reviewed camphor for topical use. The Miscellaneous External Panel concluded that OTC products containing a concentration of camphor greater than 2.5 percent have a low benefit-to-risk ratio and recommended that camphor be limited in OTC drug products for external use to less than 2.5 percent. The Miscellaneous External Panel also recommended that the quantity of camphor in a package be limited to a total of 360 mg per package and that camphor be marketed in a child-proof container to deter accidental poisoning of children (45 FR 63875).

In the **Federal Register** of September 21, 1982 (47 FR 41716), the agency published a final rule establishing that camphorated oil drug products (historically marketed primarily as topical counterirritants or liniments) are misbranded and are new drugs. The agency also initiated a recall of camphorated oil products to the retail level. In the **Federal Register** of September 26, 1980 (45 FR 63874), the agency announced that it was treating the data and information on camphor received from the Miscellaneous External Panel as a petition to reopen the administrative record on cold, cough, allergy, bronchodilator, and antiasthmatic drug products. The agency granted this petition by allowing those data and information to be included in the administrative record for these drug products. This notice served to inform interested persons of the existence of these recommendations and also invited persons or firms to submit any comments they may have. This reopening of the administrative record related only to the ingredient camphor in OTC drug products.

The agency's position on the safety of camphor containing products for topical application has been stated in the tentative final rule for OTC external analgesic drug products in the **Federal Register** of February 8, 1983 (48 FR 5854). In that document, the agency concluded that, at this time, there is no need to limit camphor content to 360 mg per package and that the camphor content will be limited to 11 percent or lower. The agency's position as stated in that document is hereby incorporated into this nasal decongestant rulemaking.

To date, no new data have been submitted to support the effectiveness of camphor as a nasal decongestant and at this time, camphor will remain in Category III as a nasal decongestant.

References

(1) Aronow, R.J., "Camphor Poisoning," *Journal of the American Medical Association*, 235:1260, 1976.

(2) Phelan, W.J., "Camphor Poisoning: Over-the-Counter Dangers," *Pediatrics*, 57:428–431, 1976.

6. One comment objected to the Panel's limiting eucalyptol, menthol, and thymol to lozenge and mouthwash dosage forms when these ingredients are used as "oral (topical) nasal decongestants." The comment contended that this limitation is arbitrary because viscous syrups and compressed tablets are just as effective as mouthwashes and lozenges. The comment recommended that "oral (topical) dosage" forms of eucalyptol, menthol, and thymol include any oral dosage form which is topically effective and which can be formulated to contain the same concentrations of these ingredients that are allowed for lozenges.

The comment's use of the term "oral (topical) nasal decongestant" apparently refers to dosage forms such as mouthwashes, lozenges, and compressed tablets, which are all used topically in the mouth, rather than swallowed, for a nasal decongestant effect. Compressed tablets and lozenges are solid dosage forms which can be used topically in the same manner and the site of application would be the same for compressed tablets, lozenges, and mouthwashes. The agency agrees that compressed tablets could also be included as a dosage form for eucalyptol, menthol, and thymol, when used as oral (topical) nasal decongestants intended to be dissolved in the mouth rather than swallowed, once the ingredients in this dosage form have been classified in Category I. The agency points out that eucalyptol, menthol, and thymol are all Category III ingredients, which, although found safe by the Panel, lack adequate data to demonstrate effectiveness as topical or inhalant nasal decongestants. Data to demonstrate effectiveness are required in order to permit final classification of these ingredients in the monograph for this use.

The comment's suggestion to allow viscous syrups as topical dosage forms in the mouth is not accepted because the agency is not aware of any data on viscous syrups containing eucalyptol, menthol, or thymol that are used as oral (topical) nasal decongestants. Interested persons are invited to submit data on viscous syrups containing these ingredients that are used as oral (topical) nasal decongestants in the mouth.

7. A comment representing the views of the staff of the Bureau of Consumer Protection of the Federal Trade Commission (FTC) requested that the active ingredients eucalyptol, menthol, and thymol used as a nasal decongestant or antitussive in a mouthwash dosage form be classified as Category II. The comment pointed out that after more than 4 months of adjudicative hearings, during which voluminous evidentiary records consisting of thousands of pages of expert testimony and exhibits were thoroughly examined for a marketed product with labeling and advertising claims that the product cured or prevented colds or sore throat, or lessened the severity or incidence of colds, cold symptoms, or sore thoats by killing germs (Ref. 1), the FTC determined that 0.91 mg of eucalyptol per milliliter (mL) of product (mg/mL), 0.42 mg/mL menthol, and 0.63 mg/mL thymol in a mouthwash solution are insufficient in concentration to provide relief for the symptoms of the common cold, including nasal congestion and cough. Expert medical and scientific witnesses testified that the process of gargling with a mouthwash containing these ingredients does not allow the ingredients to reach the critical areas of the body they need to reach to relieve the symptoms of a cold, nor do the ingredients penetrate the infected cells where the action of the cold viruses would be taking place.

The comment stated that the FTC's conclusion, after examining the records and hearing expert testimony, was consistent with the Panel's findings that there are no well-controlled studies documenting the effectiveness of eucalyptol, menthol, and thymol when usd in a mouthwash dosage form as a nasal decongestant or an antitussive. The comment pointed out that the FTC's opinion and supporting evidence were not available to the Panel during its deliberations. Therefore, the comment requested that the FDA review the FTC's opinion and the supporting evidence and use them as a basis to classify eucalyptol, menthol, and thymol in Category II for use as a nasal decongestant or antitussive in a mouthwash dosage form.

The response in this document addresses only the nasal decongestant use of these ingredients. The antitussive use will be addressed in a future issue of the **Federal Register**. The agency has reviewed the FTC's opinion and supporting evidence (Ref. 1). Medical and scientific experts testified at the FTC hearing that there is an absence of literature showing that the combination

of eucalyptol, menthol, and thymol in a mouthwash dosage form is effective in preventing colds and alleviating cold symptoms such as nasal congestion and cough. These experts in the fields of respiratory and infectious diseases, virology, pharmocology, and microbiology further stated, based upon their knowledge in their respective areas, that it is doubtful that these ingredients would be effective in treating symptoms of the common cold.

Although the Panel did not have access to the FTC's opinion and supporting evidence, it did review the St. Barnabas study, which was one of the studies discussed during the FTC hearing (Ref. 2). The St. Barnabas study was undertaken to demonstrate the effect of rinsing and gargling twice daily with an aqueous mixture of 0.91 mg/mL eucalyptol, 0.42 mg/mL menthol, and 0.63 mg/mL thymol on the incidence, duration, and severity of the common cold and its symptoms. It was a 4-year subjective study in over 4,800 schoolchildren. The experts who testified at the FTC hearing agreed that the deficiencies in the design and execution of the study precluded any meaningful interpretation of the results. The FTC concluded that the design and execution of the tests heavily biased the results in favor of the manufacturer, and therefore the tests could not support the advertising claims. The Panel concluded that although the study was not well-controlled and could not be considered proof of effectiveness, the results did reveal milder nasal symptoms and cough symptoms in individuals using the medicated mouthwash as compared with these symptoms in individuals using the placebo. Because this study did not demonstrate the effectiveness of the individual nasal decongestant ingredients, the Panel recommended that data to demonstrate effectiveness of each ingredient alone be required in accordance with its guidelines for testing OTC nasal decongestant drug products (41 FR 38415). Because safety was not at issue, and the data suggested the possibility that the combination of eucalyptol, menthol, and thymol was effective as a nasal decongestant in a mouthwash dosage form, the Panel believed that a Category III classification was justified.

At the tentative final monograph stage, FDA usually proposes Category II status for an ingredient only if there is a potential safety problem or if there are essentially no data to support the ingredient's effectiveness for its purported use. Although medical and scientific experts testified for the FTC that it is unlikely that eucalyptol, menthol, and thymol in a mouthwash would be effective as a nasal decongestant, they also stated that the studies that were done contained defects which made the results inconclusive. In view of the inconclusive results caused by deficiencies in the studies, the agency does not believe it appropriate at this time to classify the drugs as "ineffective," i.e., Category II, without allowing interested parties the opportunity to develop a well-controlled study that might demonstrate the drugs' effectiveness. Therefore, the agency is proposing that eucalyptol, menthol, and thymol in a mouthwash dosage form as a nasal decongestant remain in Category III in this tentative final monograph.

In the final monograph, any ingredient that has not been found to be safe and effective will be classified as "nonmonograph" and may not be legally marketed. To date, there have been no new data submitted to support the effectiveness of eucalyptol, menthol, and thymol in a mouthwash dosage form as a nasal decongestant, and if adequate data are not submitted before establishment of a final monograph, these ingredients for this use will be classified as "nonmonograph."

References

(1) Comment No. C0126, Docket No. 76N–0052, Dockets Management Branch.

(2) "The Effect of Listerine Antiseptic on the Incidence, Severity, and Duration of the Common Cold. A 4-Year Study," draft of unpublished paper in OTC Volume 040278, section 3.a. (referred to as the St. Barnabas Study in Comment No. C0126.)

8. One comment (Ref. 1) submitted new data from four controlled clinical studies (Refs. 2 through 5) on the effectiveness of 1-desoxyephedrine, alone and in combination with aromatics (camphor, menthol, methyl salicylate, bornyl acetate, and lavender oil), as a topical nasal decongestant (administered by a nasal inhaler). The comment requested Category I status for 1-desoxyephedrine based on the new data (Refs. 2 through 5), data submitted to the Panel (Refs. 6 and 7), and the manufacturer's marketing experience.

The agency has reviewed the data and concludes that they are adequate to reclassify this ingredient in Category I as a topical nasal decongestant. The combination of 1-desoxyephedrine and aromatics will be addressed in the combinations segment of the cold, cough, allergy, bronchodilator, and antiasthmatic tentative final monograph in a future issue of the **Federal Register.**

The agency's evaluation of study numbers 74–10A, 74–30, 74–58, and 70–24 (Refs. 2 through 4, and 6 and 7) showed significant decongestion of the nostrils treated with 1-desoxyephedrine and the combination of 1-desoxyephedrine and aromatics, when compared to baseline measurements or placebo. Study 75–45 (Ref. 5) showed that 1-desoxyephedrine did not cause rebound congestion within a 7-day period. Based on the data, the agency proposes an adult dosage of two inhalations in each nostril not more often than every 2 hours from an inhaler that delivers in each 800 mL of air 0.04 to 0.15 mg of 1-desoxyephedrine. In keeping with the guidelines established by the Panel (41 FR 38333), the agency proposes a dosage for children 6 to under 12 years of age of one-half of the adult dosage, i.e., one inhalation in each nostril not more often than every 2 hours from an inhaler that delivers in each 800 mL of air 0.04 to 0.15 mg of 1-desoxyephedrine. The data demonstrate that this ingredient does not cause rebound nasal congestion within a 7-day period. Therefore, the use of 1-desoxyephedrine as a topical nasal decongestant should be limited to not more than 7 days rather than the 3-day limit for other topical nasal decongestants that cause rebound congestion.

The agency's detailed comments and evaluations on the data are on file in the Dockets Management Branch (Ref. 8).

References

(1) Comment Nos. C0111, CR0003, and SUP015, Docket No. 76N–0052, Dockets Management Branch.

(2) Connell, J.T., "Nasal Decongestant Delta-'P' Method," draft of unpublished study (74–10A), in Comment No. C0111, Docket No. 76N–0052, Dockets Management Branch.

(3) Connell, J.T., "Inhaler," draft of unpublished study (74–30), in Comment No. C0111, Docket No. 76N–0052, Dockets Management Branch.

(4) Connell, J.T., "Inhaler," draft of unpublished study (74–58), in Comment No. C0111 (Volume 4), Docket No. 76N–0052, Dockets Management Branch.

(5) Connell, J.T., "Nasomucosal Rebound Delta-P," draft of unpublished study (75–45), in Comment No. C0111 (Volume 4), Docket No. 76N–0052, Dockets Management Branch.

(6) Turgeon, R.F., "Vick Inhaler," draft of unpublished study (70–24), dated February 11, 1971, in OTC Volume 040298.

(7) Memo to Burke, W.E., from E.B. Cohen, "Vick Inhaler: Vick Rhinorhemeter Study-Maine Research" (Supersedes Study 70–24 dated February 11, 1971), in OTC Volume 040298.

(8) Letter from W.E. Gilbertson, FDA, to G.F. Hoffnagle, Vicks Health Care Division of Richardson-Merrell, Inc., coded LET072, Docket No. 76N–052N, Dockets Management Branch.

9. One comment reported two cases in which use of nose drops containing phenylephrine hydrochloride had caused a permanent loss of the sense of

taste and smell. The comment recommended a warning statement in the labeling of these products which alerts consumers to the possibility of such an adverse reaction.

No data were submitted with the comment; however, the agency has reviewed both the Panel's discussion on the safety of phenylephrine hydrochloride (41 FR 38399) and its recommended warnings for nasal decongestants (41 FR 38422). The Panel concluded that phenylephrine hydrochloride is generally recognized as safe for use as a nasal decongestant, and it did not make any reference to the type of adverse reaction cited in the comment. Accordingly, no warning statement was recommeded.

The agency is concerned about the possibility of any adverse effects resulting from the use of drug products, and it routinely reviews and evaluates reports of those adverse reactions which are submitted. FDA's "Annual Adverse Reaction Summary Listing" for the period from 1969 to 1981 does include one reported case of parosmia (any disease or disorder of the sense of smell) that occurred in 1977 (Ref. 1). However, this case and the two cases cited in the comment are not adequate evidence to show a relationship between the permanent loss of the sense of taste and smell and the use of OTC nasal decongestant drops containing phenylephrine hydrochloride. Therefore, based upon the limited amount of information available on this type of adverse reaction, the agency does not consider it necessary at this time to require a warning statement, as the comment requested. The agency invites interested persons to submit additional comments and data on this type of adverse reaction.

Reference

(1) Department of Health and Human Services, Food and Drug Administration, "Annual Adverse Reaction Summary Listings," pertinent pages for the years 1969 through 1981, in OTC volume 04NTFM, Docket No. 76N-052N, Dockets Management Branch.

10. One comment questioned the studies used by the Panel to substantiate the effectiveness of phenylephrine hydrochloride as an oral nasal decongestant. The comment stated that numerous unpublished studies, which split evenly between mild successes and total failures, were quoted by the Panel, and in the one study (Ref. 1) published in an academically acceptable journal, no efficacy was seen even with doses higher than usually recommended. In addition, the comment cited two references which questioned the oral bioavailability of phenylephrine hydrochloride (Refs. 2 and 3). The comment recommended that phenylephrine hydrochloride not be used as an oral nasal decongestant.

The Panel concluded that phenylephrine hydrochloride was effective as an oral nasal decongestant after a thorough review of published and unpublished studies, oral and written submissions by manufacturers, and evaluations of clinical and marketing experience. The published study referred to by the comment (Ref. 1) is discussed in comment 11 below. The Panel was aware of one of the references that the comment cited as questioning the oral bioavailability of phenylephrine hydrochloride (Ref. 3), and cited this reference is discussing the safety of phenylephrine hydrochloride (41 FR 38399). This study is not relevant to the effectiveness of phenylephrine hydrochloride, but does confirm the potentiation of the effect of oral phenylephrine by a monoamine oxidase inhibitor.

The agency has reviewed the information cited by the comment, the Panel's recommendations, and all of the supporting data and concludes that, based on the studies cited by the Panel, information on clinical use and marketing experience, and the Panel's expertise in evaluating the clinical and marketing experience of this ingredient, there is sufficient basis to determine the phenylephrine hydrochloride is generally recognized as effective for OTC use as an oral nasal decongestant. The comment's recommendation is therefore not accepted.

References

(1) Rodgers, J.M., E.B. Reilly, and H.A. Bickerman, "Physiologic and Pharmacologic Studies on Nasal Airwary Resistance," *Clinical Pharmacology and Therapeutics*, 14:146, 1973.

(2) Innes, I.R., and M.L. Nickerson, "Norepinephrine, Epinephrine, and the Sympathomimetic Amines," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A. Gilman, the Macmillan Co., New York, pp. 477–494, 1975.

(3) Elis, J., et al., "Modification by Monoamine Oxidase Inhibitors of the Effect of Some Sympathomimetics on Blood Pressure," *British Medical Journal*, 2:75–78, 1967, in OTC Cough/Cold Reference Volume E, Docket No. 76N-0052, Dockets Management Branch.

11. One comment stated that a reference to a study by Rodgers, Reilly, and Bickerman (Ref. 1) cited by the Panel in three different places (in part VIII. paragraph B.d. on page 38400, in part VIII. paragraph B.e. on page 38401, and in part VIII. paragraph B.h. on page 39403) was incorrect in that the cited information was not contained in that particular reference.

The agency has reviewed the Panel's discussions on pages 38399 through 38403 and agrees with the comment that the study by Rodgers, Reilly and Bickerman (Ref. 1) does not contain the information cited by the Panel on page 38399, nor is the agency aware of what reference should have been cited there. Nevertheless, this omission does not have a bearing on the tentative status of phenylephrine hydrochloride for oral and topical use as a nasal decongestant.

The agency has determined, however, that the information in the discussions on pages 38401 and 38403 is supported in another study by Bickerman (Ref. 2) that was reviewed by the Panel and cited on page 38401. The information on pages 38401 and 38403 that was attributed to the study by Rodgers, Reilly, and Bickerman (Ref. 1) should be attributed to the Bickerman Study (Ref. 2).

References

(1) Rodgers, J.M., E.B. Reilly, and H.A. Bickerman, "Physiologic and Pharmacologic Studies in Nasal Airway Resistance," (abstract), *Clinical Pharmacology and Therapeutics*, 14:146, 1973.

(2) Bickerman, H.A., "Physiologic and Pharmacologic Studies on Nasal Airway Resistance (R^N). Current Research Methodology in the Evaluation of Proprietary Medicines. Cold and Allergy Preparations," *in* "Conference Proceedings of the Research and Scientific Development Committee of the Proprietary Association," The Proprietary Association, New York, pp. 60–72, 1971.

12. One comment claimed that certain OTC inhalant nasal decongestant products containing propylhexedrine have the capability of producing a "high" and therefore have a potential for abuse. The comment included a 1976 newspaper article which described six deaths traced to the abuse of propylhexedrine.

The Panel reviewed the data submitted on propylhexedrine and concluded that it was safe and effective for OTC use (41 FR 38402). In the dosage range recommended by the Panel, propylhexedrine has a wide margin of safety and relative freedom from toxic effects. Harvey (Ref. 1) describes propylhexedrine as a volatile indirect sympathomimetic amine that does not have central excitatory effects or addiction liability. It has a decongestant effect on the nasal mucous membrane and acts as a vasoconstrictor when inhaled once or twice through each nostril. It is considered safe for self-medication by adults, but children should not have unsupervised access to

a propylhexedrine inhaler. Side effects of propylhexedrine include rebound congestion, headache, and, in rare instances, an increase in blood pressure (Ref. 1). The Panel pointed out that 100 mg oral doses of propylhexedrine alone induce a 17- to 23-millimeter (mm) rise in blood pressure and reflex bradycardia in normal adults but no overt symptoms or euphoria, palpitation, or dry mouth (41 FR 38402).

The agency agrees with the Panel's conclusion that propylhexedrine has a wide margin of safety in the dosage range recommended for use by adults and children 6 to under 12 years of age (0.40 to 0.50 mg in two inhalations per nostril). The Panel pointed out that "the risk of misuse and/or abuse is minimized by restriction on the types of pharmacologic agents in available OTC products, limitations on dosage and concentration of active drug, and adequate and explicit directions for use coupled with appropriate warnings" (41 FR 38332).

The agency routinely reviews and evaluates reports of adverse reactions resulting from the use of OTC drug products. Annual adverse reaction summaries, compiled for the years 1969 to 1981 (Ref. 2), show that, of 21 cases of adverse reactions reported during this 12-year period for the two products mentioned by the comment, 7 cases involved the misuse of propylhexedrine in an inhaler. The six propylhexedrine-related deaths referred to by the comment occurred among individuals, most of whom had a history of drug abuse, who knowingly misused the drug. The agency is concerned about the possibility of any adverse effects resulting from the use of OTC drug products, but it also recognizes that a number of substances in the marketplace can be and are abused by some individuals. The few isolated reports on the abuse of propylhexedrine (the latest one was reported to the agency in 1977) do not indicate a widespread problem. The agency believes that propylhexedrine should be available as an inhalant nasal decongestant because it is safe and effective, when used as instructed in the labeling.

References

(1) Harvey, S.C., "Sympathomimetic Drugs," *in* "Remington's Pharmaceutical Sciences," 16th Ed., edited by A. Osol, et al., Mack Publishing Co., Easton, PA, p. 830, 1980.

(2) Department of Health and Human Services, Food and Drug Administration, "Annual Adverse Reaction Summary Listing," pertinent pages for the years 1969 through 1981, in OTC Volume 04NTFM, Docket No. 76N-052N, Dockets Management Branch.

13. Several comments strongly disagreed with the Panel's recommendation that pseudoephedrine preparations be available OTC as nasal decongestants. One comment agreed with the Panel's recommendation. The comments that objected to the OTC status of pseudoephedrine stated that pseudoephedrine causes tachyphylaxis fatigue of the beta-response mechanism and urinary retention; side effects, although rarely severe or fatal, occur frequently; pseudoephedrine is a stimulant and overuse may be very damaging; and unrestricted availability to the public may be dangerous.

The agency agrees with the Panel's recommendation that pseudoephedrine preparations (pseudoephedrine hydrochloride and pseudoephedrine sulfate) are safe and effective as oral nasal decongestants for OTC use. The comments did not submit any data in support of their reasons for objecting to the OTC status of pseudoephedrine.

It has been reported in the literature that tachyphylaxis, a condition in which effectiveness of a drug decreases after rapidly repated doses, can occur with ephedrine and its isomeric forms (i.e., d- and l-ephedrine, and d- and l-pseudoephedrine) (Refs. 1, 2, and 3). However, the agency concludes that this should not be a problem if the drug is used according to labeling directions.

Roth et al. (Ref. 4) reported that side effects of patients treated with a single oral dose of 60 mg of pseudoephedrine were minimal. Of 20 patients, 2 experienced mild elevations in pulse rate, 1 developed a moderate elevation in pulse rate, 1 experienced mild elevations in pulse rate and diastolic blood pressure, 1 developed palpitations and a slight increase in pulse rate, 2 reported tiredness, and 3 reported a light-headed feeling. Empey et al. (Ref. 5) noted that side effects were of little problem in patients taking 60 mg of pseudoephedrine three times a day. In this study, pseudoephedrine and an antihistamine were tested separately, in combination, and compared with a placebo. One patient reported dryness of the mouth when taking pseudoephedrine alone, and one patient reported excessive sweating, but there were no reports of nervousness or palpitations. The authors stated that the lower incidence of drowsiness reported with the combination, as compared with the antihistamine alone, might reflect a slight stimulant effect from pseudoephedrine; however, stimulation was not reported by anyone taking pseudoephedrine alone. In its report, the panel cited a study which indicated that mild side effects, such as drowsiness, nausea, insomnia, and headache, can occur with the use of pseudoephedrine (Ref. 6). However, these side effects are not severe and would not warrant the elimination of pseudoephedrine from the OTC marketplace. Pseudoephedrine preparations have been marketed OTC safely for many years.

The use of pseudoephedrine, as with most other sympathomimetic drugs, may cause an increase in blood pressure when taken with monoamine oxidase inhibitors. Therefore, the Panel recommended a drug interaction precaution for oral nasal decongestants in § 341.80(b)(2)(iv) (redesignated as § 341.80(c)(1)(i)(*d*) in this tentative final monograph) to warn against the use of the product when taking a prescription drug for high blood pressure or depression without first consulting a doctor. (See comment 23 below.)

Because of the vasoconstrictive properties of sympathomimetic drugs, persons suffering from urinary retention, especially elderly men with an enlarged prostate, could experience increased difficulty in urinating (Refs. 7 and 8). Males with an enlargd prostate shoud only use these drugs under the supervision of a physician. Therefore, the agency has determined that this condition will be added to the warning proposed by the Panel in § 341.80(b)(2)(iii) which appears as § 341.80(c)(1)(i)(*c*) in this tentative final monograph. This warning will read as follows: "Do not take this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor." (NOTE: The part of the warning concerning "difficulty in urination due to enlargement of the prostate gland" is not necessary for products labeled for use only in children under 12 years of age. That part of the warning is not applicable to children and its presence in the labeling would tend to distract parents from label warnings which are important. Accordingly, the revised warning for products labeled for use in children only, "Do not give this product to children who have heart disease, high blood pressure, thyroid disease, or diabetes unless directed by a doctor," has been added to the tentative final monograph in § 341.80(c)(1)(ii)(*c*)). The directions for use and appropriate warnings will inform the consumer of the proper use of the product. Based on these considerations, the agency concludes that pseudoephedrine will remain available as an OTC nasal decongestant.

References

(1) Innes, I.R., and M. Nickerson, "Norepinephrine, Epinephrine, and the Sympathomimetic Amines," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A. Gilman, Macmillan Publishing Co., New York, pp. 500–501, 1975.

(2) Patil, P.N., A. Tye, and J.B. Lapidus, "A Pharmacological Study of the Ephedrine Isomers," *Journal of Pharmacology and Experimental Therapeutics*, 148:158–168, 1965.

(3) Aviado, D.M., Jr., A.L. Wnuck, and E.J. DeBeer, "Cardiovascular Effects of Sympathomimetic Bronchodilators, Epinephrine, Ephedrine, Pseudoephedrine, Isoproterenal, Methoxyphenamine and Isoprophenamine," *Journal of Pharmacologh and Experimental Therapeutics*, 122:406–417, 1958.

(4) Roth, R.P., et al., "Nasal Decongestant Activity of Pseudoephedrine, "*Annals of Otology, Rhinology and Laryngology*, 86:235–241, 1977.

(5) Empey, M.B., et al., "A Double-Blind Crossover Trial of Pseudoephedrine and Triprolidine Alone and in Combination, for the Treatment of Allergenic Rhinitis," *Annals of Allergy*, 34:41–46, 1975.

(6) Arbesman, C.E., and R.J. Ehrenreich, "New Drugs in the Treatment of Allergies," *New York State Journal of Medicine*, 61:219–299, 1961.

(7) Innes, I.R., and M. Nickerson, "Norephinephrine, Epinephrine, and the Sympathomimetic Amines," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., edited by L.S. Goodman and A. Gilman, Macmillan Publishing Co., New York, pp. 505–507, 1975.

(8) Harvey, S.C., "Sympathomimetic Drugs," *in* "Remington's Pharmaceutical Sciences," 16th ED. edited by A. Osol, et al., Mack Publishing Co., Easton, PA, pp. 818–820, 1980.

D. Comments on Dosages for OTC Nasal Decongestants

14. One comment stated that there was an inconsistency between the dosage for naphazoline hydrochloride recommended by the Panel in § 341.20(b) and the warning for that ingredient in § 341.80(b)(6). The comment explained that in § 341.20(b) there is no dosage instruction for the use of a 0.05-percent solution in children under 12 years of age. However, § 341.80(b)(6) states that the 0.05-percent solution is not to be given to children under 6 years of age. Because the ages 6 to under 12 years are not mentioned in § 341.80(b)(6), the comment recommended that the warning in § 341.80(b)(6) should state that the 0.05-percent solution is not to be given to children under 12 years of age or, as an alternative, that dosage instructions for the 0.05-percent solution for children 6 to 11 years of age be included in § 341.20(b).

The agency agrees that the warning recommended by the Panel in § 341.80(b)(6) should be revised for clarity. The dosage instructions as stated in § 341.20(b) specify that 0.05 percent naphazoline hydrochloride is for adult use only, and that a 0.025-percent solution is to be used for children 6 to under 12 years of age. However, the warning in § 341.80(b)(6) states that the 0.05-percent solution is for adult use and should not be used in children under 6 years of age. As the comment points out, the warning in § 341.80(b)(6) neglects to mention children in the 6- to under 12-year age group. In § 341.3(a) of the advance notice of proposed rulemaking (41 FR 38419), an adult has been defined as any person 12 years of age and older. The agency has deleted the first part of the Panel's warning in § 341.80(b)(6), "For adult use only," because the product directions will specify that the 0.05-percent solution should be used only in adults. Therefore, the warning in § 341.80(b)(6) (redesignated as § 341.80(c)(2)(iv) in this document) will be revised to read as follows:

For products containing naphazoline hydrochloride identified in § 341.20(b)(6) at a concentration of 0.05 percent: "Do not use this product in children under 12 years of age because it may cause sedation if swallowed."

15. One comment proposed that § 341.20(d)(2) be revised so that an "aqueous solution" is not specified in the formulation of phenylephrine hydrochloride as a topical nasal decongestant. The comment stated that all other portions of the monograph avoid specifying inactive ingredients and that specifying an inactive ingredient was not consistent with the intent of the OTC drug review. The comment also stated that if an "aqueous solution" was specified in the formulation of phenylephrine hydrochloride to assure against the potential problem of lipid pneumonia, which can occur from the accidental aspiration of oil-based nose drops, then an appropriate limitation should be incorporated into the monograph to protect against this possibility. The comment suggested limiting the product form to "non-oil-based drops or sprays."

The purpose of the OTC drug review process is to determine the safety and effectiveness of OTC drugs. If an active ingredient is safe, but the product's inactive ingredient formulation results in an unsafe product, it was the responsibility of the Panel to address those ingredients which make the product unsafe. As the comment observes, oil-based drops or sprays may be aspirated into the lungs and may cause lipid pneumonia (Refs. 1 and 2). The Panel recognized this problem and concluded that nasal drops and sprays can only be generally recognized as safe and effective for OTC use when they are formulated as aqueous solutions. Because the designation "non-oil-based" solutions could also include types of solutions that are non-aqueous, the agency believes that a more explicit term than "non-oil-based" is necessary. Therefore, the comment's suggestion is not accepted. The phrase "aqueous solution" will remain in the topical nasal decongestant dosage for drops and sprays in § 341.20(a), (b), (c), (d)(2), and (h) (redesignated as § 341.80(d)(2)(ii)(*a*), (iii)(*a*), (iv)(*a*), and (vii)(*a*) in this document).

References

(1) Crofton, J., and A. Douglas, "Respiratory Diseases," Blackwell Scientific Publications, Oxford, England, pp. 142–150, 1969.

(2) Martin, E.W., "Hazards of Medication," 2d Ed., J.B. Lippincott Co., Philadelphia, pp. 206–207, 1978.

16. One comment (Ref. 1) stated that the Panel's recommended dosage of phenylephrine hydrochloride in § 341.20(d)(2) inadvertently allows an unnecessarily wide variation in dosage and unnecessarily restrains product formulation. The dosage allowed by the Panel is two or three sprays per nostril of a 0.25 to 0.5 percent aqueous solution. The comment stated that no effort was made to define the quantity of drug that is to be delivered in each spray; that the amount of drug delivered by a spray container can vary significantly from one container to another depending on the design and dimensions of the nozzle orifice; that container shape and fill-level also affect the amount of product delivered; that the Panel's recommendation does not limit the drug delivery system to a spray container like the one currently in common use and as a result any kind of spray mechanism could be used with even greater variability. The comment added that for all drugs in the monograph, except topical nasal decongestants, the dosages are given in concise statements of the quantity of drug to be delivered and requested that manufacturers should be permitted to formulate at percentages below 0.25 or above 0.50 as long as the total drug delivery is within the dosage range proposed by the comment. The comment submitted data to support a dosage range of 0.80 to 1.80 mg of phenylephrine hydrochloride per nostril every 4 hours.

The comment raises a number of valid points. The dosages recommended for nasal drops and sprays are not absolute amounts and are variable; however, the

Panel reviewed numerous studies on nasal drops and sprays which showed that there is a wide range of safety with these drugs. Nasal sprays and drops have been available for years, and the data that have been accumulated on these products show that the concentrations and dosages recommended by the Panel are safe and effective. Thus, although there may be some variation in the amount of drug delivered from various droppers or spray containers, the amount of drug delivered will be within the safe and effective range. The study submitted by the comment was designed to quantitatively determine the amount of phenylephrine hydrochloride delivered with one spray from a commercial nasal spray squeeze bottle. The data did not show that the measured amount of drug was either a safe or effective dose. The comment's suggestion for a milligram dosage is not accepted, and dosages for nasal drops and sprays will continue to be defined in terms of concentration.

Reference

(1) Comment No. C0135, Docket No. 76N-0052, Dockets Management Branch.

17. One comment requested that 1 percent phenylephrine hydrochloride for OTC use as a topical nasal decongestant be placed in Category I as safe and effective. The comment pointed out that the Panel recommended Category I status for aqueous solutions of phenylephrine hydrochloride in concentrations of 0.125, 0.25, and 0.5 percent. Although a submission on 1 percent phenylephrine was made, the Panel did not categorize this concentration. Two studies were submitted with the comment to document the safety and effectiveness of 1 percent phenylephrine hydrochloride (Ref. 1). The comment pointed out that nasal decongestant drops containing 1 percent phenylephrine hydrochloride have been marketed OTC for 40 years.

The agency has reviewed the two studies submitted to support the comment's request to place 1 percent phenylephrine hydrochloride in Category I for OTC use as a topical nasal decongestant. The results of the studies showed no significant difference in effectiveness between 0.5 and 1 percent concentrations of phenylephrine hydrochloride. Nasal irritation and side effects such as headache, nausea, dizziness, nasal edema, and erythema occurred with both 0.5 and 1 percent concentrations; but the differences in side effects between the two groups were not statistically significant. However, the data did suggest that the 1-percent concentration seemed more likely to induce rebound congestion. Therefore, the agency is proposing that 1 percent phenylephrine hydrochloride be classified in Category I as a topical nasal decongestant and that the product be labeled for adult use only. Additionally, because of a possible rebound effect with continued use of the 1-percent concentration of phenylephrine hydrochloride, the agency is proposing the following warning in § 341.80(c)(2)(v) for the 1-percent concentration of phenylephrine hydrochloride. "Frequent use of this product may cause nasal congestion to recur or worsen."

The agency's detailed comments and evaluation on the data are on file in the Dockets Management Branch (Ref. 2).

Reference

(1) Comment No. C0125, Docket No. 76N-0052, Dockets Management Branch.

(2) Letter from W.E. Gilbertson, FDA, to E.J. Hiross, Sterling Drug, Inc., coded LET081, Docket No. 76N-052N, Dockets Management Branch.

18. Several comments agreed with the Panel's recommendation to make 60 mg pseudoephedrine preparations available on an OTC basis. (Previously, oral nasal decongestants containing 60 mg pseudoephedrine were available only on a prescription basis. Preparations containing 30 mg pseudoephedrine have been available on an OTC basis for many years.) However, two of the comments expressed concern over the 24-hour dosage limit of 360 mg for pseudoephedrine preparations recommended by the Panel. Both of these comments recommended a dosage of 60 mg pseudoephedrine every 4 to 6 hours for a maximum of 240 mg per 24 hours rather than the 60 mg every 4 hours not to exceed a maximum of 360 mg in 24 hours recommended by the Panel. Because the maximum daily dose for the prescription 60-mg pseudoephedrine preparations was 240 mg per 24 hours, the comments argued that it does not seem reasonable to recommend a 360-mg maximum daily dose for OTC pseudoephedrine preparations.

One of the comments submitted data on the pharmacokinetics of pseudoephedrine, indicating that a 240-mg maximum dose per 24 hours may be a more appropriate dose for OTC use of 60-mg pseudoephedrine preparations (Ref. 1). In addition, information was submitted from a study showing that increasing the 24-hour dosage to 360 mg did not present a clinical advantage. The comment concluded that the risk-to-benefit ratio favors limiting the dosage to 240 mg per day.

The agency concluded from these comments and data that a dosage of 60 mg of pseudoephedrine every 4 hours might lead to accumulation of the drug and eventually marked side effects, and that a daily dosage in excess of 240 mg might be associated with significant side effects without additional therapeutic benefit. Therefore, the agency published a notice in the **Federal Register** of September 30, 1980 (45 FR 64709) changing the dosage of pseudoephedrine to 60 mg every 6 hours with a maximum 24-hour dose of 240 mg.

Three drug manufacturers subsequently submitted a petition containing new data to prove that if a 240-mg/24-hour limit is observed, a dosing interval of every 6 hours confers no added safety benefit relative to a more flexible interval of every 4 to 6 hours (Ref. 2). The petition included information on the pharmacokinetic behavior of pseudoephedrine, a review of adverse drug reactions related to pseudoephedrine, and eight studies (Refs. 3 through 10). The companies supported reduction of the maximum adult dosage of pseudoephedrine from 360 to 240 mg in 24 hours, but requested that the agency adopt a dosage interval of 60 mg every 4 to 6 hours. The petitioners also requested an extension of the May 1, 1981 effective data for compliance with the revised dosage limitations that had been set forth in the September 30, 1980 notice. In the **Federal Register** of May 5, 1981 (46 FR 25144), the agency stayed until further notice the May 1, 1981 effective date for the revised dosage interval of 60 mg every 6 hours until the new data had been reviewed. The requirement for revised labeling reflecting the maximum daily OTC dosage of 240 mg for adults and corresponding maximum daily OTC dosages for children was not stayed, but became effective on May 1, 1981.

The agency has determined that the pharmacokinetic data show that the major determinant of the half-life of pseudoephedrine is urinary pH and that the half-life varies from 4 to 8 hours in normal individuals who are representative of the population at large. The agency notes that only two of the eight studies are relevant to the issue of whether the frequency of administration of pseudoephedrine is a factor in the incidence of side effects (Refs. 3 and 4). The Kuntzman study (Ref. 3) demonstrates the influence of urinary pH on the half-life of pseudoephedrine. When urinary pH is decreased, plasma half-life of pseudoephedrine is decreased markedly. In contrast, when urinary pH is increased, plasma half-life increases. The Brater study (Ref. 4)

confirms Kuntzman's findings. After reviewing the new data, the agency finds that there is sufficient evidence to show the efficacy of a total daily dose of 240 mg of pseudoephedrine and that it is reasonable to project similar plasma levels, whether this total daily dose is given as 60 mg every 4 to 6 hours or as 60 mg every 6 hours. The agency, therefore, agrees with the comment that a more flexible adult dosage schedule for pseudoephedrine of 60 mg every 4 to 6 hours, not to exceed 240 mg daily, should be permitted. The dosage and directions for use of pseudoephedrine in § 341.80(d) (1) (ii) of the tentative final monograph will reflect this proposed revision. The dosages for children will also reflect the proposed change in dosage interval. The agency's comments on the data are on file in the Dockets Management Branch (Ref. 11).

References

(1) Comment No. C0112, Docket No., 76N–0052, Dockets Management Branch.

(2) Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(3) Kuntzman, R.G., et at., "The influence of urinary pH on the plasma half-life of pseudoephedrine in man and dog and a sensitive assay for its determination in human plasma," *Clinical Pharmacology and Therapeutics*, 12:62–67, 1971, in Citizen Petition, Docket No. 76N–052N, Dockets Managment Branch.

(4) Brater, D.C., et al., "Renal excretion of pseudophedrine," *Clinical Pharmacology and Therapeutics*, 28:690–694, 1980, in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(5) Roth, R.P., et al., "Nasal Decongestant Activity of Pseudoephedrine," *Annals of Otology, Rhinology and Laryngology*, 86:235–242, 1977, in Citizen Petition, Docket No. 76N–052N, Dockets Managmeent Branch.

(6) Yacobi, A., et al., "Evaluation of Sustained-Action Chlorpheniramine-Pseudoephedrine Dosage Forms in Humans," *Journal of Pharmaceutical Sciences*, 69:1077–1081, 1980, in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(7) Bright, T.P., et al., "Selected Cardiac and Metabolic Responses to Pseudoephedrine with Exercise," draft of unpublished study from Dow Chemical Co., in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(8) Empey, D.W., et al., "Dose-Response Study of the Nasal Decongestant and Cardiovascular Effects of Pseudoephedrine," *British Journal of Clinical Pharmacology*, 9:351–358, 1980, in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch

(9) Bye, Co., et al., "A Comparison of Plasma Levels of L (+) Pseudoephedrine Following Different Formulations, and their Relation to Cardiovascular and Subjective Effects in Man," *European Journal of Clinical Pharmacology*, 8:47–53, 1975, in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(10) Perkins, J.G., "A Bioavailability and Safety Study Comparing Actifed® Sustained-Action (SA) Capsules to Actifed Immediate-Release (IR) Tablets," *Current Therapeutic Research*, 28:650–668, 1980, in Citizen Petition, Docket No. 76N–052N, Dockets Management Branch.

(11) Letters from W.E. Gilbertson, FDA, to K.V. Crean, Buroughs-Wellcome Co., A.S. Davidson, Schering Corp., and R.L. Selman, Dow Chemical Co., coded LET077, LET078, and LET079, Docket No. 76N–052N, Dockets Management Branch.

19. One comment suggested deleting from § 341.20(c), § 341.20(d)(2), and § 341.20(h) of the Panel's recommendations the provision that topical nasal decongestant drug products containing oxymetazoline hydrochloride, phenylephrine hydrochloride, or xylometazoline hydrochloride, when administered to children 2 to under 6 years of age, should be used only in the form of nose drops and not in the form of nasal sprays. The comment stated that the Panel based this provision on the contention that a spray is difficult to use in a small nostril. The comment argued that while there may be a problem if the same nosepiece is used for both adult's and children's sprays, this problem could be resolved by using a nosepiece especially designed for the smaller nostril of children 2 to 6 years of age.

As noted in the comment, the only reason given in the Panel's report for not permitting the use of nasal decongestant sprays in children 2 to under 6 years of age is that "the spray is difficult to use in the small nostril" (41 FR 38420). The agency agrees with the comment that manufacturers should be permitted to modify the nosepiece of a nasal decongestant spray so that it can be used in a small nostril. The agency also believes that the use of a nasal spray in certain instances may be easier and more acceptable than the use of drops, especially when the obvious problems of administering drops to children in the 2- to under 6-year age range are taken into consideration.

Nasal decongestant ingredients such as phenylephrine hydrochloride have been marketed OTC for use in children in a nasal spray dosage form for many years without reports of significant adverse reactions directly attributable to the use of the spray (Ref. 1) However, the agency has concluded that oxymetazoline hydrochloride and xylometazoline hydrochloride should not be used in children under 6 years of age in any dosage form. These drugs are long-acting, potent vasoconstrictors and can cause side effects. It is often difficult to measure a correct dose of a topical nasal decongestant in a small child, and the child may inadvertently receive an excessive dose by swallowing the administered medication. Therefore, the agency believes that in the interest of safety, oxymetazoline hydrochloride and xylometazoline hydrochloride should not be used in children under 6 years of age unless directed by a doctor. (See comment 29 below.) The statement recommended by the Panel in § 341.20(c), (d)(2), and (h) "Only drops should be used in children 2 to under 6 years since the spray is difficult to use in the small nostril" will not be included in this tentative final monograph. The agency is proposing that the dosage instruction for the use of oxymetazoline hydrochloride and xylometazoline hydrochloride in children under 6 years of age be deleted from § 341.20 (c) and (h) and placed in professional labeling in § 341.90 (m) and (n). The directions for phenylephrine hydrochloride in § 341.80(d)(2)(v)(*4*) of this tentative final monograph have been revised to include the use of drops or sprays for children 2 to under 6 years of age.

Additionally, the Panel did not address topical nasal decongestants in a jelly dosage form, although these products are presently marketed. The agency has concluded that a jelly should not be used in children under 6 years of age. A jelly must be placed in the nose and then inhaled well back into the nasal passages. The small nostril of a child under 6 years of age could make insertion of a proper amount of nasal decongestant jelly very difficult, and a safe or effective dose may not be achieved. Other topical dosage forms, such as sprays or drops would be more acceptable for use by a child under 6 years of age. Therefore, for children under 6 years of age, the agency is restricting the use of any topical nasal decongestant formulated as a jelly unless directed by a doctor. This restriction has been added to the appropriate "Directions" sections of the monograph.

Reference

(1) Department of Health and Human Services, Food and Drug Administration, "Annual Adverse Reaction Summary Listing," pertinent pages for the years 1969 through 1981, in OTC Volume 04NTFM, Docket No. 76N–052N, Dockets Management Branch.

E. Comments on OTC Nasal Decongestant Labeling and Warnings

20. One comment urged that every manufacturer of a nasal decongestant drug product be required to label the product as a "nasal decongestant" instead of as a "decongestant" as many such products are labeled. Also, the comment pointed out that the consumer

often mistakenly thinks that decongestant means expectorant and therefore may self-medicate with the wrong drug.

The agency agrees that a nasal decongestant drug product should be clearly labeled as such instead of simply as a "decongestant". Under § 341.80(a) of this tentative final monograph, nasal decongestant drug products would be required to use the term "nasal decongestant" as the statement of identity.

21. Several comments pointed out that OTC drug products containing oral nasal decongestants may be labeled and marketed for use only in pediatric populations. The comments argued that the warning statement proposed by the Panel, i.e., "Do not take this product if you are presently taking a prescription antihypertensive or antidepressant drug containing a monoamine oxidase inhibitor . . .," applies only to adults and should not be required on products labeled strictly for use in children. The comments recommended that an exempting statement should be added to the monograph under § 341.50(c) stating, "Warnings which are inappropriate for children's products may be eliminated in the labeling of products containing dosage instructions for children only."

The agency does not agree that the drug interaction precaution recommended by the Panel in § 341.80(b)(2)(iv) concerning prescription antihypertensives and antidepressants containing a monoamine oxidase inhibitor should be deleted from the labeling of pediatric products. Hypertension and depression do occur in children (Refs. 1, 2, and 3). Pediatric dosages for antihypertensives are provided in a widely recognized pediatric text; however, antidepressants containing a monoamine oxidase inhibitor are not widely accepted for pediatric use and pediatric dose ranges have not been established (Refs. 4 and 5). Nevertheless, a physician might prescribe either of these drugs for children. Accordingly, this drug interaction warning will be required in the labeling of all oral nasal decongestants. (Note: The agency is proposing to simplify this warning statement, which will appear in this document as § 341.80(c)(1)(i)(*d*), to read as follows: "*Drug interaction precaution.* Do not take this product if you are presently taking a prescription drug for high blood pressure or depression, without first consulting your doctor." (See comment 22 below.))

The agency is not adding an exempting statement to the monograph as suggested by the comment. However, a portion of one warning concerning "difficuly in urination due to enlargement of the prostate gland" has been deleted for products labeled for use in children only (see comment 13 above). Additionally, warnings for products which are labeled specifically for children 2 to under 12 years of age have been reworded to reflect the administration of the products by adults rather than self administration. Warnings for products which are labeled for both adults and children have also been proposed in the tentative final monograph.

References

(1) Loggie, J.M.H., "Hypertension," *in* "Textbook of Pediatrics," edited by W.E. Nelson, 11th Ed., W.B. Saunders Co., Philadelphia, pp. 1353–1361, 1979.

(2) Forman, M.A., W.H. Hetznecker, and J.M. Dunn, "Psychopharmacology," *in* "Textbook of Pediatrics," edited by W.E. Nelson, 11th Ed., W.B. Saunders Co., Philadelphia, pp. 93–95, 1979.

(3) Etteldorf, J.N., "Noninfectious Disorders of the Urinary System," *in* "Pediatric Therapy," 4th Ed., edited by H.C. Shirkey, C.V. Mosby Co., St. Louis, pp. 722–725, 1972.

(4) Shirkey, H.C., "Table of Drugs," *in* "Pediatric Therapy," 4th Ed., edited by H.C. Shirkey, C.V. Mosby Co., St. Louis, pp. 1150–1152, 1972.

(5) Rapoport, J.L., and E. Mikkelsen, "Antidepressants," *in* "Pediatric Psychopharmacology: The Use of Behavior Modifying Drugs in Children," edited by J.S. Werry, Brunner/Mazel, New York, pp. 208–233, 1978.

22. Two comments suggested that the Panel's recommended drug interaction precaution for oral nasal decongestant drug products should be deleted from § 341.80(b)(2)(iv) of the monograph. This precaution is "Do not take this product if you are presently taking a prescription antihypertensive or antidepressant drug containing a monoamine oxidase inhibitor except under the advice and supervision of a physician." One comment argued that terms such as "antihypertensive," "antidepressant," and "monoamine oxidase inhibitor" are highly technical; that only a small percentage of the population is likely to understand this warning; and that including such a warning in the labeling of an OTC drug is contrary to the well-established principle that unnecessary or confusing precautions tend to dilute the significance of all instructions in the labeling and, hence, should be avoided. The other comment contended that it is the responsibility of the physician to instruct each patient who is taking a monoamine oxidase inhibitor on the proper means of avoiding the possible adverse reactions that can be associated with the use of this type of drug.

The agency agrees with the comment that the Panel's proposed drug interaction precaution may not be readily understood by all consumers. However, it considers a warning of this type necessary to alert consumers because antihypertensive and antidepressant drugs are widely prescribed. To simplify this precautionary statement the agency is proposing to substitute the term "high blood pressure" for the term "antihypertensive" and the term "depression" for "antidepressant." The agency also believes that the words "monoamine oxidase inhibitor" would be confusing to consumers and need not be included in the precautionary statement to convey the intended message. Accordingly, § 341.80(b)(2)(iv) (redesignated in this tentative final monograph as § 341.80(c)(1)(i)(*d*)) will be amended to read as follows: "*Drug interaction precaution.* Do not take this product if you are presently taking a prescription drug for high blood pressure or depression, without first consulting your doctor."

23. Two comments stated that the claim "relieves sinus pressure" should be in Category I rather than in Category III. One comment (Ref. 1) submitted the results of a survey conducted among sinus headache sufferers who were asked about the nature of their symptoms, i.e., whether facial pressure and/or facial congestion were present. Of 428 respondents who mentioned facial pressure 65.9 percent also mentioned facial congestion; of 380 respondents who mentioned facial congestion, 74.2 percent also mentioned facial pressure; and 704 (72.5 percent) of 971 patients taking medication to relieve the congestion of sinus headache also expected it to relieve sinus pressure. The comment concluded that consumers use the term "pressure" synonymously with "congestion." The second comment stated that the Panel's recommendations are conflicting because the Panel placed in Category I those claims relating to the relief of congestion and the promotion of sinus drainage. However, claims relating to relief of sinus pressure were placed in Category III. The comment did not submit any data in support of its position but concluded that it is a simple fact that relief of congestion and promotion of sinus drainage will relieve sinus pressure.

The agency has reviewed the survey data, including a statistical evaluation (Ref. 1), to determine whether the data support the comment's contention that "congestion" and "pressure" are synonymous terms to consumers. The details of the survey are insufficient to

support any definitive conclusions. However, it seems likely that the terms "sinus pressure" and "sinus congestion" are closely associated in the minds of consumers. "Webster's New Collegiate Dictionary" (Ref. 2) defines "pressure" as "the application of force to something by something else in direct contact with it." "Congestion" is defined as "[concentration] in a small or narrow space" (Ref. 3). "Congestion" is also defined as "excessive or abnormal accumulation of blood in a part" (Ref. 4). Using these definitions, it would follow that congestion is logically thought to be the cause of pressure. If an area (e.g., the sinuses) is congested, then whatever is causing the congestion is likely to exert pressure on the boundaries of the area. It would then follow that if congestion were relieved, pressure would be relieved also. Therefore, the agency has decided to expand the Category I indications for nasal decongestants proposed by the Panel in § 341.80(a)(9) and (10) (redesignated as § 341.80(b)(2) (iv) and (v) in this tentative final monograph). The revised indications will read as follows:

(iv) "Helps decongest sinus openings and passages; relieves sinus pressure."

(v) "Promotes nasal and/or sinus drainage; relieves sinus pressure."

References

(1) Comment No. C0056, Docket No. 76N-0052, Dockets Management Branch.

(2) "Webster's New Collegiate Dictionary," G.&C. Merriam Co., Springfield, MA, 1979, s.v. "pressure."

(3) "Webster's New Collegiate Dictionary," G.&C. Merriam Co., Springfield, MA, 1979, s.v. "congestion."

(4) "Dorland's Illustrated Medical Dictionary," 25th Ed., W.B. Saunders Co., Philadelphia, 1974, s.v. "congestion."

24. Several comments objected to the Panel's recommended warning in § 341.80(b)(ii) for topical nasal decongestants: "Do not use this product for more than 3 days . . . ." The comments contended that rebound congestion does not begin to appear until more than 7 days after starting use, that the basis for the warning is the assumption that the product will not be used according to label directions, and that the Panel cited no data to support the 3-day limitation. The comments added that "AMA Drug Evaluations" (Ref. 1) states that nasal decongestants should be used for periods not exceeding 10 to 15 days. One comment recommended that the warning be changed to limit use to no more than 10 days, and the other comments requested deletion of the warning entirely.

The agency disagrees with the comments. The comments have not submitted any data which prove that rebound congestion does not appear until after more than 7 days of use. Furthermore, individuals may respond differently to nasal congestion (Ref. 2). An individual's psychological state can affect the occurrence and degree of rebound congestion (Ref. 3 and 4).

The Panel reviewed several references (Refs. 3, 5, and 6) which provided a basis for the 3-day warning. Messek (Ref. 5) reported the occurrence of rebound congestion 90 to 120 minutes after the use of a nasal decongestant. Another nasal decongestant produced rebound congestion 6 hours after use. Rudiger (Ref. 3) reported rebound congestion approximately 4 hours after use. Biesalski (Ref. 6) found that a nasal decongestant caused rebound congestion after 5 hours. These data show that nasal decongestants can produce rebound congestion after a short period of use. Therefore, it cannot be categorically stated that rebound congestion does not begin to appear until more than 7 days after starting use of a nasal decongestant as one comment contended.

The Panel recognized that "because of the remarkable degree of nasal decongestion which follows topical application of these agents, there is a tendency on the part of patients to administer nasal decongestants too frequently and for too long a period of time." Prolonged use of topical nasal decongestants may be accompanied by a rebound phenomenon in which the initial vasoconstriction is followed by vasodilation and congestion. Thus, continued use can intensify nasal congestion. Because of the nasal congestion caused by the rebound effect, there is a tendency for an individual to habitually use a nasal decongestant. Therefore, the Panel concluded that a warning to discourage use beyond several days is necessary. The Panel reviewed references concerning persistent nasal congestion caused by the habitual use of nasal decongestants for varying periods of time, ranging from 6 to 23 months (Refs. 7 and 8). Because of the Panel's concern about the problem of rebound congestion leading to prolonged usage of nasal decongestants, it recommended a 3-day limitation on the use of these products. In addition, in order to further curb the continuous use of topical nasal decongestants, the Panel recommended that a physician be seen if symptoms persist for more than 3 days.

The agency concludes that the 3-day warning is justified in view of the above discussion. Therefore, the 3-day warning in § 341.80(b)(1)(ii) (redesignated as § 341.80(c)(2) (iii)(*a*) and (vi)) is appropriate for topical nasal decongestants except 1-desoxyephedrine which has a 7-day limit (see comment 8 above.) In addition, the agency has revised the format of the "Warnings" section in § 341.80(b) (redesignated as § 341.80(c) is this tentative final monograph) for clarity and to conform to the format of recently published monographs.

References

(1) "AMA Drug Evaluations," 2d Ed., Publishing Sciences Group, Acton, MA, p. 469, 1973.

(2) Harris, H.H., "Comparative Study of Decongestive Effectiveness of Oxymetazoline Hydrochloride in Rhinitis," *EENT Digest*, 46:41–43, 1967.

(3) Rudiger, W., "Investigations of the passability of air through the nose under the effect of a new vasoconstricting agent," (English translation), ("Ensaios sobre a permeabilidade nasal ao ar com o em prego de nova substancia vasoconstritora"), *HNO Wegweiser*, 7:77–80, 1958.

(4) Connell, J.T., "Effectiveness of Topical Nasal Decongestants," *Annals of Allergy*, 27:541–546, 1969.

(5) Messek, H., "The Effect of Different Vasoconstrictors on Various Qualities of the Nasal Mucosa," (English translation), ("Die Wirkung verschiedener Vasokonstriktoria auf einige Qualitaten der Nasenschleimhaut"), *Monatsschrift fur Ohrenheilkunde und Laryngo-Rhinologie*, 96:294–306, 1962.

(6) Biesalski, P., and K. Marquardt, "Treatment of Rhinitis of Early Childhood. Thermoelectric Studies on Decongestant Nasal Drugs," (English translation), "Zur Behandlung der Rhinitis im fruhen Kindesalter. Thermoelektrische Untersuchungen an abschwellenden Nasenmitteln"), *Schweizerische Medizinische Wochenschrift.*, 89:510–512,1959.

(7) Putnam, L.E., and R.P. Herwick, "Privine Dependence of Two Years Duration," *Journal of the American Medical Association*, 130:702–703, 1946.

(8) Thomas, J.W., and U. Fabiano, "Privine Sensitivity: A Report of Eight Cases," *Southern Medical Journal*, 39:658–664, 1946.

25. One comment proposed that the Panel's recommended warning statement for topical nasal decongestants in § 341.80(b)(1)(i) "Do not exceed recommended dosage because symptoms may occur such as burning, stinging, sneezing, or increase of nasal discharge" be required only if the active ingredient is administered topically as a drop or spray directly to the nasal mucosa. The comment contended that requiring this warning for other dosage forms is unnecessary and is not supported by available data.

The agency disagrees with the comment's contention that this warning is unnecessary for dosage forms other than those administered topically as a drop or spray. Topical nasal decongestants may be administered as

drops, sprays, jellies, or inhaled vapors. The comment did not specify which other dosage forms should not be required to be labeled with the warning recommended by the Panel § 341.80(b)(1)(i); nor did the comment submit any data to show that this warning statement is unnecessary for other dosage forms of topical nasal decongestants.

The agency believes that this warning statement should apply to all topical nasal decongestant active ingredients administered as a drop, spray, jelly, or in an inhalant dosage form. Evaluation of the studies reviewed by Panel on propylhexedrine reveals that slight stinging occurred in some cases (41 FR 38402). Because nasal decongestants when used in all of these forms, i.e., drops, sprays, inhalants, and jellies, are administered to the nasal mucosa through the nostrils, the warning statement regarding burning, stinging, sneezing, or increase in nasal discharge is appropriate on these dosage forms. Therefore, the comment is not accepted. This warning, which has been revised to read: "Do not exceed recommended dosage because burning, stinging, sneezing, or increase of nasal discharge may occur," will be required for all dosage forms of topical nasal decongestants.

26. One comment suggested that the Panel's recommended warning statement for topical nasal decongestants in § 341.80(b)(1)(ii) "Do not use this product for more than 3 days. If symptoms persist, consult a physician," should apply only if the nasal decongestant is administered topically as a drop or spray. The comment also recommended that other forms to topical administration, such as via a "lozenge or mouthwash," should appropriately use the "7-day warning" recommended by the Panel for oral nasal decongestants in § 341.80(b)(2)(ii).

The agency agrees with the Panel that topical nasal decongestants administered as a drop or spray should not be used for more than 3 days because rebound congestion is likely to occur with prolonged use. Nasal decongestants in lozenges and mouthwashes are considered to be topical nasal decongestants; however, their route of administration is different from that of ingredients administered in a drop or spray. Lozenges and mouthwashes introduce the nasal decongestant through the oral cavity and the nasopharynx. Because of this difference in routes of administration, topical nasal decongestants in lozenges and mouthwashes are unlikely to cause rebound congestion. The Panel recommended the camphor, thymol, menthol/peppermint oil, and eucalyptol/eucalptus oil be used as topical nasal decongestants in lozenges and mouthwashes. The Panel's review of these active ingredients indicates that rebound congestion does not occur with these ingredients. The ingredients in the lozenges and mouthwashes are of a different pharmacologic group from those in topical nasal decongestants administered in drop or spray dosage forms. In view of this, it would be reasonable to conclude that use of the nasal decongestants recommended by the Panel for use in lozenges and mouthwashes for a longer period than 3 days would not result in rebound congestion.

The agency concludes that, although nasal decongestants in lozenges and mouthwashes are considered to be topically administered, the specific warning statement concerning 3-day use should not apply in the labeling of these specific topical nasal decongestants and agrees with the comment that it may be more appropriate to require the use of the "7-day warning" as stated in § 341.80(b)(2)(ii) (redesignated as § 341.80(c)(1)(*b*) in this document). The agency points out that none of the ingredients listed above are included in the tentative final monograph; hence, no revisions are currently needed in the Panel's recommended monograph.

27. One comment suggested that the Panel's recommended warning statement in § 341.80(b)(1)(iii) "The use of this dispenser by more than one person may spread infection" be required only for products administered by inhalers and not for nasal decongestants administered by other routes of administration.

The Panel pointed out that the use of a dispenser by more than one person may spread infection. The comment did not specify the other routes of administration of nasal decongestants. A nasal decongestant drug may also be administered by direct application into the nostrils in the form of a drop, spray, or nasal jelly. The use of a dropper, nasal spray, or nasal jelly applicator by more than one person may also result in the spread of infection. Therefore, the agency disagrees with the comment's recommendation that the warning should be required for inhalant nasal decongestants only and concludes that this warning statement should be required in the labeling for all topical nasal decongestant products which are directly applied to the nasal mucosa or directly inhaled through the nostrils. The agency has slightly revised the Panel's warning to make it more readily understood by consumers. The warning in § 341.80(c)(2)(i)(*b*) in this tentative final monograph reads as follows: "The use of this container by more than one person may spread infection."

28. One comment stated that the Panel's recommended labeling for xylometazoline hydrochloride contains special warnings related to the use of adult and pediatric concentrations of the drug, while no special warnings are suggested for the different concentrations of oxymetazoline hydrochloride. The comment argued that the labeling requirements for similar ingredients should be standard and requested that the additional warning statements be removed from the labeling for xylometazoline hydrochloride.

The comment refers to the warning recommended by the Panel in § 341.80(b)(10) for 0.05 percent zylometazoline hydrochloride which states, "Do not give this product to children under 2 years except under the advice and supervision of a physician," and the warning in § 341.80(b)(11) for 0.1 percent xylometazoline hydrochloride which states, "For adult use only. Do not give this product to children under 12 years except under the advice and supervision of a physician." The comment argued that similar warnings were not recommended by the Panel for oxymetazoline hydrochloride.

The agency has reviewed the literature for oxymetazoline hydrochloride and xylometazoline hydrochloride used as topical nasal decongestants. Oxymetazoline hydrochloride and xylometazoline hydrochloride are vasoconstrictors which may cause side effects. They also have a longer duration of action than the other Category I topical nasal decongestants. In a small child it is difficult to measure a correct dose and the child may inadvertently receive an excessive dose by swallowing the administered medication. Because these drugs are potent, long-acting, and the possibility of systemic effects exists, the agency believes that, in the interest of safety, oxymetazoline hydrochloride and xylometazoline hydrochloride should not be used in children under 6 years of age unless directed by a doctor. Therefore, the agency is restricting the use of both xylometazoline and oxymetazoline in children under 6 years of age. The agency is proposing that labeling for the use of oxymetazoline hydrochloride and xylometazoline hydrochloride in children under 6 years of age be provided to health professionals, but not to the general public. Thus, the Panel's recommended dosage instructions for oxymetazoline

hydrochloride and xylometazoline hydrochloride for children under 6 years of age in § 341.20 (c) and (h) have been deleted and moved to professional labeling in § 341.90 (m) and (n). The Panel's recommended warnings in § 341.80 (b) (3)(ii), (4), (5), first part of (6), and (7) through (11), have been revised in order to conform to the format of recently published tentative final monographs. These warnings have been moved from § 341.80(b) and included as directions in new § 341.80(d). Therefore, although the agency is deleting the warning regarding children's dosages for 0.05 percent xylometazoline from general OTC labeling, the directions for 0.05 percent oxymetazoline and 0.05 percent xylometazoline will state that the product is for use by adults and children 6 to under 12 years of age and that for use in children under 6 years of age a doctor should be consulted.

Regarding the comment's request for deletion of the Panel's recommended warning in § 341.80(b)(11) dealing with the 0.01-percent concentration of xylometazoline, the agency concludes that, based on the Panel's recommended concentrations, which the agency has adopted in this tenative final monograph, there is a need for a statement on products containing 0.1 percent xylometazoline against use by children under 12 years of age (because the 0.05 percent concentration is to be used in this age group). Thus, although the warning in § 341.80(b)(11) has been removed from the warnings section, as noted above, the content of the warning has been retained and restated as directions in new § 341.80(d)(2)(vii) (*a*)(*1*) and (*b*)(*1*). There is, however, no need for such a statement on products containing oxymetazoline because the same strength solution (0.05 percent) is used for both adults and children 6 to under 12 years of age; there is no 0.1 percent concentration of oxymetazoline proposed for inclusion in the monograph.

29. One comment was opposed to the Panel's recommended warning for inhalant nasal decongestant products in § 341.80(b)(3)(v): "*Caution:* Not for use by mouth." The comment stated that use by mouth is not a normal or expected use of this dosage form and that the directions for use clearly indicate that the product is to be used intranasally. The comment further stated that the company's records show no evidence of inadvertent misuse in this way due to lack of understanding. The comment believed that this warning, rather than providing needed instruction, actually has a potential for inciting possible abuse by stimulating the imagination. The comment recommended that this warning not be required for inhalers.

The agency agrees with the comment's recommendation that the warning in § 341.80(b)(3)(iv), "*Caution:* Not for use by mouth" is not needed for inhalant nasal decongestants. The dosage and directions for propylhexedrine in § 341.80(d)(2)(vi) and the dosage and directions for 1-desoxyephedrine in § 341.80(d)(2)(i) of this tentative final monograph clearly indicate that these inhalants are to be used intranasally. Therefore, the warning recommended by the Panel in § 341.80(b)(3)(iv) for inhalant nasal decongestants will not be included in this tentative final monograph.

30. One comment recommended that the "warning" proposed by the Panel in § 341.80(b)(3)(i) concerning warming nasal decongestant inhalers before use should be deleted or moved to the "Directions" section. The comment expressed the opinion that, based on its extensive consumer experience with inhaler products, this instruction is unnecessary.

The agency agrees that the Panel's recommended warning in § 341.80(b)(3)(i), "This inhaler should be warmed in the hand before use to increase effectiveness," should be deleted. Inhalers are designed to release a safe and effective dose of active drug through vaporization at room temperature. The agency has reviewed the Panel's report, and additional material (Refs. 1, 2, and 3), and can find no scientific or medical data to support the inclusion of this instruction in the monograph. Therefore, the agency has deleted this instruction from § 341.80(b)(3) of the Panel's recommendations.

References

(1) Harvey, S.C., "Sympathomimetic Drugs," *in* "Remington's Pharmaceutical Sciences," 15th Ed., edited by A. Osol et al., Mack Publishing Co., Easton, PA, p. 820, 1975.

(2) Kennon, L., and J.J. Gulesich, "Some Aspects of Inhaler Technology," *Journal of Pharmaceutical Sciences*, 51:278–286, 1972.

(3) Ziment, I., "Respiratory Pharmacology and Therapeutics," W.B. Saunders Co., Philadelphia, p. 327, 1978.

F. Comments on Testing Guidelines

31. Two comments disagreed with the Panel's recommendation that smoking by test subjects should be prohibited 24 hours prior to and during the testing of nasal decongestant drugs. They argued that coryza and hay fever studies have shown that smokers constitute the majority of the target population and that it is therefore practical to attempt to determine the response of smokers to nasal decongestants. The comments also contented that this recommendation would make it more difficult to find suitable test subjects and that studies might become prohibitive in both cost and time. Another potential problem cited in the comments was the possibility that both the psychological effects of smoking withdrawal, e.g., tension and anxiety, as well as the decongestant effect of nasal decongestant drugs might modify the automatic nervous system enough during testing to result in result in studies with biased conclusions. Clinical data and a statistical analysis, which alleged that smoking has no discernible consistent effect on results obtained from testing nasal decongestants, were submitted as part of one of the comments (Ref. 1).

The agency has reviewed the results of these studies. They showed that the effect of the various drugs on the nasal flow rate as well as the clinical symptoms of both hay fever and acute coryza on smokers were frequently quite different from those observed in nonsmokers. The values sometimes differed tenfold, and the direction of the differences was unpredictable. These studies and the statistical analysis indicated that it would be advisable to use both smokers and nonsmokers in clinical trials for nasal decongestants.

The agency reviewed another study on the response of over 500 subjects to nasal decongestants (Ref. 2). The test population included 43 percent smokers. No discernible difference in nasal airway resistence or in subjective assessment of congestion existed when the subjects entered the study. The results of the study showed that the smokers' response to every one of the topical nasal decongestants tested tended to be less than that of the nonsmokers; however, that difference was great enough to be significant in only one group (phenylephrine). The results of this study support the proposal that there should be no curtailment of smoking by subjects participating in nasal decongestant studies. Considering that a significant portion of the target population is made up of smokers, it seems advisable to use both smokers and nonsmokers in clinical trials. Based on the data reviewed, the agency disagrees with the Panel's recommendation that smokers be required to obstain from smoking 24 hours prior to and during participation in the testing of nasal decongestants. An important problem in studying smokers who have abstained from cigarettes for 24 hours is the introduction of anxiety, restlessness, and autonomic responses, which may influence their nasal resistence. As an alternative to the Panel's recommendation, the agency concludes that the results of testing in smokers and nonsmokers should be tabulated separately, analyzed separately, and submitted in this form

by the manufacturer. This procedure would permit analysis of the data to establish if smokers are indeed different from nonsmokers in their response to nasal decongestants.

(Note.—In revising the OTC drug review procedures relating to Category III, published in the **Federal Register** of September 29, 1981 (46 FR 47730), the agency advised that tentative final and final monographs will not include recomended testing guidelines for conditions that industry wishes to upgrade to monograph status. Instead, the agency will meet with industry representatives at their request to discuss testing protocols. The revised procedures also state the time in which test data must be submitted for consideration in developing the final monograph. (See also part II, paragraph A.2 below—Testing of Category II and Category III conditions.))

References

(1) Comment No. C0097, Docket No. 76N–0052, Dockets Management Branch.

(2) Hamilton, L.H., "Report on Response to Nasal Decongestants by Smokers and Nonsmokers," draft of unpublished paper in OTC Volume 040298.

32. One comment contended that the method of substantiating the claim "reduction of sinus pressure" for nasal decongestants, as described in the Panel's report at 41 FR 38414 and 38415, was a pilot approach, not widely used or recognized as a clinical research tool applicable to the documentation of sinus pressure changes, and could not be properly or reproducibly executed. This method involves the insertion of a trocar or needle into the maxillary sinus under topical anesthesia. The comment pointed out that the very act of repeatedly inserting the trocar or needle causes changes in the sinus pressure which makes this method impractical as a tool to substantiate pressure changes due to the nasal decongestant. In addition, the comment opposed the use of this method on moral and ethical grounds because it involved the use of "invasive surgical techniques" in volunteer subjects to obtain clinical research data on OTC drugs and therefore would not receive approval from institutional peer review committees.

The agency agrees with the comment. Further, the agency has determined that the claim "relieves sinus pressure" will be reclassified from Category III to Category I. (See comment 24 above.) Therefore, a discussion of methods to substantiate this claim is unnecessary.

II. The Agency's Tentative Adoption of the Panel's Report

A. Summary of Ingredient Categories and Testing of Category II and Category III Conditions

1. *Summary of ingredient categories.* The agency has reviewed all claimed active ingredients submitted to the Panel, as well as other data and information available at this time, and is proposing to reclassify one nasal decongestant active ingredient from Category III to Category I. For the convenience of the reader, the following table is included as a summary of the categorization of nasal decongestant active ingredients by the Panel and the proposed classification by the agency.

Nasal decongestant active ingredients	Panel	Agency
Beechwood creosote (oral)	III	III
Bornyl acetate (topical)	III	III
Camphor (topical/inhalant)	III	III
Cedar leaf oil (topical)	III	III
1-Desoxyephedrine (inhalant)	III	I
Ephedrine (oral)	III	III
Ephedrine hydrochloride (oral)	III	III
Ephedrine sulfate (oral)	III	III
Racephodrine hydrochloride (oral)	III	III
Ephedrine (topical)	I	I
Ephedrine hydrochloride (topical)	I	I
Ephedrine sulfate (topical)	I	I
Racephedrine hydrochloride (topical)	I	I
Eucalyptol/eucalyptus oil (topical/inhalant).	III	III
Menthol/peppermint oil (topical/inhalant)	III	III
Mustard oil (allylisothiocyanate) (topical/inhalant).	II	II
Naphazoline hydrochloride (topical)	I	I
Oxymetazoline hydrochloride (topical)	I	I
Phenylephrine hydrochloride (oral)	I	I
Phenylephrine hydrochloride (topical)	I	I
Phenylpropanolamine bitartrate (oral)	I	(1)
Phenylpropanolamins hydrochloride (oral)	I	(1)
Phenylpropanolamine maleate (oral)	I	(1)
Phenylpropanolamine hydrochloride (topical).	III	(1)
Propylhexedrine (inhalant)	I	I
Pseudoephedrine hydrochloride (oral)	I	I
Pseudoephedrine sulfate (oral)	I	I
Thenyldiamine hydrochloride (topical)	III	III
Thymol (inhalant)	III	III
Turpentine oil (spirits of turpentine) (oral)	II	II
Turpentine oil (spirits of turpentine) (topical/inhalant).	III	III
Xylometazoline hydrochloride (topical)	I	I

[1] To be addressed in a future FEDERAL REGISTER document.

2. *Testing of Category II and Category III Conditions.* The Panel recommended testing guidelines for nasal decongestant drug products (41 FR 38376 and 38437). The agency is offering these guidelines as the Panel's recomendations without adopting them or making any formal comment on them. Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any nasal decongestant ingredient or condition included in the review by following the procedures outlined in the agency's policy statement published in the **Federal Register** of September 29, 1981 (46 FR 47740) and clarified April 1, 1983 (48 FR 14050). This policy statement includes procedures for the submission and review of proposed protocols, agency meetings with industry or other interested persons, and agency communications on submitted test data and other information.

B. Summary of the Agency's Changes

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the nasal decongestant section of the Panel's report and recommended monograph with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made by the agency follows.

1. The agency is amending the definitions proposed by the Panel in § 341.3 to include a definition of an "oral nasal decongestant drug" and a "topical nasal decongestant drug."

2. The agency is reclassifying 1-desoxyephedrine as a topical nasal decongestant (administered by a nasal inhaler) from Category III to Category I. Accordingly, this ingredient is included in the tentative final monograph in § 341.20(b)(1). In additon to the required labeling for all topical nasal decongestants, specific labeling requirements for 1-desoxyephedrine is being added in § 341.80(c)(2)(ii), and § 341.80(d)(2) (i) and (viii). (See comment 8 above.)

3. The agency is deleting the dosage instructions for the use of oxymetazoline hydrochloride and xylometazoline hydrochloride in children under 6 years of age that were recommended by the Panel in § 341.20 (c) and (h) and moving these dosage instructions to professional labeling in § 341.90 (m) and (n). The agency concluded that oxymetazoline hydrochloride and xylometazoline hydrochloride should not be used in children under 6 years of age unless directed by a doctor. (See comment 28 above.)

4. The agency is amending the dosage instruction for oxymetazoline hydrochloride that was recommended by the Panel in § 341.20(c) (redesignated as § 341.80(d)(2)(iv) so that the dosage interval of use will be stated in terms of "hours" as follows: "Adults and children 6 to under 12 years of age (with adult supervision): 2 or 3 drops or sprays in each nostril not more often than every 10 to 12 hours. Do not exceed 2 applications in any 24-hour period. Children under 6 years of age: consult a doctor." The Panel had recommended a topical dosage of oxymetazoline hydrochloride of "2 to 3 drops or sprays of a 0.05-percent aqueous solution in each nostril 2 times daily (in the morning and evening)." The recommended dosages for all of the other topical nasal decongestants in the Panel's monograph were stated in terms of "hours." The agency has evaluated data on the use of this drug and concludes that a dosage interval of

every 10 to 12 hours is an appropriate interval for this drug (Ref. 1).

Reference

(1) Mujik, M., and J.M. Van Rossum, "Comparative Pharmacodynamics of Sympathomimetic Imidazolines: Studies on Intestinal Smooth Muscle of the Rabbit and the Cardivascular System of the Cat," *Archives Internationales de Pharamacodynamie et de Therapie*, 155:432-449, 1965.

5. The agency is classifying 1 percent phenylephrine hydrochloride as a Category I topical nasal decongestant. Because the data suggest that the 1-percent concentration is more likely to induce rebound congestion, the agency is proposing the following warning in § 341.80(c)(v) for the 1-percent concentration of phenylephrine hydrochloride: "Frequent use of this product may cause nasal congestion to recur or worsen." (See comment 17 above.)

6. The agency is deleting from the Panel's recommendation in § 341.20(d)(2) the provision that topical nasal decongestant drug products containing phenylephrine hydrochloride when administered to children 2 to under 6 years of age should be used only in the form of nose drops and not in the form of nasal sprays. The dosage instruction for phenylephrine hydrochloride in a 0.125-percent aqueous solution idendified in § 341.80(d)(2)(v)(*a*)(*4*) in the tentative final monograph will now permit the use of drops or sprays for children 2 to under 6 years of age. (See comment 19 above.)

7. Phenylpropanolamine preparations for use as nasal decongestants are not classified in this tentative final monograph. Instead, issues related to the use of phenylpropanolamine in OTC nasal decongestant drug products, as well as in OTC weight control drug products, will be discussed in detail in a separate document to be published in the **Federal Register** in the near future.

8. The agency is deleting the statement regarding propylhexedrine proposed by the Panel in § 341.20(f): "This inhaler should retain effectiveness for a minimum of 2 to 3 months." A modification of that statement and a related statement are now included in new § 341.80(d)(2)(viii), "Other required statements," and are applicable to inhalers containing either 1-desoxyephedrine or propylhexedrine. The new statements are: "This inhaler is effective for a minimum of 3 months after first use," and "Keep inhaler tightly closed." The agency concluded that these statements are important for consumers' information because volatile substances such as 1-desoxyephedrine and propylhexedrine when used in an inhaler becomes less potent upon continued exposure to air. Manufacturers of these products recognize this fact and include such statements on their product labels (Ref. 1).

Reference

(1) Baker, C.E., et al., "Physicians' Desk Reference for Nonprescription Drugs," 3rd Ed., Medical Economics Co., Oradell, NJ, pp. 582, 583, and 659, 1982.

9. The agency is modifying the Panel's recommendations in § 341.20(g) (redesignated as § 341.80(d)(1)(ii)) by providing for a more flexible dosage interval and by reducing the adult oral dosage of pseudoephedrine preparations from 60 mg every 4 hours, not to exceed 360 mg in 24 hours, to 60 mg every 4 to 6 hours not to exceed 240 mg in 24 hours. For children 6 to under 12 years of age, the oral dosage has been reduced from 30 mg every 4 hours, not to exceed 180 mg in 24 hours, to 30 mg every 4 to 6 hours, not to exceed 120 mg in 24 hours. For children 2 to under 6 years of age, the oral dosage has been reduced from 15 mg every 4 hours, not to exceed 90 mg in 24 hours, to 15 mg every 4 to 6 hours, not to exceed 60 mg in 24 hours. (See comment 18 above.)

10. The agency is adding to § 341.80 a "Statement of identity" paragraph (designated as § 341.80(a)) to conform with the format of other recently published advance notices of proposed rulemaking or tentative final monographs. Inclusion of the new paragraph has necessitated a redesignation of § 341.80(a) to § 341.80(b), and § 341.80(b) to § 341.80(c). The agency is also redesignating Subpart D as Subpart C and placing the labeling sections of the monograph in Subpart C.

11. The agency is combining several indications that were required under § 341.80(a) (redesignated as § 341.80(b)). The agency believes that combining these indications presents them to the consumer in a clearer and more concise manner. Therefore, the indications recommended by the Panel in § 341.80(a) (1), (2), and (3) have been revised, combined, and redesignated as § 341.80(b)(1). The Panel's recommended indications in § 341.80(a) (5), (6), and (8) are also being combined, revised, and redesignated as new § 341.80(b)(2) ("Other allowable indications") which provides manufacturers the option to use additional indications in labeling.

12. The agency is reclassifying the claim "relieves sinus pressure" from Category III to Category I. Accordingly, the Category I indications for nasal decongestants recommended by the Panel in § 341.80(a) (9) and (10) (redesignated as § 341.80(b)(2) (iv) and (v)) are being expanded to include this claim in the tentative final monograph as follows:

"(iv) 'Helps decongest sinus openings and passages; relieves sinus pressure.'"

"(v) 'Promotes nasal and/or sinus drainage; relieves sinus pressure.'" (See comment 23 above.)

13. The agency is deleting the Panel's recommendation in § 341.80(a)(11) that claims relating to duration of effect for nasal decongestant products must be substantiated and accompanied by a specific time period. The agency points out that duration of effect has been included in the established dosages and directions for these products by stating the frequency of use (in terms of hours), which indirectly tells the consumer the duration of the products' effects.

14. The agency is deleting the Panel's recommendation for topical nasal decongestants in § 341.80(a)(12) regarding statements related to time to onset of action, such as fast or quick. As with all OTC drug products, nasal decongestants are expected to achieve their intended results within a reasonable period of time. However, the specific period of time within which nasal decongestants achieve these results is not related in a significant way to the safe and effective use of the products. Therefore, terms such as "fast" or "quick" are outside the scope of the OTC drug review. For other classes of products in the OTC drug review, however, statements relating to time of action may properly fall within the list of terms covered by the monograph. (See comment 2 above.)

15. The agency is deleting the Panel's recommendation in § 341.80(a)(13) which refers to claims describing a "cooling sensation" demonstrated by certain topical nasal decongestants. The agency has concluded that it has no objection to the use of terms which describe certain physical and chemical qualities of a drug, as long as these terms do not imply that any therapeutic effect might occur, are true and not misleading, and are distinctly separated from labeling indications. Terms describing product characteristics, e.g., color, odor, flavor, and feel, appear in the labeling for consumers' information and will not be specifically addressed in the monograph.

16. The agency is revising the warnings section proposed by the Panel in § 341.80(b) (redesignated as § 341.80(c)) for clarity by listing the warnings according to ingredient and dosage form (i.e., oral or topical nasal decongestants).

17. The agency is revising the warning recommended by the Panel in § 341.80(b)(1)(i) (redesignated as § 341.80(c)(2)(i)(*a*)) to read as follows: "Do not exceed recommended dosage

because burning, stinging, sneezing, or increase of nasal discharge may occur." (See comment 25 above.)

18. The agency is slightly revising the warning recommended by the Panel in § 341.80(b)(1)(iii) (redesignated as § 341.80(c)(2)(i)(*b*)) to read as follows: "The use of this container by more than one person may spread infection." (See comment 27 above.)

19. The agency is deleting the word "high" (in reference to fever) from the warning for oral nasal decongestants recommended by the Panel in § 341.80(b)(2)(ii) (redesignated as § 341.80(c)(1)(i)(*b*)). Fever can be defined as a body temperature above the normal temperature of 98.6 °F (37 °C). In the same or different disease states, however, fevers may vary significantly. Fever may be low grade, moderate, high, intermittent, or sustained. The particular characteristics of a fever depend on the disease state, and, in many cases, on the stage of development of the disease. The word "high" has been deleted from the warning because the agency believes that it is important for the consumer to recognize the presence of fever, regardless of whether the fever is high or low. Additionally, the Panel's warning in § 341.80(6)(2)(ii) (redesignated as § 341.80(c)(1)(i)(*b*)) is being revised to conform with the format of similar warnings in the tentative final monograph.

20. The agency is amending the warning for oral nasal decongestants recommended by the Panel in § 341.80(b)(2)(iii) (redesignated as § 341.80(c)(1)(i)(*c*)), to include "difficulty in urination." The amended warning will read as follows: "Do not take this product if you have heart disease, high blood pressure, thyroid disease, diabetes or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor." (See comment 13 above.) In addition, the agency has concluded that the warning in new § 341.80(c)(1)(i)(*c*)) for oral nasal decongestants should also apply to all topical nasal decongestants, except topical inhalants. Accordingly, the warning is also being added to this tentative final monograph as § 341.80(c)(2)(iii)(*b*). (See comment 4 above.) (NOTE: For oral and topical nasal decongestant warnings in the monograph, the agency is proposing to use the word "use" to denote topical use, and the word "take" to denote oral use.)

21. The agency is simplifying the warning recommended by the Panel in § 341.80(b)(2)(iv) (redesignated as § 341.80(c)(1)(i)(*d*)) to read as follows: "*Drug interaction precaution.* Do not take this product if you are presently taking a prescription drug for high blood pressure or depression, without first consulting your doctor." (See comment 22 above.)

22. The agency is deleting the warning recommended by the Panel in § 341.80(b)(3)(i) which states: "This inhaler should be warmed in the hand before use to increase effectiveness." The agency found this warning unnecessary because inhalers are designed to release a safe and effective dose of active drug through vaporization at room temperature. (See comment 30 above.)

23. The agency is moving and revising the Panel's recommended warnings in § 341.80(b) (3)(ii), (4), (5), first part of (6), (7), (8), (9) (10), and (11) and including them as part of the directions in the appropriate sections in new § 341.80(d).

24. The agency is moving the warning recommended by the Panel in § 341.80(b)(3)(iii) and is including it as part of the directions. The warning previously stated: "Children should not have unsupervised access to this inhaler." The agency believes that a statement of this should apply not only to inhalers, but also to any topical nasal decongestant product labeled for use in children because of the possibility of adverse reactions occurring from misuse or overuse of these products. Therefore, the phrase "with adult supervision" is being added to the directions for topical nasal decongestants which are labeled for use in children.

25. The agency is deleting the Panel's recommended warning in § 341.80(b)(3)(iv) for inhalant nasal decongestants which states: "*Caution:* Not for use by mouth." The agency has concluded that the directions for use of inhalant nasal decongestants as stated in § 342.80(d)(2) (i) and (vi) in the tentative final monograph clearly indicate that these products are to be used intranasally and not by mouth. (See comment 29 above.)

26. The agency is revising for clarity the warning for 0.05 percent naphazoline hydrochloride recommended by the Panel in § 341.80(b)(8) (redesignated as § 341.80(c)(2)(iv)) to read as follows: "Do not use this product in children under 12 years of age because it may cause sedation if swallowed." (See comment 14 above.)

27. The agency is adding to § 341.80 a "*Directions*" paragraph (designated as § 341.80(d)), to conform with the format of other recently published advance notices of proposed rulemaking and tentative final monographs. To simplify and clarify the labeling, FDA is also slightly modifying the Panel's directions for use.

28. The Panel did not address topical nasal decongestants in a jelly dosage form, although these products are presently marketed. The agency has concluded that a nasal jelly should not be used in children under 6 years of age and therefore this restriction is being added to the appropriate "Directions" sections. (See comment 19 above.)

29. The warning concerning enlargement of the prostate gland in § 341.80(c)(1)(i)(*c*) and § 341.80(c)(2)(iii)(*b*) proposed by the agency in this document for oral and topical nasal decongestants is being modified for products labeled for use only in children. The reference to "enlargement of the prostate gland "is not needed for products labeled for use only in children. The new warning "Do not give this product to children who have heart disease, high blood pressure, thyroid disease, or diabetes unless directed by a doctor," is being added to the tentative final monograph in § 341.80(c)(1)(ii)(*c*) and § 341.80(c)(2)(ix)(*b*). (See comments 13 and 21 above.) Additionally, all warnings for products which are labeled for use only in children 2 to under 12 years of age are being designated in the monograph and reworded to reflect the administration of the products by adults rather than self administration. Warnings for products which are labeled for both adults and children are also being proposed in the tentative final monograph.

30. In an effort to simplify OTC drug labeling, the agency proposed in a number of tentative final monographs to substitute the word "doctor" for "physician" in OTC drug monographs on the basis that the word "doctor" is more commonly used and better understood by consumers. Based on comments received to these proposals, the agency has determined that final monographs and any applicable OTC drug regulations will give manufacturers the option of using either the word "physician" or the word "doctor." This tentative final monograph proposes that option.

The agency proposes to revoke the existing warning and caution statements in § 369.20 for "nasal preparations; oil base," "nasal preparations in plastic spray containers," "nasal preparations; vasoconstrictors," and "phenylephrine hydrochloride preparations, oral" at the time that this monograph becomes effective.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the

Federal Register of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that not one of these rules, including this proposed rule for OTC nasal decongestant drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Pub. L. 96-354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC nasal decongestant drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC nasal decongestant drug products. Types of impact may include, but are limited to, costs associated with product testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC nasal decongestant drug products should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on nasal decongestant drug products, a period of 120 days from the date of publication of this proposed rulemaking in the Federal Register will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has carefully considered the potential environmental effects of this proposal and has concluded that the action will not have a significant impact on the human environment and that an environmental impact statement therefore will not be prepared. The agency's finding of no significant impact, and the evidence supporting this finding, is contained in an environmental assessment (under 21 CFR 25.31, proposed in the Federal Register of December 11, 1979; 44 FR 71741), which may be seen in the Dockets Management Branch, Food and Drug Administration.

List of Subjects in 21 CFR Part 341

OTC drugs: Anticholinergics; Expectorants; Bronchodilators; Antitussives; Nasal decongestants.

On July 9, 1982 at 47 FR 40002, FDA proposed to amend 21 CFR Subchapter B by adding a new Part 341. Proposed Part 341, as amended on October 26, 1982 (47 FR 47520) and October 19, 1983 (48 FR 48576), would be further amended as follows:

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under 21 CFR 5.11 it is proposed to make the following amendments:

PART 341—[AMENDED]

1. In proposed Subpart A, § 341.3 is amended by adding new paragraphs (h) and (i) to read as follows:

§ 341.3 Definitions.

* * * * *

(h) *Oral nasal decongestant drug.* A drug which is taken by mouth and acts systemically to reduce nasal congestion caused by acute or chronic rhinitis.

(i) *Topical nasal decongestant drug.* A drug which when applied topically inside the nose, in the form of drops, jellies, or sprays, or when inhaled intranasally reduces nasal congestion caused by acute or chronic rhinitis.

2. In Subpart B, new § 341.20 is added, to read as follows:

§ 341.20 Nasal decongestant active ingredients.

The active ingredients of the product consist of any of the following when used within the dosage limits and in the dosage forms established for each ingredient in § 341.80(d):

(a) *Oral nasal decongestants.* (1) Phenylephrine hydrochloride.

(2) Pseudoephedrine hydrochloride.

(3) Pseudoephedrine sulfate.

(b) *Topical nasal decongestants.* (1) 1-Desoxyephedrine.

(2) Ephedrine.

(3) Ephedrine hydrochloride.

(4) Ephedrine sulfate.

(5) Racephedrine hydrochloride.

(6) Naphazoline hydrochloride.

(7) Oxymetazoline hydrochloride.

(8) Phenylephrine hydrochloride.

(9) Propylhexedrine.

(10) Xylometazoline hydrochloride.

3. In proposed Subpart C, new § 341.80 is added and § 341.90 is amended by adding new paragraphs (m) and (n) to read as follows:

§ 341.80 Labeling of nasal decongestant drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as a "nasal decongestant."

(b) *Indications.* (1) The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the following phrase: "For the temporary relief of nasal congestion due to the common cold (cold), hay fever" (which may be followed by any of the following: "(allergic rhinitis)," "or other upper respiratory allergies," or "or other upper respiratory allergies (allergic rhinitis,") "or associated with sinusitus."

(2) *Other allowable indications.* In addition to the required information identified in paragraph (b)(1) of this section, the labeling of the product may contain any of the following statements provided such statements are neither placed in direct conjunction with information required to appear in the labeling nor occupy labeling space with greater prominence or conspicousness than the required information.

(i) "For the temporary relief of" (select one of the following: "stuffy nose," "stopped up nose," "nasal stuffiness," or "clogged up nose.")

(ii) (Selected one of the following: "Reduces swelling of," "Decongests," or "Helps clear") "nasal passages; shrinks swollen membranes."

(iii) "Temporarily restores freer breathing through the nose."

(iv) "Helps decongest sinus openings and passages; relieves sinus pressure."

(v) "Promotes nasal and/or sinus drainage; relieves sinus pressure."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) *Oral nasal decongestants*—(i) *For products containing phenylephrine hydrochloride, pseudoephedrine hydrochloride, or pseudoephedrine sulfate identified in § 341.20(a) (1), (2), and (3) when labeled for adults.* (*a*) "Do not exceed recommended dosage because at higher doses nervousness, dizziness, or sleeplessness may occur."

(*b*) "Do not take this product for more than 7 days. If symptoms do not improve or are accompained by fever, consult a doctor."

(c) "Do not take this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor."

(d) "*Drug Interaction Precaution.* Do not take this product if you are presently taking a prescription drug for high blood pressure or depression, without first consulting your doctor."

(ii) *For products containing phenylephrine hydrochloride, pseudoephedrine hydrochloride, or pseudoephedrine sulfate identified in § 341.20(a) (1), (2), and (3) when labeled for children under 12 years of age.* (a) "Do not exceed recommended dosage because at higher doses nervousness, dizziness, or sleeplessness may occur."

(b) "Do not give this product to children for more than 7 days. If symptoms do not improve or are accompained by fever, consult a doctor."

(c) "Do not give this product to children who have heart disease, high blood pressure, thyroid disease, or diabetes, unless directed by a doctor."

(d) "*Drug Interaction Precaution.* Do not give this product to a child who is taking a prescription drug for high blood pressure or depression, without first consulting the child's doctor."

(iii) *For oral nasal decongestant products labeled for both adults and children under 12 years of age.* The labeling of the product contains the warnings identified in paragraph (c)(1)(i) of this section.

(2) *Topical nasal decongestants*—(i) *For products containing any topical nasal decongestant identified in § 341.20(b) when labeled for adults.* (a) "Do not exceed recommended dosage because burning, stinging, sneezing, or increase of nasal discharge may occur."

(b) "The use of this container by more than one person may spread infection."

(ii) *For products containing 1-desoxyephedrine identified in § 341.20(b)(1) when used in an inhalant dosage form and when labeled for adults.* "Do not use this product for more than 7 days. If symptoms persist, consult a doctor."

(iii) *For products containing ephedrine, ephedrine hydrochloride, ephedrine sulfate, racephedrine hydrochloride, naphazoline hydrochloride, oxymetazoline hydrochloride, phenylephrine hydrochloride, or xylometazoline hydrochloride identified in § 341.20(b) (2), (3), (4), (5), (6), (7), (8), and (10) when used as nasal sprays, drops, or jellies and when labeled for adults.* (a) "Do not use this product for more than 3 days. If symptoms persist, consult a doctor."

(b) "Do not use this product if you have heart disease, high blood pressure, thyroid disease, diabetes, or difficulty in urination due to enlargement of the prostate gland unless directed by a doctor."

(iv) *For products containing naphazoline hydrochloride identified in § 341.20(b)(8) at a concentration of 0.05 percent.* "Do not use this product in children under 12 years of age because it may cause sedation if swallowed."

(v) *For products containing phenylephrine hydrochloride identified in § 341.20(b)(8) at a concentration of 1 percent.* "Frequent use of this product may cause nasal congestion to recur or worsen."

(vi) *For products containing propylhexedrine identified in § 341.20(b)(9) when used in an inhalant dosage form and when labeled for adults.* "Do not use this product for more than 3 days. If symptoms persist, consult a doctor."

(vii) *For products containing any topical nasal decongestant identified in § 341.20(b) when labeled for children under 12 years of age.* The labeling of the product contains the warnings identified in paragraph (c)(2)(i) of this section.

(viii) *For products containing 1-desoxyephedrine identified in § 341.20(b)(1) when used in an inhalant dosage form and when labeled for children under 12 years of age.* "Do not use this product for more than 7 days. If symptoms persist, consult a doctor."

(ix) *For products containing ephedrine, ephedrine hydrochloride, ephedrine sulfate, racephedrine hydrochloride, naphazoline hydrochloride, oxymetazoline hydrochloride, phenylephrine hydrochloride, or xylometazoline hydrochloride identified in § 341.20(b) (2), (3), (4), (5), (6), (7), (8), and (10) when used as nasal sprays, drops, or jellies, and when labeled for children under 12 years of age.* (a) "Do not use this product for more than 3 days. If symptoms persist, consult a doctor."

(b) "Do not use this product in children who have heart disease, high blood pressure, thyroid disease, or diabetes unless directed by a doctor."

(x) *For products containing propylhexedrine identified in § 341.20(b)(9) when used in an inhalant dosage form and when labeled for children under 12 years of age.* "Do not use this product for more than 3 days. If symptoms persist, consult a doctor."

(xi) *For topical nasal decongestant products labeled for both adults and for children under 12 years of age.* The labeling of the product contains the applicable warnings identified in paragraphs (c)(2)(i), (ii), (iii), and (vi) of this section.

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) *Oral nasal decongestants*—(i) *For products containing phenylephrine hydrochloride identified in § 341.20(a)(1).* Adults: 10 milligrams every 4 hours not to exceed 60 milligrams in 24 hours. Children 6 to under 12 years of age: 5 milligrams every 4 hours not to exceed 30 milligram in 24 hours. Children 2 to under 6 years of age: 2.5 milligrams every 4 hours not to exceed 15 milligrams in 24 hours. Children under 2 years of age: consult a doctor.

(ii) *For products containing pseudoephedrine hydrochloride or pseudoephedrine sulfate identified in § 341.20(a) (2) and (3).* Adults: 60 milligrams every 4 to 6 hours not to exceed 240 milligrams in 24 hours. Children 6 to under 12 years of age: 30 milligrams every 4 to 6 hours not to exceed 120 milligrams in 24 hours. Children 2 to under 6 years of age: 15 milligrams every 4 to 6 hours not to exceed 60 milligrams in 24 hours. Children under 2 years of age: consult a doctor.

(2) *Topical nasal decongestants*—(i) *For products containing 1-desoxyephedrine identified in § 341.20(b)(1) when used in an inhalant dosage form.* The product delivers in each 800 milliliters of air 0.04 to 0.150 milligrams of 1-desoxyephedrine. Adults: 2 inhalations in each nostril not more often than every 2 hours. Children 6 to under 12 yearas of age (with adult supervision): 1 inhalation in each nostril not more often than every 2 hours. Children under 6 years of age: consult a doctor.

(ii) For products containing ephedrine, ephedrine hydrochloride, ephedrine sulfate, or racephedrine hydrochloride identified in § 341.20(b) (2), (3), (4), and (5)—(a) *Nasal drops or sprays—For a 0.5-percent aqueous solution.* Adults: 2 or 3 drops or sprays in each nostril not more often than every 4 hours. Children 6 to under 12 years of age (with adult supervision): 1 or 2 drops or sprays in each nostril not more often than every 4 hours. Children under 6 years of age: consult a doctor.

(b) *Nasal jelly—For a 0.5-percent water-based jelly.* Adults and children 6 to under 12 years of age (with adult supervision): place a small amount in each nostril and inhale well back into the nasal passages not more often than every 4 hours. Children under 6 years of age: consult a doctor.

(iii) *For products containing naphazoline hydrochloride identified in § 341.20(b)(6)*—(*a*) *Nasal drops or sprays*—(*1*) *For a 0.05-percent aqueous solution.* Adults: 1 or 2 drops or sprays in each nostril not more often than every 6 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.025-percent aqueous solution.* Children 6 to under 12 years of age (with adult supervision): 1 or 2 drops or sprays in each nostril not more often than every 6 hours. Children under 6 years of age: consult a doctor.

(*b*) *Nasal jelly*—(*1*) *For a 0.05 percent water-based jelly.* Adults: place a small amount in each nostril and inhale well back into the nasal passages not more often than every 6 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.025-percent water-based jelly.* Children 6 to under 12 years of age (with adult supervision): place a small amount in each nostril and inhale well back into the nasal passages not more often than every 6 hours. Children under 6 years of age: consult a doctor.

(iv) *For products containing oxymetazoline hydrochloride identified in § 341.20(b)(7)*—(*a*) *Nasal drops or sprays—For a 0.05-percent aqueous solution.* Adults and children 6 to under 12 years of age (with adult supervision): 2 or 3 drops or sprays in each nostril not more often than every 10 to 12 hours. Do not exceed 2 applications in any 24-hour period. Children under 6 years of age: consult a doctor.

(*b*) *Nasal jelly—For a 0.05-percent water-based jelly.* Adults and children 6 to under 12 years of age (with adult supervision): place a small amoun' in each nostril and inhale well back into the nasal passages not more often than every 10 to 12 hours. Do not exceed 2 applications in any 24-hour period. Children under 6 years of age: consult a doctor.

(v) *For products containing phenylephrine hydrochloride identified in § 341.20(b)(8)*—(*a*) *Nasal drops or sprays—(1) For a 1-percent aqueous solution.* Adults: 2 or 3 drops or sprays in each nostril not more often than every 4 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.5-percent aqueous solution.* Adults: 2 or 3 drops or sprays in each nostril not more often than every 4 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*3*) *For a 0.25-percent aqueous solution.* Adults and children 6 to under 12 years of age (with adult supervision): 2 or 3 drops or sprays in each nostril not more often than every 4 hours. Children under 6 years of age: consult a doctor.

(*4*) *For a 0.125-percent aqueous solution.* Children 2 to under 6 years of age (with adult supervision): 2 or 3 drops or sprays in each nostril not more often than every 4 hours. Children under 2 years of age: consult a doctor.

(*b*) *Nasal jelly*—(*1*) *For a 1-percent water-based jelly.* Adults: place a small amount in each nostril and inhale well back into the nasal passages not more often than every 4 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.5-percent water-based jelly.* Adults: place a small amount in each nostril and inhale well back into the nasal passages not more often than every 4 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*3*) *For a 0.25-percent water-based jelly.* Adults and children 6 to under 12 years of age (with adult supervision): place a small amount in each nostril and inhale well back into the nasal passages not more often than every 4 hours. Children under 6 years of age: consult a doctor.

(vi) *For products containing propylhexedrine identified in § 341.20(b)(9) when used in an inhalant dosage form.* The product delivers in each 800 milliliters of air 0.04 to 0.50 milligrams of propylhexedrine. Adults and children 6 to under 12 years of age (with adult supervision): 2 inhalations in each nostril not more often than every 2 hours. Children under 6 years of age: consult a doctor.

(vii) *For products containing xylometazoline hydrochloride identified in § 341.20(b(10)*—(*a*) Nasal drops or sprays—(*1*) *For a 0.1-percent aqueous solution.* Adults: 2 or 3 drops or sprays in each nostril not more often than evey 8 to 10 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.05-percent aqueous solution.* Children 6 to under 12 years of age (with adult supervision): 2 or 3 drops or sprays in each nostril not more often than evey 8 to 10 hours. Children under 6 years of age: consult a doctor.

(*b*) *Nasal jelly*—(*1*) *For a 0.1-percent water-based jelly.* Adults: placed a small amount in each nostril and inhale well back into the nasal passages not more often than every 8 to 10 hours. Do not give to children under 12 years of age unless directed by a doctor.

(*2*) *For a 0.05-percent water-based jelly.* Children 6 to under 12 years of age (with adult supervision): place a small amount in each nostril and inhale well back into the nasal passages not more oftern than evey 8 to 10 hours. Children under 6 years of age: consult a doctor.

(viii) *Other required statements—For products containing 1-desoxyephedrine or propylhexedrine identified in § 341.20(b)(1) or (9) when used in an inhalamt dosage form.*

(*a*) "This inhaler is effective for a minimum of 3 months after first use."

(*b*) "Keep inhaler tightly closed."

(e) The word "physician" may be substituted for the word "doctor" in any of the labeling statements above.

§ 341.90 Professional labeling.

* * * * *

(m) *For products containing oxymetazoline hydrochloride identified in § 341.20(b)(7).* Children 2 to under 6 years of age: 2 or 3 drops of sprays in each nostril of a 0.025-percent aqueous solution not more often than every 10 to 12 hours. Do not exceed 2 applications in any 24-hour period.

(n) *For products containing xylometazoline hydrochloride identified in § 341.20(b)(10).* Children 2 to under 6 years of age: 2 or 3 drops or sprays in each nostril of a 0.05-percent aqueous solution not more often than every 8 to 10 hours.

Interested persons, may, or or before May 15, 1985, submit to the Docket Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the hearing of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

Interested persons, on or before January 15, 1986, may also submit in writing new data demonstrating the safety and effectiveness of those conditions not classified in Category I. Written comments on the new data may be submitted on or before March 17, 1986. These dates are consistent with

the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the Federal Register of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addresed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on March 17, 1986. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the Federal Register unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

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Tuesday
January 15, 1985

Part X

Department of Health and Human Services

Food and Drug Administration

21 CFR Part 357

Poison Treatment Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 357

[Docket No. 81N-0050]

Poison Treatment Drug Products for Over-the-Counter Human Use; Tentative Final Monograph

AGENCY: Food and Drug Administration.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is issuing a notice of proposed rulemaking in the form of a tentative final monograph that would establish conditions under which over-the-counter (OTC) poison treatment drug products are generally recognized as safe and effective and not misbranded. FDA is issuing this notice of proposed rulemaking after considering the reports and recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products and the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, public comments to the advance notices of proposed rulemaking on OTC emetic drug products and OTC drug products for the treatment of acute toxic ingestion that were based on the respective Panels' recommendations, and public comments on the agency's proposed regulation on OTC emetic drug products, which was issued in the form of a tentative final monograph. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments, objections, or requests for oral hearing on the proposed regulation before the Commissioner of Food and Drugs by May 15, 1985. Written comments on the agency's economic impact determination by May 15, 1985.

ADDRESS: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drugs and Biologics (HFN-210), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4960.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of March 21, 1975 (40 FR 12902) FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC laxative, antidiarrheal, emetic,and antiemetic drug products, together with the recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products, which was the advisory review panel responsible for evaluating data on the active ingredients in these drug classes. Interested persons were invited to submit comments by June 19, 1975. Reply comments in response to comments filed in the initial comment period could be submitted by July 19, 1975.

In the **Federal Register** of September 5, 1978 (43 FR 39544), the agency published a proposed rule, in the form of a tentative final monograph, for OTC emetic drug products. Interested persons were invited to file by October 5, 1978 written comments, objections, or requests for oral hearing before the Commissioner of Food and Drugs on the proposed regulation.

In response to the emetic tentative final monograph 16 poison control centers, 18 hospitals, 8 medical schools, 6 state health departments, 5 state pharmaceutical associations, 1 trade association, and 6 individuals submitted comments.

In a notice published in the **Federal Register** of March 21, 1980 (45 FR 18398), the agency advised that it had reopended the administrative record for OTC emetic drug products to allow for consideration of data and information that had been filed in the Dockets Management Branch after the date the administrative record previously had officially closed. The agency concluded that any new data and information filed prior to March 21, 1980 should be available to the agency in developing a proposed regulation in the form of a tentative final monograph.

In the **Federal Register** of January 5, 1982 (47 FR 444.), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC drug products for the treatment of acute toxic ingestion, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, which was the advisory review panel responsible for evaluating data on active ingredients in this drug class. Interested persons were invited to submit comments by April 5, 1982. Reply comments in response to comments filed in the initial comment period could be submitted by May 5, 1982. In response to this advance notice of proposed rulemaking, 3 poison control centers and 3 pharmaceutical companies submitted comments.

In accordance with § 303.10(a)(10), the data and information considered by the Panels and the agency are on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration (address above) after deletion of a small amount of trade secret information. Copies of the comments received are also on public display in the Dockets Management Branch.

There is considerable overlap between in the rulemaking on OTC emetic drug products and the rulemaking on OTC drug products for the treatment of acute toxic ingestion. The intent of both rulemakings is to identify those ingredients that are generally recognized as safe and effective in the treatment of poisonings. Ipecac syrup, the one ingredient included in the rulemaking on emetic drug products, was also included in the rulemaking on OTC drug products for the treatment of acute toxic ingestion. Because of the overlap between the two rulemakings and because of the large number of comments submitted to the emetic tentative final monograph, the agency has decided to combine the two rulemakings and to publish a single tentative final monograph (proposed rule) to establish Subpart A of Part 357 entitled "Poison Treatment Drug Products." Part 337, previously designated for Emetic Drug Products for Over-The-Counter Human Use, will be reserved.

In this tentative final monograph (proposed rule) to establish Subpart A of Part 357 (21 CFR Part 357, Subpart A), FDA states for the first time its position on the establishment of monograph for OTC poison treatment drug products. Final agency action on this matter will occur with the publication at a future date of a final monograph, which will be a final rule establishing a monograph for OTC poison treatment drug products.

This proposal constitute FDA's tentative adoption of the Miscellaneous Internal Panel's conclusions and recommendations on OTC drug products for acute toxic ingestion as modified on the basis of the comments received and the agency's independent evaluation of the Panel's report, and the agency's re-evaluation of the previously published proposed rule on OTC emetic drug products. Modifications have been made for clarity and regulatory accuracy and to reflect new information. Such new information has been placed on file in the Dockets Management Branch (address above). These modifications are reflected in the following summary of the comments and FDA's responses to them. Based on the comments received, the agency has proposed in this tentative final monograph a number of changes in the content and format of the labeling of posion treatment drug products. FDA recognizes that it is

important for the labeling of these products to be very easily and rapidly comprehensible, because the products would almost always be used in an emergency situation. Therefore, the agency invites specific comment on the revised labeling proposed in this tentative final monograph.

The OTC procedural regulations (21 CFR 330.10) have been revised to conform to the decision in *Cutler* v. *Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). (See the **Federal Register** of September 29, 1981; 46 FR 47730.) The court in *Cutler* held that the OTC drug review regulations were unlawful to the extent that they authorized the marketing of Category III drugs after a final monograph had been established. Accordingly, this provision has been deleted from the regulations, which now provide that any testing necessary to resolve the safety or effectiveness issues that formerly resulted in a Category III classification, and submission to FDA of the results of that testing or any other data, must be done during the OCT drug rulemaking process before the establishment of a final monograph.

Although it was not required to do so under *Cutler*, FDA will no longer use the terms "Category I" (generally recognized as safe and effective and not misbranded), "Category II" (not generally recognized as safe and effective or misbranded), and "Category III" (available data are insufficient to classify as safe and effective, and further testing is required) at the final monograph stage, but will use instead the terms "monograph conditions" (old Category I) and "nonmonograph conditions" (old Categories II and III). This document retains the concepts of Categories I, II, and III at the tentative final monograph stage.

The regulations in § 330.10(a)(7)(iii) provide for a 12-month period to submit data and information to support a condition excluded from the monograph in the tentative final order. The only ingredients reviewed and considered for poison treatment, ipecac syrup and activated charcoal, have been placed in Category I and are included in this tentative final monograph. The agency is unaware of any other ingredients that have potential for OTC use in poison treatment drug products. Therefore, the agency believes the usual 12-month period for submission of new data or information is unnecessary in developing a final monograph for OTC poison treatment drug products. Because there is no need for this 12-month period, the time for filing written comments or objections or requesting an oral hearing before the Commissioner following publication of a tentative final monograph (§ 330.10(a)(7)(i)) is 60 days. However, because of the number of OTC drug review documents being published concurrently, the agency is providing 120 days for comments or objections rather than the usual 60 days.

The agency advises that the conditions under which the drug products that are subject to this monograph would be generally recognized as safe and effective and not misbranded (monograph conditions) will be effective 12 months after the date of publication of the final monograph in the **Federal Register**. On or after that date, no OTC drug products that are subject to the monograph and that contain nonmonograph conditions, i.e., conditions that would cause the drug to be not generally recognized as safe and effective or to be misbranded, may be initially introduced or initially delivered for introduction into interstate commerce unless they are the subject of an approved new drug application (NDA). Further, any OTC drug products subject to this monograph that are repackaged or relabeled after the effective date of the monograph must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily with the monograph at the earliest possible date.

In the proposed rulemaking for OTC emetic drug products (published in the **Federal Register** of September 5, 1978 (43 FR 39544)) and in the advance notice of proposed rulemaking for OTC drug products for the treatment of acute toxic ingestion (published in the **Federal Register** of January 5, 1982 (47 FR 444), the agency suggested different effective dates for the final monographs. Experience has shown that relabeling of products covered by the monograph is necessary in order for manufacturers to comply with the monograph. New labels containing the monograph labeling have to be written, ordered, received, and incorporated into the manufacturing process. The agency has determined that it is impractical to expect new labeling to be in effect 30 days after the date of publication of the final monograph. Experience has shown also that if the deadline for relabeling is too short, the agency is burdened with extension requests and related paperwork.

In addition, some products may have to be reformulated to comply with the monograph. Reformulation often involves the need to do stability testing on the new product. An accelerated aging process may be used to test a new formulation; however, if the stability testing is not successful, and if further reformulation is required, there could be a further delay in having a new product available for manufacture.

The agency wishes to establish a reasonable period of time for relabeling and reformulation in order to avoid an unnecessary disruption of the marketplace that could not only result in economic loss, but also interfere with consumers' access to safe and effective drug products. Therefore, the agency is proposing that the final monograph be effective 12 months after the date of its publication in the **Federal Register**. The agency believes that within 12 months after the date of publication most manufacturers can order new labeling and reformulate their products and have them in compliance in the marketplace. However, if the agency determines that any labeling for a condition included in the final monograph should be implemented sooner, a shorter deadline may be established. Similarly, if a safety problem is identified for a particular nonmonograph condition, a shorter deadline may be set for removal of that condition from OTC drug products.

I. The Agency's Tentative Conclusions on the Comments and Objections

A. General Comments

1. One comment urged the agency to recognize explicitly the legal status of the monographs issued under the OTC drug review as being interpretive, as distinguished from substantive, regulations.

The agency addressed this issue in paragraphs 85 through 91 of the preamble of the procedures for classification of OTC drug products, published in the **Federal Register** of May 11, 1972 (37 FR 9464) and in paragraph 3 of the preamble to the tentative final monograph for antacid drug products, published in the **Federal Register** of November 12, 1973 (38 FR 31260). FDA reaffirms the conclusions stated there. Subsequent court decisions have confirmed the agency's authority to issue substantive regulations by rulemaking. See, e.g., *National Nutritional Foods Association* v. *Weinberger*, 512 F. 2d 688, 696–98 (2d Cir. 1975) and *National Association of Pharmaceutical Manufacturers* v. *FDA*, 487 F. Supp. 412 (S.D. N.Y. 1980), *aff'd*, 637 F. 2d 887 (2d Cir. 1981).

2. One comment argued that the indications for OTC drug products should not be limited to the precise words as set forth in quotation marks in proposed monographs. The comment

argued that since there are other ways and other words that can be used to convey the same meaning as the phrases set forth in the proposed monographs, it is unduly restrictive, unlawful, and unconstitutional to prevent the use of such alternatives. The comment further charged that this restriction is arbitrary and capricious because the agency's arguments, which support this policy (OTC Nighttime Sleep-aid and Stimulant Products Tentative Final Monographs, June 13, 1978, paragraph 5 (43 FR 25545)) as necessary to prevent consumer deception and unsafe use, are unsupported by any objective evidence that such negative effects might occur.

During the course of the OTC drug review, the agency has maintained that the terms that may be used in an OTC drug product's labeling are limited to those terms included in a final OTC drug monograph. (This policy has become known as the "exclusivity rule.") The agency's position has been that it is necessary to limit the acceptable labeling language to that developed and approved through the OTC drug review process in order to ensure the proper and safe use of OTC drugs. The agency has never contended, however, that any list of terms developed during the course of the review exhausts all the possibilities of terms that appropriately can be used in OTC drug labeling. Suggestions for additional terms or for other labeling changes may be submitted as comments to proposed or tentative final monographs within the specified time periods or through petitions to amend monographs under § 330.10(a)(12).

During the course of the review, FDA's position on the "exclusivity rule" has been questioned many times in comments and objections filed in response to particular proceedings and in correspondence with the agency. The agency has also been asked by The Proprietary Association to reconsider its position. In a notice published in the **Federal Register** of July 2, 1982 (47 FR 29002), FDA announced that a hearing would be held to assist the agency in resolving this issue. On September 29, 1982, FDA conducted an open public forum at which interested parties presented their views. The forum was a legislative type administrative hearing under 21 CFR Part 15 that was held in response to a request for a hearing on the tentative final monographs for nighttime sleep-aids and stimulants (published in the **Federal Register** of June 13, 1978; 43 FR 25544). The agency's decision on this matter will be announced in the **Federal Register** following conclusion of its review of the material presented at the hearing.

3. One comment suggested that FDA should sponsor a study on developing labeling which can be easily understood by individuals with limited education.

FDA has sponsored several labeling studies over the past few years. The first phase of the contract entitled "Consumer Comprehension of OTC Drug Labeling Language" (contract no. 223-80-3023) was completed in 1981. Unfortunately, budgeting restrictions forced the agency to cancel plans for the second phase of this study, which was designed to provide guidance in drafting labeling that can be easily understood by the public.

4. One comment objected to the current wording of the statement "In case of accidental overdose, seek professional assistance or contact a poison control center immediately," which is required for all orally administered OTC drugs. The comment argued that such a statement seems to imply that Poison Control Center personnel are not professionals. The comment suggested rewording this warning to read "In case of accidental overdose, contact a Poison Control Center or seek other professional assistance immediately."

FDA is proposing to exempt OTC poison treatment drug products from that portion of the warning in § 330.1(g) (21 CFR 330.1(g)) that is referred to by the comment. The comment is, therefore, not applicable to the labeling of these drugs. However, the agency recognizes that some change in the wording of this general warning may be necessary because the Advisory Review Panel on OTC Miscellaneous Internal Drug Products also has suggested a change in this warning (47 FR 55681). However, this issue will not be addressed in this document but will be addressed at a later date in another **Federal Register** document.

B. General Comments on Poison Treatment Drug Products

5. One comment disagreed with the Miscellaneous Internal Panel's statement that large volumes of water or milk should be ingested to dilute acidic or alkaline corrosive substances (47 FR 447). The comment pointed out that although the role of dilution with large volumes of fluid for poisoning in general is presently controversial, some evidence suggests that excessive dilution may have detrimental effects, especially in the case of caustics where large volumes of fluid may induce emesis and expose the esophagus again to the caustic. The comment suggested that it would be more prudent to suggest dilution of caustics with one glassful or less of water or milk.

Although the comment raises a valid point regarding the proper amount of fluid to be used in diluting caustics, the Panel's statement was made as part of a general discussion of poisoning and was not a specific recommendation to be included in the labeling of products covered by the monograph.

Labeling proposed in this tentative final monograph is limited to that necessary to insure the proper use of ipecac syrup and activated charcoal in treating poisoning. The labeling for both activated charcoal and ipecac syrup clearly states that these drugs are not to be administered in a poisoning that involves corrosives. Thus, there is no labeling proposed in this tentative final monograph regarding the amount of fluid to be used in diluting corrosive poisons because ipecac syrup and activated charcoal are only to be used in conjunction with noncorrosive poisons.

6. Four comments urged that the labeling be amended to include the word "pharmacist" in all phrases that include the word "physician." The comments argued that because pharmacists are readily available and extremely well informed regarding drugs, they should be named in the labeling as a contract for information regarding treatment on poisonings. Several of the comments reported the results of a recent survey as showing a good pharmacist-patient communication relationship because although 87 percent of the people surveyed were seen by more than one doctor, 86 percent will have their prescriptions filled at only one pharmacy. These comments further pointed out that former FDA Commissioner Kennedy, in a 1978 address to the American Pharmacists Association meeting in Canada, stated that "the pharmacist's knowledge of drugs, including adverse reactions, usually exceeds that of the physician."

Although physicians or pharmacists would be likely health professionals to be consulted because of their availability and recognized expertise, the agency does not believe that the labeling of OTC drug products should specify one or both of these health professionals. Many professional groups, such as nurses, nurse practitioners, and physician's assistants, are also sources of sound information on poison treatment. Consumers who are looking for poison treatment information are in the best position to choose the health professional to help them, and the warning should not limit their source of information. Therefore, the agency is revising the labeling in this tentative

final monograph for poison treatment drug products to advise consumers to contact a "health professional" for advise rather than any particular health professional.

7. A number of comments urged that the sentence "Call a physician, poison control center, or emergency room . . . ." in proposed § 337.50(c)(1) be revised to list "poison control center" first because poison control centers possess greater expertise in treating poisoning cases and are more easily reached by phone on a 24-hour basis than the other listed sources. The comments also pointed out that this change in wording would be consistent with national public education efforts to make the public aware that contacting a poison control center is the first action to take when a poisoning occurs or is suspected. Other comments suggested, in addition, that emergency room be listed second and physician last to assure that the most experienced sources are listed first.

FDA recognizes that poison control centers are the first source of information in treating poisonings and occurs with the suggested change in the labeling. The agency also believes that emergency personnel may be more readily available than other health professionals and should be listed second. (See also comment 8 below.)

8. Two comments requested that the term "emergency room" be replaced in labeling by the term "emergency medical facility" or "emergency medical center" because many emergency treatment centers are not situated within a hospital as the term "emergency room" implies. A third comment objected to the phrase "emergency medical facility" as being meaningless because the word "hospital" is the listing most often found in telephone books. The comment suggested revising the warning to read, "If you can, before using, call a poison control center, hospital, or doctor for advice."

FDA acknowledges that "emergency medical facility" or "emergency medical center" is a more descriptive term than "emergency room" because, as the comments pointed out, many emergency treatment centers are not located in hospitals. The agency does not agree that the term "emergency medical facility" is meaningless. In many parts of the United States, treatment or advise for poisoning can be obtained from hospitals, small clinics, poison control centers, medical centers, fire and emergency rescue services, etc. The term "emergency medical facility" encompasses all of these sources of information. Therefore, the agency is proposing that this term be used throughout the tentative final monograph.

9. Several comments expressed concern over the amount and complexity of labeling proposed for poison treatment drug products arguing that such labeling might be difficult to read because of the small print size and difficult to understand under rushed emergency conditions. Some of the comments urged the use of simple and brief labeling similar to the following:

> Before Use: Call your Poison Center, Physician, or Emergency Room. Do Not Use in a patient who is Comatose, Convulsing, or who has taken a Caustic. Dose: 30 mL (1 oz)—adult, 15 mL (½ oz)—child over 1 yr.

Another comment suggested the use of a package insert or an oversize bottle to allow adequate room for the labeling.

The comments raise a valid concern with respect to all poison treatment drug products. A simple, brief label is more likely to be read and understood under emergency conditions. However, it is equally important that adequate directions and warnings regarding the use of poison treatment drug products be available to the consumer when professional emergency help cannot be reached quickly.

In an effect to accomplish both objectives, FDA is proposing to divide the labeling for poison treatment drug products into two distinct segments. First, the agency proposes that the principal display panel contain the following brief emergency instructions in a conspicuously boxed area: "If possible call a poison control center, emergency medical facility, or health professional for help before using this product. If help cannot be reached quickly follow the directions (manufacturer to indicate location of directions, e.g., on the back of the bottle). Read the warnings and directions as soon as you buy this product. Insert emergency phone number(s) in space provided on the label." A space should also be provided, on the principal display panel, for writing in the phone number(s) of the appropriate poison control center or other emergency medical facility.

Second, the agency proposes that full warnings and directions be placed on a separate portion of the label. Wrap around or fold-over labels may be used to provide more label space with room for larger and more legible print. A package insert would not be acceptable because of the risk that it might become separated from the product. An oversize bottle might create confusion in the case of ipecac syrup because the quantity that may be sold OTC is limited to 30 milliliters (mL) per container, and determining a children's dose of ½ bottle as provided for in § 357.56(d)(2) of this tentative final monograph could be difficult under emergency conditions.

10. Three comments agreed with the proposed labeling for ipecac syrup (proposed § 337.50(c)(1)), which advises consumers to seek professional help before administering ipecac syrup. One of the comments stated that if consumers did not contact a professional before using ipecac syrup, it may be given many times when it is contraindicated, e.g., in instances of petroleum distillate or corrosive poisonings. Two other comments expressed the opposite opinion that attempting to contact professional help before using the product could result in a critical delay in an emergency situation. Another comment objected to a similar warning recommended for activated charcoal and poison treatment kits (recommended § 357.50(c)(1) and § 357.54(a)(1), respectively) because a written warning could be interpreted as prohibiting the administration of the product if a health professional could not be reached.

The agency believes that is any poisoning situation it would be best to seek professional help before using poison treatment drug products. However, there are times when such contact may not be possible. In those cases, the consumer should not be discouraged from using poison treatment drug products.

The agency is proposing that the principal display panel contain statements advising consumers to contact professional help if possible, but if help cannot be reached, to follow the directions provided elsewhere on the label. These statements will replace the warnings previously recommended in §§ 337.50(c)(1), 375.50(c)(1), and 357.54(c)(1). In those cases where professional help cannot be reached, the warnings contained on the labels of poison treatment drug products will list those poisoning situations in which the products should not be used.

11. One comment urged that labeling for ipecac syrup be printed in languages other than English in view of the extensive non-English speaking populations in many large cities.

The agency agrees that it would be valuable to have both emetics and adsorbents available with foreign language labeling. The regulations at 21 CFR 201.15(c) provide for labeling in other languages in addition to English. The foreign language version of the labeling statements must be a complete

and accurate translation of the required English labeling.

12. One comment pointed out that many poisoning reference sources, such as the Poisindex, recommend the administration of a saline cathartic when activated charcoal is administered in the management of poisoning. The comment questioned whether the Panel has considered the use of cathartics in poisoning.

The agency has reviewed the Miscellaneous Internal Panel's report and summary minutes of meetings and determined that the Panel did not consider the use of cathartics in acute poison treatment. A number of sources suggest the use of cathartics in poison treatment to remove unabsorbed poisons from the intestinal tract or to speed the passage of activated charcoal through the intestinal tract (Ref. 1, 2, and 3). According to Levy (Ref. 1), it has been customary to administer a saline laxative together with an adsorbent to prevent constipation or impaction. However, Levy noted that it would be advisable to use a conservative dose of a laxative to prevent excessive fluid loss and electrolyte disturbances. Dreisbach (Ref. 2) noted that catharsis or intestinal lavage can be used to remove unabsorbed poisons or poisons that have passed into the intestinal tract, but pointed out that catharsis should not be used in patients showing distrubed electrolyte balance. Cashman and Shirkey (Ref. 3) agree that laxatives may hasten transit through the bowel, thus decreasing the absorption of poisons that cannot be recovered by emesis or absorbed by activated charcoal, but believe judgment must be exercised by comparing the risk of poisoning to the theoretical value of the laxative. In view of these opinions, the agency believes that professional judgment is necessary to assess the appropriateness of using laxatives in poisoning situations. Thus, the agency does not believe that the labeling of OTC poison treatment drug products should mention the use of laxatives.

References

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(2) Dreisbach, R.H., "Handbook of Poisoning," Lange Medical Publication, Los Altos, CA, p. 23, 1980.

(3) Cashman, T.M., and H.C. Shirkey, "Emergency Management of Poisoning," *Pediatric Clinics of North America*, 17:525–534, 1970.

13. One comment stated that the Miscellaneous Internal Panel appeared to mandate the use of ipecac syrup at all times before the use of activated charcoal. The comment stated that ipecac-induced emesis is not suitable in certain cases, such as ingestion of caustic substances or petroleum distillates, because it takes an average of 19 minutes to induce emisis, and sometimes a second dose is needed to induce emesis. The comment added that these delays could permot absorption of toxins that could be prevented by prompt administration of activated charcoal (Ref. 1). The comment stated that in at least one study an average of only 28 percent (range 0 to 78 percent) of stomach contents were recovered by ipecac-induced emesis (Ref. 2). The comment added that "the consensus now emerging among clincial physicians is that the best way of handling overdoses consists of the immediate administration of large amounts (100 grams (g) or more) of powdered charcoal" (Ref. 3). The comment requested that the labeling be modified to permit the use of activated charcoal without first ingesting ipecac syrup and having vomiting occur, because activated charcoal is safe under virtually all conditions.

As the Panel discussed in its report (47 FR 448), the efficiency of activated charcoal varies considerably according to the chemical ingested. A number of substances, including inorganic acids, certain alkalies (sodium and potassium hydroxide), sodium metasilicate, cupric copper, ferrous iron, boric acid, drugs that are solids and insoluble in acidic aqueous solutions, and certain insecticides, are not very well absorbed. In addition, in those situations in which ipecac syrup is contraindicated (corrosives and petroleum distillates), activated charcoal is not very effective (see comment 51 below). Although the agency acknowledges the one report that showed an average of only 28 percent recovery of stomach contents, there are numerous reports in the literature (Refs. 4 through 8), plus vast experience reported in poison control centers and emergency medical facilities, attesting to ipecac syrup's effectiveness in treating poisonings. The agency agrees with the Panel that in the majority of poisoning cases it is best to remove as much of the ingested substance as possible from the stomach by inducing vomiting before administering activated charcoal. However, the agency recognizes that in certain specific poisoning cases, a physician or other health professional may choose to administer activated charcoal rather than ipecac syrup. Therefore, the agency is proposing that the labeling for activated charcoal be modified to include this provision. (See comment 43 below.)

References

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(2) Corby, D.G., et al., "Clinical Comparison of Pharmacologic Emetics in Children," *Pediatrics*, 42:361–364, 1968.

(3) Cooney, D.O., "Activated Charcoal, Antidotal and Other Medicinal Uses," Marcel Dikker, Inc., New York, p. 3, 1980.

(4) King, W.D., "Syrup of Ipecac: A Drug Review," *Clinical Toxicology*, 17:353–358, 1980.

(5) Krenzelok, E.P., "How to Manage Poisoning Emergencies," *Pharmacy Times*, 45:71–82, 1979.

(6) Rauber, A., "The Cardiac Safety of Ipecac Used as a Therapeutic Emetic," *Veterinary and Human Toxicology*, 20:166–168, 1978.

(7) Veltri, J.C., and A.R. Temple, "Telephone Management of Poisonings Using Syrup of Ipecac," *Clinical Toxicology*, 9:407–417, 1976.

(8) Ilett, K.F., S.M. Gibb, and R.W. Unsworth, "Syrup of Ipecacunha as an Emetic in Adults," *The Medical Journal of Australia*, 2:91–93, 1977.

14. Two comments suggested that the phase "or as directed by a physician" be deleted from the directions statement because advice on doses of ipecac syrup or activated charcoal may not be given by a physician, but may be given by a pharmacist, nurse, or other health professional working in a poison control center or emergency medical facility.

The agency agrees with the comment. The assistance from a poison control center or emergency medical facility may be provided by specially trained professional personnel other than physicians. Therefore, the agency is proposing that the phrase "or as directed by a physician" read "or as directed by a health professional" in the directions of poison treatment drug products.

15. One comment urged that the indication statement for emetics be revised to state clearly that ipecac syrup is to be used for the treatment of poisoning. A second comment suggested that the indications statement "for the treatment of acute poisoning" recommended for adsorbents and poison treatment kits be revised by deleting the word "acute" because it has no meaning to the general public in describing the type of poisoning. This comment further suggested that the indications statement for poison treatment drug products permit alternative language that is more understandable to the public, such as "emergency first aid treatment for poisoning," "emergency treatment for poisoning," "emergency treatment for accidental poisoning," "for the treatment of accidental poisoning," "emergency

first aid treatment for accidential poisoning," "emergency poison treatment," or "first aid poison treatment."

The agency believes that the labeling of any OTC drug product should clearly reflect the intended action of the product. In the case of ipecac syrup the agency believes it is important for consumers to be advised that vomiting is expected. Therefore, the agency is proposing the following statement as the indication for ipecac syrup: "For emergency use to cause vomiting of swallowed poisons." In the case of activated charcoal the agency believes that consumers should be informed that it is intended to absorb poisons and the indication proposed in this tentative final monograph reads "For emergency use to absorb swallowed poisons." The agency agrees with the one comment that the word "acute" is meaningless to the general public and has not included it in the proposed indications. The other statements suggested by the comments are acceptable as additional statements for inclusion on poison treatment drug products, but the agency does not believe that these statements should appear in conjunction with the required information.

C. Comments of Emetics

16. One comment contended that zinc sulfate, rather than ipecac syrup, is the emetic of choice in the treatment of accidental poisoning. The comment submitted an article stating that zinc sulfate, which produces vomiting by a purely local action in its action on the gastrointestinal tract, is both faster and more certain in its action then ipecac syrup (Ref. 1). The comment also emphasized that zinc sulfate lacks the central nervous system depressant action of ipecac syrup.

The agency recognizes that zinc sulfate is often effective as an emetic; however, its potential toxicity is too great to recommend its use as an OTC emetic drug product (Refs. 2, 3, and 4). The emetic dose of zinc sulfate is 2 g dissolved in 200 mL of water, repeated in 15 minutes if necessary. If emesis does not occur after the second dose, the zinc sulfate must be removed by stomach tube. If it is not removed, its absorption into the bloodstream can cause hemolytic effects and renal toxicity or even death (Refs. 2, 3, and 4). The lethal dose is estimated in the literature to be anywhere from 3 to 15 g (Refs. 2, 5, 6, and 7). The article submitted by the comment discussed a 1950 animal study conducted to develop a method for prevention of suicidal deaths caused by barbiturates. This study does not, however, support the general use of zinc sulfate as an OTC emetic.

In view of the reported toxicity of zinc sulfate and the narrow margin of safety between its effective dose (2 g) and its lowest reported lethal dose (3 g), the agency concludes that zinc sulfate is not suitable for use as an OTC emetic drug product.

References

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(2) "The United States Dispensatory," 27th Ed., J.P. Lippincott Co., Philadelphia, p. 1256, 1973.

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(5) Moeschlin, S., "Poisoning. Diagnosis and Treatment," 1st Ed., Grune and Stratton, New York, pp. 121–123, 1965.

(6) Dreisback, R.H., "Handbook of Poisoning," 9th Ed., Lange Medical Publications, Los Altos, CA, pp. 406–407, 1977.

(7) Arena, J.M., "Poisoning. Toxicology—Symptoms—Treatments," 3rd Ed., Charles C. Thomas, Springfield, IL, pp. 37–40 and 241, 1974.

17. Four comments took exception to the agency's statement at 43 FR 39545 in the preamble to the prvious emetic tentative final monograph that "ipecac acts directly on the vomiting reflex center in the brain to produce vomiting." The comments were concerned that this statement implied that this is the only mechanism by which ipecac syrup produces emesis. Two of comments submitted documentation showing that ipecac syrup induces emesis via two mechanisms (Refs. 1, 2, and 3). The first mechanism is direct irritation of the upper gastrointestinal tract by ipecac, i.e., the "gas reflex." When this mechanism is operative, vomiting usually occurs within a relatively short period of time after the ipecac syrup is ingested. The second mechanism is the action of ipecac alkaloids on the vomiting reflex center of the brain. Because absorption from the gastrointestinal tract and distribution to the brain are required before ipecac syrup can induce emesis via this second mechanism, there is usually a delay between the ingestion of the ipecac syrup and the onset of vomiting.

The agency did not intend to imply that ipecac syrup induces emesis solely by acting on the vomiting reflex center of the brain. As the comments correctly point out, ipecac may act either by direct irritation of the upper gastrointestinal tract, i.e., "gas reflex," or by central action on the vomiting center of the brain.

References

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(2) Oderda, G.M., and S. West, "Emetic and Antiemetic Products," *in* "Handbook of Nonprescription Drugs," 5th Ed., American Pharmaceutical Association, Washington, pp. 57–58, 1977.

(3) Rollo, I.M., "Drugs Used in the Chemotherapy of Amebiasis," *in* "The Pharmacological Basis of Therapeutics," 5th Ed., L.S. Goodman and A. Gilman, editors, Macmillan Publishing Co., Inc., New York, pp. 1075–1077, 1975.

18. Two comments were concerned about possible confusion between tincture of ipecac, fluidextract of ipecac, and the more dilute syrup of ipecac and the toxicity that could result if confusion occurred. One comment pointed out that vitually all published reports which discuss the toxicity of ipecac refer to toxicity resulting from the administration of fluidextract of ipecac rather than ipecac syrup. The fluidextract of ipecac contains over 10 times the concentration of the alkaloids, emetine and cephaline, found in ipecac syrup. The second comment urged that a sentence be added to the labeling of ipecac syrup advising individuals that syrup of ipecac and not the more concentrated and extremely dangerous tincture of ipecac is to be used in poisoning situations.

The first comment correctly identifies a misconception regarding the toxicity of ipecac syrup. As the comment indicated, most of the articles and reports discussing ipecac toxicity or ipecac overdose deal with situations in which the fluidextract of ipecac was administered rather than the more dilute ipecac syrup. In the past the fluidextract was frequently mistaken for the syrup. The tincture of ipecac and the fluidextract of ipecac are no longer recognized in the official compendia and are no longer commercially available. Further, such products are proposed as Category II because of their potential toxicity if incorrectly used. Therefore, the possibility of confusing the fluidextract or tincture of ipecac for the syrup of ipecac has been eliminated and the need for a label warning as suggested by the second comment is not necessary.

19. One comment urged that ipecac syrup be restricted to sale by pharmacists only because the public might consider ipecac syrup to be a specific poison antidote rather than an emetic, and may use it erroneously for

certain types of poisonings for which vomiting is contraindicated.

The issue of restricting the sale of OTC drugs to pharmacists only was discussed previously by the agency in the **Federal Register** of June 4, 1974 (39 FR 19880). There, the agency concluded that there was no public health concern that would justify the creation of a third class of drugs to be dispensed only by a pharmacist or in a pharmacy. Although the agency recognizes that the pharmacist is a health professional who can offer sound advice concerning poisoning situations, the agency believes that the proposed labeling of ipecac syrup provides adequate safeguards against its erroneous use.

20. A number of comments disagreed with the statement that ipecac syrup should be recovered by gastric lavage if a second dose does not induce vomiting (43 FR 39545). Some of the comments pointed out that the amount of ipecac syrup consumed in two doses (30 mL) is lower than the dosage (90 to 120 mL) that would have to be consumed without emesis before any cardiac arrhythmias might be induced. One comment added that a study on adults to see if syrup of ipecac in therapeutic doses would affect stress electrocardiograms (EKG's) indicated that syrup of ipecac produced no effect on the stress EKG (Ref. 1). The comments opposed any use of gastric lavage unless it was necessary to remove the poison or toxic substance that the patient had originally ingested. The comments stressed that it was not necessary to remove the ipecac syrup. One comment stated that any mention of gastric lavage in labeling is not appropriate as people of all educational levels would be using these products. An opposing comment urged that the labeling for ipecac syrup emphasize the necessity for gastric lavage if a second dose of ipecac syrup does not produce vomiting within 30 minutes. This comment was not accompanied by any supporting documentation.

The agency concluded in paragraph 9 of the emetic tentative final monograph, published on September 5, 1978 (43 FR 39545), that "gastric lavage" was inappropriate terminology for use on a label designed to be read and entirely understood by consumers in emergency situations. FDA thus deleted any mention of gastric lavage from the labeling provisions proposed in that tentative final monograph. The agency has not been presented with any data or reasoning that persuades it to change that conclusion. FDA further agrees that gastric lavage need not necessarily be performed if emesis fails to occur within 30 minutes of giving a second dose of ipecac syrup (a total of 60 mL in adults or 30 mL in children age 1 to 12), because data show that a therapeutic dose (up to 60 mL) of ipecac syrup is not cardiotoxic and produces only a mild drowsiness and diarrhea (Refs. 1 through 4). In fact as much as 105 mL of ipecac syrup have been retained by a child with only minor electrocardiograph changes occurring (Ref. 2).

References

(1) Comment No. OB0018, Docket No. 81N-0050, Dockets Management Branch.

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(4) Rauber, A., "The Cardiac Safety of Ipecac Used as a Therapeutic Emetic," *Veterinary and Human Toxicology*, 20:166-168, 1978.

D. Comments on Emetic Labeling

21. One comment suggested that it may be more appropriate to use metric units in addition to English units when indicating the volume of water to be given along with ipecac syrup in the directions in § 357.50(e).

The agency is aware of the trend towards using metric units. However, the volume of water or other clear liquid to be given after the ipecac syrup is large (120 to 480 mL). The agency believes that American consumers would be more familiar with the English volume measures (ounces) when the volume is large and that the English measures should be used in the labeling in addition to "glassful" measures. The agency would have no objection to using the metric units in addition to the English units. However, the use of metric units will not be required in this tentative final monograph.

22. Two comments suggested that the recommended doses of ipecac syrup be expressed in terms of container size, i.e., 1 tablespoonful (15 mL or ½ bottle), in addition to the presently proposed units of teaspoonful and tablespoonful, and their metric equivalents. The comments argued that this would be more meaningful to the consumer because teaspoons and tablespoons found in the home vary in size, and many people are not yet familiar with the metric system.

While there may be some variation in teaspoons and tablespoons from home to home, they represent a common form of measurement with which most people are readily familiar. The agency has no objection to manufacturers expressing the 30 mL or 15 mL dose in terms of bottle size equivalent in addition to the tablespoon measures and is proposing this option in the monograph. However, the dose for children from 6 months to 1 year of age of 1 teaspoon (5 mL) should not be expressed in terms of bottle size equivalent, i.e., ⅙ bottle, because of the obvious difficulty in accurately measuring such a dose in that manner.

23. A number of comments urged that the warning, "Do not use in semiconscious or unconscious persons," in § 337.50(c)(2) of the emetic tentative final monograph, be amended because it does not include all of the conditions which might contraindicate the use of ipecac syrup. Five comments urged that the warning be written to include persons suffering seizures or convulsions because such people might choke while vomiting. Two comments suggested that the warning be expanded to include people who are drowsy or comatose or who might be expected to lose consciousness within 20 minutes after administering ipecac syrup. Two other comments suggested that the warning could be conveyed more simply and succinctly if it was changed to read: "Do not use in persons who are not fully conscious."

FDA agrees that reference to "semi-conscious or unconscious persons" may not be correctly interpreted as including all of the conditions under which ipecac syrup should be used. Because the average consumer does not have the experience to diagnose the onset of a seizure or convulsion or that a person may lose consciousness within 20 minutes, this information should not be included in the warning. The warning "Do not use in persons who are not fully conscious," suggested by two of the comments, would more accurately and simply convey the various states of consciousness in which ipecac syrup is contraindicated. Therefore, FDA is proposing this wording in the warning included in this tentative final monograph.

24. Four comments disagreed with the statement proposed in § 337.50(c)(3) that ipecac syrup should not be used if petroleum distillates such as kerosene, gasoline, paint thinner, or cleaning fluid have been ingested. The comments argued that the ingestion of petroleum distillates or hydrocarbons is not an absolute contraindication to the use of ipecac syrup. The comments asserted that emesis can be safely induced with ipecac syrup in the alert patient who has swallowed a large quantity of a petroleum distillate (i.e., two ounces or more) or when the petroleum distillate contains a substance in a quantity that is toxic to the patient. One comment cited FDA's "Handbook of Common Poisonings in Children" (Ref. 1), an

editorial (Ref. 2), and an unpublished study (Ref. 3) as examples that current thinking among toxicologists is that emesis can be induced safely in petroleum distillate poisonings.

Four other comments urged a revision or expansion of § 337.50(c)(3). Two of these comments suggested that furniture polish be included in the warning. One of the comments states that, although the generic term "paint thinner" includes "turpentine," turpentine should be specifically mentioned in the labeling. However, the other comment countered this view stating that turpentine is not a petroleum distillate and, therefore, should not be included under the generic term "paint thinner." The comment argued that turpentine has a minimal potential for pulmonary toxicity and a high potential for central nervous system toxicity if systemically absorbed, a fact which would warrant inducing vomiting.

The agency recognizes that induction of emesis may be indicated in certain cases of hydrocarbon ingestion. However, the agency is also aware that controversy exists whether or not emesis should be induced in these cases. Some sources recommend induction of emesis when certain hydrocarbons are ingested (Ref. 2) or when the amount of hydrocarbon ingested exceeds a certain volume (Refs. 1, 2, 4, and 5). Other sources state that emetics are definitely contraindicated (Ref. 6). The major argument against inducing emesis in the pulmonary complications that occur from aspiration of the ingested substance into the lung when vomiting is induced. Some investigators have shown that vomiting is associated with a higher incidence of pulmonary complications and central nervous system involvement (Refs. 7 through 10). Others (Ref. 4) have shown that patients treated with ipecac syrup had a lower incidence of pneumonia and that the pneumonia was less severe than in those treated with gastric lavage.

In view of the controversy regarding the treatment of ingestions of hydrocarbons, the agency believes that emesis should be induced in such cases only under the guidance of a health professional. Therefore, the agency is proposing to retain in this tentative final monograph the warning that ipecac syrup should not be given in petroleum distillate poisonings unless directed by a health professional.

Because "furniture polish" is a petroleum distillate commonly found in the home, the agency agrees with the comments that it should be added to the warning as an additional example of petroleum distillates. As one comment pointed out, turpentine in not a petroleum distillate, but is a hydrocarbon commonly found in the household. Therefore, the agency proposes to add it to the warning proposed in § 337.54(c)(2). Because other paint thinners may consist of petroleum distillates, this example will be retained in the warning. The agency is proposing that the warning in § 337.54(c)(2) read, "Do not use this product, unless directed by a health professional, if turpentine, corrosives, such as alkalies (lye) and strong acids, or petroleum distillates, such as kerosene, gasoline, paint thinner, cleaning fluid, or furniture polish, have been ingested."

References

(1) American Academy of Pediatrics, "Handbook of Common Poisonings in Children," Food and Drug Administrative, pp. 1, 52, 53, and 76, 1976.

(2) Rumack, B.H., "Hydrocarbon Ingestions in Perspective," *Annals Of Emergency Medicine*, 6:172, 1977.

(3) Rumack, B.H., "Hydrocarbons-Poisoning Emesis or Not," draft of unpublished paper, in Comment No. OB0001, Docket No. 78N-0036E, Dockets Management Branch.

(4) NG, R.C., et al., "Emergency Treatment of Petroleum Distillate and Turpentine Ingestion," *Canadian Medical Association Journal*, 3:537–538, 1974.

(5) Dreisbach, R.H., "Handbook of Poisoning," Lange Medical Publications, Los Altos, CA, pp. 19 and 181–182, 1960.

(6) Gosselin, R.E., et al., "Clinical Toxicology of Commercial Products," 4th Ed., The Williams and Wilkins Co., Baltimore, pp. 188–192, 1976.

(7) Press, E., et al., "Cooperative Kerosene Poisoning Study: Evaluation of Gastric Lavage and Other Factors In the Treatment of Accidental Ingestions of Petroleum Distillate Products," *Pediatrics*, 29:648–674, 1962.

(8) Wolfsdorf, J., and H. Kundig, "Kerosene Poisoning In Primates," *South African Medical Journal*, 46:619–621, 1972.

(9) Sperling, E., "In Vivo and In Vitro Toxicology of Turpentine," *Clinical Toxicology*, 2:21–35, 1969.

(10) Beamon, R.F., et al., "Hydrocarbon Ingestion in Children: A Six-Year Retrospective Study," *Annals of Emergency Medicine*, 5:771–775, 1976.

25. Two comments asked for revision of the warning proposed in § 337.50(c)(3) for ipecac syrup which reads, "ordinarily, this product should not be used if strychnine, corrosives such as alkalies (lye) and strong acids, or petroleum distillates, such as kerosene, gasoline, paint thinner, or cleaning fluid have been ingested." One comment suggested that, although strychnine is the most rapidly acting convulsant, other convulsants such as camphor should be mentioned. The other comment argued that ingestions of strychnine are extremely rare in the United States, and the presence of strychnine in the warning may distract the consumer from the more important contradictions to ipecac-induced emesis. The comment added that the experiences of both medical and poison control centers indicate that the risks associated with inducing emesis after ingestion of convulsant drugs (e.g., camphor, amphetamines, tricyclic antidepressants, isoniazid) is small compared to the risk of allowing these extremely toxic compounds to be absorbed into the bloodstream. The comment urged that specific references to convulsant drugs be avoided.

The agency believes that in cases of overdoses of convulsants (e.g., camphor, amphetamines, tricyclic antidepressants, isoniazid), an emetic such as ipecac syrup should be given unless the patient is comatose, convulsing, has no gag reflex, or is rapidly declining in levels of consciousness (Ref. 1 through 4). The agency agrees with the latter comment that the risk of administering ipecac to a person who has ingested a toxic dose of a rapidly acting convulsant is considerably less than the risk of allowing these toxic compounds to be absorbed into the bloodstream. Therefore, the agency is proposing not to include strychnine or any other convulsant, such as camphor, in the warning. As discussed in comment 23 above, the agency is proposing the warning "do not use in persons who are not fully conscious" to include the various stages of consciousness in which ipecac syrup is contraindicated.

References

(1) Polson, C.J., "Clinical Toxicology," J.B. Lippincott Co., Philadelphia, pp. 17–20, 1959.

(2) Callahan, M., "Tricyclic Antidepressant Overdose," *Emergency Medicine*, 8:413–425, 1979.

(3) Arena, J.M., "Poisoning, Toxicology—Symptoms—Treatments," 3d Ed., Charles C. Thomas, Springfield, pp. 368–369 and 399–400, 1974.

(4) Czajka, P.A., and J.P. Duffy, "Poisoning Emergencies. A Guide for Emergency Medical Personnel," The C.V. Mosby Co., St. Louis, pp. 39, 40, and 47–50, 1980.

26. Two comments urged that ipecac syrup labeling indicates the need for prompt administration or the need for caution when a delay occurs in administering the product after ingestion of toxic doses of phenothiazines, central nervous system depressants (i.e., alcohol, barbiturates, sedative hypnotics, narcotics), or convulsants that have a slow-to-moderate onset of action. One comment cited a study which showed that, despite the antemetic action of the phenothiazines, the induction of emesis with syrup of ipecac was successful (Ref. 1). The comment also cited one case in which

emesis failed to occur and fatal ipecac cardiotoxicity resulted (Ref. 2). The comment stated that the risk of emesis failing to occur increases with the delay between the ingestion of the toxic dose and the administration of ipecac syrup because of the amount of the drug absorbed. Both comments pointed out that this delay, along with the 15 to 30 minute or longer latency period for emesis to be induced by ipecac syrup, increases the chance that the patient may lose consciousness or experience convulsions before the onset of emesis.

The comments raise a valid concern which the agency shares. However, it is usually impossible for the average consumer to determine whether a particular substance ingested is a central nervous system depressant or convulsant, let alone decide whether it possesses a slow-to-moderate onset of action. The agency is proposing a warning on the principal display panel of the ipecac syrup label instructing the consumer to "If possible call a poison control center, emergency medical facility, or health professional for help before using this product." These sources are qualified to identify the nature of the toxic substance ingested and provide guidance in the correct emergency treatment. The labeling also instructs consumers to read and follow the directions for use elsewhere on the bottle in an emergency situation when help cannot be reached quickly. The purpose of this statement is to advise consumers not to delay administering ipecac syrup in those cases when professional help cannot be contacted immediately.

The agency believes that in the case of overdoses of phenothiazines, central nervous system depressants, or convulsants, the risk of giving ipecac syrup when professional help cannot be contacted is considerably less than the risk of allowing the patient to absorb a toxic dose of these compounds. However, for the reasons stated above, a specific labeling statement mentioning these drugs in particular is not being proposed.

References

(1) Thoman, M.E., and H.L. Verhulst, "Ipecac Syrup in Antiemetic Ingestion," *Journal of the American Medical Association*, 196:147–148, 1966.

(2) MacLeod, J., "Hazards to Health. Ipecac Intoxication—Use of a Cardiac Pacemaker in Management," *The New England Journal of Medicine*, 268:146–147, 1963.

27. One comment questioned whether ipecac syrup would be effective in patients who had ingested an antiemetic drug and whether it should be contraindicated in such cases. A second comment referred to several studies that demonstrated the effectiveness of ipecac syrup in inducing vomiting in patients who had ingested a variety of antiemetic drugs including phenothiazines, tricyclic antidepressants, antihistamines, and anticholinergics (Refs. 1 and 2). The comment attributed the effectiveness of ipecac syrup in these cases to local gastrointestinal irritation rather than to an action on the vomiting center of the brain.

As discussed in comment 17 above, ipecac syrup induces vomiting either by local gastrointestinal irritation or, following systemic absorption, by the effect of its alkoloids on the vomiting reflex center of the brain. In the case of ingestion of antiemetic drugs, which may depress the vomiting center in the brain, ipecac syrup may still induce emesis by virtue of its local gastrointestinal irritation. Manoguerra and Krenzelok (Ref. 1) reported that of 63 patients who ingested drugs with antiemetic properties, 51 (81 percent) vomited following the first dose of ipecac, 9 (14 percent) vomited after a second dose, and only 3 (5 Percent) failed to vomit. These results are consistent with the studies of Ilett et al. (Ref. 2) and Thoman and Verhulst (Ref. 3) who reported that the emetic efficiency (percentage of patients vomiting) was not decreased when either phenothiozines or antihistamines were identified as the ingested substance. Ilett et al. (Ref. 2) reported 100 percent emetic efficacy in seven persons who had ingested drugs with antiemetic properties. Thoman and Verhulst (Ref. 3) reported that the administration of ipecac syrup induced vomiting in 94.5 percent of a group of 291 patients who had ingested antiemetic drugs. Based on these data, the agency concludes that there is no need to contraindicate the use of ipecac syrup in cases where antiemetic drugs have been ingested.

References

(1) Manoguerra, A.S., and E.P. Krenzelok, "Rapid Emesis from High-Dose Ipecac Syrup in Adults and Children Intoxicated with Antiemetics or Other Drugs," *American Journal of Hospital Pharmacy*, 35:1360–1362, 1978.

(2) Ilett, K.F., S.M. Gibb, and R.W. Unsworth, "Syrup of Ipecacuanha as an Emetic in Adults," *The Medical Journal of Australia*, 2:91–93, 1977.

(3) Thoman, M.E., and H.L. Verhulst, "Ipecac Syrup in Antiemetic Ingestion," *Journal of the American Medical Association*, 196:433–434, 1966.

28. A number of comments discussed the warning in proposed § 337.50(c)(4), which reads "Do not administer milk or carbonated beverages with this product [ipecac syrup]." Two comments strongly supported the reference to milk in this warning because milk reduces the effectiveness of ipecac syrup; one of these comments also supported the contraindication to the use of carbonated beverages as a diluent. Another comment suggested that the warning in § 337.50(c)(4) be revised to make it less dogmatic, i.e., *"It is preferable* not to administer milk or carbonated beverages with this product," rather than, "do not." The comment argued that the administration of fluid followed by ambulation is important to the successful induction of emesis when syrup of ipecac is used.

Several comments suggested deleting the reference to "carbonated beverages" from the proposed warning. The comments asserted that there are no reports in the published literature that contraindicate the administration of carbonated beverages, instead of water, as a diluent after giving ipecac syrup. One comment stated that the administration of carbonated beverages after giving syrup of ipecac could have been confused with the administration of carbonated beverages where caustics have been ingested and the resulting gastric distention might lead to perforation. Ipecac syrup is already contraindicated in such cases.

Two comments stated that the administration of fluid is important to successful induction of emesis; however, it is sometimes difficult to get children, who are most likely to need ipecac syrup, to drink water, and clear juices or carbonated beverages may be more acceptable. These comments cited a study showing that the use of carbonated beverages caused no adverse affects or alteration of the effectiveness of ipecac syrup in inducing emesis, leading the authors of the study to conclude that carbonated beverages do not appear to affect the patient adversely or alter the effectiveness of ipecac syrup (Ref. 1). A final comment argued that the entire warning in § 337.50(c)(4) is not warranted, is likely to be in error, and should be deleted.

After reviewing the data, the agency concludes that carbonated beverages can be safely administered after ingesting ipecac syrup. The agency agrees that administration of fluids is important to assure successful induction of emesis. The agency also recognizes the difficulty in getting children to drink water. Therefore, the agency is proposing that the directons be revised to state that water or other clear liquids are to be given with ipecac syrup. Because studies have shown that milk interfers with the ability of ipecac syrup

to induce emesis, the agency disagrees that the entire warning should be deleted (Ref. 2).

References

(1) Uden, D.L., G.J. Davison, and D.P. Kohen, "The Effect of Carbonated Beverages on Ipecac-Induced Emesis," *Annals of Emergency Medicine*, 10:79–81, 1981.

(2) Varipapa, R.J., and G.M. Oderda, "Effect of Milk on Ipecac-Induced Emesis," *Journal of the American Pharmaceutical Association*, 17:510, 1977.

29. Two comments strongly supported the need for a drug interaction precaution to guard against the use of activated charcoal in conjunction with ipecac syrup.

As discussed in the tentative final monograph for emetic drug products (43 FR 39545), the agency agrees that a drug interaction precaution is necessary on ipecac syrup to warn against the simultaneous use of activated charcoal and ipecac syrup. The agency is modifying this statement in this tentiative final monograph and proposing is as follows: "*Drug Interaction Precaution:* Activated charcoal will adsorb ipecac syrup. Do not give activated charcoal until after patient has vomited, unless directed by a health professional." This modification is being proposed in order to be consistent with the wording of a warning proposed for activated charcoal. (See comment 43 below.)

30. Two comments pointed out that the first sentence of § 337.50(d) "Drug interaction precautions" incorrectly states that "Activated charcoal will *absorb* ipecac syrup" instead of stating that "Activated charcoal will *adsorb* ipecac syrup." One comment contended that the basis of this drug interaction is the adsorption of ipecac alkaloids to the surface of activated charcoal particles.

This error was corrected in a notice published in the **Federal Register** of November 28, 1978 (43 FR 55417).

31. One comment suggested that the labeling of ipecac syrup include a statement warning that an overdose of ipecac syrup could be toxic in a child who fails to vomit. The comment stated that there is no statement in the labeling that would make the consumer aware that an overdose of ipecac syrup itself can be toxic.

FDA has reduced the likelihood of an overdose by placing a 30-mL container size limit on ipecac sprup that is sold OTC. Thirty mL of ipecac syrup is not a toxic dose, even for children. (See comment 20 above.) In addition, the labeling of ipecac syrup has been revised to instruct consumers to call a Poison Control Center, emergency medical facility, or health professional for help before using the product and to call again if the patient fails to vomit within 30 minutes. For these reasons, the agency concludes that the warning suggested in the comment is unnecessary.

32. Two comments supported the recommended dose of 15 mL (1 tablespoonful) of ipecac syrup. One comment expressed the opinion that although 15 mL of ipecac syrup is the usual dose in children less than 5 years of age, and 30 mL is the usual dose for adults and children over 5 years of age, standardizing the dose at 15 mL for everyone as proposed is a suitable alternative and would alleviate any possible confusion. However, five comments by poison control centers disagreed with the recommended 15-mL dose of ipecac syrup for persons over 1 year of age. These comments urged that this dosage be increased to 30 mL for adults. One comment submitted supporting data showing that 30 mL of ipecac produced an 81-percent incidenced of vomiting in adults. The incidence of vomiting was increased to 96-percent when a second 30-mL dose was administered to those patients who failed to vomit initially (Ref. 1). Another study (Ref. 2) demonstrated that the incidence of vomiting was only 55 to 68 percent when a 15-mL dose of ipecac was administered. The comments stated further that, in the experience of poison control centers and according to current articles (Ref. 3), the appropriate adult dose of ipecac syrup is recognized as 30 mL followed by 1 to 2 glasses of water.

FDA agrees with the position and supporting data submitted by the poison control centers. The agency is proposing that the recommended dose of ipecac syrup for adults, i.e., individuals over 12 years of age, in § 337.54(d)(1) be an initial dose of 2 tablespoonsful (30 mL) rather than the previously proposed 1 tablespoonful (15 mL) dose, with a second dose of 2 tablespoonsful to given if vomiting does not occur within 30 minutes.

References

(1) Comment OB0003, Docket No. 81N–0033, Dockets Management Branch.

(2) Ilett, K.F., S.M. Gibb, and R.W. Unsworth, "Syrup of Ipecacuahna as an Emetic in Adults," *Medical Journal of Australia*, 2:91–93, 1977.

(3) Velri, J.C., and A.R. Temple, "Telephone Management of Poisonings using Syrup of Ipecac," *Clinical Toxicology*, 9:407–417, 1976.

33. Several comments objected to the proposed directions for use, which recommend the administration of ipecac syrup in infants under 1 year of age without medical supervision. The comments argued that infants under 1 year of age need to be carefully attended when vomiting occurs in order to help the child become properly positioned to prevent aspiration of vomitus. Some comments further argued that because many people believe incorrectly that ipecac is an "antidote" rather than an emetic and because ipecac takes approximately 30 minutes to be effective, a large number of children may not be properly attended during this critical period, thereby needlessly exposing them to accidents involving aspiration of vomitus and possible death by suffocation or aspiration pneumonitis. Two other comments urged that the use of ipecac syrup for infants under 6 months of age be restricted to a physician's office or emergency room. One of the comments cited a statement in a recently published text supporting this proposed restriction (Ref. 1).

Although the agency shares the comments' concern that it is best to use ipecac syrup in infants under 1 year of age only under professional advice and guidance because of the risk that infants might aspirate their vomitus, the comments have not provided adequate or convincing justification for deletion of the dosage statement for infants under 1 year of age. The labeling contains directions to seek professional assistance before administering ipecac syrup to any age group. The agency recognizes there may be situations when professional assistance cannot be obtained and believes that the risk of aspiration may be less in such situations than the risk of allowing a toxic substance to be absorbed. The agency also recognizes that infants between the ages of 6 months and 1 year are quite mobile and thus susceptible to accidental poisoning and believes that a dosage for this age group should be provided in this tentative final monograph. Because the chance of accidental poisoning in infants under 6 months would be extremely rare, a dose for this age group is not being proposed in the monograph. A statement has been added advising that ipecac syrup should not be given to children under 6 months of age unless directed by a health professional.

Reference

(1) Goldfrank, L.R., "Managing of the Overdosed or Poisoned Patient who is Alert," *in* "Toxicological Emergencies," Appleton, Century, Crofts, New York, p. 12, 1982.

34. Three comments recommended against administering a second dose of ipecac syrup. Two of the comments stated that a second dose of ipecac syrup at home would delay treatment at

a hospital or other medical facility. The third comment stated that the only time that a second dose of ipecac syrup would be needed is for overdoses in adults who fail to vomit following the first dose. The comment stated that overdoses in adults are usually intentional and involve ingestion of large amounts of drugs and multiple combinations. According to the comment, these patients should be treated in emergency facilities and should receive psychiatric evaluation. The comment stated that, because home treatment would involve no more than administration of the first dose of ipecac syrup and then transportation of the patient to the hospital, only one dose of ipecac syrup is necessary.

The agency does not agree that directions to give a second dose of ipecac should be deleted from the monograph. One of the basic reasons for having ipecac syrup in the home is so that consumers can treat cases of poisoning even if professional help cannot be obtained. The agency fully supports the idea that professional help should be sought before ipecac syrup is used but realizes that some cases may exist where help cannot be obtained quickly. In those cases, consumers should have directions for the proper use of ipecac syrup, including directions to administer a second dose. In further support of giving a second dose Veltri and Temple (Ref. 1) report that the ability to induce emesis at home is a significant advantage because the average delay between ingestion and arrival at an emergency room has been reported to be in excess of 60 minutes, and delays longer than 60 minutes are associated with a decrease in the efficiency of emesis. The need for psychiatric evaluation is unrelated to the safe and effective use of OTC poison treatment drug products. Therefore, this subject is not covered in the monograph for OTC poison treatment drug products.

Reference

(1) Veltri, J.C., and A.R. Temple, "Telephone Management of Poisoning Using Syrup of Ipecac," *Clinical Toxicology*, 9:407–417, 1976.

35. Three comments opposed the recommendations, proposed in §§337.50 (c)(1), (e)(i), and (e)(ii), to repeat the dose of ipecac syrup if vomiting does not occur within 20 minutes. The comments noted that Rauber (Ref. 1) has reported that after administering ipecac syrup the time to emesis was as high as 26 minutes in the 24 patients studied, and, in the author's personal experience, 25 to 30 minutes is more often the time to emesis. One comment stated that in a recent series of experiments in normal healthy male volunteers, the average time to induce emesis was 22 minutes (Ref. 2). The comments, therefore, urged that the recommended time limit before repeating the dose of ipecac syrup be raised to 30 minutes. Three other comments recommended deletion of the recommendation that a second dose of ipecac syrup be given if the first dose does not induce vomiting within 20 minutes because waiting for a second dose to take effect could cause excessive delay and loss of valuable time before transporting the patient to a medical facility. One of these comments recommended that the patient be advised to call a physician immediately if vomiting does not occur within 20 minutes.

The agency has reviewed the data cited by the comments and is persuaded that the directions for ipecac syrup should be revised to indicate that a second dose of ipecac syrup should be administered if vomiting has not occurred within 30 minutes. Veltri and Temple (Ref. 2) reported that of 776 cases, 419 subjects (54 percent) vomited within 15 minutes of ipecac administration. The number increased to 689 cases (88.9 percent) within 30 minutes. This finding is supported by Rauber (Ref. 1) who found a mean time to vomiting of 26 minutes. Similar results were obtained in a study by Manoguerra and Krenzelok (Ref. 3) on 232 patients and in a study by Robertson (Ref. 4) on 214 patients. Analysis of the data from the Manoguerra and Krenzelok study shows that 144 of 232 patients (62.1 percent) vomited in the 0-to-20-minute interval, while 44 patients (18.9 percent) vomited in the 20-to-30-minute interval. Similarly, the Robertson data showed that 33 of 214 patients (15.4 percent) vomited in the 20-to-30-minute interval, while successful emesis occurred in 156 of 214 patients (72.9 percent) within the 0-to-20-minute interval. The agency believes that the increases in successful emesis shown by the above studies for the 20-to-30-minute time interval represent a significant increase in successful emesis. The agency does not agree that directions to give a second dose of ipecac should be deleted from the monograph. As discussed in response to comment 34 above, a principal reason for having ipecac in the home is to permit treatment of poisoning when professional help cannot be reached. Ideally, professional help should be sought before ipecac syrup is used; however, in some cases it may not be possible to obtain help promptly. In those cases, consumers should have directions for the proper use of ipecac syrup. If vomiting does not occur within 30 minutes, a second dose should be given to take advantage of any cumulative effect of the second dose of ipecac. In further support of giving a second dose, Veltri and Temple (Ref. 2) report that the ability to induce emesis at home is a significant advantage because the average delay between ingestion and arrival at an emergency room has been reported in excess of 60 minutes, and delays longer than 60 minutes are associated with a decrease in efficiency of emesis.

References

(1) Rauber, A., "The Cardiac Safety of Ipecac Used as a Therapeutic Emetic," *Veterinary and Human Toxicology*, 20:166–168, 1978.

(2) Veltri, J.C., and A.R. Temple, "Telephone Management of Poisoning Using Syrup of Ipeca," *Clinical Toxicology*, 9:407–417, 1976.

(3) Manoguerra, A.S., and E.P. Krenzelok, "Rapid Emesis from High-Dose Ipecac Syrup in Adults and Children Intoxicated with Antiemetics or Other Drugs," *American Journal of Hospital Pharmacy*, 35:1360–1362, 1978.

(4) Robertson, W.O., "Syrup of Ipecac—A Slow or Fast Emetic?," *American Journal of Diseases of Children*, 103:58–61, 1962.

36. Several comments supported the second portion of the warning proposed in § 337.50(c)(1), "Call a physician, Poison Control Center, or emergency room . . . immediately if vomiting does not occur within 20 minutes after a second dose has been given." However, one comment believed this information should also appear as a direction because most people would look in the directions for further advice if vomiting does not occur.

The directions being proposed in this tentative final monograph for ipecac syrup include the dosages to be given and instructions to repeat the dose if vomiting has not occurred within 30 minutes. The principal display panel of an ipecac syrup container will contain advice to call a poison control center, emergency medical facility, or health professional for help before using the product. The agency agrees that the directions should reinforce the importance of continued attempts to obtain professional help when using any poison treatment product and, therefore, proposes the following statement for inclusion in the directions of all poison treatment drug products: "If previous attempts to contact a poison control center, emergency medical facility, or health professional were unsuccessful, continue trying."

37. One comment urged that ipecac syrup labeling contain a recommendation to check the label of

the ingested substance for pertinent first aid instructions because many commercial chemical products containing caustic substances or organic solvents now carry warnings against inducing emesis in case of ingestion. The comment added that the Consumer Product Safety Commission is currently considering a requirement that labeling on all chemical products under its jurisdiction carry first aid instructions, including instructions on whether or not to induce vomiting.

The agency recognizes that the Federal Hazardous Substances Act (15 U.S.C. 1261.2(p)(1)(G)) and related regulations (16 CFR 1500.3(b)(14)(i) and 21 CFR 1230.14) contain requirements for labeling hazardous or caustic substances with instructions for first aid treatment. However, many household products are labeled with inadequate, incorrect, and potentially misleading first aid instructions. Alderman, et al. (Ref. 1) surveyed 1,019 household product labels and found that 85 percent had inadequate first aid information. In view of this information, the agency believes that it would be inappropriate and potentially harmful to include such a statement in the ipecac syrup labeling. At some future time, if product first aid labeling becomes more reliable, the agency will reevaluate its position.

Reference

(1) Alderman, D., et al., "How Adequate are Warnings and First Aid Instructions on Consumer Product Labels?: An Investigation," *Veterinary and Human Toxicology*, 24:1:8–11, 1982.

38. Three comments stressed the importance of keeping the patient ambulatory after the administration of ipecac syrup. One of these comments, from a poison control center, stated that its experience had shown that emesis is greatly delayed if the patient is kept inactive following the administration of ipecac syrup. The comment urged that labeling be modified to mention this concern. Another comment submitted a study showing no significant difference in the time it took to induce emesis in patients kept in motion versus those assigned bedrest (Ref. 1).

Keeping the person who has been given ipecac syrup active may or may not speed up emesis; however, regardless of the poison treatment used, activity may prevent loss of consciousness, which is a particular problem with people who have ingested an overdose of a central nervous system depressant. Therefore, the agency is proposing that the statement, "Keeping patient active and moving," be added to the directions for use of all poison treatment drug products.

Reference

(1) Meester, W.D., "Emesis and Lavage," *Veterinary and Human Toxicology*, 22:225–234, 1980.

39. Referring to the Miscellaneous Internal Panel's statement that, "when retching and vomiting begin, the patient should be placed face down with head lower than hips" (47 FR 447), one comment suggested that children be seated or held on an adult's lap near a basin or sink while vomiting so that the mouth can be cleared of any vomitus. The comment stated that it is difficult to expect a child or adult to be placed face down with head lower than hips, when vomiting begins.

The agency agrees with the Panel that when vomiting begins the head-lower-than-hip position helps prevent aspiration of the vomitus into the lungs. However, as the comment pointed out, this position would be difficult for a patient to maintain under some circumstances. Although the Panel included the statement in its report, it was not included in the labeling recommended in its monograph. In view of the potentially conflicting results, the agency does not believe a statement regarding positioning of the patient should be included in the monograph.

Reference

(1) Goldfrank, L.R., "Managing of the Overdosed or Poisoned Patient who is Alert," *in* "Toxicological Emergencies," Appleton, Century, Crofts, New York, p. 12, 1982.

40. Four comments urged that ipecac syrup should be packaged and marketed only in 30-mL containers, arguing that this container size provides two 15-mL doses, which would be convenient, safe, and effective; any larger amount could lead to overdoses in children and any less might be ineffective. Two other comments supported the 30-mL size, but suggested that two 15-mL containers should also be permitted. Three comments favored the 15-mL size only, arguing that 15 mL is the unit dose for a child. One of these comments suggested that the 15-mL containers should be marketed in packages of four to permit simultaneous treatment of several patients.

Current FDA regulations (21 CFR 201.308(c)) require that the OTC marketing of ipecac syrup be limited to 30 mL containers. This package size is convenient in that it provides one adult dose or two 15 mL doses for children age 1 to 12. The comments did not present any convincing arguments to warrant a change in the container size. Therefore, the 30 mL container size requirement is proposed in this tentative final monograph.

41. One comment urged that safety caps not be used on bottles of ipecac syrup.

The Poison Prevention Packaging Act (15 U.S.C. 1471–1476), which requires safety packaging for certain drug products, is administered by the Consumer Product Safety Commission (CPSC). Where necessary, FDA can request CPSC to require safety closures on OTC drugs. However, because ipecac syrup is packaged only in 30 mL containers, each of which contains a less-than-toxic dose for a small child, and the presence of safety closures could result in unwarranted delay and confusion in the administration of ipecac syrup to treat poisoning victims in emergency situations, the agency agrees that safety closures should not be used on bottles of ipecac syrup sold OTC.

42. One comment suggested that, to prevent misunderstanding by dispensing pharmacists, every bottle of ipecac syrup larger than 30 mL should bear the following statement on the label: "Remember, 30 mL may be dispensed without a prescription."

This monograph establishes conditions of marketing of OTC drugs only. It does not address prescription labeling. Thus the statement suggested by the comment is not included in the monograph. The agency has no objection to a statement similar to that suggested by the comment appearing in the labeling of prescription size bottles of ipecac syrup and is aware that such labeling is currently used (Ref. 1). However, the agency suggests that when such labeling is used it should also include a statement that complete labeling information as specified in the poison treatment drug products monograph (21 CFR Part 357 Subpart A) must be provided to consumers to whom the product is sold. The agency suggests that manufacturers of prescription size bottles of ipecac syrup provide pharmacists complete auxillary labeling to provide to consumer when smaller quantities are sold from prescription size bottles.

Reference

(1) Physician's Desk Reference, 37th Edition, Medical Economics Company, Orandell, NJ, p. 1141, 1983.

E. Comments on Adsorbents

43. Two comments objected to the OTC availability of activated charcoal as a poison adsorbent. The comments contended that poisoning cases serious enough to require the use of activated charcoal should be treated in an emergency room or other health care

facility. A comment from a poison control center stated that its experience indicates that only about 10 percent of toxic ingestion exposures are serious enough to require both the induction of emesis and the additional decontamination provided by activated charcoal. The other comment expressed that use of activated charcoal in the home may create a false sense of security and delay consultation with a poison control center.

Although syrup of ipecac has long been recognized as the first line of defense in the home treatment of poisoning, a number of studies have shown that vomiting induced by ipecac is often not complete, with recovery of stomach contents varying from 0 to 78 percent (Ref. 1). Activated charcoal has been demonstrated to be safe and effective in adsorbing poison that may remain in the gastrointestinal tract after vomiting has occurred. The Miscellaneous Internal Panel recognized (47 FR 448) and the agency concurs that, generally, the use of activated charcoal should be restricted to administration following the induction of vomiting. The agency is therefore proposing the following statement for inclusion on activated charcoal products as a drug interaction precaution: "Do not give activated charcoal until after patient has vomited unless directed by a health professional." There are situations in which activated charcoal can be administered without inducing vomiting. However, the agency believes that this decision should be made by a health professional on an individual case basis. This warning will replace the warning recommended by the panel in § 357.20(c)(3).

Reference

(1) Meester, W.D., "Emesis and Lavage," *Veterinary and Human Toxicology*, 22:225–234, 1980

44. Three comments commended the Panel for both anticipating and encouraging the development of new and more palatable dosage forms of activated charcoal, but expressed concern over the Panel's recommended criteria for comparison of the adsorptive capacity of new dosage forms with the existing dosage form. One comment urged development of a methodology for an in vivo comparison of dosage forms. Another comment asserted that the testing criteria recommended by the Panel are unnecessary because there are adequate compendial standards for measuring the adsorptive capacity of activated charcoal in the United States Pharmacopeia (U.S.P.) (Ref. 1). The comment stated that any product containing activated charcoal U.S.P. as its active ingredient would have to meet these standards for adsorptivity, and that these standards, which can be applied to final formulations, make in vivo testing scientifically and legally unnecessary.

The agency agrees that additional testing criteria for activated charcoal beyond final formulation conformity to U.S.P. adsorptivity standards (Ref. 1) should not be necessary for any activated charcoal product. The agency is proposing that the monograph specify that final formulations, in amounts equivalent to one gram (g) of activated charcoal, must meet or exceed the standards for adsorptivity for activated charcoal, U.S.P. However, the U.S.P. adsorptivity standard is specific to a dry powdered dosage form and may not be readily applicable to the testing of other dosage forms. The agency invites specific comment on suitable testing standards and methods, including modifications of the U.S.P. adsorptivity standard, for dosage forms other than the traditional dry powdered activated charcoal.

Reference

(1) "United States Pharmacopeia XX—National Formulary XV," United States Pharmacopeial Convention, Inc., Rockville, MD, pp. 128–129, 1980.

45. One comment questioned the possibility of aspiration of activated charcoal in powdered form.

Athough activated charcoal is normally packaged in powdered form, the likelihood of aspiration is minimal because the directions for use instruct the consumer to mix the activated charcoal in water before it is administered.

46. One comment supported the Miscellaneous Internal Panel's 30 g minimum dosage recommendation for activated charcoal and urged the agency to restrict the OTC marketing of activated charcoal products to a unit dose form containing a minimum of 30 g. The comment expressed concern that the dosage of activated charcoal may not be adequate if the Panel's volume measure recommendation (6 level tablespoonsful) was used because of the varying densities of charcoal powder and because 1 tablespoonful could supply from 3.5 to 6 g of activated charcoal (Refs. 1 and 2).

Another comment disagreed with the Panel's 30-g recommendations and requested that the dose be changed to 25 g. The comment supplied information indicating that a much wider effective dosage range (from 5 to 60 g) exists in actual practice and that a product containing 25 g activated charcoal is in widespread use with general acceptance by emergency medical facilities (Ref. 3).

The agency recognizes that the density of activated charcoal may vary considerably. As pointed out by one comment, a tablespoonful of activated charcoal can contain anywhere from 3.5 to 6 g (Refs. 1 and 2); thus, 6 tablespoonsful could contain from 21 to 36 g. The dose of activated charcoal generally recommended is 8 to 10 times the amount of the toxic substance ingested (Refs. 1 and 2) with the maximum limit determined only by the feasibility of administration (47 FR 449). For these reasons, the agency does not believe the dose of activated charcoal needs to be limited to a specific weight amount. Instead, the agency is proposing a range of 20 to 30 g as a dose of activated charcoal. Taking into consideration the varying densities of activated charcoal, this dosage approximates the Panel's recommendation of 6 tablespoonsful. It will also include the 25 g product that is recommended by one comment. As the comment and the Panel pointed out, there is a wide effective dosage range for activated charcoal, and the agency is proposing that a second dose be given if possible. (See comment 50 below.)

References

(1) Greensher, J., et al., "Activated Charcoal Updated," *Annals of Emergency Medicine*, 8:261–263, 1979.

(2) Dipalma, J.R., "Activated Charcoal—A Neglected Antidote," *Clinical Pharmacology*, 20:155–156, 1979.

(3) Comment No. C00005, Docket No. 81N-0050, Dockets Management Branch.

F. Comments on Adsorbent Labeling

47. One comment suggested that the statement of identity recommended in § 357.50(a) for poison treatment drug products containing activated charcoal be changed from the term "adsorbent" to a more easily understood term such as "poison antidote," "emergency poison antidote," or "first aid poison antidote."

Webster defines antidote as a remedy to counteract the effect of a poison (Ref. 1). Activated charcoal acts by means of adsorbing poisons, not by counteracting their effects. Thus, it would be false and misleading to replace the term "adsorbent" with any term implying that activated charcoal is a poison antidote. However, acceptable statements of identity are provided by replacing the word "antidote" with the word "adsorbent" in the phrases suggested by the comment, i.e., "poison adsorbent," "emergency poison adsorbent" or "first aid poison adsorbent." Therefore, the agency is proposing that any one of

these phrases may be used as the statement of identity in place of the word "adsorbent" for poison treatment drug products containing activated charcoal.

Reference

(1) "Webster's New Collegiate Dictionary," G. and C. Merriam Co., Springfield, MA, 1979, s.v. "antidote."

48. One comment believed that the Miscellaneous Internal Panel's recommended directions of mixing 4 ozs (120 mL) of water with 30 g of activated charcoal would result in too thick a slurry with increased chances of complications if aspiration of the charcoal mixture occurs. The comment cited a case in which a mixture of 9 g of charcoal in 35 mL of water was administered to a patient who regurgitated and aspirated the mixture, resulting in the immediate development of airway obstruction (Ref. 1). The comment pointed out that the water to charcoal ratio in this case (3.89:1) is very close to the ratio (4:1) recommended by the Panel. The comment recommended that the charcoal be mixed with 8 oz (240 mL) of water, adding that such a mixture allows for a better dispersion of the charcoal in water and has the advantage of making the charcoal more palatable.

Upon evaluation of the report of the case of airway obstruction resulting from the aspiration of a thick charcoal-water slurry, the agency agrees with the comment that increasing the amount of water mixed with activated charcoal will reduce this danger, aid in the dispersion of the charcoal in water, and make the mixture more palatable and thus more likely to be ingested. Therefore, the agency is proposing that the directions for activated charcoal provide that the dose is to be administrated in a minimum of 8 oz of liquid.

Reference

(1) Pollack, M.H., et al., "Aspiration of Activated Charcoal and Gastric Contents," *Annals of Emergency Medicine*, 10:528–529, 1981.

49. Several comments stated that the directions for activated charcoal recommened by the Panel in § 357.50(d) are too specific and restrictive in that they do not allow the mention of dosage forms other than aqueous solutions. The comments requested that the directions be modified to allow these alternative dosage forms to be mentioned.

The agency agrees. As pointed out in comment 44 above, the agency has no objection to alternative dosage forms as long as suitable testing methods can be developed to insure that the final product meets USP XX standards for adsorbency. Accordingly, the agency has revised the directions in this tentative final monograph to allow for alternative dosage forms.

50. Two comments suggested that the labeling of activated charcoal include a statement that the dose of activated charcoal should be repeated if possible. One comment stated that the upper limits of charcoal administration are governed only the feasibility of administration.

The agency agrees. Doses of activated charcoal up to 120 g have been administered with no reported side effects (Refs. 1 and 2) and, in general, the larger the does of activated charcoal the greater the adsorption of the ingested poison. Therefore, the agency is proposing the following statement in the directions for activated charcoal: "Repeat dose immediately, if possible."

References

(1) Greensher, J., et al., "Activated Charcoal Updated," *Annals of Emergency Medicine*, 8:261–263, 1979.

(2) Dipalma, J.R., "Activated Charcoal—A Neglected Antidote," *Clinical Pharmacology*, 20:155–156, 1979.

51. One comment suggested that the warning "Do not give activated charcoal to people who have swallowed petroleum distillate or corrosive products" be added to the warnings for products containing activated charcoal because the administration of activated charcoal is not infrequently followed by vomiting and the induction of emesis for corrosive products is contraindicated. The comment added that an additional complication to the use of activated charcoal with corrosives is that it may obscure visual observation of gastroesophageal lesions by endoscopy. The comment concluded that there is a lack of evidence documenting the beneficial effects of activated charcoal in humans who have ingested corrosives or petroleum distillates, and, therefore, activated charcoal should not be used following ingestion of these substances.

The agency agrees with the comment. Decker, Combs, and Corby (Ref. 1) found that corrosives such as inorganic acids, sodium and potassium hydroxides, and sodium metasilicate are not adsorbed to any measurable extent by activated charcoal. Picchioni, Chin, and Laird (Ref. 2) reported that, in rats, kerosene is adsorbed by activated charcoal, but that there is a lack of data on the ability of activated charcoal to adsorb other petroleum distillates. Some authors report that activated charcoal is ineffective in petroleum distillate ingestions (Ref. 3). For these reasons, the agency believes that the labeling of activated charcoal should include the same corrosive, petroleum distillate warning as that required for ipecac syrup.

References

(1) Decker, W.J., H.F. Combs, and D.G. Corby, "Adsorption of Drugs and Poisons By Activated Charcoal," *Toxicology and Applied Pharmacology*, 13:454–460, 1968.

(2) Picchioni, A.L., L. Chin, and H.E. Laird, "Activated Charcoal Preparations—Relative Antidotal Efficacy," *Clinical Toxicology*, 7:97–108, 1974.

(3) Czajka, P.A., and J.P. Duffy, "Drugs for the Management of Acute Poisonings," *in* "Poisoning Emergencies. A Guide for Emergency Medical Personnel," The C.V. Mosby Co., St. Louis, p. 15, 1980.

G. Comments on Poison Treatment Kits

52. Nine comments supported the concept of poison treatment kits containing both activated charcoal and ipecac syrup and encouraged their availability. Eight other comments, While supporting the OTC availability of ipecac syrup, opposed the OTC marketing of kits containing activated charcoal as well as ipecac syrup. The comments pointed out that the kits would be more expensive than ipecac syrup alone, that activated charcoal could be administered at the wrong time and interfere with the functioning of the ipecac syrup, and that ingestion serious enough to warrant the use of activated charcoal should properly be treated in an emergency room.

The agency appreciates the concerns and objections raised by the comments opposing the marketing of activated charcoal with ipecac syrup in poison treatment kits. The kits will undoubtedly be more expensive than ipecac syrup alone, but they are not intended to replace or prevent the sale of ipecac syrup packaged alone. Although activated charcoal can adsorb ipecac syrup and prevent its functioning if administered before the ipecac syrup has had time to induce vomiting, the agency believes that the direction and warnings for both activated charcoal and ipecac syrup being proposed in this tentative final monograph adequately caution against such use. In addition, the labeling for a poison treatment kit clearly instructs the user to ". . . call a poison control center, emergency medical facility, or health professional for help before using this product." While most cases of poisoning may call for the use of ipecac syrup only, the presence of both ipecac syrup and activated charcoal in the kit would provide the poison control center personnel or other health professional flexibility in responding to the needs of

any individual case of poisoning. In addition, when professional advice cannot be obtained, the administration of activated charcoal after vomiting had occurred provides an added margin of protection because the activated charcoal can adsorb residual poison.

The agency therefore concludes that poison treatment kits containing both activated charcoal and ipecac should be available OTC.

53. One comment urged that the poison treatment monograph contain a statement expressing a preference for ipecac syrup alone rather than the more costly dual ingredient kit containing both ipecac syrup and activated charcoal.

The agency agrees that ipecac syrup is the first line of defense in poison treatment and is less costly than the dual ingredient poison treatment kit. It would, however, be inappropriate to attempt to influence purchasing practices by requiring a label statement expressing an opinion as to the agency's preference between two products, both of which have been determined to be safe and effective.

54. Numerous comments objected to the ingredient and dosage specifications recommended by the Panel in proposed § 357.14 for a poison treatment kit. Two comments did not believe that there was any potential safety problems with the amount of ipecac syrup present in the kit. Most of the comments objected to the requirement that the kit contain 60 mL of ipecac syrup because of the potential for ipecac overdose, especially in small children. Two of these comments stated that 60 mL of ipecac syrup would not pose a safety problem if "child resistant" tops were used on the bottles, and another comment stated that a warning against overdosing could adequately handle this risk. The majority of the comments urged that the kit be limited to some smaller quantity of ipecac syrup; three suggested a limit of 15 mL of ipecac syrup, and one suggested a 45 mL limit. Thirty mL was, however, the most commonly suggested limit.

In addition, two comments objected to the requirement that the kit contain exactly four (30 g) containers of activated charcoal, with one comment suggesting that the requirement be changed from 30 g containers to 25 g containers. One of these comments also questioned the agency's authority to establish exact numerical limits on the size and type of dosage forms in such a kit.

The agency has authority under sections 502(f) and 701(a) of the Act (21 U.S.C. 352(f) and 371(a)) to establish limits on size and types of dosage forms and limits on package contents, e.g., the 36-tablet limitation per container of 1¼ grain (pediatric) aspirin tablets specified in § 201.314(c)(2). The agency has, however, reviewed both the Panel's report and the comments and agrees that the Panel's action in establishing exact ingredient and dosage specifications for a poison treatment kit, including the exact size and number of containers, is overly restrictive. The agency is proposing that the tentative final monograph establish that poison treatment kits contain one adult dose of ipecac syrup, 30 mL, and a minimum of one dose of activitated charcoal, 20 g. This requirement will provide a minimum of one dose each of both an emetic and an adsorbent. As discussed in comment 30 above, containers of ipecac syrup are limited to 30 mL due to the potential toxicity of this ingredient. The kit can therefore contain only one 30-mL container of ipecac syrup. There is no reason, however, for any restriction on the size or number of containers of activitated charcoal beyond the minimum dosage requirement of 20 g. As discussed in comment 44 above, new dosage forms of activated charcoal are also acceptable. The agency has also considered the suggestion that 60 mL of ipecac syrup could be safely packaged in a kit if placed in separate containers equipped with "child resistant" caps. The safety advantage of using such caps to permit inclusion of more ipecac syrup in the kit would, however, be offset by the risk that such caps could delay administration of the initial dose of ipecac syrup. There is, of course, no restriction on the number of kits that an individual can purchase.

55. One comment pointed out that the description of the acute toxic ingestion kit recommended by the Panel in § 357.14, which specifies charcoal containers that facilitate mixing the contents, is in contradiction to the directions in § 357.50(d) which state "Mix 6 level tablespoonfuls in ½ glassful of water."

The agency agrees that there was a discrepancy. The revisions that have been made in this tentative final monograph have resolved this discrepancy. (See comments 48 and 49 above.)

56. Three comments suggested revising the direction statements recommended by the Panel in § 357.54(d). One comment suggested deleting the direction in § 357.54(d)(1) "When professional advice is not available, first give ipecac * * * " because professional advice in the form of a poison control center, an emergency facility, or a health professional is always available by telephone. The comment contended that this direction on the outside of a poison treatment kit could cause parents not to review the additional labeling in the kit and to give activated charcoal or ipecac syrup unnecessarily.

A second comment suggested rewording the directions statements by reversing the order of § 357.54(d)(1) and § 357.54(d)(3) to give greater prominence to the statement "Save the container of poison" and to require that the statement recommended in § 357.54(d)(2) "Read instruction at time of purchase and insert phone numbers" be placed on the principal or front display panel rather than just the outside of the kit. The third comment suggested that the directions be expanded to allow inclusion of a booklet containing more detailed first aid instruction in the kit.

The agency disagrees that professional help can always be reached by telephone. There are circumstances such as in isolated locations or during severe weather when such advice will not be available. As discussed in comment 9 above, the agency has revised the labeling of poison treatment drug products to require the following statements on the principal display panel: "If possible call a poison control center, emergency medical facility, or health professional for help before using this product." "If help cannot be reached quickly, follow the directions on * * * (manufacturers to indicate location of directions, e.g., on the back of the bottle)" and "Read the warnings and directions as soon as you buy this product. Insert emergency phone number(s) in space provided on the label."

The remainder of the warnings and directions are to be placed on a separate portion of the label. The agency disagrees that the statement "Save the container of poison" should be given any special prominence as compared with other labeling. However, the agency believes that this statement is applicable to all poison treatment drug products and thus is proposing that the monograph include the statement on ipecac syrup as well as activated charcoal products. The agency has no objection to the inclusion of labeling, folders, booklets, or leaflets containing more detailed first aid or poison treatment information as long as such information does not distract from required labeling.

II. The Agency's Tentative Adoption of the Panels' Reports

A. Summary of Ingredient Categories

The agency has reviewed the only active emetic ingredient submitted to the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products, ipecac syrup, and the single claimed active adsorbent ingredient submitted to the Advisory Review Panel on OTC Miscellaneous Internal Drug Products, activated charcoal, as well as other data and information available at this time, and concurs with the Panels' Category I classification of these ingredients as OTC poison treatment drugs.

For the convenience of the reader, the following table is included as a summary of the agency's categorization of OTC poison treatment active ingredients.

	Category
Emetics:	
Ipecac fluidextract	II.
Ipecac syrup	I.
Ipecac tincture	II.
Zinc sulfate	II.
Poison Adsorbents:	
Charcoal, activated	I.

B. Summary of the Agency's Changes in the Panels' Recommendations

FDA has considered the comments and other relevant information and concludes that it will tentatively adopt the Panels' reports and recommended monographs and will combine them into a single monograph for OTC poison treatment drug products with the changes described in FDA's responses to the comments above and with other changes described in the summary below. A summary of the changes made in the Panels' conclusions and recommendations and to the previous tentative final monograph for OTC emetic drug products follows:

1. The process of combining the emetic rulemaking (proposed 21 CFR Part 337) and the acute toxic ingestion rulemaking (proposed 21 CFR Part 357, Subpart A) into the present tentative final monograph under 21 CFR Part 357 (entitled Poison Treatment Drug Products for OTC Human Use,) has required the redesignation of many section and paragraph numbers.

2. The term "health professional" is being proposed in labeling in place of the term "physician," "doctor," or "pharmacist." (See comments 6 and 14 above.)

3. The term "emergency medical facility" is being proposed in labeling in place of the term "emergency room." (See comment 8 above.)

4. Labeling for all poison treatment drug products has been revised to change the order of listing of sources of help and information for poison treatment from "physician, poison control center or emergency room" to "poison control center, emergency medical facility, or health professional." (See comment 7 above.)

5. Labeling is being divided into two distinct sections: First, the principal display panel would contain the following instruction in a conspicuously boxed area: "If possible, call a poison control center, emergency medical facility, or health professional for help before using this product. If help cannot be reached quickly, follow the directions (manufacturer to indicate location of directions, e.g., on the back of the bottle)." The statements, "Read the warnings and directions as soon as you buy this product." "Insert emergency phone number(s) in space provided on the label," must also appear prominently on the principal display panel. Second, full warnings and directions are to be placed on a separate portion of the label. (See comment 9 above.)

6. A space for writing in the phone number(s) of the appropriate poison control center or other emergency medical facility must be provided on the principal display panel. (See comment 9 above.)

7. The terms "for the treatment of poisoning," "emergency first aid treatment for poisoning," "emergency treatment for poisoning," "emergency treatment for accidental poisoning," "for the treatment of accidental poisoning," "emergency first aid treatment for accidental poisoning," "emergency poison treatment," and "first aid poison treatment" have been proposed as other allowable statements for all poison treatment drug products. (See comment 15 above.)

8. The indication statement for ipecac syrup has been revised to read "for emergency use to cause vomiting of swallowed poisons." The indication statement for activated charcoal has been revised to read "for emergency use to adsorb swallowed poisons." (See comment 15 above.)

9. The dosage of ipecac syrup for individuals 1 year of age and over has been revised to allow manufacturers to express the dosage in terms of container size i.e., 1 or ½ bottle. (See comment 22 above.)

10. The warning "Do not use in semiconscious or unconscious persons" previously proposed for ipecac syrup has been revised to read "Do not use in persons who are not fully conscious." (See comment 23 above.)

11. The corrosive-petroleum distillate warning for ipecac syrup has been revised to read "Do not use this product, unless directed by a health professional, if turpentine, corrosives, such as alkalies (lye) and strong acids, or petroleum distillates, such as kerosene, gasoline, paint thinner, cleaning fluid, or furniture polish, have been ingested." (See comment 24 above.) This same warning is being proposed for activated charcoal products. (See comment 51 above.)

12. The warning "Do not administer milk or carbonated beverages with this product" previously proposed for ipecac syrup has been revised to read "Do not administer milk with this product." (See comment 28 above.)

13. The directions for ipecac syrup have been revised to provide for water or other clear liquids to be administered following ipecac syrup. (See comment 28 above.)

14. The drug interaction precaution for emetics has been revised to read "*Drug Interaction Precaution*: Activated charcoal will adsorb ipecac syrup. Do not give activated charcoal until after patient has vomited unless directed by a health professional." (See comment 29 above.)

15. The adult dose of ipecac syrup has been increased from 15 mL to 30 mL. (See comment 32 above.)

16. A dosage of ipecac syrup for children under 6 months of age is no longer provided in the monograph. A statement advising that ipecac syrup should not be given to children under 6 months of age unless directed by a health professional has been added to the monograph. (See comment 33 above.)

17. The time interval between the first and second doses of ipecac syrup has been increased from 20 to 30 minutes. (See comment 35 above.)

18. The directions for all poison treatment drug products have been revised to include the statement "If previous attempts to contact a poison control center, emergency medical facility, or health professional were unsuccessful, continue trying." (See comment 36 above.)

19. The directions for poison treatment drug products have been revised to include the statement "Keep patient active and moving." (See comment 38 above.)

20. The warning against use of activated charcoal before vomiting has occurred has been revised to read "Do not give activated charcoal until after patient has vomited unless directed by a health professional." (See comments 29, 43, and 51 above.)

21. Formulations for activated charcoal now provide for dosage forms other than a powder. (See comment 44 above.)

22. The dosage for activated charcoal has been revised to provide a range of 20 to 30 g. (See comment 46 above.)

23. The statement of identity for activated charcoal, "adsorbent," has been revised to "poison adsorbent" or optionally "emergency poison adsorbent" or "first aid poison adsorbent." (See comment 47 above.)

24. The directions for use of activated charcoal have been revised to require that the dose be administered in a minimum of 8 oz of liquid. (See comment 48 above.)

25. The statement "Repeat dose immediately, if possible" has been added to the directions for activated charcoal. (See comment 50 above.)

26. The contents of the poison treatment kit have been revised to provide for a content of one 30-mL container of ipecac syrup and a minimum of 1 adult dose of activated charcoal (20 g). Although kit contents are limited to 30 mL of ipecac syrup, there is no restriction on the size or number of containers of activated charcoal in the kit. (See comment 54 above.)

27. The direction "Save the container of poison" has been proposed for all poison treatment drug products. (See comment 56 above.)

28. The agency advises that those portions of § 201.308 and § 369.21 applicable to ipecac syrup will be revoked at the time that the final monograph becomes effective.

The agency has examined the economic consequences of this proposed rulemaking in conjunction with other rules resulting from the OTC drug review. In a notice published in the **Federal Register** of February 8, 1983 (48 FR 5806), the agency announced the availability of an assessment of these economic impacts. The assessment determined that the combined impacts of all the rules resulting from the OTC drug review do not constitute a major rule according to the criteria established by Executive Order 12291. The agency therefore concludes that not one of these rules, including this proposed rule for OTC poison treatment drug products, is a major rule.

The economic assessment also concluded that the overall OTC drug review was not likely to have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act, Public Law 96-354. That assessment included a discretionary Regulatory Flexibility Analysis in the event that an individual rule might impose an unusual or disproportionate impact on small entities. However, this particular rulemaking for OTC poison treatment drug products is not expected to pose such an impact on small businesses. Therefore, the agency certifies that this proposed rule, if implemented, will not have a significant economic impact on a substantial number of small entities.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC poison treatment drug products. Types of impact may include, but are not limited to, costs associated with product testing, relabeling, repackaging, or reformulating. Comments regarding the impact of this rulemaking on OTC poison treatment drug products should be accompanied by appropriate documentation. Because the agency has not previously invited specific comment on the economic impact of the OTC drug review on poison treatment drug products, a period of 120 days from the date of publication of this proposed rulemaking in the **Federal Register** will be provided for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined that under 21 CFR 25.24(d)(9) (proposed in the **Federal Register** of December 11, 1979, 44 FR 71742) this proposal is of a type that does not individually or cumulatively have a significant impact on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

List of Subjects in 21 CFR Part 357

OTC drugs, Poison treatment drug products, Anthelmintic drug products, and Cholecystokinetic drug products.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371)) and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)) and under 21 CFR 5.11, it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended by adding new Part 357, Subpart A, to read as follows:

PART 357—MISCELLANEOUS INTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—Poison Treatment Drug Products

Sec.

357.1 Scope.
357.3 Definitions.
357.10 Active ingredients for poison treatment.
357.14 Poison treatment kit.
357.50 Principal display panel of all poison treatment drug products.
357.52 Labeling of activated charcoal drug products.
357.54 Labeling of ipecac syrup drug products.
357.56 Labeling of poison treatment kits.
357.58 Other allowable statements for poison treatment drug products.
357.60 Nonapplicability of § 330.1(g) to poison treatment drug products.

Authority: Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321(p), 352, 355, 371); secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704).

Subpart A—Poison Treatment Drug Products

§ 357.1 Scope.

(a) An over-the-counter poison treatment drug product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each condition in this subpart and each general condition established in § 330.1.

(b) References in this subpart of regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 357.3 Definitions.

As used in this subpart:

(a) *Adsorbent.* An agent that causes another substance to adhere to its surface.

(b) *Emesis.* Vomiting.

(c) *Emetic.* An agent that causes vomiting (emesis).

§ 357.10 Active ingredients for poison treatment.

The active ingredients of the product consist of any of the following when used within the dosage limits established for each ingredient:

(a) *Charcoal, activated.* The active ingredient is in a formulation such that the equivalent of one gram activated charcoal mets or exceeds the standards of adsorption for activated charcoal, U.S.P.

(b) *Ipecac syrup.* The active ingredient of the product is powdered ipecac. It is marketed as ipecac syrup, U.S.P. in the

quantity of 1 fluid ounce (30 milliliters) only.

§ 357.14 Poison treatment kit.

The kit is a single outer package labeled according to §§ 357.50 and 357.58 that consists of one 30 milliliter container of ipecac syrup identified in § 357.10(b) and a minimum of one dose 20 gram of activated charcoal identified in § 357.10(a).

§ 357.50 Principal display panel of all poison treatment drug products.

In addition to the statements of identity required in §§ 357.52, 357.54, or 357.56, the principal display panel contains the following information:

(a) The following statements should appear in a conspicuously boxed area.

(1) "If possible call a Poison Control Center, emergency medical facility, or health professional for help before using this product."

(2) "If help cannot be reached quickly, follow the directions" (manufacturer to indicate location of directions, e.g., on the back of the bottle).

(3) "Read the warnings and directions as soon as you buy this product. Insert emergency phone number(s) in space provided on the label."

(b) A space must also be provided for writing in phone number(s) of the appropriate Poison Control Center, emergency mecical facility, or health professional.

§ 357.52 Labeling of activated charcoal drug products.

In addition to the labeling identified in § 357.50, the labeling of the product containing the ingredient identified in § 357.10(a) contains the following:

(a) *Statement of identity.* The labeling of the product includes the established name of the drug, if any, and identifies the product as a "poison adsorbent" "emergency poison adsorbent," or "first aid poison adsorbent."

(b) *Indication.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the phrase "For emergency use to adsorb swallowed poisons."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "Do not give activated charcoal until after the patient has vomited unless directed by a health professional."

(2) "Do not use in persons who are not fully conscious."

(3) "Do not use this product, unless directed by a health professional, if turpentine, corrosives, such as alkalies (lye) and strong acids, or petroleum distillates, such as kerosene, gasoline, paint thinner, cleaning fluid or furniture polish, have been ingested."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) Oral dosage: 20 to 30 grams of activated charcoal in a minimum of 8 ounces of liquid or as directed by a health professional.

(2) "Repeat dose immediately, if possible."

(3) "If previous attempts to contact a poison control center, emergency medical facility, or health professional were unsuccessful, continue trying."

(4) "Keep patient active and moving."

(5) "Save the container of poison."

§ 357.54 Labeling of ipecac syrup drug products.

In addition to the labeling identified in § 357.50 the labeling of the product containing the ingredient identified in § 357.10(b) contains the following:

(a) *Statement of identity.* The labeling of the product includes the established name of the drug, if any, and identifies the product as an "emetic."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that is limited to the phrase "For emergency use to cause vomiting of swallowed poisons."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings":

(1) "Do not use in persons who are not fully conscious."

(2) "Do not use this product, unless directed by a health professional, if turpentine, corrosives, such as alkalies (lye) and strong acids, or petroleum distillates, such as kerosene, gasoline, paint thinner, cleaning fluid, or furniture polish, have been ingested."

(3) "Do not administer milk with this product."

(4) "*Drug Interaction Precaution:* Activated charcoal will adsorb ipecac syrup. Do not give activated charcoal until after the patient has vomited, unless directed by a health professional."

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions":

(1) Adults and children 12 years of age and over: oral dosage is 2 tablespoonsful (30 milliliters of 1 bottle) followed by 1 to 2 glasses (8 to 16 ounces) of water or other clear liquid or as directed by a health professional.

(2) Children 1 to under 12 years of age: oral dosage is 1 tablespoonful (15 milliliters or ½ bottle) followed by 1 to 2 glasses (8 to 16 ounces) of water or other clear liquid or as directed by a health professional.

(3) Children 6 months to under 1 year of age: oral dosage is 1 teaspoonful (5 milliliters) followed by ½ to 1 glass (4 to 8 ounces) of water or other clear liquid or as directed by a health professional.

(4) Children under 6 months of age: Do no administer unless directed by a health professional."

(5) "If vomiting does not occur within 30 minutes, repeat the dose."

(6) "If previous attempts to contact a poison control center, emergency medical facility, or health professional were unsuccessful, continue trying."

(7) "Keep patient active and moving."

(8) "Save the container or poison."

§ 357.56 Labeling of poison treatment kits.

The individual components of the kit must contain the labeling identified in §§ 357.52 and 357.54. The outer label of the kit must contain the information identified in § 357.50 and, in addition, the following:

(a) *Statement of identity.* The labeling of the product includes the established name of the drugs, if any, and identifies the product as a "Poison treatment kit," "Emergency poison treatment kit," or "Emergency first aid poison treatment kit."

(b) *Directions.* The labeling contains the following information under the heading "Directions": "When professional advice is not available, first give ipecac syrup to induce vomiting; after vomiting has occurred, give activated charcoal to help adsorb any remaining toxic substance."

§ 357.58 Other allowable statements for poison treatment drug products.

The following additional statements may be included in the labeling of poison treatment drug products, but should not be included in conjunction with the required labeling identified in §§ 357.50, 357.52, 357.54, and 357.56:

(a) "For the treatment of poisoning."

(b) "Emergency first aid treatment for poisoning."

(c) "Emergency treatment for poisoning."

(d) "Emergency treatment for accidental poisoning."

(e) "For the treatment of accidental poisoning."

(f) "Emergency first aid treatment for accidental poisoning.

(g) "Emergency poison treatment."

(h) "First aid poison treatment."

§ 357.60 Nonapplicability of § 330.1(g) to poison treatment drug products.

The second portion of the warning required by § 330.1(g) concerning

accidental overdose is not required on poison treatment drug products.

Interested persons may, on or before May 15, 1985 submit to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, written comments, objections, or requests for oral hearing before the Commissioner on the proposed regulation. A request for an oral hearing must specify points to be covered and time requested. The agency has provided this 120 day period (instead of the normal 60 days) because of the number of OTC drug review documents being published concurrently. Written comments on the agency's economic impact determination may be submitted on or before May 15, 1985. Three copies of all comments, objections, and requests are to be submitted, except that individuals may submit one copy. Comments, objections, and requests are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Comments, objections, and requests may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. Any scheduled oral hearing will be announced in the **Federal Register**.

These dates are consistent with the time periods specified in the agency's final rule revising the procedural regulations for reviewing and classifying OTC drugs, published in the **Federal Register** of September 29, 1981 (46 FR 47730). Three copies of all data and comments on the data are to be submitted, except that individuals may submit one copy, and all data and comments are to be identified with the docket number found in brackets in the heading of this document. Data and comments should be addressed to the Dockets Management Branch (HFA-305) (address above). Received data and comments may also be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In establishing a final monograph, the agency will ordinarily consider only data submitted prior to the closing of the administrative record on May 15, 1985. Data submitted after the closing of the administrative record will be reviewed by the agency only after a final monograph is published in the **Federal Register**, unless the Commissioner finds good cause has been shown that warrants earlier consideration.

Dated: December 31, 1984.

Frank E. Young,

Commissioner of Food and Drugs.

Margaret M. Heckler,

Secretary of Health and Human Services.

[FR Doc. 85-682 Filed 1-14-85; 8:45 am]

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Federal Register

Tuesday
January 15, 1985

Part XI

Department of the Interior

Minerals Management Service to Delineate Areas of Interest for Further Evaluation for Potential Leasing of Strategic and Nonenergy Minerals Found in the Exclusive Economic Zone and Outer Continental Shelf

Call for Information

DEPARTMENT OF THE INTERIOR

Minerals Management Service

Call for Information to Delineate Areas of Interest for Further Evaluation for Potential Leasing of Strategic and Nonenergy Minerals Found in the Exclusive Economic Zone and Outer Continental Shelf

AGENCY: Minerals Management Service, Interior.

ACTION: Call for Information.

SUMMARY: The Minerals Management Service is requesting comments and information from interested parties to assist in the delineation of areas to be included in more detailed resource, environmental and economic reviews for possible leasing of minerals other than oil, gas, and sulphur in the Exclusive Economic Zone (EEZ) and Outer Continental Shelf (OCS). Responses to this Call will be used to establish priority areas for such reviews for the possible leasing of construction materials, placer deposits, phosphorites, polymetallic sulfides, cobalt-manganese minerals, or other nonenergy minerals within the EEZ and OCS on a case-by-case basis.

DATES: Comments and information in response to this request should postmarked or hand delivered no later than May 15, 1985.

ADDRESSES: Comments and information may be mailed or delivered to the Minerals Managment Service, Office of Strategic and International Minerals, Attention: Program Director, 11 Golden Shore, Suite 260, Long Beach, California 90802.

Proprietary Information

If information of a privileged nature is submitted, it should be enclosed in a separate sealed envelope and market PROPRIETARY. This information will be exempt from disclosure pursuant to the Freedom of Information Act (5 U.S.C. 552). Indications of interest are considered to be privileged information; however, the names of persons or entities indicating interest or submitting comments will be of public record.

FOR FURTHER INFORMATION CONTACT

Mr. Reid T. Stone, Office of Strategic and International Minerals, 11 Golden Shore, Suite 260, Long Beach, California 90802, telephone (213) 548–2901. FTS 796–2901.

SUPPLEMENTARY INFORMATION:

Background

Recent task force studies, workshops, and symposia included (1) a program feasibility study on nonenergy minerals leasing (with 23 appendices) of August 1979; (2) a workshop on OCS hard minerals at OCEANS '83, San Francisco, California, in September 1980; (3) a study entitled "National Ocean Goals and Objectives for the 1980's, MARINE MINERALS: An Alternative Mineral Supply," by the National Advisory Committee on Oceans and Atmosphere, July 1983; and (4) a symposium on a National Program for the Assessment and Development of the Mineral Resources of the United States Exclusive Economic Zone by the U.S. Geological Survey, Minerals Management Service, and Bureau of Mines at Reston, Virginia, in November 1983. These have each indicated substantial potential resources of strategic and other nonenergy minerals off our shores.

The resources may be classified basically in five groups: Construction materials, including sands, gravels, shells, and other high-bulk, low unit-value materials, placer deposits of metals or minerals containing gold, platinum, tin, titanium, thorium, or rare earths; phosphorites used primarily for the production of phosphatic fertilizers and found as shallow bedded deposits or as deposits formed as nodules, sands, or encrustations on the seabed; metalliferous oxides occurring as nodules or crusts in water depths from several hundred to several thousands of meters and containing significant amounts of the metals manganese, copper, nickel, and cobalt; and metalliferous sulfides found in a variety of possible forms at the surface of the seabed and beneath the surface in water depths, generally, of several thousand meters containing significant amounts of such as copper, zinc, cadmium, molybdenum, chromium, barium, strontium, silver, or gold.

The possibility of offering leases for the exploration and possible development of both metalliferous oxides and metalliferous sulfides is being evaluated for the area of Hawaiian Islands and the Gorda Ridge off Oregon and northern California, respectively. The initial step in each case will be to prepare an impact statement on the economic, engineering, and environmental impact of exploration and development in these areas, including any unavoidable adverse effects, appropriate alternatives, and other factors. No decision has been made to offer yet in either area. In the case of the other three commodity groups, no such specific proposals are under consideration.

In keeping with the mandates of the Mining and Minerals Policy Act of 1970 and the National Materials and Minerals Policy Research and Development Act of 1980 in which the Secretary of the Interior is required among other things to promote and encourage private enterprise in the development of economically sound and stable domestic materials industries, the advisability of developing a program for leasing of nonenergy minerals on the OCS on a case-by-case basis is being considered.

Purpose of Call

The purpose of the Call is to assist the Secretary of the Interior in carrying out his responsibilities under the OCS Lands Act (43–U.S.C. 1331–1343), as amended (92 Stat. 629), and to assist various Federal/State Task Forces and Regional Technical Working Groups in delineating areas of interest for strategic and other nonenergy minerals. Interested parties are requested to outline on a map areas within the EEZ and OCS that they believe have potential for development of construction materials, placer deposits, phosphorites, polymetallic sulfides, cobalt-rich manganese crust, and/or other nonenergy minerals that may occur and for which they may have an interest in leasing. Interested parties are also requested to identify areas that they believe should be excluded from consideration for leasing and the reasons therefore.

Use of Information for Call

Information submitted in response to this Call will be considered in the advisability of examining and possibly formulating a case-by-case leasing program for strategic and other nonenergy minerals. Comments received on possible environmental effects and use conflicts may be used in the analysis of specific environmental conditions within the Call area so that the potential effects of exploration, development, and mining, other than the benefits accruing to the Nation as a result of inventorying and producing minerals, can be assessed.

Description of the Areas

Construction Materials: The potential resources of construction materials on the U.S. continental shelves are considered excellent. In 1979, the OCS Mining Policy Task Force estimated sand and gravel resources of 830, 269, 29, and 19 billion cubic meters on the Atlantic, Gulf of Mexico, Pacific, and Hawaiian offshore areas, respectively. There is a large potential for sand and gravel offshore of Alaska.

A study of the northeastern continental margin to approximately 2,000 meters of water depth showed that

much of the shelf is mantled with sand of up to 3 meters thick and of considerable lateral continuity and that gravel is also present in a more discontinuous patchy distribution. These sand deposits were estimated at 400 billion tons. The inner continental shelf areas of the Atlantic, Gulf of Mexico, and southern California have been surveyed from the shore to 20 km seaward to assess marine sand and gravel resources. The results indicate nearly 17 billion cubic meters of sand and gravel within the upper 6 m of the seafloor. Seismic data suggest that in some regions the thicknesses and volumes are considerably greater. Sand is abundant in many regions; however, it varies considerably in textural properties and in some places is admixed with or covered by mud. Gravel is most common on glaciated shelf regions of the northeast and northwest, but south of about 40°N, gravel appears limited to a carbonate shall fraction or residual coarse sediment overlying outcrops of relict fluvial channel deposits or coastal plain strata. The most promising sand and gravel deposits ar associated with glacial moraines and drift, outwash-sand plains, and glaciofluvial deltas. Also promising are ancestral river channels that crossed the shelf in the Quaternary period prior to the Holocene transgression, as well as the various classes of shoals (e.g. linear, cape-associated, and tidal-inlet-associated) that are present from the shoreface to the shelf edge.

On the Pacific coast, deposits of sand and gravel occur near Grays Harbor off central Washington within shipping distance of the Portland and Seattle metropolitan areas. Deposits offshore of California are relatively small and fine-grained, consisting of relict beach and fluvial materials. One of the most promising deposits, because of its proximity to Los Angeles and San Diego, lies off Imperial Beach and consists of reworked gravel on the submerged former delta of the Tijuana River.

In Hawaii, a potential white-sand supply is located 35 km from Honolulu on Penguin Bank in water depths of 50–60 m. This area is believed to be part of a deposit containing 350 million cubic yards. This calcareous sand is located on drowned Pleistocene sea level terraces.

Placer deposits: Placer deposits show most potential for their heavy mineral content. Heavy-mineral sands of variable composition and grade on the Atlantic shelf have been estimated to be about 1.3 billion cubic meters or more. Surficial relict sand bodies, often occurring as ridges (submarine highs), are present over most of the Atlantic shelf. They range in thickness from about 20 m to 80–140 m near the shelf edge. Some of these relict features are interpreted as ancient shore deposits that formed as the ocean transgressed the shelf at the end of the most recent glaciation. Supporting evidence for this interpretation is the presence of submerged terraces and beach ridges which are the types of features associated with interim stages of change in sea level. It has been inferred that concentrations of heavy minerals are associated with these former shoreline features.

Heavy minerals have been identified in sediments within the inner New York Bight area. Marine sediments offshore of Virginia may have greater heavy mineral concentration than offshore areas to the south and are almost as rich as an onshore control area in South Carolina. Heavy-mineral placers have been mined onshore from ancient beach sands along the coasts of New Jersey, Georgia and Florida and from coastal plain deposits in New Jersey. Kyanite, sillimanite, ilmenite, zircon, and other heavy minerals occur in beach and nearshore sediments around the Apalachicola River and in various locations along the coasts of Florida, Alabama, Louisiana, and Texas.

No quantitative estimates of heavy-mineral sand on the Gulf of Mexico continental shelf are available. Identified or indicated heavy minerals of economic interest include many of the species found on the Atlantic shelf, but very little mineralogic information is available.

In northern California, gold occurrences have been reported in offshore sediments near Crescent City and offshore of rivers in southern California. Other heavy-minerals occurrences, especially zircon and chromite, have been reported in offshore sediments near Crescent City. Platinum has been reported in beach sediments near Crescent City, north of Orick, and at Monterey Bay. Heavy-minerals occurrences have been reported offshore of Oregon, seaward of rivers including Neholem, Rogue, Siltcoas, and Umpqua to water depths of 185 meters. Heavy-minerals occurrences also have been reported seaward of Cape Blanco and near the shelf break adjacent to the Rogue Submarine Canyon.

Discontinuous placer deposits have been identified along the coast of Washington from Cape Flattery to the Columbia River. Favorable locations for placer deposits are relict sand bodies paralleling the coast, submerged beaches, and offshore of the Columbia River. On the Pacific continental shelf, heavy-mineral sand of various composition and grade is estimated to be about 2.06 billion cubic meters. Gold and heavy-mineral sand deposits occur rather extensively in relict beaches, buried river channels, and in reworked Pleistocene gravels. High-grade titanium and zircon sands have been inferred to be widespread.

Submerged shorelines and stream channels offshore Alaska near Nome and Goodnews Bay are prime localities for gold placers. A shoal north-northeast of Cape Prince of Wales may contain heavy-mineral placers including gold. Other areas where onshore lode deposits of gold are near enough to the continental shelf to merit serious investigations included Captains Bay located within the western part of Alaska; the Aleutian Islands; west of Kodiak Island; lower Cook Inlet in Kamishak Bay extending around the lower end of Kenai Peninsula; and possibly Resurrection Bay near Seaward Peninsula.

Other offshore areas possessing potential for placers include offshore of the western part of St. Lawrence Island, Shelikof Straits, offshore of the Copper River Delta, and most of southeast Alaska.

No definite estimates are available for these resources in Alaskan waters, although there are some indications that heavy-mineral deposits may far exceed those of all the remaining EEZ.

Phosphorite deposits: Phosphorite deposits are known to occur off both the east and west coasts of the United States. Phosphorite has been dredged, cored, and/or photographed at the surface of the continental shelf from the sourthern part of Florida to the shelf off North Carolina. Drilling has shown that these deposits also occur at depth beneath the shelf in Middle Tertiary rocks.

Although the size of these deposits can be only roughly estimated, they represent an enormous resource of phosphorite. Approximately 2 billion metric tons of phosphorite are present on the Blake Plateau alone. About half this much is also present as a pavement in which the phosphorite is associated with ferromanganese oxides. An equal amount of phosphorite may exist off the coast of North Carolina in the form of bedded deposits below the seabed.

Phosphorites off the coast of California have been widely recovered from the tops of submarine banks and ridges in the continental borderland and have been dredged from rather steep slopes at depths as great as 3,000 meters

and from the shelf to the north near Monterey Bay. This deposit represents a resource of approximately 115 million metric tons.

Phosphorite has been recovered from several seamounts in the Pacific Ocean, where it is usually associated with cobalt-rich ferromanganese oxides. The size of these deposits is only superficially delineated at present.

Surficial phosphorite deposits off both coasts are considered to be lag deposits that have been eroded from rocks of Middle Tertiary age. The phosphorite ranges in size from pellets to pavements but most often occurs as irregular-shaped nodules. The phosphate mineral is francolite and is associated with caronate sands. The source beds crop out on land, and in Florida they are dominantly limestones. In California, they include dolomite and highly siliceous rocks, many with high concentrations of organic carbon.

In Onslow Bay, about 100 kilometers offshore of North Carolina, preliminary evaluations have indicated a vast phosphate resource potential occurring in the Miocene Pungo River formation. This formation is a major sedimentary phosphorite unit under the coastal plain and outcrops offshore as a northeast-southwest belt about 150 kilometers long by 40 kilometers wide and dips into the subsurface to the southeast. The economically valuable beds within this formation have been estimated to contain 1.36 billion metric tons of phosphate concentrated grading between 28 to 30 percent phosphate.

Polymetallic sulfide deposits: Polymetallic sulfides have been found along several seafloor spreading centers in the Pacific Ocean. The active zone of spreading can be hundreds of kilometers long but is usually less than 2 km wide. Deeply circulating hot seawater leaches heavy metals (zinc, silver, copper, manganese, cadmium, iron, etc.) and sulphur at high temperatures from the surrounding rocks. The upward movement of these hot mineral-rich waters is confined to narrow channels. Upon reaching the seafloor, the water discharges upward in a plume called a smoker. The sudden mixing with the cold seawater causes metallic sulfide minerals to be precipitated in mounds and chimneys around the vents. Subsurface concentrations of massive metallic sulfide minerals may also be formed in the vicinity of active vents and in areas of active spreading which are covered by thick sediment. Such deposits may be preserved and carried with the spreading plate—far from the spreading centers.

More than six smokers have been found on the Juan de Fuca Ridge. A sample recovered near a smoker just outside the EEZ was almost pure zinc sulfide (55 percent zinc) and contained 300 parts per million silver.

Microscopic amounts of metallic sulfides have been identified in rock samples recently collected from the Gorda Ridge suggesting the presence of hydrothermal activity in the area.

Polymetallic sulfides may also be deposited on the flanks of active volcanoes in back arc basins such as that of the Northern Marianas and around volcanoes formed over hot spots in the crust like the Hawaiian Islands.

Cobalt-rich manganese oxide crusts: These crusts occur on flank areas of islands and seamounts in the Pacific region including the Hawaiian archipelago. Measured cobalt content ranges from 0.4 percent in the crusts in deeper water to 1.2 percent in the crusts on seamount tops in waters less than 2,500 meters. The mean crust thickness is more than 2 centimeters (cm) in upper slope areas and may be as thich as 6–8 cm. Accessible concentrations could yield 16 kg per square meter of crustal surface. The monetary value per unit area of cobalt, nickel, manganese, copper, and molybdenum in these crusts is significantly greater than in known deepwater nodules.

Reference:

Beauchamp, R.G. and M.J. Cruickshank, 1983. Placer minerals on the U.S. Continental Shelves—opportunity for development: Oceans '83 Conference Proceedings, p. 698-702.

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Department of the Interior, 1984. A national program for the assessment and development of the mineral resources of the United States Exclusive Economic Zone: Proceedings of a symposium sponsored by the Department of the Interior, Nov. 15, 16, 17, 1983, U.S.G.S. Circ. 929, p. 308.

Department of the Interior, 1979. Program feasibility document, OCS hard minerals leasing: National Technical Information Service, Springfield, VA 22161, p. 180 with 23 appendices. NTIS No. PB81–192551.

Evans, J.R., Da Bia, G.S. and Levine, C.R., 1982 Mining and Marketing of Sand and Gravel on the Outer Continental Shelf of Southern California, California Geology, Vol. 35, p. 259–276.

Riggs, S.R., and others, 1984. Phosphate resource potential in Onslow Bay, N. Carolina continental shelf: East Carolina University, Department of Geology, Greenville, NC 27834, in press.

Instructions on Call

Indications of interest should be limited to the OCS, as defined in the OCS Lands Act, which extends a minimum of 200 miles from the coasts of the states of the Union. Respondents are requested to rank areas according to priority of interest (e.g. priority 1, 2, and 3).

Dated: January 9, 1985.

William D. Bettenberg,

Director, Minerals Management Service.

[FR Doc. 85–1099 Filed 1–14–85; 8:45 am]

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federal register

Tuesday
January 15, 1985

Part XII

Department of Defense
General Services Administration
National Aeronautics and Space Administration

48 CFR Ch. 1
Federal Acquistion Regulation

DEPARTMENT OF DEFENSE

GENERAL SERVICES ADMINISTRATION

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION

48 CFR Ch. 1

[Federal Acquisition Circular 84-6]

Federal Acquisition Regulation

AGENCY: Department of Defense (DoD), General Services Administration (GSA), and National Aeronautics and Space Administration (NASA).

ACTION: Interim rule and request for comment.

SUMMARY: Federal Acquisition Circular (FAC) 84-6 amends the Federal Acquisition Regulation (FAR) with respect to the changes required to implement the publicizing provisions and the validation of proprietary restrictions of the Small Business and Federal Procurement Competition Enhancement Act of 1984 (Pub. L. 98-577), and the protest provisions of the Competition in Contracting Act of 1984 (CICA) (Pub. L. 98-369).

EFFECTIVE DATES: FAC 84-6 revisions to FAR Part 1 are effective November 29, 1984. The FAC 84-6 revision to FAR Part 27 is effective for solicitations issued on or after December 29, 1984. FAC 84-6 revisions to FAR Parts 12, 14, 33, and 52 are effective for protests filed on or after January 15, 1985. The FAC 84-6 revision to FAR Part 39 is effective January 15, 1985.

DATE: Comments must be received on or before March 18, 1985. Please cite FAC 84-6 in all correspondence on this subject.

ADDRESS: Interested parties should submit written comments to: General Services Administration, ATTN: FAR Secretariat (VR), 18th & F Street, NW., Room 4041, Washington, D.C. 20405.

FOR FURTHER INFORMATION CONTACT: Roger M. Schwartz, Director, FAR Secretariat, Room 4041, GS Building, Washington, D.C. 20405, Telephone (202) 523-4755.

SUPPLEMENTARY INFORMATION: A determination has been made under the authority of the Secretary of Defense, the Administrator of General Services, and the Administrator for the National Aeronautics and Space Administration that the regulations in FAC 84-6 must be issued as temporary regulations in compliance with section 22 of the Office of Federal Procurement Policy Act, as amended.

Item I, FAC 84-6, describes changes to FAR Part 1 to conform the regulation to the publicizing provisions of Pub. L. 98-577. The FAR revisions described in Item I are effective November 29, 1984. Under the new coverage, agencies will be required to publicize acquisition regulations that have a significant effect beyond the internal operating procedures of the agency or have a significant cost or administrative impact on contractors or offerors. Such coverage may not take effect until 30 days after a notice (see 1.501-2(b)) inviting public comment is placed in the Federal Register unless the issuing officer waives the advance comment requirement after determining that urgent and compelling circumstances make such action impracticable.

Item II, FAC 84-6, describes changes to the FAR that require civilian agencies other than NASA to implement section 203 of Pub. L. 98-577 with respect to validation of restrictions asserted by a contractor or subcontractor on the right of the Government to use technical data. The FAR revisions described in Item II are effective for solicitations issued on or after December 29, 1984.

Item III, FAC 84-6, provides new procedures for submitting protests to the General Accounting Office or the General Services Board of Contract Appeals. The FAR revisions described in Item III are effective for protests filed on or after January 15, 1985. Agencies will have to issue internal operating procedures, for implementation prior to the effective date. These regulations were previously published for a brief comment period and comments received were considered.

Item IV, FAC 84-6, revises a reference in FAR Part 39 pertaining to policies, procedures, and guidelines peculiar to automatic data processing, telecommunications, and related resources.

Roger M. Schwartz,

Director, FAR Secretariat.

January 11, 1985.

Federal Acquisition Circular

[Number 84-6]

The material contained in FAC 84-6 is effective according to the following:

—The revisions to the Federal Acquisition Regulation (FAR) described in Item I, Publicizing Proposed Regulations, are effective November 29, 1984.

—The revisions to the FAR described in Item II, Validation of Proprietary Data Restrictions, is effective for solicitations issued by civilian agencies other than NASA on or after December 29, 1984.

—The revisions to the FAR described in Item III, Protest Provisions of the Competition in Contracting Act of 1984, are effective for protests filed on or after January 15, 1985.

—The revisions to the FAR described in Item IV, Editorial, is effective January 15, 1985.

Mary Ann Gilleece,

Deputy Under Secretary, (Acquisition Management), Department of Defense.

January 10, 1985.

Ray Kline,

Acting Administrator of General Services.

January 10, 1985.

S. J. Evans,

Assistant Administrator for Procurement, NASA.

January 10, 1985.

Federal Acquisition Circular (FAC) 84-6 amends the Federal Acquisition Regulation (FAR) as specified below. The following is a summary of the amendments:

Item I—Publicizing Proposed Regulations

The Small Business and Federal Procurement Competition Enhancement Act of 1984 (Pub. L. 98-577) requires that certain acquisition regulations receive public comment. The changes to FAR Part 1 conform the regulation to these publicizing provisions. Under this new coverage, agencies will be required to publicize acquisition regulations that have a significant effect beyond the internal operating procedures of the agency or have a significant cost or administrative impact on contractors or offerors. Such coverage may not take effect until 30 days after a notice (see 1.501-2(b)) inviting public comment is placed in the **Federal Register** unless the issuing officer waives the advance comment requirement after determining that urgent and compelling circumstances make such action impracticable.

Item II—Validation of Proprietary Data Restrictions

Section 203 of Pub. L. (98-577 amended the Federal Property and Administrative Services Act of 1949 by adding coverage on validation of restrictions asserted by a contractor or subcontractor on the right of the Government to use technical data. FAR 27.401 is amended to require civilian agencies other than NASA to implement section 203 of Pub. L. 98-577 pending the publication of detailed coverage on this subject in a later FAC.

Item III—Protest Provisions of the Competition in Contracting Act of 1984

The Competition in Contracting Act of 1984 provides revised procedures for filing protests with the General Accounting Office (GAO) and new procedures for filing Automatic Data Processing protests to the General Services Board of Contract Appeals (GSBCA). These protest procedures apply to protests filed on or after January 15, 1985.

FAR Parts 12, 14, 33, and 52 contain new protest coverage. Under the new coverage, agencies will be required to implement procedures for processing protests that are filed with the GAO and with the GSBCA. The protest coverage of the FAR is removed from 14.407–8 and the revised coverage is placed in Subpart 33.1. The Disputes and Appeals coverage of Part 33 is renumbered as Subpart 33.2.

Item IV—Editorial

The reference in FAR Part 39 is corrected to read "Chapter 201 of Title 41 of the Code of Federal Regulations".

List of Subjects in 48 CFR Ch. 1

Government procurement.

Therefore, 48 CFR is amended as set forth below.

The authority for 48 CFR Ch. 1 is:

Authority: 40 U.S.C. 486(c); 10 U.S.C. Chapter 137; and 42 U.S.C. 2453(c).

PART 1—FEDERAL ACQUISITION REGULATIONS SYSTEM

1.201–1 [Amended]

1. Section 1.201–1(e)(2) is amended by removing the reference "1.501(c)" and inserting in its place the reference "1.501–2(b)".

2. Section 1.301 is amended by redesignating paragraphs (a) and (b) as (a)(1) and (a)(2) and revising new paragraph (a)(1), removing the second sentence of the new paragraph (a)(2), and adding a new paragraph (b) to read as follows:

1.301 Policy.

(a)(1) Subject to the authorities in (c) below and other statutory authority, an agency head may issue or authorize the issuance of agency acquisition regulations that implement or supplement the FAR and incorporate, together with the FAR, agency policies, procedures, contract clauses, solicitation provisions, and forms that govern the contracting process or otherwise control the relationship between the agency, including any of its suborganizations, and contractors or prospective contractors.

* * * * *

(b) Agency heads shall establish procedures to ensure that issuances (including revisions) under 1.301(a)(1) shall be publicized for public comment in the **Federal Register** in conformance with the procedures in Subpart 1.5 and as required by section 22 of the Office of Federal Procurement Policy Act, as amended, and other applicable statutes when they have a significant effect beyond the internal operating procedures of the agency or have a significant cost or administrative impact on contractors or offerors. However, publication is not required for issuances that merely implement or supplement higher level issuances that have previously undergone the public comment process, unless such implementation or supplementation results in an additional significant cost or administrative impact on contractors or offerors or effect beyond the internal operating procedures of the issuing organization. Issuances under 1.301(a)(2) need not be publicized for public comment.

3. Section 1.303 is amended by revising the title; the first sentence of paragraph (a); and paragraph (b) as follows:

1.303 Publication and codification.

(a) Agency-wide acquisition regulations shall be published in the Federal Register as required by law, shall be codified under an assigned chapter in Title 48, Code of Federal Regulations, and shall parallel the FAR in format, arrangement, and numbering system (but see 1.104–1(c)). * * *

(b) Issuances under 1.301(a)(2) need not be published in the **Federal Register**.

4. Subpart 1.5 is amended by redesignating in section 1.501 paragraph (a) as section 1.501–1; redesignating paragraphs (b), (c), and (d) as section 1.501–2; redesignating paragraph (e) as section 1.501–3; redesignating paragraph (f) as section 1.502 and redesignating section 1.502 as 1.503; and revising the subpart to read as follows:

Subpart 1.5—Agency and Public Participation

1.501 Solicitation of agency and public views.

1.501–1 Definition.

"Significant revisions," as used in this subpart, means revisions that alter the substantive meaning of any coverage in the FAR System having a significant cost or administrative impact on contractors or offerors, or a significant effect beyond the internal operating procedures of the issuing agency. This expression, for example, does not include editorial, stylistic, or other revisions that have no impact on the basic meaning of the coverage being revised.

1.502–2 Opportunity for public comments.

(a) Views of agencies and nongovernmental parties or organizations will be considered in formulating acquisition policies and procedures.

(b) The opportunity to submit written comments on proposed significant revisions shall be provided by placing a notice in the **Federal Register**. Each of these notices shall include—

(1) The text of the revision or, if it is impracticable to publish the full text, a summary of the proposal;

(2) The address and telephone number of the individual from whom copies of the revision, in full text, can be requested and to whom comments thereon should be addressed; and

(3) When 1.501–3(b) is applicable, a statement that the revision is effective on a temporary basis pending completion of the public comment period.

(c) A minimum of 30 days and, normally, at least 60 days will be given for the receipt of comments.

1.501–3 Exceptions.

(a) Comments need not be solicited when the proposed coverage does not constitute a significant revision.

(b) Advance comments need not be solicited when urgent and compelling circumstances make solicitation of comments impracticable prior to the effective date of the coverage, such as when a new statute must be implemented in a relatively short period of time. In such case, the coverage shall be issued on a temporary basis and shall provide for at least a 30 day public comment period.

1.502 Unsolicited proposed revisions.

Consideration shall also be given to unsolicited recommendations for revisions that have been submitted in writing with sufficient data and rationale to permit their evaluation.

1.503 Public meetings.

Public meetings may be appropriate when a decision to adopt, amend, or delete coverage is likely to benefit from significant additional views and discussion.

PART 12—CONTRACT DELIVERY OR PERFORMANCE

5. Section 12.505 is amended by revising paragraph (b) to read as follows:

12.505 Contract clauses.

* * * * *

(b)(1) The contracting officer shall insert the clause at 52.212–13, Stop-Work Order, in solicitations and contracts for automatic data processing under 40 U.S.C. 759 (see 33.105).

(2) Except as provided in (b)(1) above, the contracting officer may, when contracting by negotiation, insert the clause at 52.212–13, Stop-Work Order, in solicitations and contracts for supplies, services, or research and development.

(3) If a cost-reimbursement contract is contemplated, the contracting officer shall use the clause with its Alternate I.

* * * * *

PART 14—FORMAL ADVERTISING

14.407–8 [Amended]

6. Section 14.407–8 is amended by removing paragraphs (a) through (c) and inserting in their place the statement "See Subpart 33.1—Protests."

PART 27—PATENTS, DATA, AND COPYRIGHTS

7. Section 27.401 is amended by inserting a new sentence at the end of the paragraph to read as follows:

27.401 General.

* * * Civilian agencies other than NASA shall implement section 203 of Pub. L. 98–577 pertaining to validation of proprietary data restrictions.

8. Part 33 is amended by revising the title of the part and the text of section 33.000; redesignating sections 33.001 through 33.014 as sections 33.201 through 33.214 respectively; adding a new subpart 33.1; removing in the definition of "claim" in new section 33.201 the word "part" in the first sentence, the citation "33.007" in the third sentence, and the citation "33.006(a)" in the fifth sentence and inserting in their places, the word "subpart", the citation "33.207", and the citation "33.206(a)" respectively; removing in new section 33.203(b) the reference "Part 33" and inserting in its place the word "subpart"; removing in the first sentence of new section 33.208 the citation "33.007(a)" and inserting in its place the citation "33.207(a)"; removing in new section 33.210(b) the citation "33.009" and inserting in its place the citation "33.209"; and removing in the first sentence of new section 33.214 the citation "33.003" and inserting in its place the citation "33.203" as follows:

PART 33—PROTESTS, DISPUTES, AND APPEALS

Sec.

33.000 Scope of part.

Subpart 33.1—Protests

33.101 Definitions.
33.102 General.
33.103 Protests to the agency.
33.104 Protests to GAO.
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Subpart 33.2—Disputes and Appeals

33.201 Definitions.
33.202 Contract Disputes Act of 1978.
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33.210 Contracting officer's authority.
33.211 Contracting officer's decision.
33.212 Contracting officer's duties upon appeal.
33.213 Obligation to continue performance.
33.214 Contract clause.

Authority: 40 U.S.C. 486(c); Chapter 137, 10 U.S.C.; and 42 U.S.C. 2453(c).

§ 33.000 Scope of part.

This part prescribes policies and procedures for filing protests and for processing contract disputes and appeals.

Subpart 33.1—Protests

33.101 Definitions.

"Interested party," as used in this subpart, means an actual or prospective offeror whose direct economic interest would be affected by the award of or failure to award a particular contract.

"Protest," as used in this subpart, means a written objection by an interested party to a soliciation by an agency for offers for a proposed contract for the acquisition of supplies or services or a written objection by an interested party to a proposed award or the award of such a contract.

33.102 General.

(a) Contracting officers shall consider all protests, whether submitted before or after award and whether filed directly with the agency, the General Accounting Office (GAO), or for automatic data processing acquisitions under 40 U.S.C. 759 (hereinafter cited as "ADP contracts"), the General Services Board of Contract Appeals (GSBCA). The protestor shall be notified in writing of the final decision of the protest. (See 19.302 for protests of small business status and 22.608–3 for protests involving eligibility under the Walsh-Healey Public Contracts Act.)

(b) An interested party wishing to protest—

(1) Is encouraged to seek resolution within the agency (see 33.103) before filing a protest with the GAO or the GSBCA;

(2) May protest to the GAO in accordance with GAO regulations (4 CFR Part 21). An interested party who has filed a protest regarding an ADP contract with the GAO may not file a protest with the GSBCA with respect to that contract.

(3) May protest to the GSBCA regarding an award of an ADP contract in accordance with GSBCA Rules of Procedure (48 CFR Part 61). An interested party who has filed a protest regarding an ADP contract with GSBCA (40 U.S.C. 759(h)) may not file a protest with the GAO with respect to that contract.

33.103 Protests to the agency.

(a) When a protest is filed only with the agency, an award shall not be made until the matter is resolved unless the contracting officer or other designated official first determines that one of the following applies:

(1) The supplies or services to be contracted for are urgently required.

(2) Delivery or performance will be unduly delayed by failure to make award promptly.

(3) A prompt award will otherwise be advantageous to the Government.

(b)(1) When a protest against the making of an award is received and award will be withheld pending disposition of the protest, the offerors whose offers might become eligible for award should be informed of the protest. If appropriate, those offerors should be requested, before expiration of the time for acceptance of their offer, to extend the time for acceptance in accordance with 14.404–1(d) to avoid the need for resolicitation. In the event of failure to obtain such extensions of offers, consideration should be given to proceeding with award under (a) above.

(2) Protests received after award filed only with the agency shall be handled in accordance with agency procedures. The contracting officer need not suspend contract performance or terminate the awarded contract unless it appears likely that an award may be invalidated and a delay in receiving the supplies or services is not prejudicial to the Government's interest. In this event, the contracting officer should consider seeking a mutual agreement with the

contractor to suspend performance on a no-cost basis.

33.104 Protests to GAO.

The Department of Justice has advised that the GAO stay provisions in 31 U.S.C. 3553 (c) and (d) and the GAO damages provision in 31 U.S.C. 3554(c) regarding payment of costs of filing and pursuing a protest and preparing the bid and proposal are unconstitutional; therefore, they neither bind the executive branch nor serve as the basis for any coverage in this section.

(a) *General.* (1) A protester shall furnish a copy of its complete protest to the official or location designated in the solicitation or, in the absence of such a designation, to the contracting officer, no later than one day after the protest is filed with the GAO. Failure to furnish a complete copy of the protest within one day may result in dismissal of the protest by GAO.

(2) When a protest, before or after award, has been lodged with the GAO, the agency shall prepare a report. The report should include a copy of—

(i) The protest;

(ii) The offer submitted by the protesting offeror and a copy of the offer which is being considered for award or which is being protested;

(iii) The solicitation, including the specifications or portions relevant to the protest;

(iv) The abstract of offers or relevant portions;

(v) Any other documents that are relevant to the protest; and

(vi) The contracting officer's signed statement setting forth findings, actions, and recommendations and any additional evidence or information deemed necessary in determining the validity of the protest. The statement shall be fully responsive to the allegation of the protest. If the contract action or contract performance continues after receipt of the protest, the report will include the determination(s) prescribed in paragraphs (b) or (c) below.

(3) Other persons, including offerors, involved in or affected by the protest shall be given notice of the protest and its basis in appropriate cases, within one work day after its receipt by the agency. The agency shall give immediate notice of the protest to the contractor if the award has been made or, if no award has been made, to all parties who appear to have a reasonable prospect of receiving an award if the protest is denied. These persons shall also be advised that they may submit their views and relevant information directly to the GAO with a copy to the contracting officer within a specified period of time. Normally, the time specified will be 1 week.

(4) The agency shall submit a complete report (see (a)(2) above) to GAO within 25 work days after receipt from GAO of the telephonic notice of such protest, or within 10 work days after receipt from GAO of a determination to use the express options, unless—

(i) The GAO advises the agency that the protest has been dismissed; or

(ii) The agency advises GAO in writing that the specific circumstances of the protest require a longer period and GAO establishes a new date. Any new date shall be documented in the agency's protest file.

(5)(i) Timely action on protests is essential. Upon notice that a protest has been lodged with the GAO, the contracting officer shall immediately begin compiling the information necessary for a report to the GAO. To further expedite processing, when furnishing a copy of the report including relevant documents to the GAO, the agency shall simultaneously furnish a copy of the report including relevant documents to the protester and a copy of the report without relevant documents to other interested parties who have responded to the notice in (a)(3) above. Upon request the agency shall also provide to any interested party a relevant document contained in the report.

(A) Documents previously furnished to or prepared by a party (e.g., the solicitation or the party's own proposal) need not be furnished to that party.

(B) Classified or privileged information or information that would give a party a competitive advantage and other information that the Government determines under appropriate authority to withhold should be deleted from the copy of the report or relevant documents furnished to that party.

(ii) The protester and other interested parties shall be requested to furnish a copy of any comments on the report directly to the GAO as well as to the contracting officer.

(6) Agencies shall furnish the GAO with the name, title, and telephone number of one or more officials (in both field and headquarters offices, if desired) whom the GAO may contact regarding protests. Each agency shall be responsible for promptly advising the GAO of any change in the designated officials.

(b) *Protests before award.* (1) When the agency has received notice from GAO of a protest filed directly with GAO, award shall not be made until the matter is resolved, unless the contracting officer or other designated official determines in writing that—

(i) The supplies or services to be contracted for are urgently required;

(ii) Delivery or performance will be unduly delayed by failure to make award promptly; or

(iii) A prompt award will otherwise be advantageous to the Government.

(2) When a protest against the making of an award is received and award will be withheld pending disposition of the protest, the offerors whose offers might become eligible for award should be informed of the protest. If appropriate, those offerors should be requested, before expiration of the time for acceptance of their offer, to extend the time for acceptance in accordance with 14.404–1(d) to avoid the need for resolicitation. In the event of failure to obtain such extensions of offers, consideration should be given to proceeding with award under (b)(1) above.

(c) *Protests after award.* Protests received after award shall be handled in accordance with agency procedures. Although persons involved in or affected by the filing of a protest may be limited, at least the contractor shall be furnished the notice of protest and its basis. The contracting officer need not suspend contract performance or terminate the awarded contract unless it appears likely that an award may be invalidated and a delay in receiving the supplies or services is not prejudicial to the Government's interest. In this event, the contracting officer should consider seeking a mutual agreement with the contractor to suspend performance on a no-cost basis.

(d) *Findings and notice.* If the decision is to proceed with contract award, or continue contract performance under (b) or (c) above, the contracting officer shall include the written findings or other required documentation in the file. The contracting officer also shall give written notice of the decision to the protester and other interested parties.

(e) *GAO decision time.* GAO will issue its recommendation on a protest within 90 work days, or within 45 calendar days under the express option, unless GAO establishes a longer period of time.

(f) *Notice to GAO.* The head of the agency or a designee (not below the level of the head of the contracting activity) responsible for the solicitation, proposed award, or award of the contract shall report to the Comptroller General within 60 days of receipt of the GAO's recommendation if the agency has decided not to comply with the recommendation. The report shall

explain the reasons why the GAO's recommendation will not be followed by the agency.

33.105 Protests to GSBCA.

(a)(1) An interested party may protest an ADP acquisition conducted under Section 111 of the Federal Property and Administrative Services Act (40 U.S.C. 759) by filing a protest with the GSBCA. ADP acquisition protests not covered under this statute may not be heard by the GSBCA, but may be heard by the agency, the courts, or GAO. A protester shall furnish a copy of its complete protest to the official or location designated in the solicitation, or in the absence of such a designation to the contracting officer, no later than one day after the protest is filed with GSBCA. Any request for a hearing on either a suspension of procurement authority or on the merits shall be in the protest.

(2) The GSBCA procedures state that—

(i) Within one working day after receipt of a copy of the protest, the agency shall give either oral or written notice of the protest to all parties who were solicited or, if the solicitation has closed, only to those who submitted a sealed bid or offer; and

(ii) Written confirmation of notice and a listing of all persons and agencies receiving notice should be given to the Board within five working days after receipt of the protest.

(b) The GSBCA procedures state that within 10 work days after the filing of a protest, or such longer time as the GSBCA may establish, the agency shall file with the GSBCA and all other parties a protest file. Except where the agency determines under appropriate authority to withhold classified or privileged information or information that would give a competitive advantage, the protest file shall include the following:

(1) A contracting officer's decision, if any.

(2) The contract, if any.

(3) All relevant correspondence.

(4) Affidavits or statements of witnesses on the matter under protest.

(5) All documents relied upon by the contracting officer in taking the action protested.

(6) A copy of the solicitation, the protestor's bid or proposal and, if bid opening has occurred and no contract has been awarded, a copy of any relevant bids and the bid abstract.

(7) In a negotiated acquisition, a copy of offers or proposals being considered for award and relevant to the protest should be included in the GSBCA file only, for *in camera* review by the Board. The agency shall serve all parties with a list of documents provided to the Board for *in camera* review.

(8) Any additional existing evidence or information necessary to determine the merits of the protest.

(9) Any information otherwise withheld, where it is appropriate for *in camera* review by the Board.

(c) The GSBCA procedures state that within 15 work days after the filing of the protest, or such longer time as the Board may establish, the agency shall submit its answer to the Board setting forth its defenses to the protest and its findings, actions, and recommendations in the matter.

(d)(1) If a protest contains a timely request for a suspension of procurement authority, a hearing will be held whenever practicable but no later than 10 calendar days after the filing of the protest. The Board shall suspend the procurement authority unless the agency establishes that—

(i) Absent suspension, the contract award is likely within 30 calendar days; and

(ii) Urgent and compelling circumstances which significantly affect interests of the United States will not permit waiting for the decision.

(2) Circumstances in (d)(1) above shall be established by a D&F executed by the agency head or designee.

(3) The Board's decision on suspension may be oral.

(e) A hearing on the merits, if requested, will be held within 25 work days after the filing of the protest and a GSBCA decision on the merits will be issued within 45 work days, unless the Board's chairman determines a longer period is required.

(f)(1) The GSBCA may declare an appropriate interested party to be entitled to the costs of—

(i) Filing and pursuing the protest, including reasonable attorney's fees; and

(ii) Bid and proposal preparation.

(2) Costs awarded under (f)(1) above shall be paid promptly by the agency out of funds available to or for the use of the acquisition of supplies or services.

(g) The GSBCA's final decision may be appealed by the agency or by any interested party, including any intervening interested parties, as set forth in Subpart 33.2.

33.106 Solicitation provision.

The contracting officer shall insert the provision at 52.233–2, Service of Protest, in solicitations for other than small purchases.

PART 39—MANAGEMENT, ACQUISITION, AND USE OF INFORMATION RESOURCES

9. The first sentence in Part 39 is revised to read as follows: Chapter 201 of Title 41 of the Code of Federal Regulations contains policies, procedures, and guidelines peculiar to automatic data processing (ADP), telecommunications, and related resources.

PART 52—SOLICITATION PROVISIONS AND CONTRACT CLAUSES

10. Section 52.212–13 is amended by revising the introductory text to read as follows:

52.212–13 Stop-Work Order.

As prescribed in 12.505(b), insert the following clause. The "90-day" period stated in the clause may be reduced to less than 90 days.

* * * * *

11. A new section 52.233–2 is added as follows:

52.233–2 Service of Protest.

As prescribed in 33.106, insert the following provision:

Service of Protest (JAN 1985)

Protests, as defined in section 33.101 of the Federal Acquisition Regulation, shall be served on the Contracting Officer by obtaining written and dated acknowledgement of receipt from

---

[Contracting Officer designate the official or location where a protest may be served on the Contracting Officer.]

(End of Provision)

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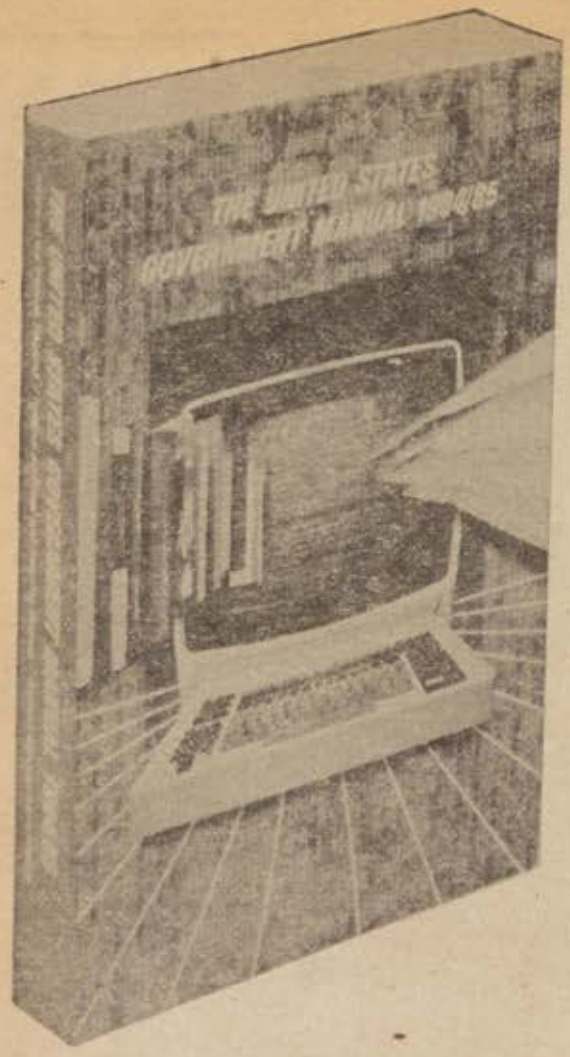
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