

Sunshine Act Meetings

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Wednesday, May 12, 1993

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).

COMMODITY FUTURES TRADING COMMISSION
"FEDERAL REGISTER" CITATION OF PREVIOUS ANNOUNCEMENT: 58 FR 26812.
PREVIOUSLY ANNOUNCED TIME AND DATE OF MEETING: 10:00 a.m., Tuesday, May 25, 1993.

CHANGES IN THE AGENDA: The Commodity Futures Trading Commission has added to the agenda applications of the Minneapolis Grain Exchange for contract designation in Frozen Shrimp futures and options on that futures contract.

CONTACT PERSON FOR MORE INFORMATION: Jean A. Webb, 254-6314.

Jean A. Webb,

Secretary of the Commission.

[FR Doc. 93-11355 Filed 5-10-93; 2:14 pm]

BILLING CODE 6351-01-M

FOREIGN CLAIMS SETTLEMENT COMMISSION
 F.C.S.C. Meeting Notice No. 9-93
 Announcement in Regard to
 Commission Meetings and Hearings

The Foreign Claims Settlement Commission, pursuant to its regulations (45 CFR Part 504), and the Government in the Sunshine Act (5 U.S.C. 552b), hereby gives notice in regard to the scheduling of open meetings and oral hearings for the transaction of Commission business and other matters specified, as follows:

Date, Time, and Subject Matter

Tues., May 25, 1993 at 10:30 a.m.—

Consideration of Proposed Decisions on claims against Iran.

Hearings on the record on objections to Proposed Decisions in the following claims against Iran:

IR-0899—Hugh E. Butler

IR-0900—John Christopher Butler

IR-0901—Patricia R. Butler

IR-1258—Patricia G. Parks

IR-1259—Perry M. Parks

IR-1346—Langston, A Division of Molins Machine Company, Inc.

IR-1737—Thomas J. Temple

IR-2091—Robert B. McCormick

Subject matter listed above, not disposed of at the scheduled meeting, may be carried over to the agenda of the following meeting.

All meetings are held at the Foreign Claims Settlement Commission, 601 D Street, NW., Washington, DC. Requests for information, or advance notices of intention to observe a meeting, may be directed to: Administrative Officer, Foreign Claims Settlement Commission, 601 D Street, NW., Room 10000, Washington, DC 20579. Telephone: (202) 208-7727.

Dated at Washington, DC on May 10, 1993.

Judith H. Lock,

Administrative Officer.

[FR Doc. 93-11408 Filed 5-10-93; 2:11 pm]

BILLING CODE 4410-01-M

FEDERAL DEPOSIT INSURANCE CORPORATION

Notice of a Matter To Be Withdrawn From Consideration at an Agency Meeting

Pursuant to the provisions of the "Government in the Sunshine Act" (5 U.S.C. 552b), notice is hereby given that the following will be withdrawn from the agenda for consideration at the open meeting of the Board of Directors of the Federal Deposit Insurance Corporation scheduled to be held at 10:00 a.m. on Tuesday, May 11, 1993, in the Board Room on the sixth floor of the FDIC Building located at 550-17th Street, NW., Washington, D.C.:

Memorandum and resolution re: Study of savings bank life insurance which makes a finding whether savings bank life insurance activities of insured banks pose or may pose any significant risk to the insurance fund of which such banks are members.

Requests for further information concerning the meeting may be directed to Mr. Robert E. Feldman, Deputy Executive Secretary of the Corporation, at (202) 898-6757.

Dated: May 7, 1993.

Federal Deposit Insurance Corporation.

Robert E. Feldman,

Deputy Executive Secretary.

[FR Doc. 93-11313 Filed 5-10-93; 9:04 am]

BILLING CODE 6714-0-M

NATIONAL CREDIT UNION ADMINISTRATION

TIME AND DATE: 9:30 a.m., Wednesday, May 19, 1993.

PLACE: Filene Board Room, 7th Floor, 1776 G Street, N.W., Washington, D.C. 20456.

STATUS: Open.

BOARD BRIEFINGS:

1. Central Liquidity Facility Report and Report on CLF Lending Rate.
2. Insurance Fund Report.

MATTERS TO BE CONSIDERED:

1. Approval of Minutes of Previous Open Meeting.
2. Request by Florida Horizons Federal Credit Union for a Community Charter Conversion.
3. Proposed Rule: Amendment to Part 704, NCUA's Rules and Regulations, Corporate Credit Unions.
4. Final Rule: Amendment to Part 710, NCUA's Rules and Regulations, Voluntary Liquidation.
5. Appeal by Farm Credit Employees Federal Credit Union, St. Paul, Minnesota, of Regional Director's Decision to Disapprove Request for Overlap of Field of Membership.

RECESS: 10:45 a.m.

TIME AND DATE: 11:00 a.m., Wednesday, May 19, 1993.

PLACE: Filene Board Room, 7th Floor, 1776 G Street, N.W., Washington, D.C. 20456.

STATUS: Closed.

MATTERS TO BE CONSIDERED:

1. Approval of Minutes of Previous Closed Meeting.
2. Administrative Actions under Section 206 of the Federal Credit Union Act. Closed pursuant to exemptions (8), (9)(A)(ii), and (9)(B).
3. Personnel Actions. Closed pursuant to exemptions (2) and (6).

FOR MORE INFORMATION CONTACT: Becky Baker, Secretary of the Board, Telephone (202) 682-9600.

Becky Baker,

Secretary of the Board.

[FR Doc. 93-11433 Filed 5-10-93; 2:57 pm]

BILLING CODE 7535-01-M

Federal Register

Wednesday
May 12, 1993

Part II

Environmental Protection Agency

40 CFR Part 82

Protection of Stratospheric Ozone;
Proposed Rule

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 82

[FRL-4625-7]

Protection of Stratospheric Ozone

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of proposed rulemaking.

SUMMARY: This action proposes the U.S. Environmental Protection Agency's (EPA) program for evaluating and regulating substitutes for the ozone-depleting chemicals being phased out under the stratospheric ozone protection provisions of the Clean Air Act (CAA). In section 612 of the amended CAA, the Agency is authorized to identify and restrict the use of substitutes for Class I and II ozone-depleting substances where other alternatives exist that reduce overall risk to human health and the environment. EPA is referring to the program that would provide these determinations as the Significant New Alternatives Policy (SNAP) program. The intended effect of this action is to expedite movement away from ozone depleting compounds.

In this Notice of Proposed Rulemaking (NPRM), EPA is both issuing preliminary decisions on the acceptability of certain substitutes and introducing its plan for administering the SNAP program. To arrive at determinations on the acceptability of substitutes, the Agency completed a cross-media analysis of risks to human health and the environment from use of various substitutes in different industrial applications. This analysis is summarized in today's proposal, and covers substitutes in the refrigeration, foam blowing, solvents cleaning, fire extinguishing, tobacco puffing, adhesives, coatings and inks, aerosols and sterilants sectors. These sectors comprise the principal industrial sectors that historically consume large volumes of ozone-depleting compounds.

DATES: Written comments or data provided in response to this document must be submitted by June 21, 1993. Any data submitted can be designated as Confidential Business Information. (See Section V.C. for more detail.) EPA will conduct a public hearing on this NPRM on May 28, 1993 beginning at 9 a.m. The record of this hearing will remain open for 30 days after the hearing for the submission of rebuttals and other supplementary material.

ADDRESSES: Written comments and data should be sent to Docket A-91-42, Central Docket Section, South

Conference Room 4, U.S. Environmental Protection Agency, 401 M Street, SW., Washington, DC 20460. The docket may be inspected between 8 a.m. and 3:30 p.m. on weekdays. As provided in 40 CFR part 2, a reasonable fee may be charged for photocopying. To expedite review, a second copy of the comments should be sent to Drusilla Hufford, Substitutes Analysis and Review Branch, Stratospheric Protection Division, Office of Atmospheric Programs, Office of Air and Radiation, 401 M Street, SW., 8205J, Washington, DC 20460. Information designated as Confidential Business Information (CBI) under 40 CFR, part 2, subpart B must be sent directly to the contact person for this notice. However, the Agency is requesting that all respondents submit a non-confidential version of their comments to the docket as well.

The public hearing on this NPRM will be held at the EPA auditorium in Washington, DC. Please call the contact person listed below for details regarding the public hearing.

FOR FURTHER INFORMATION CONTACT: Drusilla Hufford at (202) 233-9101, Substitutes Analysis and Review Branch, Stratospheric Protection Division, Office of Atmospheric Programs, Office of Air and Radiation, Washington, DC.

SUPPLEMENTARY INFORMATION:

I. Overview of This Action

This action is divided into eleven sections, including this overview:

- I. Overview of This Action
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- B. Subgroup of the Federal Advisory Committee
- III. Section 612 Program
- A. Statutory Requirements
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- VI. Effective Date of Coverage
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- A. Substitutes Reviewed under SNAP Only
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VIII. Petitions

- A. Background
- B. Content of the Petition
- C. Sufficiency of Data
- D. Criteria for Evaluating Petitions
- E. Petition Review Process
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- IX. Preliminary Listing of Substitutes
- X. Additional Information
- XI. References
- Appendix A to the preamble
- Class I and Class II Ozone-Depleting Substances
- Appendix B to the preamble
- Preliminary Listing Decisions
- Appendix C to the preamble
- Data Confidentiality Claims

II. Background

A. Regulatory History

The stratospheric ozone layer protects the earth from dangerous ultraviolet (UV-B) radiation. Depletion of stratospheric ozone allows more UV-B radiation to penetrate to the earth's surface. Increased radiation, in turn, has been linked to higher incidence of certain skin cancers and cataracts, suppression of the immune system, damage to crops and aquatic organisms, and increased formation of ground-level ozone. Further, increased radiation can cause economic losses from materials damage such as more rapid weathering of outdoor plastics. (See 53 FR 30566, August 12, 1988, for more information on the effects of ozone depletion.)

In response to scientific concerns and findings on ozone depletion, the United States and twenty-three other nations signed the Montreal Protocol on Substances that Deplete the Ozone Layer on September 16, 1987. The original agreement set forth a timetable for reducing the production and consumption of specific ozone-depleting substances, including CFC-11, CFC-12, CFC-113, CFC-114, CFC-115, Halon-1211, Halon-1301, and Halon-2402. EPA implemented the original Protocol through regulations allocating production and consumption allowances equal to the total amount of production and consumption granted to the United States under the Protocol. (See final rule promulgated on August 12, 1988; 53 FR 30566.)

The parties to the Montreal Protocol met in London June 27-29, 1990 to consider amendments to the Protocol. In response to scientific evidence indicating greater than expected stratospheric ozone depletion, the Parties agreed to accelerate the phase-out schedules for the substances already controlled by the Protocol. They also added phase-out requirements for other ozone-depleting chemicals, including

methyl chloroform, carbon tetrachloride, and other fully-halogenated chlorofluorocarbons (CFCs).

On November 15, 1990, the President signed the Clean Air Act Amendments of 1990. Title VI, section 604 of the amended CAA requires a phase-out of CFCs, halons, and carbon tetrachloride by 2000, which is identical to the London Amendments, but with more stringent interim reductions. Title VI also differs from the London Amendments in mandating a faster phase-out of methyl chloroform (2002 instead of 2005), a restriction on the use of hydrochlorofluorocarbons (HCFCs) after 2015, and a ban on the production of HCFCs after 2030. In Title VI, section 602, the CFCs, halons, carbon tetrachloride, and methyl chloroform are defined as Class I substances; HCFCs are referred to as Class II substances. Appendix A lists the Class I and Class II substances identified in the CAA.

In addition to the phase-out requirements, Title VI includes provisions to reduce emissions of Class I and Class II substances to the "lowest achievable level" in all use sectors and to maximize the use of recycling and recovery upon disposal (section 608). It also requires EPA to ban nonessential products containing ozone-depleting substances (section 610); establish standards and requirements for the servicing of motor vehicle air conditioners (section 609); mandate warning labels on products made with or containing Class I or containing Class II substances (section 611); and establish a safe alternatives program (section 612). The development and implementation of the safe alternatives program under section 612 is the subject of this action.

In October 1991, the National Aeronautics and Space Administration (NASA) announced several new findings documenting ozone depletion over the last decade that was more severe than had previously been predicted by atmospheric modeling or measurements. In particular, NASA found 2.9 per cent ozone depletion over the northern mid-latitudes over the past decade in summertime—the first time a trend showing ozone depletion had been detected in the U.S. during that time of year, when risks from depletion are greatest.

Partly in response to these findings, on February 11, 1992, President Bush announced an accelerated phase-out schedule for Class I substances as identified in the CAA. This schedule has recently been published in the *Federal Register* (58 FR 15014; March 18, 1993). The President also ordered an

accelerated review of substitutes that do less damage to the ozone layer than ozone-depleting compounds. The existence of the expedited phase-out schedule and the President's directive regarding alternatives adds a new urgency to EPA's effort to review and list substitutes for Class I and II substances under section 612.

B. Subgroup of the Federal Advisory Committee

In 1989, EPA organized the Stratospheric Ozone Protection Advisory Committee (STOPAC) in accordance with the requirements of the Federal Advisory Committee Act, 5 U.S.C. App. section 9(c). The STOPAC consists of members selected on the basis of their professional qualifications and diversity of perspectives and provides representation from industry, academia, Federal, state, and local government agencies, non-governmental and environmental groups, as well as international organizations. Since its formation, the STOPAC has provided advice and counsel to the Agency on policy and technical issues related to the protection of stratospheric ozone.

In 1991, the Agency asked STOPAC members to participate in subgroups to assist in developing regulations under Title VI of the CAA. EPA established a subgroup of the standing STOPAC to guide the Agency specifically on development of the safe alternatives program. To date, the subgroup on safe alternatives has met twice. At the first meeting in May 1991, subgroup members reviewed a detailed description of EPA's plans for implementing section 612. At this meeting, there was general agreement on the need to issue a request for data to provide the general public with an opportunity to furnish the Agency with information on substitutes. The group also agreed on the need to review substitutes as quickly as possible to avoid any delay in industry's efforts to phase out of ozone-depleting substances.

At the second meeting of the subgroup, in July 1991, subgroup members provided EPA with comments on a draft of the Advance Notice of Proposed Rulemaking (ANPRM), which was prepared in response to the conclusions of the first meeting. The comments focused primarily on the draft discussion of EPA's plans for implementing section 612 and refinements to a list of preliminary substitutes that the Agency intended to review. Based on comments received from the subgroup and other offices within EPA, a final ANPRM was prepared which was published in the

Federal Register on January 16, 1992 (57 FR 1984; January 16).

III. Section 612 Program

A. Statutory Requirements

Section 612 of the Clean Air Act authorizes EPA to develop a program for evaluating alternatives to ozone-depleting substances. EPA is referring to this new program as the Significant New Alternatives Policy (SNAP) program. The major provisions of section 612 are:

- **Rulemaking**—Section 612(c) requires EPA to promulgate rules by November 15, 1992, making it unlawful to replace any Class I or Class II substance with any substitute that the Administrator determines may present adverse effects to human health or the environment where the Administrator has identified an alternative that: (1) Reduces the overall risk to human health and the environment, and (2) is currently or potentially available.

- **Listing of Unacceptable/Acceptable Substitutes**—Section 612(c) also requires EPA to publish a list of the substitutes prohibited for specific uses. EPA must publish a corresponding list of acceptable alternatives for specific uses as well.

- **Petition Process**—Section 612(d) grants the right to any person to petition EPA to add a substance to or delete a substance from the lists published in accordance with section 612(c). The Agency has 90 days to grant or deny a petition.

- **90-day notification**—Section 612(e) requires EPA to require any person who produces a chemical substitute for a Class I substance to notify the Agency not less than 90 days before new or existing chemicals are introduced into interstate commerce for significant new uses as substitutes for a Class I substance. The producer must also provide the Agency with the producer's unpublished health and safety studies on such substitutes.

- **Outreach**—Section 612(b)(1) states that the Administrator shall seek to maximize the use of Federal research facilities and resources to assist users of Class I and II substances in identifying and developing alternatives to the use of such substances in key commercial applications.

- **Clearinghouse**—Section 612(b)(4) requires the Agency to set up a public clearinghouse of alternative chemicals, product substitutes, and alternative manufacturing processes that are available for products and manufacturing processes which use Class I and II substances.

B. Guiding Principles

EPA has followed several guiding principles in developing the SNAP program:

(1) *Evaluate substitutes within a comparative risk framework.* The Agency's risk evaluation examines risks of substitutes using risks from continued use of ozone-depleting compounds as well as risks associated with other substitutes as reference points. This evaluation will consider factors such as effects due to ozone depletion as well as effects due to direct toxicity across all substitutes. Other risk factors considered include effects on water and air quality, direct and indirect contributions to global warming, and occupational health and safety. Where such effects could be of concern, the evaluation will screen these effects. However, EPA does not believe that a numerical scheme producing a single index to rank all substitutes based on risks is appropriate. A strict quantitative index would not allow for sufficient flexibility in making appropriate risk management decisions that consider issues such as the quality of information supporting the decision, the degree of uncertainty in the data, the availability of other substitutes, and economic feasibility.

(2) *Do not require that substitutes be risk-free to be considered "safe".* Section 612(c) requires the Agency to publish a list of safe alternatives where the Agency has identified unacceptable substitutes. The Agency interprets this as a mandate to identify substitutes that reduce risks when compared to use of Class I or II compounds or to other substitutes for Class I or II substances, rather than a mandate to list as acceptable only those substitutes with zero risks. In keeping with this interpretation, the Agency believes that a key goal of the SNAP program is to promote the use of substitutes for Class I and II chemicals that minimize risks to human health and the environment relative to other alternatives. In some cases, this approach may involve designating a substitute as acceptable even though the compound may be toxic, or pose other environmental risk of some type.

(3) *Restrict only those substitutes that are significantly worse.* As a corollary to the point above, EPA does not intend to restrict a substitute if it poses only marginally greater risk than another substitute, all things considered. Drawing fine distinctions concerning the acceptability of substitutes would be extremely difficult given the variability in how each substitute can be used within a specific application and the

resulting uncertainties surrounding potential health and environmental effects. The Agency also does not want to intercede in the market's choice of available substitutes, unless a substitute has been proposed or is being used that is clearly more harmful to human health and the environment than other alternatives.

(4) *Evaluate risks by use.* Section 612 requires that substitutes be evaluated by use. Environmental and human health exposures can vary significantly depending on the particular application of a substitute. Thus, the risk characterizations must be designed to represent differences in the environmental and human-health effects associated with diverse uses.

(5) *Provide the regulated community with information as soon as possible.* The Agency recognizes the need to provide the regulated community with information on the acceptability of various substitutes as soon as possible. Given this need, EPA has decided to expedite the review process by conducting initial risk characterizations for the major substitutes now known to the Agency. The results of the risk characterizations will be used, as discussed in the previous section, to propose determinations regarding the acceptability of the substitutes.

(6) *Do not endorse products manufactured by specific companies.* While the goal of the SNAP program is to identify acceptable substitutes, the Agency will not issue company-specific product endorsements. In some cases, the Agency may base its analysis on data received on individual products, but the addition of a substitute to the approved list based on that analysis does not represent a preference for that company's product over comparable products offered by other manufacturers.

(7) *Defer to other environmental regulations when warranted.* In some cases, EPA and other federal agencies have developed extensive regulations under other statutes or other parts of the CAA that address any potential cross- or inter-media transfers that may result from the use of alternatives to Class I and II substances. For example, ceasing to use an ozone-depleting compound may in some cases entail increased use of chemicals that increase tropospheric air pollution. These chemicals, such as volatile organic compounds (VOCs) or hazardous air pollutants (HAPs), are already regulated under other sections of the CAA, and determinations under the SNAP program will take these existing regulations into account. Where necessary, the Office of Air and Radiation will confer with other EPA

program offices or federal agencies to ensure that any regulatory overlap is handled efficiently.

C. Implementation Strategy

Implementation of the SNAP program is directed towards fulfilling the general policy contained in section 612 of identifying substitutes that can serve as replacements for ozone-depleting substances, evaluating their effects on human health and the environment, and encouraging the use of those substitutes believed to present low risks to human health and the environment. Implementation of this policy involves three key activities. The first is to develop, promulgate, and administer a regulatory program for identifying and evaluating substitutes. The second activity is to undertake a review of the existing substitutes based on criteria established for the program and then to publish a list of acceptable and unacceptable substitutes by application. The third activity is to review additional substitutes as they are developed to allow their timely introduction into the marketplace.

To expedite implementation of the SNAP program, EPA has developed not only a process for examining the alternatives, as discussed in today's proposal, but has completed an initial analysis of many key substitutes based on the criteria being proposed. Section IX summarizes the results of this initial assessment. More detail on the steps leading up to today's proposal and the anticipated implementation of the SNAP program is given below.

1. Issue ANPRM and Request for Data

In January of this year, EPA published in the Federal Register an Advance Notice of Proposed Rulemaking (ANPRM) and Request for Data (57 FR 1984; January 16, 1992). The ANPRM described in general terms EPA's plans for developing the SNAP program and solicited public comment on the Agency's planned approach. The ANPRM also included an appendix listing substitutes that the Agency planned to include in its initial substitute determinations. The ANPRM invited industry to submit information on these substitutes and to identify additional alternatives to be considered in the SNAP program.

The Agency received approximately one hundred comments from industry, trade groups, and other federal agencies. These comments contained information on potential substitutes for ozone-depleting chemicals, as well as comments on the SNAP program as described in the ANPRM. In some cases, the information provided on substitutes

did not contain sufficient data for the Agency to immediately incorporate these alternatives into the risk characterizations. The Agency is working now to gather additional information on these alternatives to ensure that they can be included in the list of reviewed substitutes in the final rule.

Comments on the SNAP program itself focused primarily on issues such as effective dates, small uses, the desirability of assured minimum periods of use for substitutes, how mixtures will be handled by the SNAP program, and how specific the lists of "acceptable" and "unacceptable" substances will be. These comments, and the Agency's response to them, are addressed in later sections of today's proposal.

2. Develop Preliminary Determinations on Substitutes

To arrive at its SNAP determinations, the Agency has been collecting and evaluating information on substitutes since the President's signing of the Clean Air Act Amendments in November 1990. In some cases, this information has been furnished directly by companies manufacturing, selling, or using the substitutes. In others, the Agency has initiated its own studies to characterize, for example, worker exposures where toxicity was anticipated to present a potential problem. Response to the request for data in the January ANPRM augmented the Agency's available data, both by helping to identify substitutes that merit consideration in the SNAP program and by providing additional information on substitutes already under consideration.

There are, however, still omissions in the Agency's list of substitutes under consideration. In some cases, engineering and use profile data are missing; in others, information on potential market applications may not yet be available. The Agency today is repeating the data request issued in the ANPRM, and is encouraging companies that manufacture substitutes to provide information.

3. Publish Proposed SNAP Process and Proposed Determinations

This NPRM represents the third implementation step, which is to describe the proposed structure and process for administering the SNAP program and to propose determinations on the acceptability of key substitutes. The notice also contains the proposed regulatory language that will serve as the legal basis for administering and enforcing the SNAP program.

EPA believes that notice-and-comment rulemaking procedures are necessary to establish these regulations governing the SNAP program. EPA further believes that rulemaking is also required to place any substance on the list of prohibited substances, to list a substance as acceptable only under certain conditions, or to remove a substance from either the list of prohibited or acceptable substitutes. EPA requests comment, however, on the need to remove a substance from the list of acceptable substitutes through rulemaking.

EPA does not believe that rulemaking procedures are required to list alternatives as acceptable with no limitations. Such listings do not impose any sanction, nor do they remove any prior license to use a substance. Consequently, once this rule is promulgated, EPA will be adding substances to the list of acceptable alternatives without first requesting comment on new listings.

Because EPA's SNAP regulations are not yet final, however, manufacturers and users may have additional information that could help EPA in making this first round of SNAP determinations. Recognizing this, EPA has elected to propose the list of acceptable alternatives identified in this notice, and to request public comment on these listings. This should not in any way be taken as a precedent for future listings of acceptable substitutes. Once the SNAP program regulations are finally adopted and EPA has received SNAP notices from manufacturers and users, EPA will add substances to the list of acceptable substitutes without notice-and-comment procedures.

Any approvals or prohibitions on substitutes described in this notice are preliminary and will not be final until the SNAP program is promulgated. Even though they are preliminary, the Agency is issuing the SNAP decisions now because many companies are awaiting Agency guidance before switching out of ozone-depleting substances. The Agency believes that by publishing these preliminary determinations, it has met the intent of section 612 to inform the public of Class I and II substitutes believed to present minimal risks to human health and the environment. Moreover, given the accelerated pace of the phase-out of Class I compounds, the Agency wants to encourage the earliest possible shift to the alternatives identified on today's list of acceptable substitutes.

The Agency may revise these decisions in the future as it reviews additional substitutes and receives more data on substitutes already covered by

the program. However, EPA expects future changes to the SNAP lists to be minor, and thus not to represent an undue burden on the regulated community. The principal types of changes the Agency expects to make in the future would be to add new substitutes or sectors to the lists, rather than to change a substitute's approval status. Further, once a substitute has been finally placed on either the acceptable or the unacceptable list, EPA will conduct notice-and-comment rulemaking to subsequently remove a substitute from either list, as described below in Section VII. Again, the Agency requests comment on whether formal rulemaking is necessary to remove a substance from the acceptable list.

4. Issue Final Regulation

As discussed above, the final rule will promulgate the SNAP process and the first set of determinations on SNAP substitutes. The final regulation will address comments that the Agency receives on today's NPRM, and will also incorporate any further data on substitutes that are received during the comment period.

5. Maintain and Update SNAP Determinations

Three mechanisms exist for revising or expanding the list of SNAP determinations published in the final regulation. First, under section 612(d), the Agency will review and either grant or deny petitions to add or delete substances from the SNAP list of acceptable or unacceptable alternatives. Section VIII of this notice presents EPA's proposed method for handling petitions.

The second means of revising or expanding the list of SNAP determinations is through the notifications, which must be submitted to EPA 90 days before introduction of a chemical into interstate commerce for significant new use as an alternative to Class I or Class II substances. These 90-day notifications are required by section 612(e) of the CAA and by EPA regulations today proposed to be issued under sections 114 and 301 of the Act to implement section 612(c). In Section VII, this notice discusses the Agency's proposed approach for processing these notifications, including a proposed strategy for integrating the SNAP notifications with other chemical review programs already being implemented by EPA under authorities provided in the Toxic Substances Control Act (TSCA) and the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). Other parts of this action also explain how the Agency will address the overlap

between SNAP regulations and regulations issued under other titles of the Clean Air Act.

Finally, the Agency believes that section 612 authorizes it to initiate changes to the SNAP determinations independent of any petitions or notifications received. These amendments can be based on new data on either additional substitutes or on characteristics of substitutes previously reviewed.

6. Perform Outreach and Operate Clearinghouse

Outreach and the clearinghouse comprise the technical assistance component of the SNAP program. The purpose of this effort is to provide information for companies to use in selecting among the approved substitutes. Section VII.A.3.f. describes the Agency's proposed approach for establishing the clearinghouse and performing outreach.

IV. Scope of Coverage

A. Definition of Substitute

1. Statutory Language

Based on the language of section 612(a) of the CAA, the Agency is proposing in the SNAP program to define a "substitute" as any chemical, product substitute, or alternative manufacturing process, whether existing or new, that could replace a Class I or Class II substance. While subsequent subsections of section 612 refer only to "substitute substances" or "substitute chemicals," EPA is proposing a definition that interprets these provisions as incorporating the general definition of substitute presented in 612(a). The Agency believes that this definition is consistent with the overall intent of section 612 and is necessary to enable EPA to identify and analyze the universe of substitutes for Class I and II substances.

Section 612(c) prohibits users from replacing Class I or II substances with any substitute substance which the Administrator determines may present adverse effects to human health and the environment, where the Administrator has identified an alternative to such replacement that (1) reduces overall risk to human health and the environment, and (2) is currently or potentially available. EPA believes that in addition to authorizing the Agency to ban the use of a given substitute substance, section 612 confers the legal authority to allow the use of a substance only under certain use conditions, such as with mitigation measures. EPA only intends to use this authority where a viable substitute exists, but would otherwise

have to be disallowed because of risk associated with its uncontrolled use. EPA anticipates imposing use conditions only in the rare instances where clear regulatory gaps exist, and where an unreasonable risk exists in the absence of any condition.

In imposing conditions, EPA does not intend to preempt other regulatory authorities, such as those exercised by the Occupational Safety and Health Administration (OSHA), or other standard setting bodies. Rather, EPA hopes to fill existing regulatory gaps during the interim period of substitution away from ozone-depleting compounds, and provide the needed margin of protection to human health and the environment until other regulatory controls or standards are developed under appropriate authorities. Once existing gaps are filled, EPA will rescind any conditions which have become redundant. The mechanism for informing the public of this change will be the quarterly Federal Register notices updating the status of the SNAP lists. These are discussed further below in section VII.A.

The Agency, however, requests comment on the general issue of the need for use conditions. In particular, EPA requests comment on whether section 612 in fact confers upon the Agency the authority to go beyond the listing of acceptable and unacceptable alternatives and to set such use conditions. Further, EPA requests comment on the capability and practicality of EPA enforcing use conditions which may, for example, closely resemble workplace safety standards, which are typically within the enforcement purview of other regulatory authorities.

EPA also requests comment on whether, when an unreasonable risk might exist due to a gap in regulatory coverage, the appropriate means to address these risks is through the existing regulatory framework of other federal authorities. For example, rather than using EPA's use conditions to address existing gaps in workplace safety standards, EPA could refer the matter to the appropriate OSHA authorities and request appropriate action to mitigate an otherwise unreasonable risk.¹

Alternatively, where the length of time required to address a problem under another authority may be unacceptably long given the nature of

the risk, there may be cases in which EPA would simply consider unacceptable the use of a given substitute, pending the development of a regulatory framework to control the risk it poses in its use as a substitute for an ozone-depleting compound.

Section 612(e) makes clear that a chemical can be a substitute whether it is existing or new. Also, the language in section 612(c) clearly states that a substitute may be "currently or potentially available." The Agency is proposing to define as potentially available any alternative that the Agency reasonably believes to be technologically feasible and economically viable, even if not all testing has yet been completed and it is not yet produced and sold in commercial quantities. EPA solicits comment on this approach.

The language included in section 612 is written broadly to allow for an all-encompassing evaluation of substitutes that will be introduced as replacements for ozone-depleting chemicals. However, additional clarification is presented below to further explain the Agency's definition of a "substitute" based on section 612.

2. Additional Clarification

a. *Chemicals Already Listed as "Existing" under TSCA.* Many commenters have expressed the view that any compound already existing (e.g., listed on the TSCA inventory, either through the grandfathering provisions or by undergoing new-chemical review under section 5 of TSCA) is not subject to review under section 612. Nothing on the face of section 612(c), however, suggests that any "new" compound can be considered a substitute for purposes of that subsection. Moreover, section 612(e) explicitly requires producers of chemicals, both "new and existing," to notify the Agency before introducing such chemicals into interstate commerce for significant new uses as Class I alternatives. In addition, section 612(c) requires the Agency to produce lists of acceptable and unacceptable substitutes, without regard to the status of each chemical, whether new or existing.

These interrelated provisions of section 612 serve as the basis for the Agency's belief that all substitutes, whether "new or existing" chemicals, are subject to SNAP review. This regulatory purview would thus necessarily extend to those chemicals already listed on the TSCA inventory. EPA believes SNAP review is critical given the differing statutory objectives of TSCA and the CAA, and the new and

¹ 29 U.S.C. 654, OSHA General Duty Clause, requires that each employer "shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees. * * *

expanded applications of many existing chemicals as Class I and Class II replacements, which could alter existing release and exposure profiles.

b. Expanded Use of Existing Alternatives. There has also been some question regarding whether an existing alternative already being sold commercially (e.g., use of semi-aqueous cleaners in the electronics industry) would be subject to review under section 612. The Agency believes that they would. Because of the phase-out, uses of existing substitutes can be expected to increase significantly beyond current consumption. This increased use could translate into greater releases and risks, and existing substitutes are therefore subject to SNAP approval where their use could significantly expand to new users or product lines. Users should note that preliminary SNAP determinations discussed in Section IX of this action demonstrate that with few exceptions, all substitutes already on the market meet the conditions for SNAP approval.

c. Authority to Review Substitutes for Class II Compounds. Section 612(c) authorizes the Administrator to prohibit the use of substitutes for Class II, as well as Class I substances, and requires the Agency to compile lists of substitutes for Class II as well as Class I compounds upon making the requisite findings. This is in part because of the considerable overlap in sectors that use Class I and II substances. More importantly, this mirrors the statute's general emphasis on moving away from Class I compounds in a way that does not create new and unintended environmental problems. Clearly, for the same reasons Class I substitutes require review, Class II substitutes should also be reviewed.

To obtain the data necessary to analyze Class II substitutes, the Agency is proposing to use statutory authority provided in sections 114 and 301 of the CAA with 612(c). These sections together authorize the Administrator to promulgate regulations needed to require companies to provide information EPA may reasonably require to identify acceptable and unacceptable substitutes for Class II substances. EPA proposes to exercise this authority so that Class I and Class II substitutes are subject to the same information reporting requirements and listing process.

d. Designation of Class I and Class II Chemicals as Substitutes. EPA believes that the review authority under section 612 extends also to use of Class I and Class II chemicals as substitutes, even though these chemicals are subject to the phase-out provisions of the CAA.

While some comments received by the Agency in response to the ANPRM question EPA's authority under section 612 to review Class I and Class II chemicals as substitutes (e.g., methyl chloroform used to replace CFC-113), it is clear that these compounds can be used as substitutes for other Class I and II substances in certain applications. Since section 612 authority extends to "any" substitutes, they are subject to review under the SNAP program just as any other substitute. Given the potential for the Class I and Class II chemicals to continue depleting stratospheric ozone and thus affect human health and the environment, a close examination of these alternatives in the context of both their effect on the environment and the availability of other substitutes for particular uses is warranted under section 612.

e. Alternative Substances and Manufacturing Processes. Section 612(c) broadly charges EPA to identify alternatives to ozone-depleting substances. For example, EPA believes that alternative substances can include no-clean fluxes for solvent cleaning, substituting for solvents using Class I or II compounds. Several commenters disagree with this interpretation of the language in section 612. However, EPA believes it appropriate to consider substitute substances in its reviews under the SNAP program, since many of these alternatives are viable substitutes and could reduce overall risks to human health and the environment.

Similarly, new production techniques and/or processing equipment are important developments that can minimize environmental releases. Accordingly, alternative manufacturing processes will also be examined under section 612 in the context of use and emissions of substitutes. Section 612's reference to "alternative", instead of "alternative substance", or "alternative chemical", implies a statutory intent that "alternative" be read broadly.

EPA will encourage, where appropriate, alternative processes that reduce environmental and human health effects. In many applications, reliance on alternative processes and/or equipment may be associated with the use of substitute chemicals. In these instances, EPA encourages the filing of joint submissions where information is provided by both the chemical manufacturer and, for example, an equipment manufacturer. Such joint filings will provide the most comprehensive data on an alternative and its effect on human health and the environment.

f. Feedstock Substitutes. Other commenters have questioned the

applicability of section 612 to substitutes that could replace Class I chemicals which are used solely as intermediates in the production of other chemicals. To the extent that any feedstock substitutions occur, the Agency believes that there will be no incremental risk to human health and the environment. This is because intermediates are used as inputs in production of other compounds, and as a result are largely consumed in the chemical manufacturing process. For instance, in analyzing uses of carbon tetrachloride as a feedstock, the Agency determined that greater than 99 per cent of this chemical was consumed in the production process. The Agency is therefore proposing that feedstock substitutes be exempt from reporting and review under section 612.

g. Second-Generation Substitutes. A key issue is whether there exists a point at which an alternative should no longer be classified as a Class I and Class II substitute as defined by section 612. The Agency believes that as long as Class I and Class II chemicals are being used, any first-generation substitute designed to replace these applications is subject to the regulatory provisions implemented under section 612. However, the Agency is proposing today that second-generation replacements, if they are replacing non-ozone depleting first-generation alternatives, are exempt from reporting requirements under section 612. Other regulatory programs (e.g., other sections of the CAA, or section 6 of TSCA) exist to ensure protection of human health and the environment in these situations.

Several commenters agreed with the need to exempt second-generation substitutes. On the other hand, EPA is proposing that second-generation substitutes replacing first-generation substitutes that deplete stratospheric ozone (e.g., HCFCs) should be bound by the same notification and review requirements under section 612 as first-generation substitutes.

For example, if a hydrofluorocarbon (HFC) is introduced as a first-generation refrigerant substitute for either a Class I (e.g., CFC-12) or Class II chemical (e.g., HCFC-22), it is subject to review and listing under section 612. However, future substitutions to replace the HFC would be exempt from reporting under section 612 because the first-generation alternative did not deplete stratospheric ozone. However, if a Class I (interim only) or Class II chemical is used as a first-generation substitute (e.g., use of HCFC-141b as a transitional replacement in foam blowing), the second-generation substitute is still subject to review under section 612.

because it is replacing a Class I or II chemical.

h. Formulation Changes Accompanying the Use of Class I and Class II Substitutes. In general, the Agency believes that changes in formulation needed to accommodate replacement of Class I and II compounds are not subject to the provisions of section 612. Such auxiliary changes may be necessary, for example, when a new blowing agent in foam blowing necessitates the replacement of the catalyst formerly used in conjunction with the Class I blowing agent.

This position was also supported by comments received in response to the ANPRM. However, if the potential SNAP notice submitter has reason to believe that such changes will significantly influence the environmental and human health risk characteristics associated with the use of any Class I or Class II substitute, this must be communicated to the Agency. Alternatively, if EPA has reason to suspect such concerns may exist, it may request the review of any such changes in formulation in connection with review of substitute compounds.

B. Who Must Report

1. General Provisions

As required by section 612(e), anyone who produces a substitute for a Class I substance must provide the Agency with that person's unpublished health and safety studies on the substitute, as well as notify the Agency at least 90 days before introducing the substitute into interstate commerce for significant new use as an alternative. Also, as discussed in section IV.A.2.c of this notice, pursuant to sections 114, 301 and 612(c), producers of Class II substitutes must abide by the same reporting requirements.

Under the authority of sections 114, 301(a) and 612(c), EPA is proposing that in certain cases, formulators or end-users of substitutes could be considered to be producers and would therefore be subject to reporting requirements. This approach is discussed in the following section, IV.A.2.j.(2). To analyze alternative substitutes under section 612(c), the Agency finds it necessary under section 301(a) to require all producers of substitutes, whether a chemical manufacturer, formulator, or end-user, to submit information under section 114 describing such substitutes. With respect to substitutes for both Class I and II substances, EPA needs all of the types of information described below, not just health and safety studies. This is needed to allow EPA to

fully analyze the overall risks to human health and the environment presented by alternative substitutes, as required by section 612(c).

2. Designated Submitters

a. Chemical Manufacturers. Chemical manufacturers making a substitute for direct commercial sale are required to notify the Agency about the existence of that substitute. This requirement is especially applicable to chemical manufacturers that have developed new compounds for specific, targeted uses as substitutes for Class I or II substitutes. For instance, if a chemical manufacturer intends to market a new chemical as a substitute foam blowing agent to companies that manufacture insulation products, that manufacturer would be required to notify the Agency about the existence of the substitute. The reporting requirement would also apply to chemical manufacturers that intend to sell an existing chemical to a particular user group.

b. Formulators. A formulator is a person or organizational entity engaged in the preparation or formulation of a substitute, after chemical manufacture of the substitute or its components, for distribution or use in commerce. Formulators usually only sell substitutes based on existing chemicals, since they do not ordinarily possess chemical manufacturing capabilities. Chemicals used in such substitutes are frequently in common use and have already been approved for general use through other chemical review programs such as under TSCA or FIFRA.

However, to the extent that these formulators can be considered to be directly responsible for production of the substitute, for example by offering a tailored formulation or blend for an industrial cleaning process, these formulators would be subject to reporting requirements as outlined in this proposal. In such cases, the formulator is best suited in the manufacture-to-use chain to present information on how substitutes based on existing chemicals are or could be used.

In cases where the manufacturer of a chemical is also the formulator, the manufacturer would then be responsible for meeting reporting requirements on the chemical. Similarly, if an end-user has developed a process to replace an ozone-depleting compound, this end-user would be required to provide EPA with information on the substitute.

The simplest approach to allocating responsibility for reporting requirements would be to place the reporting burden in all cases on chemical manufacturers. However, the

Agency believes that the approach outlined above provides the best correlation between burden for reporting and benefit from securing approval for a substitute. For instance, it would be inappropriate to require a manufacturer of a chemical in widespread industrial use to report on every possible application for that chemical as a substitute. The Agency requests comment on this aspect of the proposed reporting requirements.

c. End-users. In general, end-users of substitutes will not be obligated to meet the reporting requirements discussed in this proposal, except in rare cases where the end-user and the producer of the substitute are one and the same company and the company intends to sell that substitute into inter-state commerce. While the Agency expects that this situation will occur only seldom, it has already received notice from several large companies who developed a substitute for use in their own manufacturing process and subsequently decided to offer that substitute for commercial sale. The Agency hopes that evaluating and listing such substitutes will help provide other potential end-users with information on viable substitutes, rather than stifling research and development innovations by end-users. The Agency solicits comment on this aspect of today's proposal.

3. Exemptions from Reporting

The Agency has identified several situations in which notification under the provisions of section 612(e) will not be required. These exemptions from reporting are discussed below.

a. Substitutes Already Listed by EPA. As part of today's proposal, the Agency has already completed a preliminary review of several Class I and Class II alternatives and has proposed that these substitutes be either acceptable or unacceptable. In preparing these proposed determinations, the Agency evaluated information either on file or supplied in response to the ANPRM published in the *Federal Register* on January 16, 1992. The preliminary substitutes list and the supporting risk screen are described in more detail in Section IX. No submission is needed for those substitutes and applications already proposed as acceptable in today's NPRM.

Any specific comments on the proposed substitute determinations found in this action should be provided to the Agency, along with any supporting information, during the comment period. If information is not received by the Agency during the comment period, a formal submission to

add substitutes will be required once the final rule is promulgated.

b. *Small Sector and Application Use.* Most ozone-depleting substances have been or are currently used in large industrial sectors such as refrigeration or fire extinguishing. However, there are also numerous small uses of Class I or II substances that fall outside of these major use sectors. Most of these small uses of ozone-depleting compounds are for solvents in applications other than industrial cleaning operations, such as solvents used as book preservers, drilling and machining coolants, extraction or bearer media, or mold release agents. While small-use applications for Class I and Class II compounds are varied and numerous, in the aggregate these small uses do not contribute substantially to ozone depletion. The Agency estimates that across all sectors, including the solvents sector, these varied but small volume uses comprise in aggregate at most seven per cent of total U.S. consumption of ozone-depleting substances.

Because the potential for adverse effects on human health and the environment is related to the aggregate amount of ozone-depleting material consumed in an end-use or sector, the Agency proposes to focus the SNAP determinations on large-volume applications in major use sectors. Given the breadth of EPA's required "overall" risk assessment, the imposition on small sectors, and on small uses within any sector, of a full SNAP submission for each small use seems unjustified by the potential for risk posed by these small uses.

Moreover, a key policy interest of EPA's in designing and implementing the SNAP program is promoting the quickest possible shift from the phase-out compounds into alternatives posing lower overall risk. The speed and orderliness of this shift depends in part on clear early determinations from EPA on the acceptability of key substitutes. Focusing the SNAP program on all possible substitutes in every conceivable use could diminish EPA's ability to provide an early and clear message on those substitutes which constitute the bulk of the problem SNAP is aimed at ameliorating.

Accordingly, eight major industrial use sectors are covered in today's proposal. They are refrigeration, foam blowing, fire extinguishing, solvent cleaning, adhesives, coatings, and inks, aerosols, sterilization, and tobacco puffing. Analysis of substitutes in a ninth sector, pesticides, will be completed, and the resulting decisions will be added to the SNAP determinations in the final rule. EPA

does not plan to add sectors other than the nine principal sectors listed above to the formal analyses performed under SNAP, unless the Agency in future receives additional data indicating that inclusion of additional sectors is warranted based on the potential for high risks to human health and the environment.

Further, the Agency does not plan individual analyses of all small uses within major industrial sectors. Specifically, EPA is today proposing not to review any uses of substitutes of less than 10,000 lbs per year within a sector as defined in the SNAP determinations. Companies producing, formulating or using substitutes for ozone-depleting compounds in annual quantities under 10,000 lbs per year need not notify EPA of their activities under SNAP.

However, the Agency encourages companies to maintain documentation describing the basis for their view that any substitute being used meets this small use definition. This documentation could be necessary in the event the Agency receives a petition to add such substitutes to its evaluation.

The Agency's decision to focus the SNAP program on high-volume sectors does not imply the complete absence of any risk from use of substitutes in small use applications. Instead, the Agency believes that focusing the listing decisions on the largest sectors and uses will allow the Agency to target its regulatory efforts to those applications that offer the maximum risk reduction potential. If other sectors are subsequently added to the Agency's analysis, the Agency will provide notice in the *Federal Register* of the need to furnish the Agency with data on substitutes. The Agency requests comment on this approach to small sectors and small uses within all sectors of substitutes for ozone-depleting compounds. In particular, EPA requests comment and data on risks associated with small sector and small volume uses.

c. *Test Marketing.* Use of alternatives for the sole purpose of test marketing is exempt from any reporting requirements under section 612. However, once a company decides to sell an alternative as a Class I or II substitute, it must provide the Agency with notification at least 90 days prior to the introduction of the substitute into interstate commerce for significant new use as a substitute for a Class I or Class II chemical.

For new substitute chemicals that are being test marketed, the producer must abide by the provisions of section 5(h)(1) of TSCA, which authorizes the EPA, upon application, to grant

exemptions from TSCA-reporting requirements, provided that test marketing will not present an unreasonable risk to human health or the environment. When submitting the TSCA application, it would also be advantageous if the producer would notify EPA's Office of Air and Radiation; however, such notification is not mandated under section 612.

d. *Research.* Substitutes manufactured or imported solely for research and development are exempt from notification requirements under section 612. Several commenters, including Federal agencies involved in research on CFC-related substitutes, support this exemption. Amounts used in research are assumed to be the minimum necessary for reasonable scientific experimentation. For new chemicals, the provisions of section 720.36 of the PMN rule (40 CFR Part 720) are in effect. The Agency solicits comment on appropriate use levels to allow in research applications.

e. *Second-Generation Substitutes.* As discussed in section IV.A.2.h., substitutes replacing first-generation alternatives that are not ozone-depleting chemicals are exempt from any additional reporting and review under section 612. However, if the second-generation substitute is replacing a compound that contributes to stratospheric ozone depletion (e.g., a HCFC), information must be submitted to the Agency for review under the SNAP program.

f. *Formulation Changes.* As discussed in section IV.A.2.i., the Agency is proposing that changes in formulation that accompany the use of substitutes for Class I and Class II substances need not be reviewed under section 612. The Agency believes that other regulatory mechanisms (e.g., TSCA) are available for examining and controlling, as needed, any adverse environmental and human health effects associated with subsequent formulation modifications. However, the manufacturer overseeing the formulation change is required to notify the Agency if these modifications may significantly influence the environmental and human health risk characteristics associated with the Class I or Class II substitute. Also, the Agency reserves the right to examine formulation changes if a problem appears to exist.

g. *Substitutes Produced for Export.* Substitute manufacturers producing solely for export and use by non-U.S. entities outside the U.S. are not subject to the requirements of section 612. EPA believes that its authority under section 612 extends only to use of substitutes in areas under the jurisdiction of the

United States government, regardless of their place of manufacture. This exemption does not apply to substitutes introduced as replacements for Class I and II chemicals offered for sale or use at offshore U.S. installations (e.g., U.S. military bases located in foreign countries) that are subject to the legal provisions of section 612, since 612(c) applies to use rather than to manufacture of substitutes.

h. Substitutes Used as Feedstock. The Agency is proposing to exempt substitutes used as feedstock from the reporting and review requirements of section 612. Because feedstock chemicals are largely consumed as intermediates, except for trace amounts, the Agency does not believe that such substitutions would cause any increase in ozone depletion or other adverse effects on human health and the environment.

V. Information Submission

A. Overview

To develop the list of unacceptable and acceptable substitutes as required by section 612(c), the Agency must assess and compare the "overall risks to human health and the environment" posed by use of substitutes, and this assessment must be performed in the context of particular applications. This "overall" examination will consider a wide range of health and environmental factors. In the section that follows, the Agency presents information that will be required in the SNAP program notice to help EPA evaluate Class I and Class II substitutes. A copy of the notification form can be obtained from the SNAP coordinator at the address listed in the beginning of this action.

B. Information Required

1. Name and description of the substitute. The substitute should be identified by its (1) commercial name, (2) chemical name, (3) trade name(s), (4) identification numbers (e.g., Chemical Abstract Service (CAS) registry, National Institutes of Occupational Safety and Health Registry of Toxic Effects of Chemical Substances (NIOSH RTECS), EPA hazardous waste identification number, OHM-TADS, DOT/UN/NA/IMCO shipping, HSDB, National Cancer Institute (NCI), (5) chemical formula, and (6) chemical structure.

2. Physical and chemical information. Key properties needed to characterize the substitute are: molecular weight; physical state; melting point; boiling point; density; odor threshold; solubility; partition coefficients (Log

K_{ow} , Log K_{oc}); vapor pressure; and Henry's Law Constant.

3. Substitute applications.

Identification of the applications in which the substitutes are likely to be used is required. It is essential to provide a complete list of potential uses because the substitute listing required by section 612(c) is specific to application.

4. Process description. For each application identified, the Agency requires descriptive data on processing, including in-place pollution controls. Such information will be used to characterize workplace and environmental releases and exposures.

5. Ozone depletion potential. The predicted ozone depletion potential (ODP) of substitute chemicals is required. The submitter should also provide sufficient supporting documentation—either a citation or the background information used to develop the ODP. For purposes of calculating ODP, the Agency recommends the methodology used in the most recent *Scientific Assessment of Ozone Depletion: 1991*, which was prepared for the United Nations Environment Programme. [1]

6. Global warming potential. The Agency requires data on the total global warming potential (GWP) of the substitute in its particular application (e.g., as a refrigerant, foam blowing agent, etc.). The total GWP considers both direct and indirect effects. Direct effects means the direct global warming effects of using a substitute. The Agency is requesting that all GWPs be referenced to CO₂ using the methodology recommended by the Intergovernmental Panel for Climate Change (IPCC). [2] Indirect effects explicitly consider the effect on global warming arising from changes in energy consumption associated with the use of a substitute (e.g., an alternative refrigerant). This latter measure can be identified as changes in energy efficiency or demand resulting from use of the substitute relative to that of the substance being replaced.

7. Toxicity data. To assess the overall risks to human health and the environment, information is required on the acute and chronic toxicity effects of a substitute chemical, its impurities, and its degradation products on any organism (e.g., humans and other mammals, fish, wildlife, and plants). To characterize the risk to humans, the Agency is requesting a minimum submission of the following mammalian tests: a range-finding study that considers the appropriate exposure pathway for the specific use (e.g., inhalation, oral, etc.), and a 90-day

subchronic repeated dose study in an appropriate rodent species (for example, rats or mice). For substitutes that are being evaluated as fire suppressants, a cardiotoxicity study, usually in the dog, is also required. Additional mammalian toxicity tests will be identified by EPA on a case-by-case basis depending on the particular substitute and application being evaluated. To sufficiently characterize aquatic toxicity, both acute and chronic toxicity data for a variety of species are required. The Agency is proposing a minimum aquatic data set to be submitted as described in "Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and Their Uses," which is available through the National Technical Information Service (#PB 85-227049).

Other relevant hazard information and data summaries, such as the Material Safety Data Sheets, must also be submitted. Submission of the actual toxicity studies is recommended; however, it is not necessary to submit these reports if they have been supplied to the Agency as part of other regulatory submissions. If the actual studies are not submitted, however, the submitter must provide sufficiently clear references or citations that the Agency can locate the studies without delay. As discussed below in Section V.C.3., data concerning the objectives, methodology, results or significance of any toxicity, metabolism, translocation, or persistence test for a substitute and its degradation products cannot be held as CBI where such data are also submitted under TSCA and FIFRA. The Agency is proposing that submitters providing information on new chemicals for joint review under the TSCA and SNAP programs adhere to the TSCA minimum testing requirements described in TSCA section 4.

8. Environmental Fate and Transport. Where available, EPA requests information on the environmental fate and transport of substitutes. Such data shall include information on bioaccumulation, biodegradation, adsorption, volatility, transformation, and other data necessary to characterize a substitute's movement and reaction in the environment.

9. Flammability. Data on the flammability of a substitute chemical or mixture are required. Specifically, data on flash point and flammability limits are needed, as well as information on the procedures used for determining the flammability limits. For substitutes that will be used in consumer applications, documentation of testing results conducted by independent laboratories (e.g., Underwriters Laboratories) should

be submitted where appropriate. Detail on any suggested abatement techniques to minimize the risks associated with the use of flammable substances or blends should also be provided. The Agency recognizes that many promising alternatives may be considered marginally flammable, but can be used safely and effectively.

10. *Exposure data.* The submitter must provide modeling or monitoring data on exposures associated with the manufacture, formulation, transport, and use of a substitute. Descriptive process information for each substitute application, as required above, will be used to develop exposure estimates where exposure data are not readily available. Depending on the application, exposure profiles will be needed for workers, consumers, and the general population.

11. *Environmental release data.* Data on emissions from the substitute application and equipment, as well as pollutant releases or discharge to all environmental media (ambient air, surface and groundwater, hazardous/solid waste) are needed to complete the risk characterization. Submitters should provide information on release locations, if known. Any information on any pollution controls that are used or could be used in association with the substitute (e.g., emissions reduction technologies, wastewater treatment, treatment of hazardous waste) and the costs of such technology is also requested.

12. *Replacement ratio for a chemical substitute.* The Agency also requires information on the replacement ratio for a chemical substitute versus the Class I or II substances being replaced. The term "replacement ratio" refers to how much more or less of the substitute chemical is needed to substitute for the original ozone-depleting compound being replaced. This ratio will affect the estimated incremental cost and environmental effects associated with use of the substitute.

13. *Required changes in technology.* Data on any changes in technology needed to use the alternative are required. Such information should include a description of whether the substitute can be used in existing equipment—with or without some retrofit—or only in new equipment. Data on the cost (capital and operating) and estimated life of the technology modifications should also be submitted. These economic data are essential to understanding the near-term potential of using an alternative.

14. *Cost of substitute.* The Agency requires data on the expected average cost of the alternative. The cost of the

substitute can be expressed, for example, in terms of \$/pound (for a chemical substitute) or as incremental capital and operating costs associated with a retrofit or new equipment. In addition, information is needed on the expected equipment life for an alternative technology. Other critical cost considerations should be identified, as appropriate. For example, it is important to understand the incremental costs associated with losses or gains in energy efficiency associated with use of a substitute relative to current experience with existing substances.

15. *Availability of substitute.* The Agency needs to understand the extent to which a substitute is already commercially available or the date on which it is expected to become available. The timing of availability is an important factor in assessing the overall health and environmental effects of the substitute.

16. *Anticipated market share.* Data on the anticipated near-term and long-term (over the next ten years) nationwide substitute sales is also required. This information can be presented in several ways, for example: a percentage of existing nationwide use of Class I or Class II chemicals in a particular application; number of units/products to be produced; or pounds of substitute sold. This information is required to assess the potential effects of a substitute related to total consumption and environmental releases.

17. *Applicable regulations under other environmental statutes.* The submitter is required to provide information on whether the substitute(s) are regulated under other statutory authorities, in particular the Clean Water Act, Safe Drinking Water Act, the Resource Conservation and Recovery Act, the Federal Insecticide, Fungicide, and Rodenticide Act, the Toxic Substances Control Act, the Comprehensive Environmental Response, Compensation and Liability Act, the Emergency Planning and Community Right-to-Know Act, as well as other titles of the CAA. The Agency will evaluate substitutes under the SNAP program subject to existing regulatory constraints.

18. *Information already submitted to the Agency.* Individuals may have already submitted information being required in the SNAP program notice to the Agency as part of past regulatory and information-gathering activities. In this case, to minimize reporting burden, the submitter should provide the following information to help EPA locate the data already maintained at EPA: type of information submitted; the

date of submission; the EPA office to which the data were sent; description of the regulatory program; and a document-control number, if assigned (e.g., a PMN number). If the submitter cannot provide references for data sent previously to the Agency, he or she should include all required information in the SNAP notice. To facilitate review, reports already submitted to the Agency as part of other regulatory submissions should be resubmitted if the original information was claimed as CBI.

19. *Information already available in the literature.* If any of the data needed to complete the SNAP program notice are available in the literature, the submitter should provide the Agency with references for such information. Failure to provide the Agency with an accurate and complete citation may delay review of the notice. Additionally, submitters are encouraged to provide copies of any literature to expedite review, particularly if the citation is from a source not readily available. Any references from sources in foreign languages should be translated into English prior to submission.

All submissions must be provided in three complete identical copies. If information is to be claimed as confidential, all confidential information must be excised from the third copy, which will be placed in the public docket. When portions of a submission are claimed as confidential, the first two copies will include the confidential material. If no claims of confidentiality are made for the submission, the third copy should be identical to the other two. (See below, as well as Appendix C, for further guidance on handling of confidential information under SNAP.)

C. Submission of Confidential Business Information

1. Clean Air Act Provisions

Anyone submitting information for which Confidential Business Information (CBI) status is requested must assert a claim of confidentiality at the time of submission. Failure to assert a claim of confidentiality at the time of submission may result in disclosure of the information by the Agency without further notice. Further, it should be noted that information which is publicly available (e.g., in journals, trade magazines, product literature, etc.) cannot be claimed as CBI. Therefore, requesting CBI status for such information could delay review under section 612. All claims of confidentiality will be treated in a manner consistent with 40 CFR part 2, subpart B.

2. Substantiation of Confidentiality Claims

At the time of submission, EPA requires a substantiation of any confidentiality claims. In making these claims, the following provisions apply:

- The specific information to which the claim applies must be clearly marked in the body of the study as subject to a claim of confidentiality;
- A Supplemental Statement of Data Confidentiality Claims must be submitted, identifying each section claimed confidential and describing in detail the basis for the claim. (A list of points to address in such a statement is included in Appendix C);
- The Supplemental Statement of Data Confidentiality Claims must be signed and dated and must include the typed name and title of the official who signed it.

The submitter should be advised that under the Clean Air Act section 114(c), emissions data may not be claimed as confidential. Moreover, there are further instances in which confidentiality assertions may later be reviewed even when confidentiality claims are received. These are provided in the provisions of 40 CFR part 2, subpart B. The submitter will be contacted as part of this evaluation process. However, if required substantiation is not provided along with the submission of information claimed as confidential, EPA may make the complete submitted information available to the public without further notice to the submitter.

3. Confidential Provisions for Toxicity Data

In the event that toxicity or health and safety studies are listed as confidential, the submitter should be advised that this information cannot be maintained as confidential where such data is also submitted under TSCA or FIFRA, because of specific disclosure provisions in those statutes. However, any information other than emissions data contained in the toxicity study that is not relevant to the effects of a substance on human health and the environment (e.g., discussion of process information, proprietary blends) can be maintained as confidential subject to the provisions of 40 CFR, part 2, subpart B. The Agency is therefore requesting that submitters not identify the following information as confidential when submitting information under TSCA or FIFRA: all information concerning the objectives, methodology, results, or significance of any toxicity test or experiment performed on or with a substitute or its degradation products; any information concerning the effects

of the substitute on any organism (e.g., fish, wildlife, humans and other mammals) or the environment (e.g., studies related to persistence, translocation, and fate); and pharmacokinetics/metabolism studies.

4. Federal Register Requirements

As discussed below in Section VII.A.3., the Agency intends to publish quarterly notices in the Federal Register updating the list of acceptable and unacceptable alternatives. The Agency is proposing that if the name of a specific chemical contained in any studies supporting such notices must be maintained as confidential, the submitter and the Agency will together develop a generic name that will protect the proprietary nature of the chemical, but will provide sufficient detail for the public to evaluate the health and safety studies. If appropriate, the submitter may reference any generic names identified for use in the PMN program.

VI. Effective Date of Coverage

A. General Provisions

In general, EPA's rules listing substitutes as unacceptable become effective thirty days after final rulemaking. However, EPA is authorized to permit the continuation of activities otherwise restricted where the balance of equities supports such grandfathering. Consequently, where appropriate, EPA may grandfather uses of particular substitutes by setting the effective date of unacceptability listings at some future date.

The United States District Court for the District of Columbia Circuit has established a four-part test to judge the appropriateness of Agency grandfathering (see *Sierra Club v. EPA*, 719 F.2d 436 (D.C. Cir. 1983)). This test involves balancing the results of four analyses, including whether the new rule represents an abrupt departure from previously established practice, the extent to which a party relied on the previous rule, the degree of burden which application of the new rule would impose on the party, and the statutory interest in applying the new rule immediately. In each rulemaking listing a substitute as unacceptable where grandfathering seems appropriate, EPA will conduct these four analyses and weigh their results. Where the balance of equities favors grandfathering, EPA will set a delayed effective date for such listings.

In keeping with the discussion above, then, for restrictions on use of unacceptable substitutes, the Agency will in selected cases set the effective date differently for each banned

substitute. The effect of this will be in these selected cases to tailor the implementation dates to individual applications. EPA will establish these effective dates in the rulemakings on each substitute to be banned.

Setting effective dates for specific chemicals and uses will allow the Agency to avoid penalizing those who in specific applications may have already invested in good faith in alternatives the SNAP program ultimately prohibits. For example, the Agency in this action is proposing to find unacceptable the use of HCFC-141b in certain solvent applications. New information on stratospheric ozone depletion has increased concern over possible adverse human health and environmental effects, and the Agency's unacceptable determination in the case of HCFC-141b reflects these increased concerns. However, the Agency recognizes that some solvent users may have switched to HCFC-141b in good faith, expecting that this substitute would sufficiently lower the risk of ozone depletion relative to earlier materials. To provide for these users, the Agency is today proposing a tailored effective date for certain uses of HCFC-141b. See the listing determination narrative discussion in Section IX, as well as the listing tables in Appendix B, for a full discussion of HCFC-141b and associated effective dates. Finally, to balance the desire not to penalize those who switched early in good faith with the need to avoid creating an incentive for continued investment in alternatives the Agency wishes to discourage, the longer-term effective dates discussed above will affect only existing equipment.

Until the Agency reaches a final decision restricting the use of a substitute, vendors are not barred from selling such substitutes. However, manufacturers, formulators, users or other individuals involved in sale or use of a substitute are still required to notify the Agency of any sale or use of a Class I or Class II substitute as required by the SNAP program.

This action includes a proposed list of acceptable substitutes and a proposed list of banned substitutes. The list of restricted substitutes becomes binding 30 days after the date of publication of the final rule. In contrast, the list of acceptable substitutes is not binding, but rather is furnished for the purpose of assisting users in understanding the full range of available, acceptable substitutes in each application. Before issuing the final rule, the Agency hopes to supplement the list of acceptable substitutes with substitutes not yet on the proposed list.

As noted above, the Agency does not believe determinations that substitutes are acceptable need be made through rulemaking. Consequently, EPA believes that it is within its discretion to supplement the list of acceptable substitutes upon making determinations consistent with the criteria to be established in this rulemaking. In the interest of informing users as soon as possible of acceptable substitutes, EPA expects to add to the list of substitutes those substitutes for which it can make such a determination during the pendency of the rulemaking, consistent with the criteria promulgated.

The Agency therefore encourages vendors and users of substitutes to use this opportunity to provide EPA with information necessary to issue a SNAP determination. Many potential users of substitutes have asserted that they want the benefit of EPA's SNAP determinations when transitioning out of Class I and Class II compounds. In addition, vendors of substitutes have also claimed they will derive significant benefits from having their substitutes added to the SNAP lists of approved substitutes, where possible.

VII. Notice, Review, and Decision-Making Procedures

The purpose of this section is to summarize the proposed procedures for submitting the required information to the Agency, and the steps EPA will take in reviewing SNAP program submissions, and making determinations based on them. This section focuses on three procedures, summarized in Exhibit 1, depending on the nature of the submission received by the Agency. Some substitutes may already have received approval or may not need approval under other environmental statutes, especially TSCA and FIFRA. These substitutes, in consequence, would only require review under the SNAP program. Section VII.A. discusses the submission and review process for alternatives that fall into this category in greater detail. In other cases, a substitute will require approval under section 612 as well as relevant provisions of TSCA and FIFRA. In these cases, any substitute that is a new chemical (i.e., not currently listed on the TSCA inventory) must be submitted to the Agency for review under the SNAP program, as well as the PMN program. Section VII.B. describes steps

for this review in more detail. For alternatives to Class I and Class II chemicals that will be used in pesticide products, the substitute manufacturer will need to file notification jointly with EPA's Office of Pesticide Programs (OPP) and EPA's SNAP program. Section VII.C. discusses the latter procedure. EPA has coordinated closely with each of these regulatory programs to establish a joint review process that will ensure consistency in the final decisions, while minimizing the time for review, the reporting burden, and the costs for the submitter and the Agency.

A. Substitutes Reviewed Under SNAP Only

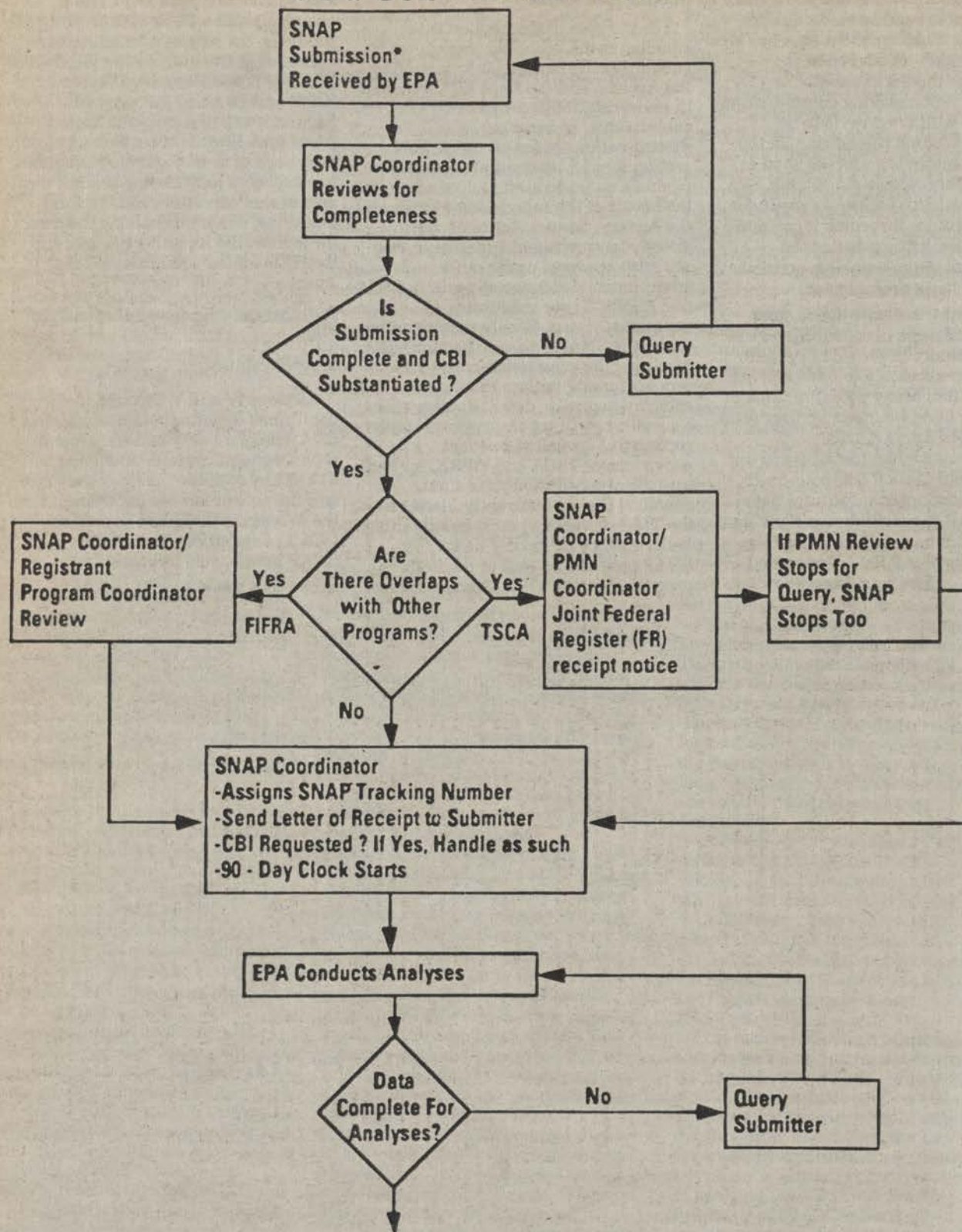
1. Applicability

Sections IV and V describe the conditions dictating review under the SNAP program only and the general reporting requirements under section 612. If any of these conditions are met and the substitutes are not exempt from the process as described in section IV.B.3., Exemptions from Reporting, a SNAP notice must be submitted.

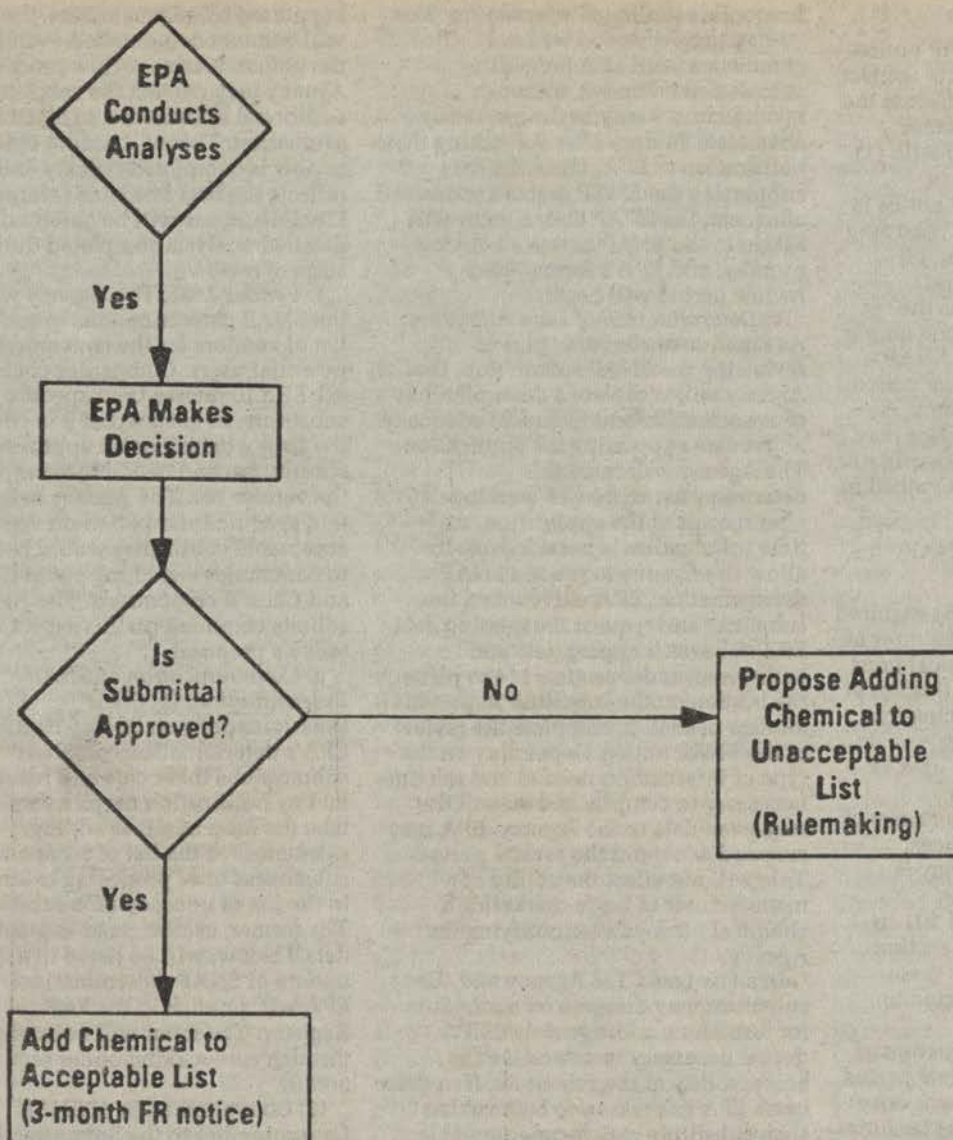
BILLING CODE 6560-50-P

SNAP Determination Process

EXHIBIT 1



*Petitions are handled through the same process, and are subject to the same information requirements. Please see Section VIII on petitions.



Note: All determinations will be made public in EPA's quarterly Federal Register notices updating the SNAP program lists. All determinations which have the effect of changing the unacceptable list (e.g., banning a chemical for a specific application or removing it from the acceptable list), will also be subject to the rulemaking process.

2. Pre-Notice Communication

Prior to submitting the SNAP notice, each submitter is encouraged to contact EPA's SNAP Coordinator to discuss the notification process. Among other things, the SNAP Coordinator will: (1) assist the potential submitter in determining whether a SNAP notice is needed; (2) answer questions regarding how to complete a submission; (3) provide all necessary forms and guidance manuals; (4) serve as the initial point of contact when the notice is submitted; and (5) assign a SNAP program tracking number to the notice once it is received by the Agency. A copy of the SNAP program notice may be obtained from the SNAP Coordinator. Specific data requested are described in Section V.

3. Processing of Completed SNAP Submission

a. 90-Day Review Process. As required under section 612(e), a manufacturer of a substitute for a Class I chemical must provide the Agency with notification at least 90 days prior to introducing into commerce any new or existing chemicals for significant new uses as Class I alternatives. The same requirements apply to manufacturers of substitutes for Class II substances, although in this case the Agency is drawing on general authorities contained in sections 114 and 301 in order to fulfill the purpose of section 612(c). EPA intends to review these chemicals within a 90-day period to ensure prompt response for manufacturers initiating production of substitutes. EPA's 90-day review period for SNAP submissions will begin once EPA receives a submission that includes data that are adequate, as described in Section V.B. above. If a submission does not include adequate data, EPA may return the submission to request specific additional information. Section 114 and in the case of petitions section 612(d) authorizes EPA to require manufacturers to support their SNAP submissions with data adequate to facilitate EPA's review.

b. Initial Receipt of the SNAP Submission. (1) Letter of Receipt. The SNAP Coordinator will send a letter of receipt to the submitter once the Agency receives the SNAP submission.

(2) Initial Review of Submission. Once received, the SNAP Coordinator will review the notice to ensure that basic information necessary to process the submission is present (i.e., name of company, identification of substitute, etc.). A more detailed review of supporting technical data will then ensue, as well as an examination of the substantiation provided for any claim

for confidentiality of information. The 90-day review period will not commence until EPA judges the submission complete, although manufacturers may begin marketing chemicals 90 days after submitting their notification to EPA. Once the data supporting the SNAP notice are deemed adequate, the SNAP Coordinator will assign to the SNAP notice a tracking number, and EPA's formal 90-day review period will begin.

c. Determination of Data Adequacy. As mentioned above, as part of reviewing the SNAP submission, the Agency will complete a determination of the scientific and technical adequacy of the data supporting the application. The Agency will issue this determination within 15 working days after receipt of the application. Any time information is not adequate to allow the Agency to reach a SNAP determination, EPA will contact the submitter and request the missing data. EPA believes it appropriate and authorized under section 114 to place the burden on the submitter to provide all data needed to complete the review of the SNAP notice. Depending on the type of information needed and the time necessary to compile and submit the requested data to the Agency, EPA may suspend or extend the review period. This will not affect the ability of a manufacturer to begin marketing a chemical 90 days after notifying the Agency.

In a few cases, the Agency and the submitter may disagree on a schedule for furnishing additional data EPA deems necessary to determine the acceptability of the substitute. If in these cases EPA has reason to believe that such substitute may be unacceptable, the Agency may exercise the option of proposing to list the substitute as unacceptable until the necessary data are provided, due to the uncertainty of the risks associated with use of the substitute.

d. Availability of New Information During Review Period. If critical new information becomes available during the review period that may influence the Agency's evaluation of a substitute, the submitter must notify the Agency about the existence of such information within ten days of learning of such data. The submitter must also inform the Agency of new studies under way, even if the results will not be available within the 90-day review period. The Agency may extend or suspend the review period depending on the type of information at issue and the stage of review.

e. Completion of Detailed Review. Once the submission is found to be

supported by adequate data, the Agency will commence a detailed evaluation of the notice. As this review proceeds, the Agency may contact the submitter for additional information to assist in the evaluation. This will ensure that the review is completed quickly and that it reflects the best available information. Final decisions will be based on the detailed analysis completed during this stage of review.

f. Vendor Lists. The Agency will use the SNAP determinations to compile a list of vendors for the convenience of potential users. Companies could then ask EPA to review their specific substitute, to ensure that it is covered by the listing decisions on approved substitutes, and to add the company to the vendor list. The Agency believes that specific information on vendors of acceptable substitutes would be useful to companies switching out of Class I and Class II compounds. The Agency solicits comment on this aspect of today's proposal.

g. Communication of SNAP Determination. (1) SNAP Determinations on 90-Day Notifications. EPA's determinations on SNAP submissions that come as a result of the 90-day notification requirement will take the form of either adding substances to the list of acceptable substitutes or of proposing to add them to the list of unacceptable substitutes. The former, as discussed in greater detail below, will be listed in a quarterly update of SNAP determinations which EPA will publish in the **Federal Register**. The latter will be made final through rule-making under section 307(d).

(2) Communication of SNAP Determination to the Submitter. Once review has been completed, the submitter will be notified in writing of the determination under SNAP. At this time, the submitter will also be informed if any conditions are attached to the approval of a substitute. Companies may continue uninterrupted sale or manufacture of their substitutes until the Agency places a substitute on the list of unacceptable substitutes as a result of rulemaking. Sale or manufacture may continue if the Agency fails to reach a decision or notify the submitter of that decision within 90 days of initial notification of EPA.

(3) Communication of SNAP Determination to the Public (a) **Federal Register Notice**

To provide the public with updated information on SNAP determinations, the Agency is proposing to publish in the **Federal Register** a complete list of

the acceptable and unacceptable alternatives that have been reviewed to date. This list will be published four times each year and will include recent decisions made under the SNAP program. In addition to the quarterly publications, the Agency will communicate decisions through a clearinghouse and various outreach programs, as discussed in the next section, as well as through the stratospheric ozone program hotline, which the Agency has already established.

(b) Outreach and Clearinghouse

Section 612(b) requires the Administrator to assist users in identifying alternatives to Class I and II compounds. The Agency has long operated an outreach program for users of ozone-depleting compounds, and this new mandate along with the accelerated phase-out of Class I and II substances adds impetus to these efforts.

Section 612(b)(4) requires the Agency to maintain a public clearinghouse of alternative chemicals, product substitutes, and alternative manufacturing processes that are available as replacements for Class I and Class II chemicals. The clearinghouse will distribute information on those substitutes that are approved under the SNAP program. For the convenience of companies wishing to identify substitutes with low relative environmental risks, the Agency will maintain a list of vendors selling substitutes that meet EPA's criteria for approval, as discussed in section VII.A.3.f.

In addition, the Agency is proposing to enter data on substitutes into the Pollution Prevention Information Exchange System (PPIES) database, which is maintained by EPA's Office of Research and Development. This database contains information on numerous pollution prevention options for a wide variety of industrial sectors and chemicals. PPIES can also be accessed from a variety of other pollution prevention databases maintained by other Federal agencies and industry. The Agency requests comment on this proposed approach to providing the public with information on available alternatives.

4. Decision-Making Framework

a. Decisions by Substitute and Use. As required by section 612(c), the Agency must publish a list of substitutes prohibited under the SNAP program and a list of acceptable alternatives for particular applications. Given that environmental exposure and risk profiles can change significantly from

one application to the next, it is essential to evaluate and list substitute decisions in the context of their intended use. The Agency has initially identified a number of use sectors by which to list substitutes, and Section IX provides preliminary risk management decisions for many substitutes in each of the principal use sectors. Other substitutes in each of these sectors exist as well, and these substitutes will be covered in subsequent analyses undertaken in the SNAP program.

In listing the substitutes, the Agency will be as specific as possible, by providing exact chemical names of substitutes. The Agency anticipates two possible exceptions to this practice. The first is where release of the chemical identity of a substitute constitutes release of proprietary information. In that event, the Agency will report generic chemical names based on chemical classes as described in Section V.C. The other exception would be in cases where the Agency believes that a more general categorization is needed to account for the diversity of possible chemicals used in a particular set of substitutes. For example, in the solvents cleaning sector, many substitutes are formulations composed of compounds drawn from several categories of chemicals. In this case, the toxicity profile of each chemical is similar to those of other chemicals in that class. Yet for most substitutes, a broad chemical classification (e.g., aromatic hydrocarbons, or HCFCs) is not specific enough because of differences among chemicals belonging to each of these groups. Thus, where appropriate, EPA will provide a more specific description of the substitute by application.

b. *Decision Categories.* Under section 612, the Agency has considerable discretion in the risk management decisions it can make in SNAP. The Agency has identified several possible decision categories, as described below. However, these types of risk management decisions should not be construed as comprising all possible options that the Agency will exercise under section 612. Depending on the particular characteristics of the submission, alternative approaches may be warranted.

(1) *General Acceptance.* Where the Agency has reviewed a substitute and found no reason to prohibit its use, it will list the alternative as acceptable for the applications listed. Where appropriate, the Agency may provide some additional comment (e.g., general recommendations encouraging recapture and recycling). However, these comments are not conditions for use of the substitute.

(2) *Approval Subject to Conditions.* After reviewing a notice, the Agency may determine that a substitute is acceptable only if certain conditions are met. The Agency cannot predict at this time all necessary restrictions, but already anticipates some conditions based on substitute reviews already completed.

For example, the Agency may impose conditions on the use of a substitute and require recycling equipment to limit workplace and ambient releases or require use of other control practices within a certain application. Alternatively, EPA may approve a compound not for general use, but for use only in certain narrow applications. Clearly, any limitations imposed will depend on the risks involved and the substitute and application in question. To provide adequate opportunity for comment by the regulated community, EPA will complete notice-and-comment rulemaking before promulgating any finding to approve a substitute subject to a condition on use.

In implementing its use of conditions, the Agency has sought to avoid overlap with other existing regulatory authorities. EPA has taken a number of steps to mitigate this potential for duplication. First, EPA intends to limit the use of conditions to cases in which clear regulatory gaps exist. Second, these existing regulatory gaps must render the use of a substitute an unreasonable risk in the absence of any additional controls. Third, in the limited cases in which conditions may be necessary, the Agency will impose them only after going through formal notice-and-comment rulemaking. Finally, the Agency intends to withdraw existing conditions when they are superseded by appropriate regulatory controls under other authorities.

The Agency, however, requests comment on the general issue of the need for use conditions. In particular, EPA requests comment on whether section 612 in fact confers upon the Agency the authority to go beyond the listing of acceptable and unacceptable alternatives and to set such use conditions. Further, EPA requests comment on the capability and practicality of EPA enforcing use conditions which may, for example, closely resemble workplace safety standards, which are typically within the enforcement purview of other regulatory authorities.

EPA also requests comment on whether, when an unreasonable risk might exist due to a gap in regulatory coverage, the appropriate means to address these risks is through the existing regulatory framework of other

federal authorities. For example, rather than using EPA's use conditions to address existing gaps in workplace safety standards, EPA could refer the matter to the appropriate OSHA authorities and request appropriate action to mitigate an otherwise unreasonable risk.²

Alternatively, where the length of time required to address a problem under another authority may be unacceptably long given the nature of the risk, there may be cases in which EPA would simply consider unacceptable the use of a given substitute, pending the development of a regulatory framework to control the risk it poses in its use as a substitute for an ozone-depleting compound.

For example, in this action, EPA has proposed conditions on the acceptability of certain halon substitutes when used as total flooding agents in normally occupied areas. EPA has imposed these conditions because of the risk of cardiotoxic levels of exposure to personnel in areas where substitute agents may be discharged in the event of fire. Existing OSHA standard 1910.160 applies certain general controls to the use of fixed extinguishing systems in occupied workplaces, whether gaseous, dry chemical, water sprinklers, etc., and EPA has not reproduced those. These include, for example, the requirements for discharge and pre-discharge alarms, and availability of Self Contained Breathing Apparatus (SCBA) for emergency entry into an area where agent has been discharged.³

² 29 U.S.C. 654, OSHA General Duty Clause, requires that each employer "shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees. * * *

³ 29 CFR 1910.160(b) includes general provisions to ensure the safety of all fixed extinguishing systems. Paragraph (c) stipulates requirements for systems with "potential health and safety hazards to employees" such as might be posed by gaseous agents.

(b)(3) "The employer shall provide a distinctive alarm or signaling system * * * capable of being perceived above ambient noise or light levels * * * to indicate when the extinguishing systems is discharging. Discharge alarms are not required on systems where discharge is immediately recognizable."

(b)(4) "The employer shall provide effective safeguards to warn employees against entry into discharge areas where the atmosphere remains hazardous to employee safety or health."

(b)(5) "The employer shall post hazard warning or caution signs at the entrance to, and inside of, areas protected by fixed extinguishing systems which use agents in concentrations known to be hazardous to employee safety and health."

(b)(6) "The employer shall assure that fixed systems are inspected annually * * * to assure that the system is maintained in good operating condition."

While section 1910.162 can apply generally to gaseous agents, it includes cardiotoxic levels specific to Halon 1301. Section 1910.162 paragraphs (b)(5) and (b)(6) provide alternative workplace requirements based on specific design concentrations of Halon 1301. (These design concentrations are not identified as the cardiotoxic NOAEL or LOAEL, so one cannot generalize a rule for use with alternative agents.) For this reason, EPA is concerned that halon substitute agents could be used in the absence of enforceable compound-specific cardiotoxic exposure levels. Should OSHA create compound-specific cardiotoxicity values to be applied to the use of halon substitutes as gaseous total flooding agents in occupied spaces, these conditions would no longer be necessary and EPA would rescind them.

However, EPA is also aware that existing OSHA regulations may provide adequate coverage against exposure to toxic levels of agents or their decomposition products. Section 1910.162 (b)(3) states, "(t)he employer shall assure that employees are not exposed to toxic levels of gaseous agent or its decomposition products," and paragraph (b)(4) states, "(t)he employer shall provide a distinctive pre-discharge employee alarm * * * when agent design concentrations exceed the maximum safe level for employee exposure." EPA invites comment on the adequacy of 1910.162 (b)(3) to provide workplace protection against toxic exposures to agents that differ from Halon 1301.

(3) Substitutes Pending Completion of Review. The Agency will describe submissions for which it has not yet reached a final decision as pending. For all substitutes in the pending category, the Agency will contact the submitter to determine a schedule for providing the missing information if the Agency needs to extend the 90-day review period. EPA will use the authority under section 114 to gather this information, if necessary.

(4) General Prohibition. The Agency has the authority under section 612(c) to prohibit the use of a substitute believed to present adverse effects to human health and the environment where alternatives that reduce overall risk are available. The Agency will only use this provision where it has identified other

(b)(10) "The employer shall train employees designated to inspect, maintain, operate, or repair fixed extinguishing systems. * * *

(b)(17) "The employer shall provide and assure the use of personal protective equipment needed for immediate rescue of employees trapped in hazardous atmospheres created by an agent discharge."

(c)(3) "On all total flooding systems the employer shall provide a pre-discharge employee alarm * * * which will give employees time to safely exit from the discharge area prior to system discharge."

substitutes that are currently or potentially available and that have lower overall risks. Substitutes will be listed as unacceptable through the rulemaking process.

(5) Prohibition with Limited Exemptions for Critical Uses. In some applications, even though the Agency restricts the use of a substitute based on the potential for adverse effects, it may be necessary to grant a limited number of exemptions because of the lack of alternatives for specialized uses within the general application area. The Agency will refer to such exemptions as "critical use exemptions." For example, the Agency could list a substitute as generally unacceptable for solvent applications, but allow for limited exemptions for critical uses within the sector of solvent cleaning. These critical use exemptions will be granted only for the period necessary to develop and implement alternatives not yet available.

At this time, the Agency cannot know and list all critical use applications that will be exempted. Section VIII.F. discusses the petition process for critical use exemptions in more detail. Critical use exemptions will be granted through notice-and-comment rulemaking.

c. Time Certainty of Decisions. In response to the ANPRM, several comments suggested that the Agency establish assured minimum periods of use for substitutes listed as acceptable. For example, one commenter recommended that the Agency consider any substitute decision, once made, valid for a minimum of fifteen years before making any changes. Clearly, there are advantages to having a guaranteed period within which a substitute can be used without concern for future changes in the acceptability of a substitute. In particular, such certainty would encourage reduced reliance on Class I chemicals in the near term.

Despite this benefit, the Agency believes that providing time certainty to its decisions on balance could discourage continued research on substitutes. In addition, the Agency believes that in certain limited cases, new data on previously approved or disapproved substitutes may warrant changes to an existing SNAP determination. Such changes, however, will only be considered in cases where new information indicates a need to reassess the risk of a previously evaluated substitute. For example, new toxicity data may become available that point to a dramatically different hazard profile for a chemical, and which changes the risk the substitute poses to human health and the environment

relative to other substitutes. Similarly, if the Agency previously listed a high-risk substitute as acceptable only because no other alternative exists for a specific end-use, this determination may be subject to change if a new substitute with demonstrably lower overall risks becomes available.

In such instances, which the Agency expects will occur infrequently, EPA will provide consideration for companies who earlier made a switch to a substitute believed to be acceptable. In particular, the Agency proposes to examine capital expenditures made by affected industries to manufacture and use a substitute when it evaluates whether the availability of another alternative should render the first alternative unacceptable.

d. *Implications of Other Regulatory Requirements.* The Agency is proposing that the SNAP program in evaluating substitutes take into consideration the regulatory requirements of other environmental and health protection statutes (e.g., the Clean Water Act or the Occupational Safety and Health Act). By considering existing regulatory constraints, the Agency's evaluation of alternatives will explicitly recognize compliance with provisions designed to reduce workplace and environmental releases. However, it will not be possible to factor in regulatory requirements that are still under development (e.g., more stringent requirements to control volatile organic compounds and hazardous air pollutants under Title I and Title III of the CAA). Clearly, in these instances, a substitute, although approved, must comply with all future regulations. Should future regulations severely limit the availability of the only substitute for a prohibited substance, EPA would reconsider the advisability of keeping that substance on the list of unacceptable substitutes.

Several commenters felt that the goal of section 612 was to encourage use of substitutes for Class I and Class II chemicals by relaxing regulatory requirements in other areas. The Agency does not believe that it was the intent of Congress to use the authority under section 612 to compromise existing regulatory requirements. Instead, EPA intends to evaluate substitutes in the framework of protection provided by current regulatory standards.

5. EPA-Generated Review of Substitutes

In addition to notices received under section 612 for substitute review, the Agency is authorized by section 612(c) to add or delete alternatives to the list of reviewed substitutes on its own initiative. EPA has many efforts under

way to identify and communicate the availability of promising new alternatives. These include support for research efforts to study and focus attention on future substitutes, involvement in the United Nations Environment Programme biannual assessment of technologies for key sectors currently using ozone-depleting chemicals, and technology transfer projects with industry, other Federal agencies, and developing nations. Based on information available through these activities, EPA may initiate review of new substitutes under section 612. In each case, the next planned quarterly Federal Register notice updating the status of SNAP determinations will inform the public that EPA is initiating a review, subject to the provisions discussed in this proposal. Similarly, determinations ultimately reached as a result of these internally-generated reviews will be publicly noticed every three months.

B. Joint Review of New Substitutes under SNAP and TSCA PMN

1. Applicability

Any potential SNAP submitter who intends to introduce a new chemical (i.e., a chemical not currently included in the TSCA inventory) as an alternative for a Class I or Class II chemical must undergo review not only under section 612, but under section 5 of TSCA (the Premanufacture Notice program) as well. Because of the overlap in statutory authority, the Agency has established a joint review process between the SNAP and TSCA Premanufacture Notice (PMN) programs. This process has been structured to minimize reporting burden and to ensure consistency in decisions between the two programs. The following sections describe the joint review and decision-making process in more detail.

2. Data Submission Requirements and Process

a. *SNAP and PMN Forms.* The Agency has reviewed the data submission needs for the SNAP and PMN programs and found significant overlap. In general, the Agency has identified only a few additional data elements beyond those already required by the PMN program that should be included for review under the SNAP program. These elements are:

- Ozone depletion potential.
- Global warming potential.
- Explicit quantification of the cost of using the substitute, including:
 - Chemical replacement data
 - Chemical cost data

—Incremental equipment expenditures (either new or retrofit) needed to use substitute

—Information on the cost implications of changes in energy consumption (e.g., from the use of a less or more energy-efficient refrigerant)

• Documentation of testing results, where available, regarding the flammability of substitutes that will be used in consumer applications.

Given this overlap, the Agency is proposing that a submitter requesting a review under both the SNAP and PMN programs provide the above information by following these steps:

• Complete the PMN form (EPA Form 7710-25) following the Instructions Manual currently available through the TSCA Assistance Information Service.

• Indicate on page 11 of the PMN form, "Optional Pollution Prevention Information," that the chemical to be reviewed is also to be considered under the SNAP program.

• Complete a SNAP addendum that requests information only on those items listed above. (The addendum can be obtained from the SNAP Coordinator.)

The completed PMN form (EPA Form 7710-25) will remain the basis for all information needed to complete review of the new chemical under section 5 of TSCA. The completed PMN form and the SNAP addendum together will comprise the data submission for section 612 review and listing decisions for new chemicals. This approach is intended to minimize the reporting burden on submitters.

The Agency will modify the PMN Instructions Manual in the future to provide more explicit direction on how to complete the SNAP addendum. A SNAP submitter may also consult the SNAP Guidance Document, which will be available for potential submitters at the time the SNAP program is promulgated. Any questions regarding the completion of these forms can be directed to either the PMN pre-notice coordinator or the SNAP Coordinator.

b. *Submission of Completed Forms.* Both the PMN and SNAP programs have a review period of 90 days, subject to suspensions and extensions described in Section VII.A. for the SNAP program and in the Preamble to the PMN final rule (40 CFR 720.75). To ensure that new chemical submissions are reviewed and decided on jointly, the Agency encourages submitters to provide both the PMN form and SNAP addendum to the PMN and SNAP coordinators. Failure to provide both programs with the requested information at the same time could result in delays in the review

of a submitter's notice seeking approval of a new chemical as a CFC substitute approved by EPA where it would result in delay of EPA's approval under the PMN program.

c. Procedures for Handling Confidential Business Information. The Agency recognizes that, where appropriate, information submitted to the PMN and SNAP programs may need to be confidential. EPA is proposing that all CBI submitted as part of the joint PMN/SNAP review be maintained and treated in a manner consistent with TSCA requirements. Confidentiality claims will be processed and may be reviewed in a manner consistent with 40 CFR part 2, subpart B. This approach is being proposed because the majority of data provided to SNAP under the joint review process will come from the PMN form. Submitters should note that while TSCA and CAA may have different language describing CBI handling procedures, there is no substantive difference in how CBI is maintained under the two statutes.

3. Joint Review of New Substitutes Under PMN and SNAP

a. Preparation of Public Docket and Federal Register Notices. Once the letter of receipt has been issued, the PMN program will prepare a public docket and Federal Register notice, as described in the Preamble to the final rule for the PMN program (40 CFR 720.75). The PMN program manager will consult with the SNAP Coordinator in preparing the notice. The Agency is proposing this approach for joint PMN/SNAP reviews because it believes it will reduce the reporting burden imposed on manufacturers.

b. Joint Review Process. EPA is proposing to complete joint evaluations of new chemicals serving as Class I or Class II substitutes under section 5 of TSCA and section 612 of the CAA. This joint review process will be coordinated to ensure that there is consistency in the final decisions made under the PMN and SNAP programs. To ensure agreement in the decisions, Agency offices will work in concert to develop toxicity, exposure, and risk profiles for those substitutes and applications that come under joint TSCA and CAA review authority. The Agency will also coordinate its review of the completeness of the information supplied and subsequent data requests to minimize the reporting burden on the submitter.

Submitters should note that Agency decisions to restrict production of particular chemicals under TSCA will, in the case of joint PMN/SNAP applications, also have the effect of

restricting production of substitutes undergoing review under the SNAP program. However, companies that produce substitutes only being reviewed under the SNAP program are not required to cease production during the SNAP review period.

As part of the review, the PMN and SNAP programs will work to arrive at a consistent decision regarding the new chemical under review. Consequently, listing decisions under SNAP will reference any conditions also incorporated into the PMN review (e.g., submission of additional toxicity information, restrictions on use, etc.).

If a substitute meets the conditions for general PMN approval but not for SNAP approval, the company may produce and market the substance in question. However, EPA will commence a rulemaking to prohibit as unacceptable the description or use of the substitute as an EPA-approved Class I or II substitute. If the chemical fails to meet the conditions for PMN approval, the submitter is barred from producing the chemical and consequently also from marketing the product as a CFC substitute. Submitters should note, however, that the CAA section 612 places considerable emphasis on identifying and promoting the use of substitutes which, relative to others, reduce overall risks to human health and the environment. To the extent a substitute offers such risk reduction, EPA under the CAA will make every effort to facilitate production and use of that alternative.

c. Communication of Decision. The PMN program will use the existing TSCA regulatory framework for communicating decisions to submitters of the decision on the new substitute. The SNAP program will provide public notice of decisions regarding the acceptability or unacceptability of a substitute following the process described in Section VII.A.3.h. EPA will contact the submitter to determine how best to list the substitute under the SNAP program if necessary to protect the confidentiality of the alternative.

C. Joint Review of Substitutes Under SNAP and FIFRA

1. Background on Use of Ozone-Depleting Chemicals in Pesticides

Certain pesticides are formulated with Class I and Class II chemicals. The most prominent example is the use of methyl chloroform (1,1,1-trichloroethane) as an inert ingredient. Pesticide products that contain Class I and Class II compounds must be reformulated as these chemicals are phased out of production under the Clean Air Act. This section describes

how the Agency proposes to handle reviews of these changes.

2. Applicability

Any new pesticide or amendment of an existing formulation is already subject to Agency approval under current provisions of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), P.L. 100-460, 100-464 to 100-526, and 100-532. However, as of the effective date of the SNAP program, new pesticides or formulation changes based on Class I or Class II substitutes will also be subject to review under section 612 of the CAA. These authorities apply in all cases where a manufacturer amends a pesticide product to replace chemicals being phased out under section 602. Similarly, registrations of new pesticide products will also be subject to SNAP review if the new formula contains chemicals functionally replacing Class I or II compounds.

3. Review Responsibilities Under FIFRA and CAA/SNAP

In general, review responsibilities for pesticide products under the CAA SNAP program will focus on a substance's ozone depletion and global warming potential. The FIFRA reviews will address factors commonly examined during pesticide amendments and registrations. The two program offices responsible for these reviews will coordinate their efforts at critical junctures and share pertinent data to ensure appropriate technical consideration of the substitute.

4. Data Submission Requirements and Process

a. Preparation of Applications. The Agency has reviewed the data submission needs for the SNAP and FIFRA pesticide amendment/registration process and found no significant overlap. Because there is so little overlap, the Agency is proposing that a submitter requesting review under both SNAP and the Office of Pesticide Programs' pesticide amendment/registration process submit all information ordinarily required for the OPP process as well as a fully completed SNAP submission form. A copy of the FIFRA form should be submitted to the OPP, and a copy of the SNAP form should be submitted to the SNAP Coordinator. The SNAP form can be obtained from the SNAP Coordinator. For further guidance, SNAP submitters may also consult the SNAP Guidance Document, which will be available for review at the time the SNAP program is promulgated.

If a registrant is submitting an amendment to a product registration under FIFRA that currently contains a Class I or II substance, he or she should note in Section II ("Amendment Information") of the FIFRA form that the amendment was prompted by the CAA production phase-out. Similarly, if a registrant is submitting an application for a new pesticide registration that would otherwise have been based on a Class I or II compound, he or she should note in Section II of the FIFRA form that the registration includes a Class I or II substitute.

The submitter should also identify in Section II both the substitute chemical and the Class I or II compound it is replacing. Further, if a registrant is aware that a particular chemical intended for use as a Class I or Class II substitute in a pesticide formulation has already been approved through earlier SNAP/FIFRA determinations, the registrant should also reference the relevant part of the prior review. This additional information will allow EPA to identify quickly those registrants whose proposed substitutes have already been the subject of listing determinations under SNAP, and thereby streamline the SNAP review.

b. *Review of Applications.* When the Agency receives the FIFRA application and SNAP submission, it will log each into the relevant tracking systems: the Office of Pesticide Program's (OPP) tracking system for the FIFRA application and the SNAP tracking system for the SNAP submissions. If the FIFRA application is identified in Section II as a Clean Air Act substitution, the FIFRA program coordinator will contact EPA's SNAP coordinator to establish whether the substitute has been the subject of any prior SNAP reviews. If the registrant's substitute is on the list of unacceptable substitutes, EPA will notify the registrant that the amendment request cannot be granted. If the registrant's substitute is on the list of acceptable substitutes, EPA will proceed with the standard FIFRA application review. If a chemical substitute is not listed under existing SNAP determinations but is a substitute for an ozone depleting compound, EPA will inform the registrant of the need for a SNAP review.

5. *Communication of Decision.* Once the EPA review is complete, the Agency will notify the registrant whether the new formulation or proposed formulation change is acceptable. At the same time, the Agency will amend the SNAP determinations to reflect these findings and will publish the revised determinations in the next quarterly

Federal Register notice. Submitters should note that, because of the shared authority to review substitutes under both SNAP and FIFRA, formulators may not sell amended or new formulations until they have received FIFRA approval.

D. Shared Statutory Authority With the Food and Drug Administration

The Federal Food, Drug and Cosmetic Act (FDCA), 21 U.S.C. 321, provides for the safety and effectiveness of drugs and therapeutic devices, the purity and wholesomeness of foods, and the harmlessness of cosmetics. Under this statute, the Food and Drug Administration (FDA) regulates the packaging of food products and incidental additives and requires predistribution clearance of medical devices.

As defined in the FDCA, medical devices can include any devices, diagnostic products, drugs, and drug delivery systems. Devices covered under this jurisdiction are subject to review under the FDCA. Some medical devices and food packaging currently contain Class I or II compounds. The Agency is proposing that such products be exempt from further review for human health effects under the SNAP program where FDA approval of such effects is required before a product can be introduced into commerce. EPA will rely in its SNAP determination on FDA's conclusions regarding health effects. The Agency believes this exemption is justified because of the higher burden of proof placed on submitters under the FDCA. However, the Agency will continue to evaluate all other environmental effects of the proposed substitute, and will consult with the FDA to determine the appropriate course of action.

VIII. Petitions

A. Background

1. Role of Petitions

Section 612(d) in the CAA explicitly states that "any person may petition the Administrator to add a substance . . . or to remove a substance from either of such [prohibited or safe use] lists." The petition provision serves two principal needs. The first is to permit the appeal of existing Agency determinations under the SNAP program. The second is to provide a mechanism for individuals and organizations to bring to the Agency's attention new information on substitutes that could affect existing listing determinations or result in new ones.

The opportunity for outside parties to comment on existing listing decisions is an important aspect of the petition

process. As discussed in the section on notifications, companies that produce substitutes must submit specific data on the substitutes to the Agency for review. However, organizations and private citizens other than those required to submit SNAP notices may have additional information about existing substitutes or information on new substitutes not yet reviewed by the Agency. To ensure that the SNAP determinations are based on the best information on substitutes, it is essential that the Agency offer a means for such information to be incorporated into the SNAP analyses on a continuing basis.

Before individuals, organizations, or companies may initiate court action against EPA for the purpose of changing the lists of acceptable or unacceptable substitutes, they must first exhaust all administrative remedies for receiving such relief, including remedies like the petition process described in this section.

2. Types of Petitions

Four types of petitions exist:

- (1) Petitions to add a substitute not previously reviewed under the SNAP program to the approved list;
- (2) Petitions to add a substitute not previously reviewed under the SNAP program to the prohibited list;
- (3) Petitions to delete a substitute from the approved list and add it to the prohibited list; and
- (4) Petitions to delete a substitute from the prohibited list and add it to the approved list.

Petitioners should note that the first type of petition is comparable to the 90-day notifications, except that the latter are submitted by substitute producers prior to the introduction into interstate commerce of the substitute for a significant new use as a Class I or Class II substitute. The first type of petition, by contrast, would be initiated by entities other than the company responsible for the substitute.

Companies that manufacture, formulate, or use a substitute themselves and want to have their substitutes added to the approved list should submit information on the substitute under the 90-day review program.

3. Basis for Petition

A petitioner may submit a petition for several reasons, including:

- Availability of information on substitutes or applications not covered in the existing SNAP determinations;
- New toxicity data on a substitute;
- New technologies or practices that reduce exposures to a substitute previously prohibited under SNAP due to toxicity concerns; or

• Requests for approval for specialized uses for a prohibited substitute where no other technologically viable substitute can be found in a particular niche use. All of the above are examples of valid justifications for submitting a petition. Other bases for petitioning the Agency may exist as well, and all petitions with adequate supporting data will receive equal consideration under the SNAP program.

4. Nature of Response

The Agency will only review and grant or deny petitions based on the industrial use category identified in the petition. For example, simply because the Agency ultimately deletes a substitute from the list of approved substitutes for solvents cleaning does not mean the substitute is from then on prohibited for use as a refrigerant. A similar caveat applies for petitions on uses within industrial sectors. If a substitute, for instance, is approved for a specific application within a use sector, it will not automatically be approved for all other applications in that sector.

B. Content of the Petition

A petition must contain the information described in Section V.B. of this notice, which lists the items to be submitted in a 90-day notification. Information requirements for petitions and 90-day notifications are the same, since the Agency will be applying equal rigor to analyses of petitions submitted by outside parties as to notifications received from the producing companies themselves. As with SNAP submissions, the Agency will issue a determination on the completeness of the petition within 15 days of receiving the petition.

For petitions, the Agency also requires the following information:

- *Action requested:* A brief statement describing the type of petition; and
- *Rationale:* A brief summary of the basis for the petition and the data that support the petition.

Specifically for petitions that request approval for substitutes on "critical use" grounds, the Agency proposes to require additional information documenting a company's efforts to find and implement substitutes. This information is discussed below.

For petitions that request a re-examination of a substitute previously reviewed under the SNAP program, the submitter may reference the prior submittal rather than submitting separate information. In this case, the petitioner should specifically summarize in the rationale for the petition any new or additional data.

C. Sufficiency of Data

Petitioners should be aware that insufficient data may prevent the Agency from reaching a speedy decision on whether to grant or deny a petition. EPA will not consider a petition "received" for the purposes of triggering the 90-day review prescribed by section 612(d) until the submission includes as much of the information needed to rule on the petition as the petitioner can reasonably be expected to obtain. As provided in section 612(d), any petition must "include a showing by the petitioner that there are data on the substance adequate to support the petition." Petitioners may provide citations to scientific literature, where appropriate. However, submitters are advised that furnishing copies of supporting articles, reports, or letters will expedite the review process.

Any time the Agency receives a petition with insufficient data, EPA will not commence review until the petitioner submits the missing information to the best of the petitioner's ability. To the extent the petitioner does not have the required information, EPA may also seek data from sources other than the petitioner, including manufacturers or users of products that contain the substitute. As with the 90-day SNAP notices, EPA may also decide, based on preliminary information, to propose to list the substitute in question as unacceptable pending the receipt of additional data. In such cases, section 612(d) explicitly provides that "the Administrator shall use any authority available to the Administrator, under any law administered by the Administrator, to acquire such information." These authorities include section 114 of the CAA as well as information collection provisions of other environmental statutes. Where EPA cannot obtain sufficient data, the Agency may deny the petition for lack of adequate technical support.

D. Criteria for Evaluating Petitions

In evaluating petitions, the Agency will follow the same criteria as for review of pre-commercialization notices. This will ensure that both petitions and notifications are judged by the same standards.

E. Petition Review Process

1. *Petition Submittals.* Today's proposal describes a generic petition process. Petitions should be sent to the docket number listed in the beginning of this action as well as to the SNAP staff.

2. Petition Reviews

When the Agency receives a petition, it will log the petition into the SNAP petition tracking system. If the petition concerns a substitute previously either approved or restricted under the SNAP program, the Agency will as a courtesy contact the manufacturer of that substitute. Decisions to remove any substitutes from either list will be made as a result of notice-and-comment rulemaking. The Agency requests comment on whether notice-and-comment rulemaking procedures are required when removing a substitute from the acceptable list.

As explained above, the Agency will grant or deny the petition within 90 days of receiving a complete application. If the Agency grants a petition to either add a substance to the list of unacceptable substitutes or remove a substance from this list, this decision will be formally promulgated as a rulemaking. Otherwise, responses to petitions including explanations of petition denials will be noticed in the next 3-month *Federal Register* notice updating the SNAP determinations. Regardless of the nature of the final determination, the Agency will inform petitioners within 90 days whether their request has been granted or denied.

If a petition is denied, the Agency will publish in the *Federal Register* an explanation of the determination. If a petition is granted, the Agency will publish the revised list incorporating the petition decision within 6 months of reaching a determination. Where EPA must complete rulemaking to alter the lists, the statute requires EPA to propose, take comment on, complete final action, and publish the revised lists within six months of the grant of the petition.

F. Critical Use Exemption Petitions

In some cases, it may be necessary to allow limited exemptions for specialized uses of a substitute that has been designated as an unacceptable for a broad application within a sector. For example, even though the Agency may restrict the general use of a compound, it could still grant exemptions for use of that compound in specific applications where it can be demonstrated that no other substitute exists. The Agency will refer to such petitions as critical use exemptions. EPA believes that it will receive few such requests for exemptions, since the Agency is not proposing broad restrictions unless other alternatives exist for the application in question.

These petitions are in a special category, since they are based on a claim

that a particular substitute should be exempted from broad regulatory restrictions because no other substitute exists that meets performance or safety standards. The Agency can either grant the critical use exemption based on information independently collected, or it can base the exemption on a petition from a vendor or end user. Any exemptions will be granted for specific uses, and companies will not have to apply for exemptions on a company-by-company basis.

Section 612 provides the Agency with the authority to grant such exemptions. In section 612(c), the Clean Air Act states that "it shall be unlawful to replace any Class I or Class II substance with any substitute substance which the Administrator determines may present adverse effects to human health or the environment, where the Administrator has identified an alternative to such replacement that—(1) reduces the overall risk to human health and the environment; and (2) is currently or potentially available." As a result, the Agency is not authorized to restrict use of a substitute if that substitute is the only currently or potentially available alternative to the Class I or Class II substance.

However, in publicizing critical use exemptions for niche applications, the Agency will encourage other companies or vendors to challenge each critical use exemption. It is EPA's hope that this may bring to light new alternatives or processes of which the petitioner and EPA are unaware, and that these new alternatives may pose lower overall risks than the substances which have been the subject of the critical use exemption. If an exemption is revoked based on the availability of a new, lower-risk alternative, companies that have made investments in technology which was earlier deemed a "critical use" may be granted permission to extend their use for a limited period of time.

If this approach to critical use exemption petitions is adopted in the final rule, the Agency will issue guidance describing additional documentation petitioners should include. This information could include descriptions of:

- Substitutes examined and rejected;
- Process or product in which the critical use substitute is needed;
- Reason for rejection of other alternatives, e.g., performance, technical or safety standards; and/or
- Anticipated date other substitutes will be available and projected time for switching.

In addition to this basic information, the guidance will also include specific

data for critical use petitions in each sector.

For example, to evaluate critical use applications for solvent cleaning substitutes, the Agency will also need information on the soils to be removed, the substrate, and the type of part being cleaned. This information is requested not only to aid the evaluation of the petition, but also so that the Agency can help the petitioner identify other potential alternatives. As noted previously, critical use exemption petitions will be processed through notice-and-comment rulemaking.

IX. Preliminary Listing of Substitutes

A. Overview

This section presents EPA's proposed listing decisions for Class I chemical substitutes in the following applications: refrigeration, foam blowing, solvent cleaning, fire extinguishing, sterilants, aerosols, tobacco expansion and adhesives, coatings and inks. Parts D through J below present a detailed discussion of the proposed substitute listing determinations for each of the major use sectors. Tables that summarize the key proposed listing decisions in this section are included in Appendix B. As discussed earlier in this action, the Agency is proposing to exclude substitutes in other applications from the listing decisions.

To develop the lists of unacceptable and acceptable substitutes, EPA conducted screens of health and environmental risks posed by various substitutes for Class I compounds in each use sector. These screens are presented in individual background documents entitled "Risk Screen on the Use of Substitutes for Class I Ozone-Depleting Substances" for each use sector. Based on these analyses, EPA classified as "unacceptable" only uses of substitutes that pose significantly higher human health and environmental risks than those risks that would accrue through either continued use of the Class I substances themselves or through use of other available substitutes.

The assessments presented in the background documents are screens of the comparative risks posed by use of substitutes, not assessments or rankings of the absolute risks associated with use of each substitute. Designating a substitute as "acceptable" does not imply the absence of risks for that substitute, but rather that the substitute in question is believed to present lower overall risks than the Class I compound it is replacing. For instance, in some cases, ozone-depleting substances can

be replaced by chemicals with known toxicity or ability to contribute to ground-level ozone formation. The Agency's risk screen analyzes these effects, and the SNAP determinations describe as "acceptable" those substitutes for which any risks from replacements would be small compared to aggregate risks from other existing, similar sources or for which such risks could be managed by developing and implementing appropriate regulatory controls.

The risk characterization does not at present include assessment of the environmental transformation products of the substitutes. Research efforts of the Agency in cooperation with the Alternative Fluorocarbons Environmental Acceptability Study (AFEAS) are in progress and are intended to define the chemical, biological and photochemical sinks for these substances in the biosphere. Ultimately, these research activities will contribute to the development of ecological risk assessment for substitutes.

Additionally, in cases where the Agency has proposed listing a substitute as unacceptable, it has assessed—as required in section 612—the availability of other substitutes and concluded that alternatives were currently or potentially available. This assessment includes a review of the affordability of other available substitutes.

As a rule, the Agency did not evaluate the technical performance of a substitute, since the purpose of the SNAP program is to examine environmental effects of substitutes identified as being of commercial interest regardless of technical acceptability. However, in certain sectors, performance of the substitute does pertain directly to environmental or health effects. For example, in refrigeration, the ability of a refrigerant replacement to serve as a coolant will directly influence the substitute's energy efficiency, which in turn will affect the substitute's environmental effects. Similarly, in fire extinguishing, the ability of a substitute to put out fires and thereby save human lives will directly affect a substitute's health effects. Further, in the case of critical use exemption petitions, the Agency's decision to grant or deny such a petition may hinge on questions of technical performance. For example, in the case of certain specialized solvents, some substitutes otherwise considered unacceptable may require critical use exemptions because they are the only available substitute offering performance characteristics deemed essential in a certain application. In

cases such as these, the SNAP analyses do consider the performance of a substitute.

EPA's evaluation of each substitute in each end use is based on the following types of information and analyses:

- **Atmospheric effects** are assessed by predicting ozone depletion and global warming. Ozone depletion is based on market penetration of a substitute and is measured in terms of cumulative Cl_x loadings and its effect in terms of increased incidence of skin cancer cases and skin cancer mortalities. Changes in global temperatures may result from releases of the substitutes themselves or from changes in fossil fuel use due to increases or decreases in energy efficiency resulting from production or use of the substitutes. The model used by the Agency to determine these effects—the Atmospheric Stabilization Framework model—has been used by the Agency in calculating the benefits from the phase-out of Class I substances. This model was peer-reviewed in connection with this earlier analysis. Although scientific studies have pointed to the possibility of ecological effects due to ozone depletion, such as crop damage, the scope of existing studies is limited and therefore these effects were not considered as part of this analysis. As the sophistication of analyses on this topic advances, the Agency will include estimates of ecological effects in its modeling of atmospheric impacts.

- **Exposure assessments** are used to estimate concentration levels of substitutes to which workers, consumers, the general population, and environmental receptors may be exposed, and over what period of time. These assessments are based on personal monitoring data or area sampling data if available. Otherwise, exposures are assessed using measured or estimated releases as inputs to mathematical models. Exposure assessments may be conducted for many types of releases, including releases in the workplace and in homes, releases to ambient air and surface water, and releases from the management of solid wastes.

- **Toxicity data** are used to assess the possible health and environmental effects from exposure to the substitutes. If Occupational Safety and Health Administration (OSHA)-approved or EPA-wide health-based criteria such as Permissible Exposure Limits (PELs; for occupational exposure), inhalation reference concentrations (RfCs; for noncarcinogenic effects), or cancer slope factors (for carcinogenic risk) are available for a substitute, exposure information is combined with this toxicity information to determine

whether there is reason for concern. Otherwise, toxicity data are used in conjunction with existing EPA guidelines to develop health-based criteria for interim use in these risk characterizations.

- **Flammability** is examined as a possible safety concern for workers and consumers. EPA assesses flammability risk using data on flash point and flammability limits (e.g., OSHA flammability/combustibility classifications), test data on flammability in consumer applications conducted by independent laboratories (e.g., Underwriters Laboratories), and information on flammability risk minimization techniques.

- Some of the proposed substitutes are *volatile organic compounds* (VOCs), chemicals that increase tropospheric air pollution by contributing to ground-level ozone formation. Local and nationwide increases in VOC loadings from the use of substitutes is also evaluated.

In conducting these assessments, EPA made full use of previous analyses performed by the Agency, including the 1990 interim hazard assessments and supporting documentation. These analyses were modified in some cases to incorporate more recent data or to accommodate different analytical approaches as needed. Where possible, EPA incorporated data submitted in response to the ANPRM; EPA will continue to review data provided in these submissions between proposal and promulgation of the SNAP rulemaking. Finally, these analyses assume that the regulated community complies with applicable requirements of other statutes and regulations administered by EPA (e.g., recycling requirements promulgated under the CAA) and other Federal agencies (e.g., any enforceable occupational exposure limits set by OSHA).

Where further data become available at a later date that would help characterize the risks of substitutes, the Agency will incorporate this data into its risk screens. For example, as mentioned above, the risk screen does not at present include assessment of the environmental transformation products of substitutes. Research efforts of the Agency in cooperation with the Alternative Fluorocarbons Environmental Acceptability Study (AFEAS) are in progress and are intended to define the chemical, biological and photochemical sinks for these substances in the biosphere. Ultimately, these research activities will contribute to the development of more complete ecological risk assessments for substitutes. However, the Agency

generally does not believe that a more detailed characterization of risks would lead to a different listing decision for individual substitutes, since the critical comparison for policy purposes remains the adverse effects posed by continued use of a Class I compound.

The Agency requests comment on its application of the proposed decision criteria in the listing determinations proposed today, which include acceptable and unacceptable substitutes by sector. EPA further solicits additional information on substitutes. However, the decisions included in today's proposal will not be final until the SNAP program is promulgated.

It should be noted that the listing of acceptable and unacceptable substitutes is an on-going process. Thus, if a company is not yet able to provide the Agency with the information needed to complete a review of a substitute, a review can be completed in the future, when data become available. Once this rule is promulgated, the substitute may be submitted to the Agency for review as part of the formal SNAP program, as discussed in Sections IV through IX of today's proposal.

B. Format for SNAP Determinations

Sections D through J below present the proposed decisions on acceptability of substitutes that EPA has made based on available information and the proposed evaluation criteria (see Section V of today's proposal). These sections describe the application (e.g., industrial-process refrigeration), the substitutes evaluated, the proposed decision (i.e., acceptable or unacceptable) and associated rationale, conditions for use of the substitute, and any general comments.

In most cases, the application descriptions have been written broadly to encompass numerous industrial uses. Based on discussions with industry, the Agency felt that this approach was preferable to listing substitutes by narrowly-defined applications, which would increase needlessly the number of SNAP notices that would be received by the Agency. The objective of section 612 is to ensure that replacements of Class I and Class II substances with available substitutes will reduce adverse effects on human health and the environment. In general, the Agency can look at exposures from very broad classifications of use (e.g., metals cleaning) and perform the screening analysis to ensure that this statutory objective is being met. It is not necessary or helpful, for example, to list acceptable substitutes by each specific type of metal being cleaned in the solvents sector. This is especially true

when conservative assumptions used in the screening analysis demonstrate the acceptability of a wide range of alternatives. EPA requests comment on the descriptions of industrial applications and solicits comment and data, in particular, on those instances where more detail may be needed.

Where possible, the substitutes presented in sections D through J have been identified by their chemical name. Generally speaking, EPA has not listed substitutes by product or company name in order to avoid implied endorsement of one substitute over another.

However, there are two instances in which specific chemical names have not been included. First, where proprietary blends have been identified as substitutes, the Agency has worked with the manufacturers to identify generic ways in which the substitute could be listed. Before a user invests in a substitute in these categories, they may wish to contact the SNAP coordinator to confirm that the substitute they intend to use has been reviewed and approved by EPA. However, if a potential user identifies the substitute by a product name that EPA has on record, but has not included on the list for the reasons stated above, EPA will confirm the listing of the substitute without violating any proprietary business information provided in confidence to the Agency. The Agency requests comment on this proposed approach for listing and disseminating information on confidential substitutes.

The second situation in which EPA does not anticipate listing specific chemicals arises in the solvent-cleaning sector, primarily for aqueous and semi-aqueous cleaners. In this area, numerous cleaning formulations exist and are comprised of a wide variety of chemicals. As discussed in the section below on solvent-cleaning alternatives (see Section IX. F.), the Agency performed its screening assessment by identifying representative chemicals. These were then used to screen a wide variety of chemicals grouped into categories of solvent-cleaning constituents (e.g., saponifiers, surfactants, etc.). Rather than require users to compare the toxicity of chemicals in the formulations they wish to use to this set of reference chemicals, the Agency is proposing to use its risk screen to establish a list of common types of chemicals found in cleaning formulations. This list could then be used by companies as guidance on the types of chemicals expected to be found in a cleaning formulation.

EPA proposes this strategy for listing acceptable aqueous and semi-aqueous

cleaners for several reasons. First, it should minimize the need to submit SNAP notices for blends of compounds that are combinations of the chemicals on the cleaning formulation components list. Second, it will allow EPA to avoid listing proprietary formulations. The Agency requests comment on the usefulness of this proposed approach for listing aqueous and semi-aqueous cleaners.

Any conditions for use included in listing decisions are part of the decision to identify a substitute as acceptable. Thus, users would be considered out of compliance if using a substitute listed as "acceptable" without adhering to the conditions EPA has stipulated for acceptable use of the alternative. The conditions, if any, are listed when it is clear that a substitute can only be used safely if certain precautions are maintained. As noted previously, listing of substitutes as approved subject to conditions will be done through rulemaking.

The comments contained in the table of listing decisions found in summary form in Appendix B are intended to provide additional information on a substitute. Since comments are not part of the regulatory decision, they are not mandatory for use of a substitute. However, EPA encourages users of approved substitutes to apply any comments in their use of these substitutes. In many instances, the comments simply allude to good operating practices that have already been identified in existing industry and/or building-code standards. Thus, many of the comments, if adopted, would not require significant changes in existing operating practices for the affected industry.

C. Decisions Universally Applicable

Recently, the Agency has become aware of substitute mixtures that are being marketed as replacements for both Class I and Class II chemicals. In situations where these mixtures are a combination of Class I and Class II chemicals, they may serve as transitional chemicals because they offer environmental advantages in that they have a lower combined ODP than use of a Class I compound by itself. However, where EPA has identified an alternative in addition to the Class I and Class II mixture and that alternative reduces overall risk to human health and the environment, such mixtures shall be unacceptable.

There have been a few instances in which mixtures of Class I and Class II chemicals have been marketed as replacements for Class II chemicals. Because the ODP of these alternatives is

clearly higher than the Class II substances, the Agency is proposing to prohibit the use of any Class I and Class II mixture as a replacement for a Class II chemical. Where the Agency is aware of specific mixtures falling into this category, they are listed by individual use sector below. The remainder of this section presents the initial listing decisions for each of the following end use sectors:

- D. Refrigerants
- E. Foam Blowing
- F. Solvents Cleaning
- G. Halons
- H. Sterilants
- I. Aerosols
- J. Tobacco Expansion
- K. Adhesives, Coatings and Inks

D. Refrigerants

1. Overview

The refrigeration industry was the first to make widespread use of CFCs after this class of chemical compounds was discovered in the 1930s. In 1990, refrigeration and air conditioning accounted for almost 22 per cent of the total use of Class I substances in the United States. Over 500 million pieces of refrigeration and air conditioning equipment use these chemicals as the working fluids in a vapor compression cycle.

Many Class I substances exhibit desirable thermophysical properties for use in refrigeration cycles. They are relatively nontoxic, nonflammable, and inexpensive to produce; all these characteristics have contributed to their appeal as refrigerants. CFC-12 is the most widely used refrigerant, with applications in mobile air conditioners (MACs), household refrigerators and freezers, various appliances, chillers, retail food refrigeration equipment, cold storage warehouses, refrigerated transport systems, and industrial equipment. CFC-11 is most commonly used to provide cooling for large buildings, while CFC-115, as a component in the refrigerant blend R-502, is used for low temperature applications. CFC-113 and CFC-114 are used in special application chillers.

Of the Class II controlled substances, HCFC-22 is the refrigerant of choice in small to medium air conditioning systems, and some types of retail food and industrial process refrigeration systems.

Chillers used for commercial air conditioning can be categorized by cooling capacity. The lowest cost options for capacities below 200 tons are usually reciprocating chillers operating with HCFC-22. These chillers are usually air-cooled. Water cooling

requires the use of cooling towers and a ready supply of water.

There is a greater range of options for air conditioners in the cooling capacity range of 150 to 1200 tons. Low-pressure centrifugal chillers using HCFC-123 are available for this capacity. In addition, screw and centrifugal chillers using higher pressure refrigerants such as HCFC-22 or HFC-134a are also available for these capacities.

For chiller cooling capacities above 1200 tons, high-pressure centrifugal chillers currently dominate the market. At least two manufacturers offer factory-packaged HCFC-22 centrifugals up to roughly 2000 tons. Field-erected systems are available in larger sizes. Multiple low-pressure HCFC-123 centrifugals are also an option.

Alternative substances, such as lithium bromide/water absorption chillers, are also available with cooling capacities up to 1500 tons or more. These systems use heat, usually from steam or natural gas, to power the refrigeration cycle. Ideal applications are those where waste heat above 200 °F is available to power the chiller.

Another application is for heat recovery when a great deal of heat below 150 °F is required and there is a significant cooling load. Still another application, mainly for cold storage warehouses, involves lowering the pressure at which natural gas travels through pipelines at pressure drop stations to achieve cooling of a transfer medium, such as methanol/water or ethylene glycol.

EPA has divided the refrigeration and air conditioning sector into the following general end uses:

- commercial comfort air conditioning (chillers)—centrifugal, reciprocating, and screw chillers used to provide air conditioning;
- residential refrigerators;
- residential freezers;
- residential dehumidifiers used to control the humidity in homes;
- cold storage warehouses—public and private facilities used to store meat, produce, dairy products, frozen foods, and other perishable goods;
- commercial ice machines—equipment used to produce ice for commercial purposes;
- industrial process refrigeration systems used in the chemical, pharmaceutical, petrochemical, and other manufacturing and food processing industries, as well as industrial ice machines and ice rinks;
- transport refrigeration, including refrigerated ship holds, trucks and truck trailers, railway freight cars, and shipping containers;
- retail food refrigeration, including equipment found in supermarkets,

convenience stores, restaurants, hotel and institutional kitchens, and other food service establishments;

- mobile air conditioning used to control passenger compartment humidity and temperature in cars, trucks, buses, planes and other vehicles;
- residential and commercial air conditioning and heat pumps—window units, packaged terminal air conditioners, central air conditioners, direct expansion commercial air conditioners, and heat pumps.

Industry has invested heavily in the search for suitable alternative refrigerants that exhibit the favorable characteristics of the controlled substances, but that do not contribute to stratospheric ozone depletion or global warming. The hydrochlorofluorocarbons (HCFCs) and hydrofluorocarbons (HFCs) have received the most attention, along with expanded use of traditional refrigerants such as ammonia and hydrocarbons. In some cases, the most promising solution appears to be a blend of refrigerants. The 1991 report by UNEP's Refrigeration, Air Conditioning, and Heat Pumps Technical Options Committee contains detailed information about the status of alternative refrigerants in various applications.

Clearly, an important role will be played by blends of refrigerants. There are currently multiple blends in various stages of research, testing and market development, and as the search for optimal replacements continues, the number of blends will increase. Because of the impossibility of performing full SNAP analyses for all possible blends in all conceivable permutations, the Agency, between proposal and issuance of the final rule, will explore ways to streamline EPA's consideration of substitute refrigerant blends under the SNAP program.

One issue which EPA will be investigating further with respect to refrigerant blends is differential fractionation which may result in flammability and energy efficiency problems. For example, in a centrifugal chiller system equipped with a flooded evaporator (liquid refrigerant is situated on the outside of tubes through which water is flowing), the evaporator may act as a distillation device for the blend. The higher-pressure components may boil first and change to vapor, while the lower-pressure components remain as a liquid. This process artificially lowers the refrigerant pressure in the evaporator which, in turn, reduces the efficiency and capacity of the chiller. Similar reductions also can occur when using a low refrigerant velocity blend shellside in a condenser. In this

situation, the low-pressure components condense first, leaving the vapor "rich" in high pressure components and causing an increase in condensing pressure.

The section which follows discusses specific determinations on individual substitutes by application. Appendix B at the end of this notice summarizes in tabular form the Agency's proposed determinations on substitutes in the refrigerants sector, which are presented here in narrative form. These proposed determinations are based on the risk screen described in the draft background document entitled "Risk Screen on the Use of Substitutes for Class I Ozone-Depleting Substances: Refrigerants".

2. Alternative Refrigerants

a. Hydrochlorofluorocarbons. EPA believes that hydrochlorofluorocarbons (HCFCs) have a potentially important role to play as transitional refrigerants, both in retrofit applications and in new equipment. HCFCs have the disadvantage that they contribute to the destruction of stratospheric ozone, although to a much lesser extent than CFCs. Use of HCFCs until safer alternatives are available will allow industry to move away from CFC refrigerants more rapidly. EPA believes that this approach will have environmental and health benefits over one that allows continued use of CFCs until equipment that uses other alternatives is available.

HCFCs are chemically similar to CFCs except that they contain hydrogen in addition to chlorine and fluorine. Because their thermophysical properties are, in many cases, similar to CFCs, equipment designed to use CFCs can sometimes be retrofitted to operate with HCFCs. HCFC-22 has been used as a refrigerant for many years. It is the primary refrigerant used in small to medium sized air conditioners, and has found increasing application in medium temperature retail food refrigeration systems. HCFC-123 holds promise as the primary replacement for CFC-11 in low pressure centrifugal chillers. HCFC-124 has potential applications in blends as a refrigerant in chillers and other refrigeration equipment.

Because they contain hydrogen, the HCFCs break down more easily in the atmosphere, and therefore have lower ODPs. They also have global warming potentials lower than the CFCs. Production of HCFCs is controlled by the Clean Air Act and was initially scheduled to be phased out by 2030. EPA, however, is reexamining these dates in response to new data indicating greater risks of ozone depletion. Based

on these new concerns, EPA may propose an earlier phase-out for some of the HCFCs, particularly those with higher ozone-depleting potentials.

As noted above, EPA believes that HCFCs will play an important role as transitional refrigerants. There are clear environmental and health benefits to be gained by allowing their use until better substitutes are developed. Future EPA analysis under the SNAP program will focus on HCFC-22 applications and substitutes.

b. Hydrofluorocarbons.

Hydrofluorocarbons (HFCs) do not contain chlorine and do not contribute to destruction of stratospheric ozone. HFCs have zero ODPs, but some HFCs contribute to global warming. Their general use is one or more years away in some applications; in other applications, the shift to their use has already begun. Although a few HFCs have been in use for some time (HFC-152a is a component in the azeotropic blend CFC-500 used in smaller tonnage reciprocating equipment and large tonnage centrifugal equipment), the potential for HFCs as a replacement for CFCs has grown rapidly over the last several years. HFC-134a and HFC-152a hold the most promise as currently available replacements for Class I and Class II refrigerants and development of HFC-32 as a possible alternative has progressed.

c. Hydrocarbons. Since hydrocarbons do not contain chlorine or bromine, they do not contribute to ozone depletion. They degrade in the lower atmosphere, contributing to smog, but not significantly to global warming.

Propane, ethane, propylene, and to some extent butane are used as refrigerants in specialized industrial applications, primarily in oil refineries and chemical plants, where they are frequently available as part of the process stream and where their use contributes only slightly to the incremental risk of fire or explosion. These systems are designed to meet rigid requirements for reliability, durability, and safety. ASHRAE Standard 15, "Safety Code for Mechanical Refrigeration," and Standard 34, "Refrigerants," are incorporated into building codes in most of the U.S. These standards limit use of flammable refrigerants in many applications. Hydrocarbon refrigerants are also used in limited applications in some small appliances.

d. Ammonia. Ammonia has been used as a refrigerant in vapor compression cycles for more than 100 years. It is by far the refrigerant of choice in the meat packing, chicken processing, dairy, frozen juice, brewery, cold storage, and

other food processing and industrial applications. It is also widely used to refrigerate holds in fishing vessels. Industrial process refrigeration equipment uses rotary screw or reciprocating compressors. Ammonia is mainly used when moderate to low temperatures are required. Ammonia has a characteristic pungent odor, excellent refrigerant properties, no long term atmospheric drawbacks, and is low in cost. However, it is moderately flammable and toxic, although it is not a cumulative poison. OSHA standards specify a 15 minute short-term exposure limit of 35 ppm for ammonia.

e. Perfluorocarbons. Perfluorocarbons (PFCs) are fully fluorinated compounds, unlike CFCs, HCFCs, or HFCs. The principal environmental characteristic of concern for these compounds is that they have extremely long atmospheric lifetimes, often orders of magnitude longer than the CFCs. These long lifetimes cause the PFCs to have very high global warming potentials. Technology for containment and recycling of PFCs is commercially available and is recommended by manufacturers to offset any possible adverse environmental effects. An important advantage of the PFCs is that, unlike CFCs or HCFCs, they do not contribute to ozone depletion. In addition, these chemicals are nonflammable, essentially nontoxic, and they are exempted from Federal VOC regulations since they do not contribute to ground-level ozone formation.

Under Section 612, the Agency has completed an analysis showing the global warming that might be expected from atmospheric emissions of these compounds. The Agency further anticipates that additional, more detailed analysis of the environmental effects of PFCs will show that in widespread use, these compounds would pose higher overall risk relative to other available alternatives. Due to these concerns, the Agency has found acceptable only certain narrowly defined uses of perfluorinated compounds. EPA has described these limited acceptable uses as specifically as possible. The Agency requests comment on whether further narrative is needed to adequately describe these uses. Further, users should be aware that, because of the environmental concerns detailed above, any uses of PFCs outside those described herein should be submitted for future review and approval under SNAP.

f. Absorption refrigeration systems. Absorption refrigeration systems are the only major existing alternative to systems based on vapor compression cycles. Ammonia is also used in

absorption refrigeration and air conditioning systems. Small ammonia refrigeration units are popular in recreational vehicles and in some household applications as they need no electrically driven mechanical compressor, relying instead on a propane flame as an energy source. Small refrigerators using absorption technology are produced for use in hotel rooms, where the focus is on their silent operation rather than the lack of a suitable supply of electricity. Small absorption systems use hydrogen to maintain a system pressure high enough to allow the ammonia refrigerant to evaporate at low pressure and temperature (and condense at room temperature), and are constructed to withstand high internal operating pressures. The absorption mechanism itself is a sealed unit, which usually needs no servicing over its operating life.

Commercial ammonia absorption systems are used for air conditioning comfort cooling, particularly where waste heat is available. As with all chillers, these produce chilled water, which is circulated to the space being cooled. Lithium bromide is also used in commercial absorption systems, where it serves as an absorber. Such systems operate at very low pressure to allow water to act as a refrigerant. Lithium bromide is a relatively nontoxic, nonflammable, nonexplosive, chemically stable compound. Both types of absorption chiller systems have been traditional competitors of electrically driven CFC chillers.

g. New technologies. Chlorine has been proposed as a Class I substitute refrigerant for use in chlorine liquefaction, a processing step in the manufacture of the chemical. When chilled below its boiling point, chlorine can be stored as a liquid at atmospheric pressure, a method that for safety reasons is preferable to storing the chemical as a pressured gas at ambient temperatures. Compatibility of the refrigerant with liquid chlorine is critical because of chlorine's high reactivity; CFC-12 has been widely used because it does not react with chlorine.

Chlorine compressors would be specialized units made to resist chemical attack by liquid and gaseous chlorine. Because a chlorine refrigeration system would use part of the process stream as the refrigerant, the proposed use of chlorine as a refrigerant is analogous to that of hydrocarbon refrigerants in the oil and gas industry. EPA has determined that if the refrigeration system is placed so that any leakage or losses of chlorine would

be contained and neutralized by the process safety mechanisms, chlorine can be used safely in these specialized applications.

3. Preliminary Listing Decisions

a. *General Conditions.* (1) *The use of HCFCs is acceptable.* This determination shall not be considered to release any user from conformance with all other regulations pertaining to Class II substances. These include: (a) the prohibition against venting during servicing under section 608, which was effective July 1, 1992; (b) recycling requirements under section 608 once they are promulgated; (c) section 609 regulations in the case of motor vehicle air conditioners; and (d) the production phase-out of Class II substances under section 605, which is currently being revised as part of EPA's efforts to accelerate the phase-out of ozone-depleting chemicals.

(2) *The use of HFCs is acceptable.* This determination shall not be considered to release any user from conformance with the venting prohibition under section 608(c)(2), which takes effect November 15, 1995, at the latest.

b. *Acceptable Substitutes.* Substitutes are listed as acceptable by end use. Accordingly, the following list of acceptable substitutes are only approved for those end uses explicitly identified as acceptable. These substitutes are not identified as acceptable alternatives in any other end use described in this section until and unless a determination of acceptability has been made for any other end use. EPA recommends that the users of HCFCs, HFCs and any other alternative refrigerants adhere to the provisions of ASHRAE Standard 15—Safety Code for Mechanical Refrigeration, and ASHRAE Standard 34—Number Designation and Safety Classification of Refrigerants.

(1) *HCFC-123* is acceptable as a substitute for CFC-11 in centrifugal chillers, both in new equipment and in retrofits. HCFC-123 is also acceptable as a substitute for CFC-12 and CFC-500 in new centrifugal chillers. As noted above, users of HCFC-123 should adhere to ASHRAE Standards 15 and 34. EPA worker-monitoring studies of HCFC-123 show that 8-hour TWA can be kept within 1 ppm (less than the interim OEL of 10 ppm) when recycling and ASHRAE standards are followed.

(2) *HCFC-22* is acceptable for use in new equipment in the following end uses:

- As a substitute for CFC-11 in centrifugal chillers;
- As a substitute for CFC-12 in centrifugal chillers, reciprocating

chillers, cold storage warehouses, residential dehumidifiers, residential freezers, commercial ice machines, industrial process refrigeration equipment, refrigerated transport equipment, retail food systems, vending machines, and water coolers;

- As a substitute for CFC-500 in centrifugal chillers, dehumidifiers and refrigerated transport systems;
- As a substitute for CFC-502 in cold storage warehouses, residential freezers, commercial ice machines, industrial process refrigeration systems, refrigerated transport systems, and retail food systems.

HCFC-22 is acceptable for use in existing equipment, or retrofits, in the following end uses:

- As a substitute for CFC-12 in cold storage warehouses, industrial process refrigeration equipment, retail food systems, and vending machines;
- As a substitute for CFC-502 in cold storage warehouses, industrial process refrigeration equipment, retail food systems and refrigerated transport systems.

HCFC-22 is already used in a variety of air conditioning and refrigeration end uses. As a result, it is more widely available than any of the HFC substitutes.

(3) *HCFC-22/HFC-152a/HCFC-124 blend* is acceptable as a substitute for CFC-12 in retrofits of cold storage warehouses, residential dehumidifiers, residential freezers, residential refrigerators, commercial ice machines, industrial process refrigeration equipment, refrigerated transport systems, retail food systems, vending machines, water coolers, and mobile air conditioners. Although the blend is acceptable in these end uses, the extent to which retrofit changes are required varies by equipment. HCFC-22/HFC-152a/HCFC-124 blend is acceptable as a substitute for CFC-500 in retrofits of centrifugal chillers, residential dehumidifiers and refrigerated transport. As with all blends, precautions must be taken during recycling to avoid mixing with other refrigerants.

(4) *HFC-124* is acceptable as an alternative to new and retrofit CFC-114 centrifugal chillers in all applications.

(5) *HCFC-22/Propane/HFC-125 blend* is acceptable as a substitute for CFC-500 in refrigerated transport, both in new equipment and in retrofits. This blend is also acceptable as a substitute for CFC-502 in cold storage warehouses, industrial process refrigeration, refrigerated transport, and retail food equipment, both in new equipment and in retrofits. Flammability has been studied and shown to be controllable.

As with all blends, care must be taken in recycling to avoid mixing with other refrigerants.

(6) *HFC-134a* is acceptable for use in new equipment in the following end uses:

- As a substitute for CFC-11 in centrifugal chillers;
- As a substitute for CFC-12 in household refrigerators; cold storage warehouses, residential dehumidifiers, residential freezers, commercial ice machines, industrial process refrigeration, centrifugal chillers, reciprocating chillers, refrigerated transport, retail food, vending machines, water coolers, and mobile air conditioners;
- As a substitute for CFC-500 in centrifugal chillers, dehumidifiers, and refrigerated transport; and
- As a substitute for CFC-502 in industrial process refrigeration and refrigerated transport.

HFC-134a is acceptable for use in existing equipment, or retrofits, in the following end uses:

- As a substitute for CFC-12 in centrifugal chillers, reciprocating chillers, cold storage warehouses, residential dehumidifiers, industrial process refrigeration equipment, refrigerated transport systems, retail food systems, vending machines, and mobile air conditioners;
- As a substitute for CFC-500 in centrifugal chillers and refrigerated transport systems; and
- As a substitute for CFC-502 in industrial process refrigeration equipment, and refrigerated transport systems.

HFC-134a is potentially the most versatile substitute identified to date as it may be possible to use it in a broad range of applications. However, HFC-134a may be less energy efficient than HCFC-22 in some end uses;

(7) *HFC-152a* is acceptable as a substitute for CFC-12 in new household refrigerators and residential freezers.

(8) *Ammonia* is acceptable for use in new equipment in the following end uses:

- As a substitute for CFC-11 in centrifugal chillers;
- As a substitute for CFC-12 in centrifugal chillers, cold storage warehouses, commercial ice machines, industrial process refrigeration equipment, and retail food systems;
- As a substitute for CFC-500 in centrifugal chillers; and
- As a substitute for CFC-502 in cold storage warehouses, retail food systems, commercial ice machines, and industrial process refrigeration equipment.

(9) *Butane* is acceptable for use in new equipment as a substitute for CFC-

12 in industrial process refrigeration equipment. EPA recommends but does not require that butane only be used at industrial facilities which manufacture or use hydrocarbons in the process stream.

(10) *Chlorine* is acceptable for use in new equipment as a substitute for CFC-12 in industrial process refrigeration equipment, and as a substitute for CFC-502 in new industrial process refrigeration equipment. EPA recommends but does not require that chlorine only be used at industrial facilities which manufacture or use chlorine in the process stream.

(11) *Propane* is acceptable for use in new equipment as a substitute for CFC-12 in industrial process refrigeration equipment. EPA recommends but does not require that propane only be used at industrial facilities which manufacture or use hydrocarbons in the process stream.

(12) *Lithium bromide* is acceptable for use in absorption refrigeration systems. It is acceptable as a substitute for CFC-11, CFC-12 and CFC-500 in new centrifugal chillers.

(13) *High to Low Pressure Stepdown Process* is acceptable for use in energy recovery systems as a substitute for CFC-12 in new cold storage warehouse equipment.

(14) *HCFC-142b* is acceptable as a substitute for CFC-114 in new centrifugal chillers.

c. *Unacceptable Substitutes.* (1) *HCFC-22/HCFC-142b/CFC-12 blend* is proposed unacceptable in all HCFC-22 refrigeration and air conditioning end uses. Because this blend contains CFC-12 (which has an ODP 20 times that of HCFC-22), it poses a greater risk to stratospheric ozone than the use of HCFC-22 alone.

(2) *HCFC-141b* is proposed unacceptable as a substitute for CFC-11 in new centrifugal chillers. Flammability may be an issue. Further, this material is not generally available in new equipment. Finally, the material has a high ozone depletion potential.

(3) *HCFC-22/HCFC-142b/Isobutane blend* is proposed as unacceptable for use as a substitute for CFC-12 in retrofits of mobile air conditioners. Flammability may be an issue, and the Agency's final determination in this case will depend on receiving adequate data on flammability and likely fractionation through permeable hoses. Submission of information from industry groups, such as from the Society for Automotive Engineers, for example, regarding refrigerant retrofit guidelines for specific equipment in motor vehicle air conditioners, would help EPA evaluate such issues as

flammability and the effect of blends on recycling and recovery efforts.

(4) *Hydrocarbon Blend A* is proposed as unacceptable for use as a substitute for all CFC-12 refrigeration uses. Flammability may be an issue. The Agency's final determination will depend on receiving adequate data on factors such as flammability and materials compatibility.

EPA has not found any other substitutes to be unacceptable but may do so at a later date based on new data.

E. Foams

1. Overview

Foam plastics accounted for approximately 18 per cent of all U.S. consumption of ozone-depleting chemicals on an ODP-weighted basis in 1990. Five Class I chemicals—CFC-11, CFC-12, CFC-113, CFC-114, and methyl chloroform—are used as blowing agents in foam production. These five compounds are used in a wide variety of applications.

The manufacture of foam plastics relies on the use of gas or volatile liquid blowing agents to create bubbles, or cells, in the plastic foam structure. Suitable blowing agents must conform to a number of criteria. They must be soluble in liquid but not in solid plastic, possess a suitable boiling point and vapor pressure, and they must not react with plastic. In addition, blowing agents with low thermal conductivity are desirable for use in insulating foams. CFCs possess these desirable properties, and hence have found widespread use as blowing agents in many foam plastics.

Some foam plastics are characterized by a structure of closed cells that traps the blowing agent, while others have open cells that allow the blowing agent to escape. Although some rigid polyurethane packaging foams are open celled, most rigid foams have closed-cell structures. Many of these closed-cell, rigid foams are excellent insulating materials, because the blowing agent trapped within the cells can serve as a thermal insulator. Flexible foams, on the other hand, generally have open cells and are poor thermal insulators.

Foam plastics manufactured with CFCs fall into four major categories: Polyurethane, phenolic, extruded polystyrene, and polyolefin. Historically, CFC-11 and CFC-113, which remain in a liquid state at room temperature, have been used as blowing agents in polyurethane and phenolic foams. CFC-12 and CFC-114, which have lower boiling points than CFC-11 and CFC-113 and are gases at room temperature, are used in polyolefin and

polystyrene foams. In addition to CFCs, methyl chloroform is used as a blowing agent in some flexible polyurethane foams.

The major applications for foams are cushioning, packaging, and thermal insulation. In general, cushioning and packaging foams include flexible polyurethane foams, polyurethane integral skin foams, polyolefin foams, and polystyrene sheet foams, while insulating foams include rigid polyurethane foams, polystyrene insulation board, and phenolic insulation board. However, some rigid polyurethane foams and extruded polystyrene board have non-insulating uses in flotation and packaging products, and certain polyolefin foams have thermal insulating applications.

Due to the wide variety of end uses that foams represent, the Agency has decided to divide its analysis of foam plastics into the following ten distinct end-use sectors:

- rigid polyurethane laminated boardstock;
- rigid polyurethane appliance;
- rigid polyurethane spray and commercial refrigeration, and sandwich panels;
- rigid polyurethane slabstock and other foams;
- polystyrene extruded insulation board;
- phenolic insulation board;
- flexible polyurethane;
- polyurethane integral skin;
- polystyrene extruded sheet; and
- polyolefin.

The SNAP determinations proposed today distinguish between these ten end-use sectors because the mix of potential alternatives to Class I blowing agents is different for each.

Rigid polyurethane foams, which serve primarily as insulation for appliances, buildings, and refrigerated transport containers, rely heavily on the use of CFC-11 as a blowing agent. These foams also find use as pipe and tank insulation and as flotation material. The low thermal conductivity of CFC-11 endows many rigid polyurethane foams with excellent thermal insulating qualities. Moreover, low toxicity, low flammability, and compatibility with key materials have made CFC-11 the blowing agent of choice in most rigid polyurethane applications.

Extruded polystyrene insulation board, which has traditionally used CFC-12 as a blowing agent, serves as insulation for roofs, walls, and floors in residential and agricultural buildings, as insulation against frost heave in roads and railways, and as the insulating core material in sandwich panels.

Phenolic insulation board, a closed-cell insulating foam that relies primarily

on a blowing agent mixture of CFC-113 and CFC-11 for its manufacture, accounts for only a small proportion of the total CFC consumption in foam plastics. Closed-cell phenolic foam serves mainly as building insulation. The foam's primary use is as roof insulation, although it also finds use as wall insulation in commercial applications and as sidewall sheathing in residential applications.

CFC-11 use was, at one time, prevalent in flexible polyurethane foams. However, the period between 1986 and 1990 saw a decrease of over 90 per cent in the use of CFC-11 as an auxiliary blowing agent in flexible polyurethane foams. The reduction in CFC-11 use has, to some extent, been compensated for by an increase in methylene chloride use. Polyurethane flexible slabstock foam is an open-celled flexible foam manufactured in a variety of densities and degrees of firmness that finds use in many cushioning applications. Polyurethane flexible molded foam, which is also open-celled, serves primarily as cushioning in motor vehicles.

The production of integral skin foams, which has also traditionally relied on CFC-11 as a blowing agent, has seen a reduction in CFC-11 consumption in recent years. Integral skin foams combine a flexible, semi-rigid, or rigid foam core with a tough outer skin. The skin results from the tendency of physical blowing agents such as CFC-11 to condense at the mold surface during manufacture. Rigid integral skin foams have applications in products such as computer cabinets, skis, and tennis rackets, while uses for semi-rigid integral skin foams include steering wheels, head rests, arm rests, office furniture, and certain other minor applications.

Extruded polystyrene sheet foam, which traditionally used CFC-12, has already switched to non-CFC alternatives. Extruded polystyrene sheet serves as food packaging in items such as meat trays, egg cartons, and clam-shell containers. The foam also finds use as loose fill packaging material and as art board.

Traditionally, CFC-114 and CFC-12 have been the main blowing agents used in the production of extruded polyolefin foams, although some CFC-11 has been used as well. Polyolefin foams include products manufactured from either polyethylene or polypropylene resins. Extruded polyethylene sheet products serve primarily as protective packaging for furniture, electronics, and other goods. Extruded polyethylene planks are mainly used as packaging for electronics and other high-value goods

but have a number of other applications in areas such as military packaging, flotation, construction, and aircraft seating. Extruded polypropylene sheet serves as packaging in applications such as interleaving, protective furniture covering, and protective wrap for delicate food items.

2. Alternative Blowing Agents

The foam industry in the U.S. has been successful in identifying, developing, and introducing substitutes for CFC blowing agents. However, the choice of future alternatives for CFCs will depend on a number of factors. These include toxicity, flammability, environmental concerns, and, in the case of insulating foams, the insulating efficiency of alternatives.

Toxicity concerns associated with the use of alternative chemicals relate to the exposure of workers and consumers to the chemicals or to the decomposition products these chemicals may form slowly over time in foam products. The likely degree of human health risk associated with an alternative depends not only on the nature of a substitute chemical but also on the chemical composition, manufacturing process, and product applications that characterize the foam end-use sector into which that substitute will be introduced.

Flammability concerns, like toxicity concerns, have to do with possible danger to workers and consumers. Such danger includes possible ignition of materials during manufacturing, storage, or transportation and the fire hazard posed by the final product. Alternatives to CFCs have varying degrees of flammability. As in the case of toxicity, however, the composition, production processes, and end-use applications that characterize each foam type will dictate the potential risks associated with flammability.

In addition to posing toxicity and flammability risks, alternatives may have deleterious effects on the environment. Such deleterious effects may include stratospheric ozone depletion, global warming, and contribution to smog formation. HCFCs have, in varying degrees, the potential to deplete ozone; both HCFCs and HFCs have global warming potential; and various potential alternatives, especially hydrocarbons, are volatile organic compounds (VOCs) that contribute to the formation of ozone, or smog, in the lower atmosphere.

The use of alternative blowing agents can have an adverse effect on the insulating capability of foam products. Based on initial tests, for example, the replacement of CFCs with HCFCs in

insulating foams reduced insulating efficiency. However, formulation changes and modifications to the foam technology have yielded HCFC-blown products with insulating efficiency equivalent to CFC-blown products. In fact, most efforts to replace CFC blowing agents in insulating foams over the near term involve HCFCs, although HFCs and hydrocarbons may serve as alternatives in a limited number of applications.

In the flexible and packaging foam sectors, there has already been widespread movement away from CFCs to alternative, non-HCFC auxiliary blowing agents and production processes. Water, which generates CO₂, is the primary blowing agent for flexible polyurethane foams. Auxiliary blowing agents like CFC-11, methylene chloride or acetone confer certain desirable physical characteristics, such as softness or low density, to the finished product. This trend away from use of CFCs is likely to continue in light of EPA's proposed regulations under section 610 of the CAA that would, beginning on November 15, 1993, ban the sale of CFCs in flexible and packaging foams. Also, beginning on January 1, 1994, section 610 bans sale of noninsulating foams manufactured with Class II substances. Foam used in food packaging must in addition meet the regulatory requirements of the FDA.

a. Hydrochlorofluorocarbons. Hydrochlorofluorocarbons (HCFCs) and HCFC blends have been, and will continue to be, important as transitional alternatives to CFC blowing agents, particularly in insulating foams. Two HCFCs, HCFC-123 and HCFC-141b, can serve as virtual drop-in replacements for CFC-11 in many end-use applications. Because of toxicity, the resultant low interim occupational exposure level (OEL), and the lack of commercial availability of HCFC-123, HCFC-141b represents the more likely short-term possibility for replacing CFC-11 in several insulating foam sectors. As a result, the Agency has determined that HCFC-141b, despite its relatively high ODP of 0.11, represents an important transitional alternative to CFC-11. Other HCFC alternatives are HCFC-22 and HCFC-142b. Although these compounds are commercially available and have lower ODPs than HCFC-141b, each has a boiling point significantly lower than CFC-11. As a result, conversion to HCFC-22 or HCFC-142b from CFC-11 generally entails significant investment in technical and process modification. HCFC-22 and HCFC-142b do, however, present viable, near-term alternatives to CFC-12 in extruded polystyrene foams.

The continued availability of HCFCs, even those with relatively high ODPs, is necessary to ensure the continued replacement of CFC blowing agents with alternative compounds in the short term. Production of HCFCs is controlled by the Clean Air Act and under section 605 is scheduled for phase-out by 2030. However, due to new data concerning greater risks of ozone depletion, EPA has proposed an accelerated phase-out schedule. Given the technical and safety concerns associated with many non-HCFC alternatives, however, disallowing the interim use of HCFCs in all foam sectors, including the use of HCFC-141b and HCFC-22, would have adverse effects on human health and the environment.

Additional restrictions on HCFC use may be made subject to final promulgation of section 610 for non-essential uses. Section 610 states that after January 1, 1994, it shall be unlawful for any person to sell or distribute, or offer for sale or distribution, in interstate commerce, any plastic foam product which contains, or is manufactured with, a Class II substance. Section 610(d)(2) authorizes EPA to grant exceptions to the Class II ban for foam insulation products, or foam used for motor vehicle safety in accordance with section 103 of the National Traffic and Motor Vehicle Safety Act on federal motor vehicle safety standards.

b. Hydrofluorocarbons. Hydrofluorocarbons (HFCs) represent a zero-ODP alternative to CFC blowing agents in many sectors. From the standpoint of stratospheric ozone depletion alone, HFCs are preferable to HCFCs as alternative blowing agents. However, other considerations such as flammability and cost may limit the feasibility of HFC alternatives, especially over the short term. Moreover, the relatively high thermal conductivity of HFCs is likely to hamper the insulating capabilities of HFC-blown foams. This, in turn, could result in energy efficiency losses.

Two HFCs, HFC-134a and HFC-152a, are under consideration as substitutes in a number of applications. Because both compounds have boiling points that are significantly lower than that of CFC-11, significant technical and process modifications would be required to introduce them as replacements for CFC-11. The HFCs hold more promise as near- or intermediate-term alternatives for CFC-12 in extruded polystyrene foams, particularly in extruded polystyrene sheet foams. However, issues such as flammability, cost, commercial availability, and the solubility of HFCs in polystyrene

polymer remain of concern for extruded polystyrene foams.

Both HFC-134a and HFC-152a have significantly higher thermal conductivities than do any of the CFCs. Although formulation changes and process modifications can be introduced to increase the thermal insulating efficiency of HFC-blown foams, it is unlikely that such changes can compensate fully for the disparity in thermal conductivity between HFCs and CFCs, especially in the near term. As a result, conversion to HFCs would likely lead to the production of foams with lower insulating efficiency and, possibly, to a reduction in the energy efficiency of buildings, appliances, refrigerated transport containers, and other insulated items.

Even if technical difficulties and problems associated with thermal conductivity can be overcome, the commercial availability and cost of HFC-134a, and the flammability of HFC-152a, remain of concern. Conversion to HFC-152a may entail significant capital investment in order to ensure worker safety against fire hazards. Moreover, in the case of insulating foams, manufacturers will need to guarantee that foams blown with HFC-152a meet the building code requirements that apply to the flammability of building materials.

The Agency has determined that, although HFCs represent an attractive alternative to CFC blowing agents in the intermediate and long term, HFC-134a and HFC-152a are unlikely to replace CFCs to a significant extent in the short term, especially in insulating foams.

c. Hydrocarbons. Like HFCs, hydrocarbons represent a zero-ODP alternative to CFC blowing agents in many sectors. From the standpoint of ozone depletion potential and global warming potential alone, hydrocarbons are preferable to HCFCs as alternative blowing agents. However, other considerations such as flammability and concerns over ground-level air pollution may limit the adequacy of hydrocarbons as alternatives, especially over the short term. Moreover, the relatively high thermal conductivity of hydrocarbons is likely to hamper the insulating capabilities of hydrocarbon-blown foams. This, in turn, could result in energy efficiency losses.

Hydrocarbons have significantly higher thermal conductivities than do any of the CFCs. Although formulation changes and process modifications can be introduced to increase the thermal insulating efficiency of hydrocarbon-blown foams, it is unlikely that such changes can compensate fully for the disparity in thermal conductivity

between hydrocarbons and CFCs, especially in the near term. As a result, conversion to hydrocarbons would likely lead to the production of foams with lower insulating efficiency and, possibly, to a reduction in the energy efficiency of buildings, appliances, refrigerated transport containers, and other insulated items.

Conversion to hydrocarbons may entail significant capital investment in order to ensure worker safety against fire hazards. Moreover, in the case of insulating foams, manufacturers will need to guarantee that foams blown with hydrocarbons meet the building code requirements that apply to the flammability of building materials.

Hydrocarbons are VOCs that contribute to the formation of ozone, or smog, in the lower atmosphere. Any use of hydrocarbon blowing agents is subject to the federal and regional restrictions that apply to VOCs, and conversion to hydrocarbons could involve the capital investment necessary to comply with these restrictions.

Hydrocarbons have proven effective as replacements for CFCs in many noninsulating foams. However, the Agency believes that, although hydrocarbons have the potential to replace CFC blowing agents in insulating foams, they are unlikely to replace CFCs in insulating foams over the short term.

d. Other. Two other blowing agents, methylene chloride and acetone, have proven effective as substitutes for CFC-11 in flexible polyurethane foams. Methylene chloride, which already serves as an auxiliary blowing agent for most grades of flexible polyurethane foam, is commercially available, has relatively low cost, and provides a technically feasible alternative to CFC-11. However, because of concerns over its high toxicity, methylene chloride use is restricted in several states and localities; and is subject to review under Title III of the CAA.

Acetone, when used as a blowing agent, is capable of yielding all grades of flexible polyurethane foam. It can serve as an alternative blowing agent where methylene chloride use is infeasible. Acetone is a VOC and must be controlled as such. In addition, plant modifications may be necessary to accommodate acetone's flammability.

The AB Technology is a commercially available and technically feasible process for replacing CFCs or other auxiliary blowing agents for most conventional flexible foam grades. AB Technology employs formic acid in conjunction with water as the blowing agent for producing flexible polyurethane foam. The process is based

on using the reaction of formic acid with an isocyanate to produce carbon monoxide in addition to the water/isocyanate reaction normally used to generate carbon dioxide gas for the expansion of foam. OSHA has set a permissible exposure level (PEL) for carbon monoxide of 35 ppm of a time weighted average with a ceiling not to exceed 200 ppm.

Carbon dioxide (CO₂) is an acceptable substitute for all foam end-uses. One hundred percent CO₂ blowing is achieved by further increasing the water content in the foam formulation, thereby eliminating the need for a physical blowing agent. CO₂ blends acceptable as long as the other constituents of the blend are acceptable under SNAP.

3. Primary Listing Decisions

a. Acceptable Substitutes

(1) Polyurethane, Rigid Laminated Boardstock. (a) HCFC-123

HCFC-123 is acceptable as an alternative blowing agent to CFC-11 in rigid polyurethane laminated boardstock foam. From the standpoint of technical feasibility, HCFC-123 represents a viable alternative to CFC-11 as a potential blowing agent. More specifically, the physical properties, thermal conductivity, and aging of foams blown with HCFC-123 are similar to those blown with CFC-11. As a result, HCFC-123, which has an ozone depleting potential significantly lower than that of CFC-11, has the potential to replace CFC-11 in many applications. Nonetheless, availability of HCFC-123 is limited at present, and furthermore industry may be unable to meet the relatively low interim OEL of 10 ppm set by the manufacturer. However, recent worker monitoring studies indicate that an interim OEL of 10 ppm can be achieved through the use of increased ventilation, good housekeeping and work practices, and dust collection. HCFC-123 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(b) HCFC-141b

HCFC-141b is acceptable as an alternative to CFC-11 in rigid polyurethane laminated boardstock foam. Although its ODP of 0.11 is relatively high, HCFC-141b, because it can serve as a virtual drop-in substitute for CFC-11, offers almost immediate transition out of CFCs in this sector. Not only does HCFC-141b offer a technically feasible alternative to CFC-11, but it is currently available or will soon be available in sufficient quantities to meet industrial demand. The Agency has proposed restricting the use of

HCFC-141b in the proposed accelerated phase-out of HCFCs in light of its relatively high ODP and the fact that other zero-ODP substitutes should be available by the phase-out dates. HCFC-141b is currently subject to the phase-out of Class II compounds under section 605 of the CAA.

(c) HCFC-22

HCFC-22 is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. HCFC-22 offers an alternative with significantly less potential to deplete ozone than CFC-11. Foams blown with HCFC-22 have been developed that have thermal insulating capabilities equivalent to foams blown with CFC-11. However, technical problems remain. New laminate materials may be needed to counteract the solvent characteristics of HCFC-22, and significant process changes would be necessary to accommodate the low boiling point of HCFC-22. HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(d) HCFC-142b

HCFC-142b is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. HCFC-142b offers an alternative with significantly lower potential to deplete ozone than CFC-11. Nevertheless, certain technical problems persist. Namely, plant modifications are required to allow use of blowing agents like HCFC-142b that have low boiling points, and the compound's chemical and physical characteristics may lead to rapid aging of the foam. Finally, the use of HCFC-142b results in potentially significant losses in thermal insulating efficiency. HCFC-142b is subject to the phase-out of Class II compounds under section 605 of the CAA.

(e) HCFC-22/HCFC-141b

The HCFC-22/HCFC-141b blend is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. Because both components of the blend are commercially available in large enough quantities to meet industry demand, it offers a near-term vehicle for replacing CFC-11 in laminated boardstock foams. HCFC-22 has an occupational exposure limit of 250 ppm, whereas HCFC-141b has an OEL of 1000 ppm. Use of the blend, because of its HCFC-141b component, will be restricted under the proposed accelerated phase-out of HCFCs, since other non-ODP substitutes should become available. The HCFC-22/HCFC-141b blend is presently subject to the phase-out of Class II

compounds under section 605 of the CAA.

(f) HCFC-22/HCFC-142b

The HCFC-22/HCFC-142b blend is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. The blend offers an alternative with significantly less potential to deplete ozone than CFC-11. Nevertheless, certain technical problems persist. Namely, plant modifications are required to allow use of blowing agents like HCFC-22 and HCFC-142b that have low boiling points, and the blend's chemical and physical characteristics may lead to rapid aging of the foam. Finally, use of the blend results in potentially significant losses in thermal insulating efficiency. The HCFC-22/HCFC-142b blend is subject to the phase-out of Class II compounds under section 605 of the CAA.

(g) HCFC-141b/HCFC-123

The HCFC-141b/HCFC-123 blend is acceptable as an alternative to CFC-11 in rigid polyurethane laminated boardstock foam. As noted above, HCFC-141b, because of its commercial availability and ability to serve as a virtual drop-in substitute for CFC-11, offers an immediate opportunity to replace CFC-11. HCFC-123, although it has the technical requirements necessary to replace CFC-11, suffers from limited availability and concerns over whether the interim OEL can be met. The HCFC-141b/HCFC-123 blend offers an opportunity to use HCFC-123 while at the same time allaying those concerns to some degree. Moreover, because the ODP of HCFC-123 is lower than that of HCFC-141b, the blend has a lower ODP than HCFC-141b alone. Nevertheless, the blend, because of the HCFC-141b component, is subject to the proposed accelerated phase-out of HCFCs. The HCFC-141b/HCFC-123 blend is also currently subject to the phase-out of Class II compounds under section 605 of the CAA.

(h) HFC-134a

HFC-134a is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in rigid polyurethane laminated boardstock foams. The use of HFC-134a as a blowing agent in rigid polyurethane laminated boardstock foams is currently not commercially feasible. Plant modifications may be necessary to accommodate the use of HFC-134a because its boiling point is lower than that of CFC-11. In addition, there are

concerns over commercial availability, the cost of HFC-134a is likely to be high, and the use of HFC-134a may cause significant increases in thermal conductivity, with a concomitant loss in the insulating capacity of foams blown with HFC-134a.

(i) HFC-152a

HFC-152a is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. HFC-152a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in rigid polyurethane laminated boardstock. The use of HFC-152a as a blowing agent in rigid polyurethane laminated boardstock foam is currently not commercially feasible, and there are concerns over the potential for significant increases in thermal conductivity. Process changes may be necessary to accommodate the use of HFC-152a, and plant modifications may be necessary to manage its flammability. Also, foams blown with HFC-152a will need to conform with building code requirements that relate to flammable materials.

(j) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-11 in rigid polyurethane laminated boardstock foam. Of the hydrocarbons, pentane has the greatest potential as a replacement for CFC-11 in this sector of the foam industry. However, the use of pentane as a blowing agent in rigid polyurethane laminated boardstock foam is currently not commercially feasible. Moreover, extensive plant modifications may be necessary to accommodate the use of pentane and other hydrocarbons. In addition, these materials pose flammability concerns. Further, there is a potential for significant increases in thermal conductivity that could reduce insulating capacity; studies suggest that pentane could increase thermal conductivity by 15 to 20 per cent over CFC-11, for example. Foams blown with hydrocarbons will need to conform with building code requirements that relate to flammable materials. Finally, pentane and other hydrocarbons are VOCs and must be controlled as such under Title I of the CAA.

(k) 2-Chloropropane

2-Chloropropane is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam. At present, because 2-chloropropane is a proprietary technology, its commercial availability may be limited. Moreover, 2-chloropropane is flammable and its use

may require extensive modification of existing equipment.

(l) Carbon Dioxide

Carbon dioxide is acceptable as a substitute for CFC-11 in rigid polyurethane laminated boardstock foam.

(2) Polyurethane, Rigid Appliance Foam

(a) HCFC-123

HCFC-123, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 in rigid polyurethane appliance foam.

(b) HCFC-141b

HCFC-141b, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 in rigid polyurethane appliance foam.

(c) HCFC-22

HCFC-22, for reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as a substitute for CFC-11 in rigid polyurethane appliance foam.

(d) HCFC-142b

HCFC-142b is acceptable as a substitute for CFC-11 in rigid polyurethane appliance foam. HCFC-142b offers an alternative with significantly less potential to deplete ozone than CFC-11. Nevertheless, certain technical problems persist. Namely, plant modifications are required to allow the use of blowing agents like HCFC-142b that have low boiling points. HCFC-142b is subject to the phase-out of Class II compounds under section 605 of the CAA.

(e) HCFC-22/HCFC-142b

The HCFC-22/HCFC-142b blend is acceptable as a substitute for CFC-11 in rigid polyurethane appliance foam. The blend offers an alternative with significantly less potential to deplete ozone than CFC-11. Foams blown with the blend have been developed that have thermal insulating capabilities equivalent to foams blown with CFC-11. However, technical problems remain. New plastic materials may be needed for appliances to counteract the solvent characteristics of HCFC-22, and significant process changes would be necessary to accommodate the low boiling point of the HCFC-22/HCFC-142b blend. The blend is subject to the phase-out of Class II compounds under section 605 of the CAA.

(f) HCFC-22/HCFC-141b

The HCFC-22/HCFC-141b blend is acceptable as a substitute for CFC-11 in rigid polyurethane appliance foam. Because both components of the blend are commercially available in large enough quantities to meet industry demand, it offers a near-term vehicle for replacing CFC-11 in rigid appliance foams. Use of the blend, because of its HCFC-141b component, will be restricted under the proposed accelerated phase-out of HCFCs, since other non-ODP substitutes should become available. The problem of toxic decomposition byproducts, although present, is controllable. However, new plastic materials may be needed for appliances to counteract the solvent characteristics of HCFC-22, and some process changes may be necessary to accommodate the low boiling point of HCFC-22. The HCFC-22/HCFC-141b blend is presently subject to the phase-out of Class II compounds under section 605 of the CAA.

(g) HCFC-123/HCFC-141b

The HCFC-123/HCFC-141b blend, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 in rigid polyurethane appliance foam.

(h) HFC-134a

HFC-134a, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 in rigid polyurethane appliance foam.

(i) HFC-152a

HFC-152a, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 in rigid polyurethane appliance foam.

(j) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-11 in rigid polyurethane appliance foam. Hydrocarbons offer the potential of a non-ozone-depleting alternative to the use of CFC-11 blowing agents in rigid polyurethane appliance foam. However, the use of hydrocarbon blowing agents in rigid polyurethane appliance foams is currently not commercially feasible. Moreover, extensive plant modifications may be necessary to accommodate the flammability of hydrocarbons. In addition, the potential for significant increases in thermal conductivity may reduce insulating capacity. Foams blown with hydrocarbons must conform

with building code requirements that relate to flammable materials. Hydrocarbons are VOCs and will be subject to control as such under Title I of the CAA.

(k) Carbon Dioxide

Carbon dioxide is acceptable as a substitute for CFC-11 in rigid polyurethane appliance foam.

(3) Rigid Polyurethane Commercial Refrigeration Foam, Spray Foam, and Sandwich Panels (a) HCFC-123

HCFC-123, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(b) HCFC-141b

HCFC-141b, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(c) HCFC-22

HCFC-22 is acceptable as a substitute for CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels. HCFC-22 offers an alternative with significantly less potential to deplete ozone than either CFC-11 or CFC-12. However, significant process changes would be necessary to accommodate the low boiling point of HCFC-22. HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(d) HCFC-142b

HCFC-142b, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(e) HCFC-22/HCFC-142b

The HCFC-22/HCFC-142b blend, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(f) HFC-134a

HFC-134a, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(g) HFC-152a

HFC-152a, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(h) Hydrocarbons

Hydrocarbons, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, are acceptable alternative blowing agents for CFC-11 and CFC-12 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(i) Carbon Dioxide

Carbon dioxide is an acceptable alternative blowing agent for CFC-11 in rigid polyurethane commercial refrigeration foam, spray foam, and sandwich panels.

(4) Polyurethane Slabstock and Other Foams (a) HCFC-123

HCFC-123 is acceptable as an alternative to CFC-11 in rigid polyurethane slabstock and other foams. From the standpoint of technical feasibility, HCFC-123 represents a viable alternative to CFC-11 as a potential blowing agent. More specifically, the physical properties, thermal conductivity, and aging of foams blown with HCFC-123 are similar to those blown with CFC-11. As a result, HCFC-123, which has an ozone depleting potential significantly lower than that of CFC-11, has the potential to replace CFC-11 in many applications. Nonetheless, commercial availability of HCFC-123 is limited at present, and it is unclear that industry can meet the relatively low interim OEL of 10 ppm set by the manufacturer. Nevertheless, recent worker monitoring studies indicate that an interim OEL of 10 ppm can be achieved through the use of increased ventilation, good housekeeping and work practices, and dust collection. Certain slabstock and other foams manufactured with HCFC-123 may be subject to the January 1, 1994 ban on Class II substance use in noninsulating foams. HCFC-123 is

subject to the phase-out of Class II compounds under section 605 of the CAA.

(b) HCFC-141b

HCFC-141b is acceptable as an alternative to CFC-11 in rigid polyurethane slabstock and other foams, provided that these foams are used for insulating or flotation purposes. Although its ODP of 0.11 is relatively high, HCFC-141b, because it can serve as a virtual drop-in substitute for CFC-11, offers almost immediate transition out of CFCs in this sector. Not only does HCFC-141b offer a technically feasible alternative to CFC-11, it is currently available in sufficient quantities to meet the demands of industry. The Agency will be proposing to restrict the use of HCFC-141b in the accelerated phase-out of HCFCs because other non-ODP substitutes should become available. The problem of toxic decomposition byproducts, although present, is controllable. With the exception of flotation foams, EPA believes that HCFC-141b is not acceptable for use in noninsulating applications, such as rigid polyurethane packaging or floral foams. The Agency has decided to allow the use of HCFC-141b in rigid polyurethane flotation foams until January 1, 1994, the effective date of the section 610 ban on Class II noninsulating foams manufactured with HCFCs becomes effective. HCFC-141b is also subject to the phase-out of Class II compounds under section 605 of the CAA.

(c) HCFC-22

HCFC-22 is acceptable as a substitute for CFC-11 in rigid polyurethane slabstock and other foams. HCFC-22 offers an alternative with significantly less potential to deplete ozone than either CFC-11 or CFC-12. However, significant process changes may be necessary to accommodate the low boiling point of HCFC-22. Certain slabstock and other foams manufactured with HCFC-22 may be subject to the January 1, 1994 ban on Class II substance use in noninsulating foams. HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(d) Hydrocarbons

Hydrocarbons, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, are acceptable alternative blowing agents for CFC-11 and CFC-12 in rigid polyurethane slabstock and other foams.

(e) Carbon Dioxide

Carbon dioxide is an acceptable alternative blowing agent for CFC-11 and CFC-12 in rigid polyurethane slabstock and other foams.

(5) Extruded Polystyrene Insulation Board. (a) HCFC-22

HCFC-22 is an acceptable alternative blowing agent for CFC-12 in extruded polystyrene boardstock foam. HCFC-22 offers an alternative with significantly less potential to deplete ozone than CFC-12. HCFC-22, however, has a relatively high permeation rate out of polystyrene thus affecting insulation performance. HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(b) HCFC-142b

HCFC-142b is an acceptable alternative blowing agent for CFC-12 in extruded polystyrene boardstock foam. HCFC-142b offers an alternative with significantly less potential to deplete ozone than either CFC-11 or CFC-12. HCFC-142b is subject to the phaseout of Class II compounds under section 605 of the CAA.

(c) HCFC-22/HCFC-142b

The HCFC-22/HCFC-142b blend is acceptable as a substitute for CFC-12 in extruded polystyrene boardstock foam. The blend offers an alternative with significantly less potential to deplete ozone than CFC-12. The blend is subject to the phase-out of Class II compounds under section 605 of the CAA.

(d) HFC-134a

HFC-134a is acceptable as a substitute for CFC-12 in extruded polystyrene insulation board foam. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-12 blowing agents in extruded polystyrene insulation board. HFC-134a, because of its low flammability and encouraging performance in toxicological testing, exhibits definite advantages from the standpoints of environmental risk and worker and consumer safety. However, HFC-134a has relatively high thermal conductivity and cost. In addition, the compound has poor solubility in polystyrene polymer, which could limit its usefulness as an alternative blowing agent from a technical standpoint.

(e) HFC-152a

HFC-152a is acceptable as a substitute for CFC-12 in extruded polystyrene insulation board foam. HFC-152a offers the potential for a non-ozone-depleting alternative to CFC-12 blowing agents in extruded polystyrene

boardstock. However, the high flammability of HFC-152a when combined with its properties of high thermal conductivity, low solubility in polystyrene polymer, and high permeability through polystyrene limit the extent to which HFC-152a is likely to replace CFC-12. Plant modifications may be needed to accommodate the flammability of HFC-152a, and foams blown with HFC-152a will need to conform with building code requirements that relate to flammable materials.

(f) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-12 in polystyrene insulation board foam. Of the hydrocarbons, pentane, isopentane, butane, and isobutane have been demonstrated as feasible blowing agents in polystyrene. In fact, hydrocarbons have been used for years in the manufacture of extruded polystyrene sheet products. However, hydrocarbons have several disadvantages as blowing agents in extruded polystyrene boardstock. Replacement of CFC-12 blowing agents with hydrocarbons is likely to reduce significantly the insulating efficiency of extruded polystyrene boards. Moreover, hydrocarbon-blown foams cannot presently attain the thickness that CFC-blown foams do. Controlling the flammability of hydrocarbons entails significant investment in plant conversion to accommodate them as alternatives to CFC-12. Also, foams blown with hydrocarbons will need to conform with building code requirements that relate to flammable materials. Finally, hydrocarbons are VOCs and must be controlled as such under Title I of the CAA.

(g) HCFC-22/Hydrocarbons

Blends of HCFC-22/hydrocarbons, for the reasons described and with the caveats outlined above for HCFC-22 and hydrocarbons, are proposed as acceptable substitutes for CFC-12 in extruded polystyrene boardstock foam.

(h) Carbon Dioxide

Carbon dioxide is an acceptable alternative blowing agent for CFC-12 in extruded polystyrene boardstock foam.

(6) Phenolic Insulation Board. (a) HCFC-141b

HCFC-141b, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-113 in phenolic insulation board.

(b) HCFC-142b

HCFC-142b, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, is acceptable as an alternative to CFC-11 and CFC-113 in phenolic insulation board.

(c) HCFC-22

HCFC-22, for the reasons described and with the caveats outlined in the section on rigid polyurethane commercial refrigeration foams, spray foams, and sandwich panels, is acceptable as an alternative to CFC-11 and CFC-113 in phenolic insulation board.

(d) HCFC-22/HCFC-142b

The blend HCFC-22/HCFC-142b, for reasons described above and with the caveats outlined above for HCFC-22 and HCFC-142b, is acceptable as an alternative to CFC-11 and CFC-113 in phenolic insulation board.

(e) Hydrocarbons

Hydrocarbons, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock, are acceptable alternatives to CFC-11 and CFC-113 in phenolic insulation board.

(f) HCFC-22/Hydrocarbons

HCFC-22/Hydrocarbon blends are acceptable a substitute for CFC-11 and CFC-113 in phenolic insulation board. HCFC-22/hydrocarbon blends offer an alternative with significantly less potential to deplete ozone than either CFC-11 or CFC-113. However, extensive plant modifications may be necessary to accommodate use of these blends. In addition, there are concerns about the potential for significant increases in thermal conductivity resulting from the replacement of CFC-11 and CFC-113 with a blend. Also, foams blown with hydrocarbons will need to conform with building code requirements that relate to flammable materials. Hydrocarbons are VOCs and must be controlled as such under Title I of the CAA, and HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(g) 2-Chloropropane

2-Chloropropane is acceptable as a substitute for CFC-11 and CFC-12 in phenolic insulation board. At present, because 2-chloropropane is a proprietary technology, its commercial availability may be limited. Moreover, 2-chloropropane is flammable and its use may require extensive modification of existing equipment.

(h) Carbon Dioxide

Carbon dioxide is an acceptable alternative blowing agent for CFC-11 and CFC-12 in phenolic insulation board.

(7) Flexible Polyurethane Foam. (a) Methylene Chloride

Methylene chloride is acceptable as a blowing agent in flexible polyurethane foams, provided that it is used in accordance with relevant OSHA standards and that its use meets future ambient air controls for hazardous pollutants under Title III of the CAA. Methylene chloride is already used as an auxiliary blowing agent in the manufacture of most flexible polyurethane slabstock foams and has proven adequate in yielding foams of many densities and degrees of softness. Replacement of CFC-11 or methyl chloroform blowing agents with methylene chloride can reduce the potential for stratospheric ozone depletion resulting from the production of flexible polyurethane foams.

Nevertheless, there is widespread concern over the potential health and safety hazards that methylene chloride poses. In fact, due to these concerns, some local and regional restrictions apply to the use of methylene chloride. To assess these risks in the application under discussion, EPA used data collected by the Occupational Safety and Health Administration (OSHA) for the proposed revision of the permissible exposure level (PEL) for methylene chloride. The Agency's estimate for total population risk for methylene chloride was based on average plant emissions derived from OSHA's values, and while not negligible, was within the range of existing Agency decisions on acceptable risk. The Agency solicits comment on risks associated with the use of methylene chloride in open-cell foam blowing. For further detail, refer to the background document entitled "Risk Screen on Use of Substitutes for Class I Ozone-Depleting Substances: Foams".

In light of toxicity concerns, the Agency has decided to allow the use of methylene chloride subject to existing or future restrictions. Methylene chloride use must meet all future ambient air controls for hazardous air pollutants under Title III of the CAA. In addition, use of the compound must conform to all relevant workplace safety standards; OSHA has proposed permissible exposure levels (PELs) for methylene chloride of 25 ppm on a time-weighted average (TWA).

(b) Acetone

Acetone is acceptable as a blowing agent for flexible polyurethane foams,

provided that it is controlled as a VOC under Title I of the CAA. In those areas where methylene chloride use is deemed unacceptable, acetone may provide another non-ODP alternative to CFC-11 and methyl chloroform. All grades of flexible polyurethane foam produced with CFCs can be produced using acetone as an auxiliary blowing agent. Acetone does not have an ozone depletion potential, its global warming potential is negligible. Nevertheless, acetone is highly flammable and its use requires special precautions to ensure adequate ventilation. In addition, the compound may be subject to controls as a VOC under Title I of the CAA.

(c) HCFC-123

HCFC-123, for the reasons described and with the caveats outlined in the section on rigid polyurethane laminated boardstock is acceptable as a blowing agent in flexible polyurethane foams.

(d) HFC-134a

HFC-134a is acceptable as a substitute for CFC-11 in flexible polyurethane foam. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in flexible polyurethane foam. The use of HFC-134a as a blowing agent in flexible polyurethane foams is currently not commercially feasible. Plant modifications may be necessary to accommodate the use of HFC-134a because its boiling point is lower than that of CFC-11. In addition, the cost of HFC-134a is high compared to CFC-11.

(e) HFC-152a

HFC-152a is acceptable as a substitute for CFC-11 in flexible polyurethane foam. HFC-152a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in flexible polyurethane foam. Process changes may be necessary to accommodate the use of HFC-152a, and plant modifications may be necessary to manage its flammability.

(f) AB Technology

AB Technology is acceptable as an alternative process in flexible polyurethane foams, provided that it is used in accordance with relevant OSHA standards. The AB Technology generates carbon monoxide as the chemical blowing agent. Actions to insure the safety of workers from exposure to elevated levels of carbon monoxide should be taken, particularly at the latter phases of production where ventilation is generally not as efficient as on the foam line. OSHA has set a permissible exposure level (PEL) for carbon monoxide of 35 ppm on a time-

weighted average (TWA) with a ceiling of 200 ppm.

(g) Carbon Dioxide

Carbon dioxide is an acceptable alternative process in flexible polyurethane foams.

(8) Polyurethane Integral Skin Foams. (a) HCFC-123

HCFC-123 is acceptable as an alternative to CFC-11 in integral skin foams. From the standpoint of technical feasibility, HCFC-123 represents a viable alternative to CFC-11 as a potential blowing agent in integral skin foams. More specifically, the physical properties and aging of foams blown with HCFC-123 are similar to those blown with CFC-11. As a result, HCFC-123, which has an ozone depleting potential significantly lower than that of CFC-11, has the potential to replace CFC-11 in many integral skin applications. Nonetheless, commercial availability of HCFC-123 is limited at present, and it is not clear that industry can meet the relatively low interim OEL of 10 ppm set by the manufacturer. Nevertheless, recent worker monitoring studies indicate that an interim OEL of 10 ppm can be achieved through the use of increased ventilation, good housekeeping and work practices, and dust collection. The use of HCFC-123 is subject to the provisions of section 610 of the CAA, which bans the use of Class II substances in noninsulating foams after January 1, 1994. The ban does not apply to certain integral skin foams used to provide for motor vehicle safety. HCFC-123 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(b) HCFC-141b

HCFC-141b is acceptable as an alternative to CFC-11 in integral skin foams used for automotive safety, although its use will be subject to the proposed accelerated phase-out of HCFCs. Although its ODP of 0.11 is relatively high, because it can serve as a virtual drop-in substitute for CFC-11, HCFC-141b offers almost immediate transition out of CFC-11 in integral skin foams. Not only does HCFC-141b offer a technically feasible alternative to CFC-11, but it is currently available in sufficient quantities to meet the demands of industry. The Agency has chosen to restrict the use of HCFC-141b in light of the fact that other non-ODP substitutes should become available. Section 610 of the CAA, which bans the use of Class II substances in noninsulating foams after January 1, 1994, excludes certain automotive safety foams from the ban. The allowable use

of HCFC-141b shall be limited to those integral skin foams excluded from the ban under section 610. HCFC-141b is currently subject to the phase-out of Class II compounds under section 605 of the CAA.

(c) HCFC-22

HCFC-22 is acceptable as a substitute for CFC-11 in integral skin foam, although its use will be subject to the proposed accelerated phase-out of HCFCs. HCFC-22 offers an alternative with significantly less potential to deplete ozone than CFC-11. However, process changes may be necessary to accommodate the low boiling point of HCFC-22. The use of HCFC-22 in integral skin foams shall be subject to section 610 of the CAA, which bans the use of Class II substances in noninsulating foams after January 1, 1994. The ban does not apply to certain foams used to provide for motor vehicle safety. HCFC-22 is also subject to the phaseout of Class II compounds under section 605 of the CAA.

(d) HCFC-22/HCFC-141b

HCFC-22/HCFC-141b blend, for reasons described and with the caveats outlined above for HCFC-22 and HCFC-141b, is an acceptable substitute for CFC-11 in integral skin foam used for automotive safety.

(e) HFC-134a

HFC-134a is acceptable as a substitute for CFC-11 in polyurethane integral skin foam. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in polyurethane integral skin foam. The use of HFC-134a as a blowing agent in flexible polyurethane foams is currently not commercially feasible. Plant modifications may be necessary to accommodate the use of HFC-134a because its boiling point is lower than that of CFC-11. In addition, the cost of HFC-134a is high compared to CFC-11.

(f) HFC-152a

HFC-152a is acceptable as a substitute for CFC-11 in polyurethane integral skin foam. HFC-152a offers the potential for a non-ozone-depleting alternative to CFC-11 blowing agents in polyurethane integral skin. Process changes may be necessary to accommodate the use of HFC-152a, and plant modifications may be necessary to manage its flammability. Also, foams blown with HFC-152a will need to conform with any requirements that relate to flammable materials.

(g) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-11 in integral skin foams. Hydrocarbons offer the possibility of a non-ODP replacement for CFC-11 in integral skin foams. However, the use of hydrocarbon blowing agents in integral skin foams is not commercially feasible at present. Moreover, extensive process modifications would be necessary to accommodate the flammability of hydrocarbons and to make the necessary technical and process modifications. Also, foams blown with hydrocarbons will need to conform with any requirements that relate to flammable materials. Hydrocarbons are VOCs and must be controlled as such under Title I of the CAA.

(h) Methylene Chloride

Methylene chloride is acceptable as a blowing agent in integral skin foam. See methylene chloride discussion under Polyurethane Flexible Foams for additional details on toxicity.

(i) Carbon Dioxide

Carbon dioxide is acceptable as a blowing agent in integral skin foams.

(9) Extruded Polystyrene Sheet Foam.

(a) HFC-134a

HFC-134a is acceptable as a substitute for CFC-12 in extruded polystyrene sheet foam. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-12 blowing agents in polystyrene sheet foam.

(b) HFC-152a

HFC-152a is acceptable as a substitute for CFC-12 in extruded polystyrene sheet foam. HFC-152a offers the potential for a non-ozone-depleting alternative to CFC-12 blowing agents in extruded polystyrene sheet foams. The compound is commercially available and its low molecular weight suggests that its blowing efficiency will be double that of CFC-12. Plant modifications may be needed to accommodate the flammability of HFC-152a.

(c) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-12 in extruded polystyrene sheet foam. Hydrocarbons offer the potential of a non-ozone-depleting alternative to the use of CFC-12 blowing agents in extruded polystyrene sheet. At present, pentane and butane are used extensively as blowing agents in extruded polystyrene sheet. These compounds are widely available at low cost and offer excellent solubility with the polystyrene polymer.

However, extensive plant modifications may be necessary to accommodate the use of hydrocarbons in place of CFC-12. In addition, hydrocarbons are VOCs and will be subject to control as such under Title I of the CAA.

(d) Carbon Dioxide

Carbon dioxide is acceptable as a substitute for CFC-12 in extruded polystyrene sheet foam.

(10) Polyolefin Foams. (a) HCFC-22

HCFC-22 is acceptable as a substitute for CFC-11, CFC-12, and CFC-114 in polyolefin foams. HCFC-22 offers an alternative with significantly less potential to deplete ozone than CFC-11, CFC-12, or CFC-114. The use of HCFC-22 in polyolefin foams may be restricted under section 610 of the CAA, which bans the use of Class II substances in noninsulating foams after January 1, 1994. HCFC-22 is subject to the phase-out of Class II compounds under section 605 of the CAA.

(b) HCFC-142b

HCFC-142b is acceptable as a substitute for CFC-11, CFC-12, and CFC-114 in polyolefin foams. HCFC-142b offers an alternative with significantly less potential to deplete ozone than CFC-11, CFC-12, or CFC-114. The use of HCFC-142b in polyolefin foams may be restricted under section 610 of the CAA, which bans the use of Class II substances in noninsulating foams after January 1, 1994. HCFC-142b is subject to the phase-out of Class II compounds under section 605 of the CAA.

(c) HCFC-22/HCFC-142a

HCFC-22/HCFC-142a blends are acceptable, for reasons described and the caveats outlined above, as a substitute for CFC-11, CFC-12 and CFC-114 in polyolefin foam.

(d) HFC-134a

HFC-134a is acceptable as a substitute for CFC-11, CFC-12, and CFC-114 in polyolefin foams. HFC-134a offers the potential for a non-ozone-depleting alternative to CFC-11, CFC-12, and CFC-114 in polyolefin foams. HFC-134a, because of its low flammability and encouraging performance in toxicological testing, exhibits definite advantages from the standpoints of environmental risk and worker and consumer safety.

(e) HFC-152a

HFC-152a, for the reasons described and with the caveats outlined in the section on extruded polystyrene sheet foam, is acceptable as an alternative to

CFC-11, CFC-12, and CFC-114 in polyolefin foams.

(f) Hydrocarbons

Hydrocarbons are acceptable as substitutes for CFC-11, CFC-12, and CFC-114 in polyolefin foams. Use of hydrocarbon blowing agents in polyolefin foams is not now commercially feasible. Extensive plant modifications may be necessary to accommodate hydrocarbon use due to flammability and technical considerations. Finally, hydrocarbons are VOCs and must be controlled as such under Title I of the CAA.

(g) HCFC-22/Hydrocarbons

HCFC-22/hydrocarbons blends, for the reasons described and with the caveats outlined above, are acceptable substitutes for CFC-11, CFC-12 and CFC-114 in polyolefin foams.

(h) Carbon Dioxide

Carbon dioxide is acceptable as a substitute for CFC-11, CFC-12, and CFC-114 in polyolefin foams.

b. *Proposed Unacceptable Substitutes.* The final listing of a foam blowing agent as unacceptable in a specific foam use sector constitutes a ban on the use of that alternative to Class I or Class II compounds in commerce. The Agency solicits comments on these proposed decisions. These decisions will be effective 30 days after publication of the final rule.

(1) Rigid Polyurethane Slabstock and Other Foams (Rigid Polyurethane Packaging Foams). (a) HCFC-141b

The use of HCFC-141b (or blends thereof) is proposed unacceptable as an alternative blowing agent in rigid polyurethane packaging foams with the exception of insulating and flotation foams. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives, or alternatives with lower ODPs, are sufficiently available to render the use of HCFC-141b unnecessary in this application.

(2) Flexible Polyurethane Foams. (a) HCFC-141b

The use of HCFC-141b (or blends thereof) is proposed unacceptable as an alternative blowing agent in flexible polyurethane foams. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives are sufficiently available to render the use of HCFC-141b unnecessary in this application.

(3) Integral Skin Foams. (a) HCFC-141b

Use of HCFC-141b (or blends thereof) is proposed unacceptable as an alternative blowing agent in integral skin foams, except where used for the purpose of motor vehicle safety. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives, or alternatives with lower ODPs, are sufficiently available to render the use of HCFC-141b unnecessary in this application. However, the use of HCFC-141b will be allowed in those integral skin automotive foams excluded from the ban on noninsulating foams under section 610 of the CAA.

(4) Polyolefin Foams. (a) HCFC-141b

The use of HCFC-141b (or blends thereof) is proposed unacceptable as an alternative blowing agent in polyolefin foams. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives, or alternatives with lower ODPs, are sufficiently available to render the use of HCFC-141b unnecessary in this application.

F. Solvents Cleaning

1. Overview

On an ozone-depletion weighted basis, solvents constitute approximately 15 per cent of the chemicals targeted for phase-out under the Montreal Protocol. In the U.S., the two Class I chemicals used as industrial solvents are CFC-113 ($C_2F_3Cl_3$ —trifluorotrchloroethane) and methyl chloroform ($C_2H_3Cl_3$ —1,1,1-trichloroethane). The SNAP determinations proposed today focus on substitutes for these chemicals when used as industrial cleaning solvents, since this application comprises the largest use of CFC-113 and methyl chloroform (MCF).

Other cleaning applications for CFC-113 and MCF exist as well, such as in dry cleaning of textiles. In addition, these solvents are used as bearer media (such as lubricant carriers), mold release agents, component testing agents, coolants, or in other non-cleaning applications. For the reasons described earlier in this Preamble, the Agency proposes to exclude substitutes for these smaller uses from the SNAP determinations. As a result, the Agency is not at this time issuing any determinations on acceptability of such substitutes, and will neither approve nor restrict their uses.

The three major cleaning applications that use CFC-113 and MCF are metals cleaning, electronics cleaning, and

precision cleaning. Metals cleaning applications usually involve removing cutting oils and residual metal filings. This sector relies principally on MCF as a cleaning solvent. In contrast, the electronics industry uses principally CFC-113, for instance, to remove flux residues left after mounting parts on printed circuit boards. Precision cleaning also uses mostly CFC-113. This last application comprises a broad category of industrial cleaning operations and can cover uses ranging from cleaning pacemakers to cleaning direct access storage devices on computers.

Appendix B at the end of this Preamble lists in tabular form the Agency's proposed determinations on substitutes in the cleaning sector. These proposed determinations are based on the risk screen described in the draft background document entitled "Risk Screen on the Use of Substitutes for Class I Ozone-Depleting Substances: Solvent Cleaning." The table also includes as "pending" a number of substitutes that the Agency will issue determinations on in the next round of SNAP analyses. This table was compiled in part based on information on substitutes that companies submitted to the Agency in response to the January 16, 1992, Advance Notice of Proposed Rulemaking. In some cases, the Agency did not have adequate engineering or environmental information on these substitutes to permit a SNAP determination. Vendors or users of cleaning substitutes not described in Appendix B should submit information on these uses, so that the Agency can issue a SNAP determination.

In general, the solvents cleaning industry has been extremely successful at finding non-ozone-depleting alternatives to cleaning with CFC-113 and MCF. Numerous alternatives are already commercially available, and ongoing research and development promises to generate additional innovative solutions. The most creative approaches focus on changing the manufacturing process to remove the cleaning stage altogether. This change, in which producers rely on "no-clean" technologies, embodies one of the success stories in the search for alternatives—a pollution prevention approach that relies on cutting out the manufacturing step that creates the environmental problem rather than simply transferring the pollutants from one medium to another. The electronics industry in particular has many such cleaning alternatives that eliminate the need for CFC-113 and MCF. In metals cleaning, few "no-clean" alternatives are currently available, since the

manufacturing process is so heavily dependent on the use of oils as lubricants. However, no-clean approaches and products, such as vanishing oils, are being developed for cleaning metal parts and may soon be more broadly available.

Finding alternatives for CFC-113 and MCF in precision cleaning has been more difficult. Here, the industry has tried where possible to find and implement other cleaning options, but in some cases currently available alternatives simply do not meet the performance or safety criteria that would permit them to be used successfully.

2. Alternatives in Solvents Cleaning

a. Hydrochlorofluorocarbons (HCFCs) HCFC-141b or HCFC-141b blends with alcohols are the principal HCFC alternative solvents to CFC-113/MCF cleaning. These alternatives can be used in vapor degreasing equipment, principally for electronics or precision cleaning, and in some cases existing CFC-113 or MCF equipment can be retrofitted for use with HCFC-141b alternatives. From an environmental standpoint, the critical characteristic of HCFC-141b is that it has a relatively high ODP—0.11—the highest of all the HCFCs.

Another HCFC, HCFC-123, is generally not considered to have widespread application as a cleaner. Although this HCFC has the capacity to remove many soils, it is such an aggressive cleaner that it frequently degrades the surface of the part being cleaned. Additionally, toxicity concerns have limited commercial interest in HCFC-123 as a cleaning substitute. The Agency is currently investigating whether industry exposure standards for HCFC-123 can be met, and has therefore listed this chemical as "pending" approval.

HCFC-225, a third HCFC, is widely viewed as having potential as a cleaner, especially for precision cleaning. However, this chemical is not yet in widespread production or use. Further, HCFC-225 is still undergoing toxicity testing. Preliminary findings suggest that of the two HCFC-225 isomers, HCFC-225ca and HCFC-225cb, toxicity concerns associated with the ca-isomer may limit its commercial viability.

b. Semi-Aqueous Cleaning. Semi-aqueous cleaning is an alternative for cleaning in all three cleaning sectors. This process employs hydrocarbon/surfactant cleaners either emulsified in water solutions or applied in concentrated form and then rinsed with water. Since both approaches involve water as part of the formulation, the

process is commonly referred to as "semi-aqueous." The principal categories of chemicals used in this process are terpenes, petroleum distillates, or alcohols. Surfactants are sometimes added to the formulation to increase wetting, emulsification and rinsing properties. Within each category of compounds, formulators draw from a wide variety of specific chemicals. For example, even though terpene-based cleaning often uses d-limonene, other terpene cleaners formulated with terpineols or terpinenes exist. A similar range of choices is available when selecting the surfactant.

To characterize environmental releases, EPA developed model processes intended to represent generic semi-aqueous cleaning scenarios. The purpose of developing the model processes was to portray the average use scenario, rather than to depict specific examples of cleaning applications. An extensive discussion of various semi-aqueous cleaning processes may be found in the Industry Cooperative for Ozone Layer Protection (ICOLP) documents on the subject.

c. Aqueous Cleaning. Aqueous cleaning, unlike semi-aqueous cleaning, uses water as the primary solvent. This process is used mostly for metals cleaning, but companies are beginning to explore options using these substitutes in other cleaning applications.

In aqueous cleaning, detergents and surfactants are combined in water with a variety of additives such as organic solvents (e.g., high-boiling point alcohols), builders, saponifiers, inhibitors, emulsifiers, pH buffers and anti-foaming agents. Builders such as alkaline salts usually make up a large portion of the formulation (other than water), and they are often used in blends of several chemicals. Surfactants comprise the other major portion; these chemicals are chosen for their detergent, emulsification or wetting properties.

The cleaning process is comparable to that used in semi-aqueous applications and consists of combinations of a wash phase, a rinse phase, and a drying phase. An important difference is that the wash tank is frequently heated to improve soil removal. The final step, drying, can be accomplished by use of heat or a drying agent.

A critical feature of aqueous cleaning, as with semi-aqueous cleaning, is the wide variety of chemicals chosen for the formulations. For each cleaning need, a vendor can tailor a formulation to the soils and parts—a process that produces innumerable combinations of chemicals in different concentrations. To capture this diversity, the Agency has chosen to

adopt a screening approach that parallels the methodology described in the section on semi-aqueous cleaners.

d. Organic Solvents. Organic solvents can be used to replace CFC-113 and MCF in certain cleaning operations. The classification of organic solvents typically includes conventional organic solvents such as alcohols, ethers, esters and ketones. These compounds are commonly used in solvent tanks at room temperature, although the solvents can also clean in in-line systems or be heated to increase solvency power. If heated, the solvents must be used in equipment designed to control vapor losses.

These solvents, unlike Class I and II compounds, do not contribute to stratospheric ozone depletion, and generally have short atmospheric lifetimes. Yet many of the organic solvents are regulated as VOCs because they can contribute to ground-level ozone formation. In addition, certain of the organic solvents are toxic to human health and are subject to workplace standards set by OSHA.

e. Other Chlorinated Solvents. In addition to MCF and CFC-113, the three other commonly used chlorinated solvents are trichloroethylene ("TCE"), methylene chloride ("meth"), and perchloroethylene ("perc"). Unlike MCF and CFC-113, these chlorinated solvents have very short atmospheric lifetimes and are not considered to contribute to ozone depletion. However, all three have known toxicity problems and are regulated as Hazardous Air Pollutants under Title III of the Clean Air Act. They are also subject to stringent workplace standards set by the Occupational Health and Safety Administration. Additionally, TCE and perc exhibit photochemical reactivity, and are regulated as smog precursors.

The phase-out of CFC-113 and MCF has prompted a renewed interest in meth, TCE, and perc, despite these toxicity concerns. The three solvents are mostly viewed as potential metal cleaning substitutes, especially since they can be used in conventional vapor degreasing equipment. In fact, these three solvents were the preferred industrial solvents until concerns about their toxicity and anticipated lowering of the Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs) resulted in a switch by some users to MCF.

In response to such concerns, equipment vendors have now developed processes for using these solvents that significantly limit their emissions. The availability of such equipment has prompted environmental agencies in other western countries, such as

Germany, to relax restrictions on the use of these chemicals. Such equipment, although expensive, can now be purchased in the United States.

f. No-Clean Alternatives. No-clean alternatives involve the use of fluxes or cutting oils that need not be removed after the manufactured part is fully formed. It offers an efficient solution to the cleaning problem, since it sidesteps the cleaning process altogether. Water-removable products are products where the soils or fluxes can be removed using water as opposed to other types of solvents. In electronics cleaning, where these two approaches are in more widespread use, no-clean or water-removable alternatives rely either on special fluxes or on a soldering process that eliminates or reduces the residues otherwise removed through the cleaning step.

g. Perfluorocarbons. Perfluorocarbons (PFCs) are fully fluorinated compounds, unlike either CFCs, HCFCs or HFCs. These compounds are being discussed as part of innovative cleaning processes to replace ozone-depleting solvents. These processes would use an aqueous or solvent cleaner bath with a PFC vapor zone for rinsing and/or drying. Although these processes have the technical potential to meet a number of cleaning needs, the expense of the PFCs may limit wide-spread commercial interest in processes that use these compounds.

The principal environmental characteristic of concern for the PFCs is that they have extremely long atmospheric lifetimes, often orders of magnitude longer than the CFCs. Environmental concerns associated with use of PFCs are discussed in the refrigerants chapter. Technology for containment and recycling of PFCs is commercially available and is recommended by manufacturers to offset any possible adverse environmental effects.

h. Monochlorotoluene/chlorobenzotrifluorides. Monochlorotoluene and chlorobenzotrifluorides are of commercial interest as solvent substitutes in a variety of cleaning applications. These compounds can be used either in isolation or in various mixtures, depending on desired chemical properties. The Agency recently received information on these formulations, and will issue a SNAP determination for these substitutes in the next set of listing decisions.

i. Volatile Methyl Siloxanes. Cyclic and linear volatile methyl siloxanes (VMSs) are currently undergoing investigation for use as substitutes for Class I compounds in electronics and

precision cleaning. Because of their chemical properties, these compounds show promise as substitutes for cleaning precision guidance equipment in the defense and aerospace industries. In addition, the volatile methyl siloxanes have high purity and are therefore relatively easy to recover and recycle. In the cleaning process using VMS, the fluids are used to clean parts in a closed header system using a totally enclosed process. The parts are drained and then dried using vacuum baking.

j. Supercritical Fluid Cleaning, Plasma Cleaning, UV-Ozone Cleaning. Supercritical fluid cleaning, plasma cleaning, UV-ozone cleaning are all three high-technology methods of cleaning parts. These substitutes are mostly of interest for cleaning electronic parts or for precision cleaning.

k. Brominated Hydrocarbons. The Agency recently received notification that brominated hydrocarbons can be used as substitute cleaning agents, and will issue a SNAP determination on these chemicals in the next set of listing decisions.

3. Preliminary Listing Decisions

a. Acceptable Substitutes. (1) Metals Cleaning.—(a) Semi-Aqueous/Aqueous Processes. *Semi-aqueous and aqueous processes are approved as substitutes in metals cleaning.* The determinations in this action cover semi-aqueous processes using terpenes, petroleum distillates, and alcohols.

To complete its modeling of the ability of aqueous and semi-aqueous substitutes to replace CFC-113 and MCF in existing applications, the Agency examined their ability to meet the cleaning requirements posed in the metals cleaning sector. Each of these alternatives has the potential to service as much as 70 percent of the metals cleaning market. To date, companies have shown the greatest interest in aqueous cleaners for metals cleaning, which is why the Agency has made every effort to include review of this option in its first round of SNAP determinations.

The concern with the water-based processes has historically been the potential for adverse effects on aquatic life following discharge of wastewaters to surface water bodies. Examples of these effects include death to aquatic microorganisms, fish teratogenicity, or ecosystem effects such as inhibition of algal growth or bioconcentration. In this case, the Agency wanted to ensure that, in restricting the use of CFC-113 and methyl chloroform, it would not simply be replacing risks from air emissions with equal risks from contaminated water effluent.

To complete its risk analysis for the aqueous and semi-aqueous cleaners, the Agency developed a screening methodology designed to characterize risks presented by typical processes using these cleaners. The diversity of chemicals used in aqueous and semi-aqueous cleaning formulations turned this exercise into a complex undertaking. To complete its screen, the Agency projected concentrations in water for the "worst" or most toxic chemical that could be used in the water-based processes. These concentrations were based on the maximum possible concentration in the formulation and case studies documenting actual release profiles for several sample processes. The predicted concentrations obtained using this approach were then compared with toxicity values for this "worst" chemical.

The risk screen performed by the Agency did show a potential for adverse effects on aquatic life due to the inherent toxicity of chemical constituents in the cleaners. These findings point to the need to control unnecessary and irresponsible discharge of these chemicals.

However, the Agency believes that most risks presented by use of water-based processes can be controlled by adhering to requirements for wastewater treatment imposed by municipal or state authorities. In addition, the screen performed by the Agency that indicated the possibility of risks to aquatic life is likely to have overstated potential risks. For example, the screen did not account for several complex biological processes, including biodegradation and volatilization. The Agency is developing scientific studies to address these factors, and believes that once these factors are incorporated that the risk screen will demonstrate clearly that the water-based processes present acceptable risks to aquatic life.

The Agency believes that this approach to screening risks, although it does not examine the toxicity of each chemical and mixture or project exposures for each possible process, provides adequate perspective on the risks of these compounds compared with risks from the CFCs. The Agency solicits comment on this approach and data that could help refine the analysis of individual chemicals and mixtures. For example, the Agency's analysis did not specifically examine risks from mixtures of various chemicals where there could be synergistic effects. Although the Agency does not anticipate that such data would change the decision to list these substitutes as acceptable, the Agency hopes that a

better understanding of ecological effects of such substitutes will enhance its ability to assist users in choosing among substitutes and among formulations.

In an effort to further assist users in choosing substitutes with low environmental impacts, the Agency is currently developing a list of chemicals commonly used in the types of cleaners deemed acceptable under the SNAP program. The Agency encourages companies to ensure that substitutes sold as CFC-113/MCF replacements be formulated based on this list.

In addition, the Agency urges companies to adopt closed-loop recycling and recovery systems wherever possible to limit discharge of these chemicals. Users should also note that EPA is preparing new effluent guidelines under the Clean Water Act for this industry. These guidelines, expected to be issued by 1994, will address any remaining, uncontrolled risks deriving from the use of water-based cleaners in this industry.

(b) Organic Solvents. *Organic solvents are acceptable substitutes for CFC-113 and MCF in the metals cleaning sector.* Although these compounds can be toxic to human health, and are considered VOCs, the Agency's risk screen shows that these risks can be addressed through existing regulatory controls. In occupational settings where toxicity is a concern, such as for acetone or for certain ketones, OSHA has set Permissible Exposure Limits designed to control any risks.

Similarly, controls exist for sources of VOC emissions, and the Agency's analysis indicates that increased use of the organic solvents would increase VOC levels in the troposphere by only very small amounts.

(c) Other Chlorinated Solvents. *Trichloroethylene (TCE), perchloroethylene (perc) and methylene chloride (meth) are all acceptable substitutes for CFC-113 and MCF in the metals cleaning sector.* These alternatives have the chemical properties to meet the cleaning needs of up to 80 percent of the metals cleaning sector, although the Agency anticipates that the actual market share for the non-ozone-depleting chlorinated solvents will not expand to the maximum extent feasible.

Because of the high toxicity of these compounds, they have the potential to pose risks to workers and residents in nearby communities. However, the Agency's analysis of use of these compounds as cleaning agents indicates that these risks can be controlled by adhering to existing regulatory standards. OSHA has determined, for

instance, that it is possible to use these solvents in a manner that minimizes risks to workers. To reach this conclusion, OSHA conducted extensive analyses of the toxicity and technical feasibility of using perchloroethylene, trichloroethylene, or methylene chloride (54 FR 2329-2984, January 19, 1989, and 56 FR 57036-57141, November 7, 1991). OSHA found that the new Permissible Exposure Limit (PEL) of 50 ppm for trichloroethylene was feasible in metal cleaning operations (54 FR 2433) and after conducting an extensive study of metal degreasing control technologies, NIOSH concluded that an exposure limit of 25 ppm for TCE could also be achieved. More recently, in its proposed standard for methylene chloride, OSHA found that a PEL of 25 ppm is technically feasible during metal cleaning operations with the use of appropriate local exhaust ventilation and work practices.

Additionally, the Agency is in the process of addressing residual risks to the general population under Title III of the new Clean Air Act. Title III requires EPA to establish Maximum Achievable Control Technology (MACT) standards for use of Hazardous Air Pollutants (HAPs). All three non-OD chlorinated solvents are listed as HAPs, and the Agency expects to issue MACT rules governing their use as solvent cleaning agents by 1994.

The Agency also believes that risks from waste generation due to use of these solvents are unlikely to be significantly different from risks of waste disposal of spent CFC-113 and methyl chloroform. The risks from spent cleaning solvents derive in large part from the soils removed in the cleaning process. Since the composition of the soils would not change as a result of substitution, risks are also not expected to increase significantly.

The Agency also notes that the voluntary "33/50" program is encouraging companies to decrease emissions of TCE, perc, and meth, in addition to 14 other specific chemicals. Participating companies voluntarily commit to decreasing emissions 33 per cent by the end of 1992 and 50 per cent by the end of 1995, using pollution prevention strategies. The Agency is committed in the long term to urge companies to participate in pollution prevention programs such as "33/50", and continue to find new ways to use and emit less polluting and lower toxicity compounds. The Agency requests comment on the decision to list these compounds as acceptable substitutes for CFC-113 and MCF.

(2) Electronics Cleaning (a) Semi-Aqueous/Aqueous Cleaners

In the area of electronics cleaning, semi-aqueous and aqueous cleaners were deemed to be acceptable substitutes. The justification for this determination is described in the section on metals cleaning. In this case, the Agency estimated that up to eighty per cent of the cleaning market could be captured by semi-aqueous processes and that up to 60 per cent of the market could be served by aqueous cleaners.

As in metals cleaning, the Agency urges companies to adopt pollution prevention practices and to formulate cleaners based on the cleaner constituent list.

(b) No-Clean Substitutes. *No-clean processes are acceptable substitutes for ozone-depleting chemicals used in electronics cleaning.* The Agency's analysis estimates that, over time, as much as seventy per cent of the electronics cleaning market could switch to no-clean processes—a projection that is borne out by the high degree of interest shown by electronics companies in these substitutes.

Concerns for risks deriving from use of no-clean processes focus primarily on worker safety. To examine these risks, the Agency looked at critical factors that distinguish no-clean processes from conventional electronics assembly. These differences center on changes in the proportions of chemicals used in formulations, rather than on differences in the identity of chemicals selected. The analysis determined that occupational risks deriving from these differences are already well-documented and controlled, for example, through requirements specified on key Materials Safety Data Sheets and existing workplace regulations implemented by OSHA.

Additionally, the shifts in proportions of chemicals used in the formulation result in less waste than is normally generated through the traditional manufacturing process, resulting in a lower probability of adverse effects to the general population. The Agency also investigated the production of waste before and after the actual cleaning process and found that waste generation at these points in the production process would not be affected.

(c) Organic Solvents. *Organic solvents are acceptable substitutes for CFC-113 and MCF in the electronics cleaning sector.* The Agency's justification for this decision is described in the section on acceptable substitutes for metals cleaning.

(d) Other Chlorinated Solvents. *Trichloroethylene (TCE),*

perchloroethylene (perc) and methylene chloride (meth) are all acceptable substitutes for CFC-113 and MCF in the electronics cleaning sector, for the reasons described in the metals cleaning discussion. Although these solvents have not received as much commercial interest for electronics cleaning as for metals cleaning applications, the Agency did receive a request to review and approve these chemicals for electronics cleaning.

Although the Agency's risk screen focused on use of these chemicals in metals cleaning operations, the screen suggests that release profiles for these chemicals in electronics cleaning will be either the same or lower. As a result, the Agency has reached the same conclusion in the metals cleaning analysis, namely that any risks due to the inherent toxicity of these chemicals could be controlled by existing and future regulatory standards.

However, the Agency has received some indication from industry experts that these solvents do not fill any special cleaning niche for the electronics industry. Based on a desire to control any unnecessary use of chemicals with such high inherent toxicity, the Agency requests comment on the availability of other alternatives and on whether there is a genuine need to use these chemicals in electronics cleaning applications.

(e) Perfluorocarbons. Use of perfluorocarbons (PFCs) in spot-free cleaning and drying of high-performance computer components is an acceptable substitute in cases where no other alternative exists that meets performance or safety standards. This would not include defluxing of printed circuit boards or cleaning of standard metal parts, since many other viable alternatives exist for these applications.

Global warming concerns associated with PFC use are discussed in the refrigerants chapter. Despite these concerns, the Agency has listed this niche application as an acceptable use of perfluorocarbons because it is aware that, for certain computer components, a PFC-based process may be the only viable process available to replace use of Class I or II compounds.

For example, in manufacture of certain direct access storage devices (DASDs) for computers, spot-free cleaning and drying using PFCs appears at the present time to be the only cleaning process that yields the necessary product performance (as opposed to cosmetic appearance). To make the technical improvements demanded of the storage devices, such as faster access times and higher recording densities, companies have

been required to use magnetically superior materials. These materials are extremely prone to corrosion from water and are vulnerable to any contamination introduced in the manufacturing process, such as organic or particulate matter. Consequently, the storage device itself must be a miniature "clean room" if it is to perform correctly. Manufacturers of some DASDs can use water-based cleaners in much of the production process, but may need to rely on the PFCs as water-displacement agents to achieve the required high degree of cleanliness while protecting the water-sensitive materials in the device.

Another example of components where PFC-based cleaning may be necessary is data storage media.

In cases where users must rely on PFCs due to lack of other options, they should make every effort to:

- Adopt closed systems and recover, recycle and destroy where possible
- Reduce emissions to a minimum through conservation practices that address idling losses, liquid dragout, and operator variables
- Continue to search for long-term alternatives.

Examples of appropriate measures to reduce emissions include freeboard chillers, welded piping, and programmable handling devices. The Agency believes that it is reasonable to expect users to achieve favorable CFC/PFC replacement ratios since PFCs have relatively higher boiling points. In addition, the high price of PFCs makes additional containment cost-effective.

Prospective users should also note that companies investigating PFC use currently contend that within 3-8 years, it will be possible to replace the PFCs in cleaning equipment with other chemicals that have zero ozone depletion potential and very low global warming potential. As a result, they view use of the PFCs as an important but transitional solution to their cleaning needs. If PFCs are chosen, it is important for users to begin working with chemical manufacturers to start testing and qualifying these new materials to help speed conversion when the chemicals become commercially available.

In addition to the case cited earlier, the Agency is examining other possible necessary uses for PFCs as rinse agents to follow a water-free cleaning process or as drying or rinsing agents to follow a water-based cleaning process. Parts typically cleaned in these applications are characterized by vulnerable substrates, complex geometries, and exceptionally stringent cleanliness standards and include:

- Precision mechanical or electro-mechanical parts such as gyroscopes and accelerometers with complex structures and capillary spaces that could trap water or solvent residue
- Plastic parts with embedded iron or parts made from steel, lead or other materials subject to corrosion, oxidation or other damage from water (e.g., gallium arsenide, silicon nitride or magnesium parts)
- Plastic parts for the medical industry where extremely rigorous standards of cleanliness are necessary to ensure patient survival (e.g., kidney dialysis, implants, etc.)
- Electro-optical devices for weapon-targeting systems
- Ceramic or other porous materials for military, medical, safety or other high-value products, where any conductive residue could interfere with the component's performance
- Temperature-sensitive materials that cannot maintain component integrity at aqueous drying temperatures (e.g., where loss of dimensional stability is at issue)
- High-performance analytical devices where any residue could interfere with equipment accuracy.

The Agency solicits comment on the need to use PFCs in these applications or in any other specialized cleaning applications. In addition, the Agency seeks comment on the availability, performance, and economic feasibility of any cleaning alternatives that would eliminate the need for PFCs in these applications.

(f) Supercritical Fluid Cleaning, Plasma Cleaning, UV-Ozone Cleaning. Supercritical fluid cleaning, plasma cleaning, UV-ozone cleaning are all approved as substitutes in electronics cleaning. The Agency did not identify any environmental issues associated with use of these substitutes. Ozone is hazardous to human health, however, the Occupational Safety and Health Administration has already set standards for use of this compound in the workplace.

(3) Precision Cleaning. (a) Semi-Aqueous/Aqueous Processes.

Semi-aqueous and aqueous processes are approved for precision cleaning. The reasons for this decision are the same as those described in the metals cleaning section. Each of these alternatives has the potential to service approximately 65 per cent of the precision cleaning market. This figure may overestimate the technical potential for water-based processes in this sector, since industry feedback indicates that this end use sector faces the greatest technical

constraints in implementing new cleaning alternatives.

The Agency did not specifically examine risks from water-based processes used in precision cleaning. Instead, the analysis assumed that these risks would be either comparable to or less than risks associated with use of water-based processes for electronics cleaning.

(b) Other Chlorinated Solvents. *These alternatives, for reasons described in the section on metals cleaning, are deemed acceptable substitutes for precision cleaning.* For the analysis of risks from these substitutes in the precision cleaning end use sector, the Agency made the same assumptions as in its analysis for electronics cleaning applications of water-based processes, namely that exposures would be equal or less than exposures in the metals cleaning sector. Consequently, the Agency believes that risks would also be either equal or less.

(c) Organic Solvents. *Organic solvents are acceptable substitutes for CFC-113 and MCF in the precision cleaning sector.* The Agency's justification for this decision is described in the section on acceptable substitutes for metals cleaning.

(d) Perfluorocarbons. *Use of perfluorocarbons (PFCs) in spot-free cleaning and drying of high-performance computer components is an acceptable substitute in cases where no other alternative exists that meets performance or safety standards.* This would not include deflusing of printed circuit boards or cleaning of standard metal parts. While the Agency is concerned about increased uses of PFCs due to global warming concerns as discussed in the refrigerants chapter, it believes that cases exist where a PFC-based process may be the only process available to replace use of Class I or II compounds. These cases are discussed in the section on acceptable substitutes for electronics cleaning.

(e) Supercritical Fluid Cleaning, Plasma Cleaning, UV-Ozone Cleaning. *Supercritical fluid cleaning, plasma cleaning, UV-ozone cleaning are all approved as substitutes in precision cleaning.* The Agency did not identify any environmental issues associated with use of these substitutes. Ozone is hazardous to human health, however, the Occupational Safety and Health Administration has already set standards for use of this compound in the workplace.

b. Proposed Unacceptable Substitutes

(1) Metals Cleaning. (a) HCFC-141b and its Blends

HCFC-141b and its blends are proposed to be prohibited as substitutes for CFC-113/MCF in metals cleaning, with limited critical use exceptions for CFC-113 replacements. The proposed effective date for this prohibition is 30 days after the date of the final rule for new equipment and as of January 1, 1996, for existing equipment. As discussed earlier in this action in Section VI.A., the Agency is authorized to grandfather existing uses from a proposed prohibition where appropriate under the four-part test established in *Sierra Club v. EPA*, supra.

The Agency has conducted the four analyses required under this test, and it has concluded that the balance of equities favors a grandfathering period of two years for existing equipment in this application. The prohibition proposed in this action clearly represents a departure from previously established practice, as use of the substitute was allowed previously. Existing users of HCFC-141b who switched from Class I substances into this solvent invested in this substitute on the assumption that it would be a sufficient improvement. Prohibiting their use of the substitute immediately would impose a severe economic burden on these users. These factors taken together outweigh any statutory interest in applying the new rule immediately to existing users. This is especially true since the restriction applies immediately to new equipment using HCFC-141b, which creates no incentive for continued investment in equipment using HCFC-141b in this application.

The Agency's basis for proposing to restrict use of HCFC-141b is that this compound has a comparatively high ODP—0.11. This is the highest ODP of all the HCFCs; in fact, the ODP for 141b is nearly equal to the ODP for MCF (0.12). For this reason, the Agency proposes not to grant any exceptions for replacing MCF with 141b, since using 141b in place of MCF would negate the environmental benefits that the phase-out was designed to achieve.

To analyze the impacts from use of 141b as a CFC-113 replacement, the Agency estimated 141b use over time in each of the cleaning end uses, and projected health effects due to ozone depletion with the help of the Atmospheric Stabilization Framework model. The modeling period starts in 1990 and measures health effects expected for people born before 2030.

The findings of this modeling show adverse health effects of the magnitude commonly associated with the use of ozone-depleting compounds. For example, in the case of metals cleaning, the Agency projected that use of HCFC-141b to replace MCF where technically feasible could yield approximately 40,000 additional skin cancer cases and approximately 1,000 additional skin cancer fatalities compared to use of non-ozone-depleting substitutes.

The Agency believes that these figures and the availability of superior substitutes as described in the section on acceptable substitutes justify the proposal to list 141b as an unacceptable substitute. The Agency believes that, in almost all applications, other solvent cleaning substitutes are available that meet industry performance and safety criteria. To reach its decision on 141b use, the Agency also took into account the cost of other alternatives. The analysis suggested that, although 141b can be used with modification to existing equipment, the capital costs for the retrofit and the materials costs in combination would be so high as to render other alternatives comparatively affordable, even though they require new equipment.

Readers should note that 141b will be restricted as a substitute only where other alternatives exist to CFC-113 for the application in question. Several companies have already contacted the Agency, indicating that they have tested available alternatives to CFC-113, and that in some cases only HCFC-141b meets performance or safety criteria. The most commonly cited reasons for needing to use HCFC-141b are either applications where a non-flammable solvent is required for cleaning operational equipment or where sensitive parts could be destroyed by use of other cleaning processes.

For these applications of 141b, which the Agency refers to as "critical uses," users may receive an exemption from the SNAP restrictions. Procedures for receiving a critical use exemption are described in Section VIII.F. of today's Preamble. Companies interested in these exemptions who believe they may qualify are encouraged to review this section. Companies who have already notified the Agency and requested permission for continued use of 141b will be contacted after this proposal so that the Agency can issue a formal critical use determination.

Companies should note that uses of 141b in existing solvent cleaning equipment would be permitted to continue until two years after the date of the final rule, as discussed above. The

Agency solicits comment on the proposed effective date.

The Agency believes that the decision to restrict 141b use as a CFC-113/MCF substitute for metals cleaning will have little effect on industry since few vendors of HCFC 141b have been selling 141b as a metals cleaning substitute. Companies in this end use sector that want to replace CFC-113 with 141b and feel they qualify for an exemption should review the section referenced above. The Agency expects to receive few such petitions, however, since most metals cleaning is currently performed with MCF.

(2) Electronics Cleaning. (a) HCFC-141b and its Blends

HCFC-141b and its blends are proposed to be prohibited as substitutes for CFC-113/MCF in electronics cleaning, with limited critical use exceptions for CFC-113 replacements. The reasons for this prohibition are the same as those for the decision on 141b as a metals cleaning substitute. As in the metals cleaning sector, the Agency proposes to grant limited critical use exemptions to this prohibition. The proposed effective date for this prohibition is 30 days after the date of the final rule for new equipment and January 1, 1996 for existing equipment. As discussed earlier in this action in Section VI.A., the Agency is authorized to grandfather existing uses from a proposed prohibition where appropriate under the four-part test established in *Sierra Club v. EPA*, supra.

The Agency has conducted the four analyses required under this test, and it has concluded that the balance of equities favors a grandfathering period of two years for existing equipment in this application. The prohibition proposed in this action clearly represents a departure from previously established practice, as use of the substitute was allowed previously. Existing users of HCFC-141b who switched from Class I substances into this solvent invested in this substitute on the assumption that it would be considered an acceptable substitute. It would impose a severe economic burden on these users to prohibit their use of the substitute immediately, with no provision of time to allow them to recover their investment in existing equipment or acquire new equipment in a timely fashion. These factors taken together appear to outweigh any statutory interest in applying the new rule immediately to existing users, especially since the restriction would apply immediately to new equipment using HCFC-141b, which would serve

to prevent further ozone depletion from use of HCFC-141b in this application.

As with metals cleaning applications for 141b, the Agency modeled potential 141b use in electronics cleaning applications over time, and projected health effects due to ozone depletion with the help of the Atmospheric Stabilization Framework model. For electronics cleaning, the maximum market penetration for 141b as a replacement for CFC-113 is 90 per cent. With this penetration, the model predicted approximately 400 additional skin cancer fatalities and 30,000 additional skin cancer cases compared to uses of non-ozone-depleting substitutes.

(3) Precision Cleaning. (a) HCFC-141b

For the same reasons described in the section on metals cleaning, HCFC-141b and its blends are proposed to be prohibited as substitutes for CFC-113/MCF in precision cleaning, with limited critical use exemptions for CFC-113 replacements. The proposed effective date for this prohibition is 30 days after the date of the final rule for new equipment and as of January 1, 1996, for existing equipment. As discussed earlier in this action in Section VI.A., the Agency is authorized to grandfather existing uses from a proposed prohibition where appropriate under the four-part test established in *Sierra Club v. EPA*, supra.

The Agency has conducted the four analyses required under this test, and it has concluded that the balance of equities favors a grandfathering period of two years for existing equipment in this application. The prohibition proposed in this action clearly represents a departure from previously established practice, as use of the substitute was allowed previously. Existing users of HCFC-141b who switched from Class I substances into this solvent invested in this substitute on the assumption that it would be considered an acceptable substitute. It would impose a severe economic burden on these users to prohibit their use of the substitute immediately, with no provision of time to allow them to recover their investment in existing equipment or acquire new equipment in a timely fashion. These factors taken together outweigh any statutory interest in applying the new rule immediately to existing users, especially since the restriction would apply immediately to new equipment using HCFC-141b, which would serve to prevent further ozone depletion from use of HCFC-141b in this application.

In the case of precision cleaning uses of HCFC-141b, the Agency's modeling

of 141b use as a CFC-113 replacement projected approximately 5,000 additional skin cancer cases when compared to use of non-ozone-depleting substitutes.

As in the case of other cleaning applications, the Agency proposes to prohibit substitutions of 141b to replace MCF, since these compounds have nearly identical ODPs. Here again, Agency will propose to grant a limited number of critical use exemptions. Companies in this sector wishing to replace CFC-113 with 141b that may qualify for an exemption should review the section in today's Preamble on critical use exemption petitions. The Agency expects most requests for permission to use 141b will come from this end use sector, and has already received a number of inquiries from companies that either use or want to use 141b as a substitute for cleaning with CFC-113.

G. Halons

1. Overview. Halons are gaseous or easily vaporizable halocarbons used primarily for putting out fires, but also for explosion protection. The two halons used most widely in the United States are Halons 1211 (chlorodifluorobromomethane) and 1301 (trifluorobromomethane). Halon 1211 is used primarily in streaming applications in which it is manually dispensed through a nozzle from a hand-held or portable extinguisher. Halon 1301 is used in total flooding and explosion protection applications in which a predetermined quantity of the gas is dispensed into a fixed location in order to achieve a specific extinguishing concentration of gas.

The principal use for Halon 1211 is in handheld extinguishers in fixed facilities such as homes, offices, and military and government buildings. A small percentage of handheld 1211 extinguishers are also used on aircraft in accordance with FAA regulations. Portable systems are used by military and commercial "crash/rescue" teams at airports. In order to evaluate 1211 substitutes in the variety of applications described above, the Agency has divided streaming applications into three categories: residential, commercial/industrial, and military. This subdivision of the sector allows the Agency to properly account for differences in the types of fires likely to be encountered and in the types of proposed extinguishers.

Halon 1301 systems are used in combination with automatic fire detection equipment as total flooding agents in contained areas. Most Halon 1301 total flooding systems are used to

protect electronics facilities, such as computer rooms and telecommunications switching facilities. Halon 1301 is also used to protect oil production facilities, records storage facilities, aircraft cargo bays, flammable liquid storage facilities, laboratories, public places such as libraries, museums, shopping malls and tourist facilities, and much more.

Halon total flooding systems are particularly important in protecting normally unoccupied facilities, where typically no personnel are present to detect and extinguish fires. Halon total flooding systems are also used in occupied areas in which large numbers of workers or large capital investments may be at risk. In this latter case, precautions must be taken to avoid exposing occupants to toxic levels of extinguishant. Typically, these chemicals are used in conjunction with fire detection devices, alarm devices to warn occupants of impending discharge, as well as manual abort mechanisms to delay discharge until occupants are evacuated or to prevent accidental discharges. Some systems also incorporate a 'lockout' mechanism to prevent discharge of agent in the event personnel must enter the area in an emergency. Some occupational or military settings involve flammable liquids or vapors (Class B fires) where the speed of the potential fire event precludes evacuation prior to discharge. The design of a system that reacts quickly to the threat of fire or explosion must consider the effects of human exposure to the fire suppression agent.

Halon 1301 can also be used in explosion protection applications which include explosion inertion and explosion suppression. In inertion, the atmosphere is filled with an explosion protection agent at the concentration needed to prevent an explosion. The inerting agent must disperse uniformly and remain at the required concentration for a specified amount of time. Effective inertion systems require the timely detection of conditions likely to cause an explosion. In suppression, an agent is discharged to mitigate an explosion, or deflagration, that has already begun. The agent must surround the expanding fireball at a specified concentration. Both inertion and suppression require rapid discharge of agent, often without providing time for evacuation of personnel. Again, possible exposure of occupants to toxic levels of the compound must be carefully controlled and balanced against the risk of explosion.

Some limited use of Halon 2402 also exists in the United States, but only as an extinguishant in engine nacelles (the

streamlined enclosure surrounding the engine) on older aircraft and in the guidance system of Minuteman missiles. Halons also find limited application in other use sectors such as plasma etching. Decisions proposed in this notice do not address these other sectors, but instead focus on fire protection applications which comprise the vast majority of halon applications.

Halons are used in a wide range of fire protection applications because they combine five characteristics. First, they are highly effective against solid, liquid/gaseous, and electrical fires (referred to as Class A, B, and C fires, respectively). Second, they are clean agents; that is, they dissipate rapidly, leaving no residue and therefore do not cause "secondary damage" to the property they are protecting. Third, halons do not conduct electricity and can be used in areas containing live electrical equipment. Fourth, halons are gaseous substances that can penetrate in and around physical objects to extinguish fires in otherwise inaccessible areas. Finally, halons are generally safe for limited human exposure when used with proper exposure controls.

Despite these advantages, halons are among the most ozone depleting chemicals in use today. Halon 1301 has an estimated ODP of 16; Halon 1211 has an estimated ODP of 4. Thus, while total halon production (measured in metric tons) comprised just 2 per cent of the total production of Class I substances in 1986, halons represented 23 per cent of the total estimated ozone depletion potential of CFCs and halons combined. Halons therefore make up the largest use sector in terms of ozone depleting potential.

The greatest releases of halon into the atmosphere occur not in extinguishing fires, but during testing and training, service and repair, and accidental discharges. Data generated as part of the Montreal Protocol's technology assessment indicate that only 15 per cent of annual Halon 1211 emissions and 18 per cent of Halon 1301 emissions occur as a result of use to extinguish actual fires. These figures indicate that significant gains can be made in protecting the ozone layer by revising testing and training procedures and by limiting unnecessary discharges through better detection and dispensing systems for halon and halon alternative systems. Additional information on specific halon uses can be found in the Montreal Protocol 1991 Assessment or in other background material in the public docket. The initial determinations found in this section are based on the risk screen described in the draft background document entitled

"Characterization of Risk from the Use of Substitutes for Class I Ozone-Depleting Substances: Fire Extinguishing and Protection (Halon Substitutes)."

2. *Substitutes for Halons.* The fire protection community has made considerable progress in identifying and developing substitutes for halons in fire protection applications. Several manufacturers have submitted information regarding substitute streaming and total flooding agents, and the National Fire Protection Association (NFPA) has initiated efforts to develop standards for their use in total flooding scenarios. In addition, manufacturers are seeking Underwriters Laboratories (UL) and Factory Mutual (FM) certification for systems employing the new agents. The Agency's review of halon substitutes is intended not to replace, but to complement the guidance of the fire protection community in directing the transition away from halons to substitutes that are less destructive to the stratosphere.

Most recent efforts to develop substitutes for halon have focused primarily on halocarbon chemicals. These are considered potential "replacements" for halon because they possess halonlike properties (gaseous, non-conducting) and because they can be used on Class A, B, and C fires. These halocarbon replacements can be distinguished by the mechanism by which they extinguish fires. Chemical action agents, like halons, suppress fires by interfering with the free radical chain reactions that sustain a fire. Physical action agents cool, dilute, or smother the fire (separating the air and fuel). In general, chemical action agents are much more effective fire suppressants than physical action agents.

Halocarbons represent only a portion of agents available for fire protection. Water mist or fog is a newly developing technology that uses fine water droplets to suppress and extinguish fires. Studies indicate that water mist can be used in a wide variety of applications for occupied and unoccupied areas including electronics, machinery spaces, enclosed spaces, etc. Several other "alternative" agents such as water, carbon dioxide, foam, and dry chemicals are already in widespread use as fire extinguishants and can be expected to find limited use as substitutes for halon. Unlike some halocarbons, these alternative agents are not effective against all types of fire. They do not all have the same penetration capability, nor are they all non-conducting and non-toxic. Thus, each can be used only in specified applications as directed by

manufacturers and by fire protection authorities such as the NFPA. However, these alternatives should seriously be considered as appropriate replacements to halons where systems are being redesigned.

Substitutes for halons, whether other halocarbons or alternatives such as water, must meet four general criteria. They must be effective fire protection agents, have an acceptable environmental impact, have low toxicity, and they must be relatively clean or volatile. In addition, they must be commercially available as a halon replacement in the near future.

The halon sector requires special evaluation of consumer and worker exposures to discharges of halon substitutes during fire emergencies and accidental discharges. In these acute, episodic exposures to the halon substitutes, cardiac sensitization is of particular interest. The term cardiac sensitization refers to an increased susceptibility of the heart to adrenaline (or other catecholamines) which may result in potentially fatal heart arrhythmias.

Human heart arrhythmias and sudden deaths resulting from overexposure to CFCs, halons, and other halogenated hydrocarbons have been documented in workplace settings, and in volatile substance abuse (i.e. glue-sniffing). Several studies involving human exposure in a laboratory setting establish the potential significance for human health of animal data on cardiac sensitization. (See the background document "Characterization of Risk from the Use of Substitutes for Class I Ozone-Depleting Substances: Fire Extinguishing and Protection" for more details.) Evaluating the safety of potential halon substitutes requires the measurement of the No-Observed-Adverse-Effect-Level (NOAEL) and the Lowest-Observed-Adverse-Effect-Level (LOAEL) of cardiac sensitization in an appropriate species, usually the dog. The Agency uses the NOAEL value as the basis to ensure protection to the worker population.

The determination of the safety of either a flooding or streaming agent substitute is also dependent on a number of other related factors. For total flood systems, the magnitude of exposure will depend on the design concentration of the flooding agent (as determined by the substitute's extinguishing concentration plus 20 percent, as specified by NFPA guidelines) and the length of time it takes a person to evacuate the area in which the agent is released. Because total flood systems are designed to achieve a uniform concentration of

agent within a space, the magnitude of exposure is independent of the size of space, size of fire, or proximity of person to the fire. In assessing exposure and consequent use restrictions, the design concentration of a total flood substitute is compared to its cardiotoxic NOAEL and LOAEL levels. Generally, if the design concentration is higher than the agent's NOAEL level, conditions are placed on the use of the agent to ensure human safety. For example, if the NOAEL is 1 percent and the LOAEL is 2.5 percent, but the substitute requires 4 percent concentration to extinguish a fire, all personnel must be evacuated from an area before the concentration exceeds the 2.5 percent LOAEL. If there is a possibility that someone must enter a room while the agent is likely to exceed the NOAEL level, Self Contained Breathing Apparatuses (SCBA) must be worn in accordance with OSHA safety requirements.

In contrast, exposure to substitute streaming agents can be expected to vary greatly depending on the amount of agent released, the time needed to extinguish a fire, the size of the room or enclosure in which a fire occurs, the size of the fire, the proximity of the person to the point of discharge of the agent, the rate at which fresh air infiltrates the space, and the air exchange rate near the fire. Assessment of exposure in streaming applications is much more complicated and requires development of a model and testing of the values assumed for the variables described above. The resulting modeled peak exposure rate is compared to the NOAEL in our assessments. For some proposed substitutes, the Agency requires personal monitoring data in order to complete the assessment.

Evaluating halon substitutes also requires assessing the efficacy of substitute agents. The efficacy of a fire protection agent can be measured by the extinguishing concentration required to put out a burning fire. With substitutes for handheld extinguishers and for total flood systems on weight-constrained systems (such as aircraft and space systems), designers are also concerned with the weight of substitute required to replace the halon. This factor is referred to as the weight equivalency ratio and relates the number of pounds of substitute required to replace each pound of halon to achieve the same fire extinguishing capability. In other applications, such as with existing equipment, required storage volume for a substitute is of greatest concern. This quantity can be measured by the storage volume equivalency ratio which is defined as the ratio of the storage volume of substitute to the storage

volume of halon required to achieve the same fire extinguishing capability. These three measures will be used throughout this proposed rule to evaluate halon substitutes.

After concluding the analysis of alternatives to halon, the Agency in some cases proposes to approve the use of an agent contingent on certain conditions. In implementing its use of conditions, the Agency has sought to avoid overlap with other existing regulatory authorities. EPA has taken a number of steps to mitigate this potential for duplication. First, EPA intends to limit the use of conditions to cases in which clear regulatory gaps exist. Second, these existing regulatory gaps must render the use of a substitute an unreasonable risk in the absence of any additional controls. Third, in the limited cases in which conditions may be necessary, the Agency will impose them only after going through formal notice-and-comment rulemaking. Finally, the Agency intends to withdraw existing conditions when they are superseded by appropriate regulatory controls under other authorities.

The Agency, however, requests comment on the general issue of the need for use of conditions. In particular, EPA requests comment on whether section 612 in fact confers upon the Agency the authority to go beyond the listing of acceptable and unacceptable alternatives and to set such use conditions; and on the capability and practicality of EPA enforcing use conditions which may, for example, closely resemble workplace safety standards which are typically within the enforcement purview of other regulatory authorities.

EPA also requests comment on whether, when an unreasonable risk might exist due to a gap in regulatory coverage, the appropriate means to address these risks is through the existing regulatory framework of other federal authorities. For example, rather than using EPA's use conditions to address existing gaps in workplace safety standards, EPA could refer the matter to the appropriate OSHA authorities and request appropriate action to mitigate an otherwise unreasonable risk.⁴

Alternatively, where the length of time required to address a problem under another authority may be unacceptably long given the nature of the risk, there may be cases in which

⁴ 29 USC 654, OSHA General Duty Clause, requires that each employer "shall furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees. . . ."

EPA would simply consider unacceptable the use of a given substitute, pending the development of a regulatory framework to control the risk it poses in its use as a substitute for an ozone-depleting compound.

Finally, EPA requests comment on the use of conditions where no regulatory gap, *per se*, exists, but where the use of an alternative poses risk to the public. By imposing such conditions, EPA would be establishing a new regulatory framework where one did not previously exist. For example, explosion-inertion agents are not currently regulated by OSHA or any other regulatory body. However, design concentrations for systems protecting from explosion of various gases or flammable liquids may expose personnel to cardiotoxic levels of inertion agents. While the Agency is not currently proposing to place conditions for the use of alternatives in occupied areas, it may do so in the final rule subject to public comment as well as further analysis with agencies such as OSHA and OMB. EPA could place a condition for use of alternative agents in occupied areas which would identify the cardiotoxic LOAEL and would prohibit design concentrations that exceed that level.

The primary candidate substitutes for halons in fire protection applications are discussed below by category. No SNAP submissions have been received for substitutes to replace halons in explosion suppression applications. However, in the listing decisions, explosion suppression is included with the explosion-inertion decisions. The Agency is requesting comment on this.

a. Brominated Hydrofluorocarbons.—Brominated hydrofluorocarbons (HBFCs) are an effective halon substitute. Because these substances contain bromine, they act as chemical action agents in the same manner as the halons. In fact, some HBFCs are more effective than Halons 1211 and 1301 in specific applications. For this reason, HBFCs can replace Halons 1211 and 1301 on nearly a one-to-one basis and appear to have significant applicability in existing systems. However, the presence of bromine also means that these agents have higher ozone-depleting potentials than other halon substitutes.

At this time, only one HBFC, HBFC-22B1, is expected to be commercially available in the near term. Extinguishment testing indicates that HBFC-22B1 can replace Halon 1211 at a ratio of 1.08 by weight, making it a substitute for handheld extinguishers. HBFC-22B1 can also replace Halon 1301 at a ratio of 1.4 by weight and 1.3

by storage volume, making it technically suitable for use in existing total flood systems.

HBFC-22B1 can, however, serve only as an interim substitute for halons. The substance has an estimated ODP of 0.74 and will soon be added to the list of Class I substances in accordance with section 602(d) of the Clean Air Act. Under the Montreal Protocol, production of HBFC-22B1 is required to be completely phased out by January 1, 1996. In addition, this agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40 CFR 721.1296). The provisions of today's proposed rule do not supersede those of the TSCA regulations presently in effect, and readers should note that, at present, the terms of the TSCA requirements are more restrictive than the provisions of this rule.

b. Hydrochlorofluorocarbons

A number of hydrochlorofluorocarbons (HCFCs) have also been suggested as halon replacements. These include HCFC-22, HCFC-123, and HCFC-124. These HCFCs are effective fire-fighting agents, but because they are physical action agents, they are considerably less effective than halons or HBFCs and thus exhibit high extinguishing concentrations. Further, although the ozone depletion potential of HCFCs is considerably lower than that of either halons or HBFCs, they are listed as Class II chemicals under the Clean Air Act and their production will be phased out. As a result, these chemicals can serve only as interim halon substitutes.

HCFC-22 has been suggested as a total flooding agent. HCFC-22 has a low acute toxicity, but its ODP (0.05) is higher than other candidate HCFCs. The extinguishing concentration is 11.6 percent, the highest of the candidate HCFCs, while its cardiotoxicity LOAEL is 5.0 percent. It also is somewhat inferior in terms of weight and storage volume equivalents. For these reasons, this compound is unlikely to be used as a single agent.

HCFC-123 is being considered as a streaming agent to replace Halon 1211. Because of its relatively high effectiveness, HCFC-123 could replace Halon 1211 at a ratio of 1.8 by weight—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC

substitutes. However, HCFC-123, has a cardiotoxic level of 2.0 percent in the dog, with no effect apparent at 1.0 percent. Potential users have expressed concern about using HCFC-123, or blends containing HCFC-123 as the primary constituent, in small enclosed areas. However, actual exposures were assessed using personal monitoring, and the Agency concludes that likely exposure levels do not exceed safe levels.

HCFC-124 is being considered as both a total flooding agent and a streaming agent, both alone and in blends. HCFC-124 demonstrates average performance compared to other halon substitutes as a fire extinguishant and has relatively low ODP and GWP values. Testing indicates that the substance may be lethal at levels ranging from 24 percent to 36 percent. Cardiotoxicity occurs in the dog at 2.5 percent with no effect apparent at 1.0 percent. Potential users express concerns regarding exposures in small enclosed spaces.

c. Hydrofluorocarbons

Hydrofluorocarbons (HFCs) have also been suggested as halon substitutes. HFCs are physical action agents and are less effective than halons or HBFCs. Due to their reduced efficacy, considerably larger storage volumes are required for use in fire protection systems. Their great advantage over halons, HBFCs, and HCFCs is that HFCs have an ozone depletion potential of zero. However, when exposed to fires, HFCs potentially decompose into greater amounts of hydrogen fluoride (HF) than do HCFCs, depending on the number of fluorines in the molecule. Discharge of these chemicals onto a fire must be rapid to prevent the buildup of large amounts of these decomposition products.

In addition, some HFCs can potentially contribute to global warming. The Agency examines the atmospheric lifetime and global warming potential (GWP) of each substitute to establish a risk balanced listing decision. If an agent's atmospheric lifetime or GWP is unusually large relative to other available substitutes, the use of these agents may be allowed only for specific limited uses to prevent widespread adoption.

HFC-23, HFC-32, HFC-125, HFC-134a, and HFC-227ea have all been proposed as total flooding agents. HFC-227ea has also been proposed as a streaming agent. Required extinguishing concentrations vary from 5.9 percent for HFC-227ea to 12.4 percent for HFC-23. Required storage volumes will vary from 2.5 to 4.5 times that required for 1301. Weight equivalency ratios compared to 1301 vary from 1.1 for HFC-32 to 2.65

for HFC-125. All have low acute toxicity levels.

Not all of these substances have been fully investigated for commercialization. Specifically, HFC-32 is considered flammable with a flammability range that is very large, and would probably require blending with another material to make a nonflammable mixture.

d. Perfluorocarbons.

Perfluorocarbons (PFCs) are effective fire protection agents, having the lowest required extinguishing concentration of any of the suggested substitutes other than HBFCs. However, these compounds have high molecular weights which create weight and storage replacement ratios that are somewhat higher than the HCFCs and many of the HFC candidates. Two PFCs have been submitted as halon replacements: perfluorobutane (FC 3-1-10) as a total flood replacement for Halon 1301, and perfluorohexane (FC 5-1-14) as a Halon 1211 replacement primarily for USAF flightline applications.

As discussed in the section on refrigerants, PFCs are of concern due to long atmospheric lifetimes and their potential to contribute to global warming. The intent of SNAP is to reduce the overall risk to health and the environment. Since there is no other regulatory authority controlling the emissions of such long-lived agents, the Agency intends to take conservative decisions regarding substances with the potential to cause significant environmental, and ultimately human health, impacts. Therefore, the Agency is proposing to prohibit discharge testing and training with these agents, and to require recapture and recycling in order to minimize emissions of these agents. Eighty to eighty-five percent of all halon emissions are due to testing, training, leakage and accidental discharge, and it is likely that such emission patterns will occur with the alternative agents as well. In addition, the Agency proposes to allow use of PFCs only for applications involving critical military uses, the protection of public safety or national security, or life support functions. The Agency invites comment about the niche these agents can best serve in light of the fact that the Agency seeks to prevent their widespread use. The Agency specifically invites comment on the cost of these restrictions and benefits in terms of reduced potential for global warming.

e. Chlorofluorocarbons.

Chlorofluorocarbons (CFCs) have also been proposed as halon alternatives, either individually or in blends. However, since production of CFCs is to be phased out by the end of 1995,

sufficient quantities of recycled CFC would have to be available for halon applications, making it improbable that significant shifts to these compounds will occur. CFCs are relatively effective fire extinguishants and have well-understood toxicity characteristics. While CFCs deplete stratospheric ozone, their ODPs are significantly lower than those of Halons 1211 and 1301.

f. Blends.—A number of manufacturers have proposed proprietary blends of chemicals for fire protection applications. These blends combine a variety of CFCs, HCFCs, HFCs, PFCs, inert gases, and other additives to achieve desired levels of effectiveness, toxicity, and decomposition products. Most of these blends have non-zero ODPs and GWPs. Toxicity varies with the exact composition of the blend.

Where possible, the Agency has examined both the blend and its individual constituents. Characteristics of the overall combination, in some cases, were examined to estimate a weighted average of the characteristics of the individual components.

g. Non-halocarbon Alternative Agents. Non-halocarbon alternative agents such as CO₂, dry chemical, foams, inert gas blends and water that are currently in widespread use may also be used as substitutes for halon. However, as noted above, these agents are not as widely applicable as are the halons and must be used in end uses recommended by the manufacturers and approved by standard-setting entities such as the NFPA.

CO₂ can be used as a streaming or a total flooding agent. In the past, CO₂ systems were used in many of the applications now served by halons. As a total flooding agent, CO₂ has an extinguishing concentration ten times that of Halon 1301 and requires 1.4 times the storage volume required by 1301 systems; it is also an asphyxiant in the concentrations required for total flooding. Streaming CO₂ extinguishers must also be larger and heavier than 1211 extinguishers and have no Class A fire rating. Additionally, depending on the exposure characteristics discussed above, CO₂ may reach dangerous levels in small areas.

One manufacturer has developed a blend of CO₂ mixed with inert gases as a Halon 1301 substitute in total flood systems. This agent would not be considered a 'drop in' replacement due to its high extinguishing concentration. As it is a non-reactive, non-halocarbon substance, and thus is not carcinogenic, mutagenic or teratogenic, the toxicity and cardiotoxicity tests normally applied to halon substitutes do not

apply here. Rather, this agent is a potential asphyxiant. It is designed to decrease the oxygen level to 12 to 14 per cent, at which combustion cannot be supported. OSHA requires oxygen levels to be at least 19.5 per cent for human safety. It has been suggested that this particular blend increases breathing rates, thus making the oxygen deficient atmosphere breathable for short periods of time. Data submitted by the manufacturer was peer-reviewed by pulmonary, cardiac, and stroke specialists. All have agreed that the blend does not pose significant risk to the working population and may even pose less risk than does exposure to halocarbon agents.

Dry chemical extinguishers are suitable for Class A, B, and some Class C fires. Total flooding systems using dry chemical are rare, but some "localized applications" exist around deep fat fryers and textile machines. Generally, dry chemical extinguishers are more effective than halons, but dry chemical is not a clean agent and cannot be used without potentially damaging precision machinery and other equipment.

Water is an effective fire protection agent that can be used with either total flooding or streaming systems. Water is primarily a Class A fire extinguishant, but can be used against Class B when applied as a fine mist. Water also produces a cooling effect that prevents re-ignition. Water, typically cannot be used against Class C electrical fires and may cause considerable secondary damage in some applications. However, a promising new technology incorporates fine water droplets to create a water mist or fog. It has been suggested that water mist systems are safe for use on Class A and B fires, and even on Class C electrical fires without causing secondary damage.

Foams are extremely effective in extinguishing flammable liquids (Class B fires) and to some degree against Class A fires. Portable and handheld systems are available for use as streaming agents, but high- and medium-expansion foams are also marketed for total flooding applications in inaccessible areas (such as between floors or in marine machinery spaces). Use of high- and medium-density foams can be dangerous in large, cluttered or hazardous enclosures in which people might be present, but foams are not typically considered toxic. Nevertheless, foams can cause secondary damage and, due to their water content, cannot be used with electrical fires. They do not penetrate as well as gaseous agents.

3. Preliminary Listing Decisions

In order to evaluate the acceptability of proposed halon substitutes, the Agency divided the fire protection sector into six end-uses: (1) Residential/Consumer Streaming Agents, (2) Commercial/Industrial Streaming Agents, (3) Military Streaming Agents, (4) Total Flooding Agents for Occupied Areas, (5) Total Flooding Agents for Unoccupied Areas, and (6) Explosion Inertion. The table in Appendix B provides a summary of decisions by end use.

For some substitutes, data required by the Agency to complete a risk assessment is not yet available or has not been submitted to the Agency as requested. As a result, not all candidate substitutes have been fully evaluated by the Agency. Those substitutes which the Agency is currently reviewing, but for which a final determination cannot yet be made, are listed as pending in the table in Appendix B. The Agency will make every effort to evaluate these chemicals before promulgation of the final rule.

a. Acceptable Substitutes.—(1) Streaming Agents: Consumer Applications.

(a) HBFC-22B1. HBFC-22B1 is proposed acceptable as a streaming agent in consumer applications for nonresidential uses only. Given the potential market penetration and the high ODP of HBFC-22B1, use of HBFC-22B1 in consumer applications was estimated to cause unacceptable damage to the ozone layer and an excessively high number of skin cancer cases and deaths. The total estimated skin cancer cases and fatalities from the use of 22B1 as a halon 1211 replacement in all uses including consumer uses is approximately 30,000 and approximately 600, respectively. In light of the availability of other fire protection agents with lower associated risks, the Agency determined that the risks posed by HBFC-22B1 were too large to justify widespread use in the consumer sector.

In addition to concern about its ODP, use of HBFC-22B1 in residential applications may present exposure risks of cardiotoxicity. To assess this risk, the Agency modeled the peak concentration of HBFC-22B1 that would be expected if such an extinguisher were used to suppress a kitchen fire and estimated the decline from the peak. Such analysis indicated that peak concentrations of HBFC-22B1 would exceed 3300 ppm. This is in excess of NFPA ceilings for exposure.

Because of its effectiveness, the Agency is approving use of HBFC-22B1

as a streaming agent only for nonresidential uses only. However, it can only be considered a transitional agent, because it will be phased out as a Class I substance in accordance with the Clean Air Act and with the requirements of the Montreal Protocol.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40-CFR 721.1296). Under the terms of the Consent Order, it may be used only for outdoor automotive and marine applications. In addition, to ensure safe use, the sale of this product is restricted to a size discouraging residential use, with a minimum UL rating of 5BC. The unit must be properly labeled indicating that residential use is prohibited due to danger of cardiotoxicity; indicating proper space volume restrictions limiting exposure to 1 per cent; and indicating proper evacuation and reentry requirements. In addition, the agent may only be sold in rechargeable units to encourage reuse and recycling and to discourage the potential for the agent to escape to the atmosphere through improper disposal.

(b) HCFC-123. HCFC-123 is acceptable as a streaming agent for consumer applications. Because of its relatively high effectiveness, HCFC-123 could replace Halon 1211 at a ratio of 1.8 by weight—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. However, since HCFC-123, has a cardiotoxic level of 2.0 per cent in the dog, with no effect apparent at 1.0 per cent, potential users have expressed concern about using HCFC-123 or blends containing HCFC-123 as the primary constituent. However, actual exposures were assessed using personal monitoring devices, and the Agency concludes that likely exposure levels from its use as a streaming agent do not exceed safe levels.

(c) [HCFC Blend] B

[HCFC Blend] B is acceptable as a streaming agent for consumer applications.—This blend consists largely of HCFC-123, therefore, as with HCFC-123, it has been shown in tests to have a relatively high effectiveness with a weight equivalency ratio to Halon 1211 of 1.8—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest

ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. While HCFC-123 has a cardiotoxic level of 2.0 per cent in the dog, with no effect apparent at 1.0 per cent, actual exposures from use of this blend as a streaming agent were assessed using personal monitoring devices. The Agency concludes that likely exposure levels do not exceed safe levels.

(d) [CFC-Blend]

[CFC-Blend] is acceptable as a streaming agent for nonresidential consumer use.—While [CFC-Blend] contains CFCs, its overall ODP is 0.95, which is less than one-fourth that of Halon 1211. [CFC-Blend] is the most effective of all other halon substitutes except for HBFC-22B1 and HCFC-123, and does not pose the exposure risk of HBFC-22B1 in certain scenarios. [CFC-Blend] is generally considered non-toxic but in light of its high ODP relative to other substitute agents and the large potential market for consumer/residential extinguishers, alternative agents such as water and dry chemical are considered sufficient for residential uses. In addition, this substitute will be phased out by December 31, 1995.

(e) Dry Chemical

Dry chemical extinguishers are approved for use in residential streaming applications as a Halon 1211 substitute.—Dry chemical extinguishers can be used as a substitute for Halon 1211 in most residential applications. While dry chemical extinguishers can be used on Class A, B, or C fires depending upon the type of powder used, they do not always penetrate well around obstacles, they do not inhibit re-ignition of fires, they do not cool surfaces, they can cause secondary damage, and discharge in confined spaces can result in temporary loss of visibility. Dry chemical extinguishers should be used only in accordance with manufacturer's guidelines and with relevant NFPA standards.

(f) Carbon Dioxide

Carbon Dioxide extinguishers are approved for use in residential streaming applications as a Halon 1211 substitute.—Carbon dioxide can be used as a direct substitute for Halon 1211 in specified applications. Carbon dioxide systems have no rating versus Class A fires and so must be used in conjunction with another type of extinguisher to ensure that all possible fire scenarios can be appropriately handled. In addition, discharge of carbon dioxide into confined spaces may result in CO₂

concentrations above the Immediately Dangerous to Life and Health (IDLH) level. Areas into which carbon dioxide is discharged should be immediately evacuated and ventilated. Carbon dioxide extinguishers should be used only in accordance with manufacturer's guidelines and applicable NFPA standards.

(g) Water

Water extinguishers are approved for use in residential streaming applications as a Halon 1211 substitute. Users should be aware, however, that water extinguishers cannot act as a substitute for Halon 1211 in all applications. Water is primarily a Class A (solid) fire extinguisher and should not be used with Class B (flammable liquid) or C (electrical) fires. Water may damage objects onto which it is discharged. Water extinguishers should be used only in accordance with manufacturer's guidelines and with NFPA standards.

(h) Foam

Foam extinguishers are approved for use in residential streaming applications as a Halon 1211 substitute. Foam extinguishers cannot be used as a substitute for halon in all applications. Portable foam extinguishers are intended primarily for use on flammable liquid fires and are somewhat effective on Class A fires. Foams can also cause secondary damage on objects onto which it is discharged. Foam extinguishers should be used in accordance with manufacturer's guidelines and with NFPA standards.

(2) Streaming Agents: Commercial/Industrial Use

(a) HBFC-22B1

HBFC-22B1 is approved for use as a streaming agent in commercial/industrial applications. Despite its high ODP, this chemical will enable industry to more rapidly shift away from 1211 extinguishants which have an even higher ODP. Moreover, as the chemical will be phased out as a Class I substance on January 1, 1996, only limited use is expected to be made of this substitute.

Worker exposure may be a concern in small office areas, but in larger offices, modeling efforts indicate that HBFC-22B1 can be used safely. In most office/industrial fire scenarios, proper procedures should be in place regarding the operation of the extinguisher and ventilation of extinguishment areas after dispensing the extinguishant to minimize concerns about exposure.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to

requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40 CFR 721.1296). Under the terms of the Consent Order, to ensure safe use, the sale of this product is restricted to a size discouraging residential use, with a minimum UL rating of 5BC. The unit must be properly labeled indicating that residential use is prohibited due to danger of toxicity, listing proper space volume restrictions limiting exposure to 1 per cent, and indicating proper evacuation and reentry requirements. In addition, the agent may only be sold in rechargeable units to encourage reuse and recycling and to discourage the potential for the agent to escape to the atmosphere through improper disposal. EPA invites comment on these use restrictions.

(b) [CFC-Blend]

[CFC-Blend] is acceptable as a streaming agent for use in commercial/industrial streaming applications. While [CFC-Blend] contains CFCs, its overall ODP is 0.95, which is less than one-fourth that of Halon 1211. [CFC-Blend] is the most effective of all other halon substitutes except for HBFC-22B1 and HCFC-123, and does not pose the exposure risk of HBFC-22B1 in certain scenarios. [CFC-Blend] is generally considered non-toxic and could serve as a transitional substitute in many streaming applications, but will be phased out by December 31, 1995.

(c) HCFC-123

HCFC-123 is acceptable as a streaming agent for commercial/industrial applications.

Because of its relatively high effectiveness, HCFC-123 could replace Halon 1211 at a ratio of 1.8 by weight—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. However, since HCFC-123, has a cardiotoxic level of 2.0 percent in the dog, with no effect apparent at 1.0 percent, potential users have expressed concern about using HCFC-123, or blends containing HCFC-123 as the primary constituent. However, actual exposures were assessed using personal monitoring devices, and the Agency concludes that likely exposure levels from its use as a streaming agent do not exceed safe levels.

(d) [HCFC-Blend] B

[HCFC-Blend] B is acceptable as a streaming agent for commercial/industrial applications.

This blend consists largely of HCFC-123, therefore, as with HCFC-123, it has been shown in tests to have a relatively high effectiveness with a weight equivalency ratio to Halon 1211 of 1.8—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. While HCFC-123 has a cardiotoxic level of 2.0 percent in the dog, with no effect apparent at 1.0 percent, actual exposures from use of this blend as a streaming agent were assessed using personal monitoring devices. The Agency concludes that likely exposure levels do not exceed safe levels.

(e) Dry Chemical

Dry Chemical, for the reasons described and with the limitations suggested in the section on consumer streaming applications, are approved for use as a commercial/industrial streaming agent.

(f) Carbon Dioxide

Carbon Dioxide, for the reasons described and with the limitations suggested in the section on consumer streaming applications, is approved for use as a commercial/industrial streaming agent.

(g) Water

Water, for the reasons described and with the limitations suggested in the section on consumer streaming applications, is approved for use as a commercial/industrial streaming agent.

(h) Foam

Foams, for the reasons described and with the limitations suggested in the section on consumer streaming applications, is approved for use as a commercial/industrial streaming agent.

(3) Streaming Agents: Military Applications (a) HBFC-22B1

(a) HBFC-22B1

HBFC-22B1 is approved for use as a streaming agent in military applications. Despite its high ODP, HCFC-22B1 will enable the military to more rapidly shift away from 1211 extinguishants which have an even higher ODP. Moreover, as this chemical will be phased out under the Montreal Protocol (with possible essential use exemptions) as a Class I substance on

January 1, 1996, only limited use is expected to be made of this substitute.

Worker exposure may be a concern in small, enclosed areas, but in larger areas and outdoor areas, modeling efforts indicate that HBFC-22B1 can be used safely. In most realistic fire scenarios, proper procedures should be in place regarding the operation of the extinguisher, workers will be properly trained in fire-fighting procedures, and ventilation of extinguishment areas can be expected after dispensing the extinguishant.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40 CFR 721.1296). Under the terms of the Consent Order, to ensure safe use, the sale of this product is restricted to a size discouraging residential use, with a minimum UL rating of 5BC. The unit must be properly labeled indicating that residential use is prohibited due to toxicity; indicating proper space volume restrictions limiting exposure to 1 percent; and indicating proper evacuation and reentry requirements. In addition, the agent may only be sold in rechargeable units to encourage reuse and recycling and to reduce the potential for the agent to escape to the atmosphere through improper disposal.

(b) HCFC-123

HCFC-123 is acceptable as a streaming agent for military applications.

Because of its relatively high effectiveness, HCFC-123 could replace Halon 1211 at a ratio of 1.8 by weight—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. However, since HCFC-123 has a cardiotoxic level of 2.0 percent in the dog, with no effect apparent at 1.0 percent, potential users have expressed concern about using HCFC-123, or blends containing HCFC-123 as the primary constituent. However, actual exposures were assessed using personal monitoring devices, and the Agency concludes that likely exposure levels from its use as a streaming agent do not exceed safe levels.

(c) [HCFC Blend] B

[HCFC Blend] B is acceptable as a streaming agent for military applications.

This blend consists largely of HCFC-123, therefore, as with HCFC-123, it has been shown in tests to have a relatively high effectiveness with a weight equivalency ratio to Halon 1211 of 1.8—a figure considerably better than that of most other streaming substitutes. HCFC-123 has the lowest ODP of all the HCFCs proposed as halon substitutes, and its global warming potential (GWP) is half that of other proposed HCFC substitutes. While HCFC-123 has a cardiotoxic level of 2.0 percent in the dog, with no effect apparent at 1.0 percent, actual exposures from use of this blend as a streaming agent were assessed using personal monitoring devices. The Agency concludes that likely exposure levels do not exceed safe levels.

(d) FC 5-1-14

FC 5-1-14 is acceptable in streaming applications for military flightlines, inside military aircraft, and in military computer and telecommunication facilities.

Due to the long atmospheric lifetime of FC 5-1-14, the Agency urges that the chemical be used only in those instances in which a viable alternative is not available. The Agency proposes that the only acceptable uses involve national security or public safety where no other substitute has been proven to be as effective.

For example, military flightlines are ground-based operations which typically involve fuel spills and fires in engine nacelles. Flightlines require a clean agent that is capable of extinguishing three-dimensional fires, and that is non-corrosive and leaves no residue in order to leave engines intact. These are typically smaller, easily contained fires. Crash Rescue Vehicles may have a combination of agents available, but agents such as foam are usually used for larger fires.

The Agency proposes to permit use of this agent in operational military electronics facilities such as computer and telecommunication rooms, which are critical to national security or public safety.

In order to reduce emissions of FC 5-1-14 into the atmosphere, the Agency is proposing to require that FC 5-1-14 not be used in system discharge tests or for training. In addition, the Agency is proposing to require that FC 5-1-14 be recovered before servicing and recycled for later use.

In most streaming applications, the Agency believes that alternatives to FC 5-1-14 exist. These include the halocarbon replacements identified above as well as alternative agents such as water, CO₂, foam, and dry chemicals.

Users should attempt to use these other agents before deciding on a FC 5-1-14 system.

(e) [CFC-Blend]

[CFC-Blend] is acceptable as a substitute to Halon 1211 for use in military streaming applications. While [CFC-Blend] contains CFCs, its overall ODP is 0.95, which is less than one-fourth that of Halon 1211. [CFC-Blend] is the most effective of all other halon substitutes except for HBFC-22B1 and HCFC-123, and does not pose the exposure risk of HBFC-22B1 in certain scenarios. [CFC-Blend] is generally considered non-toxic and could serve as a transitional substitute in many streaming applications until it is phased out on December 31, 1995.

(f) Dry Chemical

Dry chemical, for the reasons described in the section on consumer streaming applications, is approved for use as a military streaming agent.

(g) Carbon Dioxide

Carbon Dioxide, for the reasons described and with the limitations suggested in the section on streaming applications, is approved for use as a military streaming agent.

(h) Water

Water, for the reasons described and with the limitations suggested in the section on streaming applications, is approved for use as a military streaming agent.

(i) Foam

Foams, for the reasons described and with the limitations suggested in the section on streaming applications, is approved for use as a military streaming agent.

(4) Total Flooding Agents: Occupied Areas

In analyzing the acceptability of substitutes for occupied total flooding applications, the Agency considered cardiotoxicity one of the primary decision variables. Current limitations on use of Halon 1301 in total flooding applications assure that these uses do not pose a cardiotoxic risk to personnel, if flooding does not exceed the design concentration. Halon 1301 has a cardiotoxic NOAEL of 7.5 percent, and a LOAEL of 10.0 percent; its required extinguishing concentration for total flooding is only 2.6 percent, according to testing results. OSHA promulgated a safety and health standard governing fire protection systems used at all workplaces (29 CFR 1910 Subpart L) which is designed to limit employee

exposures to toxic levels of gaseous agents used in fixed total flood systems. In addition to alerting employees of impending system discharge by suitable alarms (Section 1910.160), the standard requires that employees be provided sufficient time to leave before system discharge if the discharge is designed to exceed 10 percent (Section 1910.162). For Halon 1301, the standard prohibits the use of halon concentration greater than 7 percent (the cardiotoxic NOEL) where egress cannot be accomplished in less than 1 minute and prohibits the use of concentrations greater than 10.0 percent (the cardiotoxic LOEL) where egress requires more than 30 seconds. In addition, if there is a possibility that someone must enter a room while an agent is likely to exceed the NOEL level, Self Contained Breathing Apparatuses (SCBA) must be worn.

Since most of the proposed substitutes for use in normally occupied areas pose a risk of cardiotoxic exposure, EPA has concluded that their use must be governed by conditions similar to those for Halon 1301. While the OSHA regulation section 1910.160 generally applies to all fire protection systems, section 1910.162 addresses specific allowable concentrations only for halon. While it is not the intent of EPA to preempt OSHA regulation in this area, the Agency is seeking to ensure public safety until OSHA develops appropriate regulations for the new substitute gaseous agents. Therefore, while all agents used in normally occupied areas must meet OSHA regulations under section 1910.160, the Agency is setting conditions for use in normally occupied areas similar to those found in the OSHA regulation section 1910.162.

For example, in this action, EPA has proposed conditions on the acceptability of certain halon substitutes when used as total flooding agents in normally occupied areas. EPA has imposed these conditions because of the risk of cardiotoxic levels of exposure to personnel in areas where substitute agents may be discharged in the event of fire. Existing OSHA standard 1910.160 applies certain general controls to the use of fixed extinguishing systems in occupied workplaces, whether gaseous, dry chemical, water sprinklers, etc., and EPA has not reproduced those. These include, for example, the requirements for discharge and pre-discharge alarms, and availability of Self Contained Breathing Apparatus (SCBA) for

emergency entry into an area where agent has been discharged.⁵

While section 1910.162 can apply generally to gaseous agents, it includes cardiotoxic levels specific to Halon 1301. Section 1910.162 paragraphs (b)(5) and (b)(6) provide alternative workplace requirements based on specific design concentrations of Halon 1301. That is, if the design concentration is 7 percent, employees must be able to egress in one minute, but if the design concentration is 10 percent, employees must be able to egress in 30 seconds. These design concentrations are not identified as the cardiotoxic NOEL or LOEL, so one cannot generalize a rule for use with alternative agents which have different LOEL and NOEL values. For this reason, EPA is concerned that halon substitute agents could be used in the absence of enforceable compound-specific cardiotoxic exposure levels. On the other hand, requiring other gaseous agents to meet the 7 percent or 10 percent requirements specified in 1910.162 will preclude their use because the design concentrations of the alternative agents vary greatly, as does their cardiotoxic values. Should OSHA create compound-specific cardiotoxicity values to be applied to the use of halon substitutes as gaseous total flooding agents in occupied spaces, these conditions would no longer be necessary and EPA would rescind them.

⁵ 29 CFR 1910.160(b) includes general provisions to ensure the safety of all fixed extinguishing systems. Paragraph (c) stipulates requirements for systems with "potential health and safety hazards to employees" such as might be posed by gaseous agents.

(b)(3) "The employer shall provide a distinctive alarm or signaling system * * * capable of being perceived above ambient noise or light levels * * * to indicate when the extinguishing systems are discharging. Discharge alarms are not required on systems where discharge is immediately recognizable."

(b)(4) "The employer shall provide effective safeguards to warn employees against entry into discharge areas where the atmosphere remains hazardous to employee safety or health."

(b)(5) "The employer shall post hazard warning or caution signs at the entrance to, and inside of, areas protected by fixed extinguishing systems which use agents in concentrations known to be hazardous to employee safety and health."

(b)(6) "The employer shall assure that fixed systems are inspected annually * * * to assure that the system is maintained in good operating condition."

(b)(10) "The employer shall train employees designated to inspect, maintain, operate, or repair fixed extinguishing systems. * * *"

(b)(17) "The employer shall provide and assure the use of personal protective equipment needed for immediate rescue of employees trapped in hazardous atmospheres created by an agent discharge."

(c)(3) "On all total flooding systems the employer shall provide a pre-discharge employee alarm * * * which will give employees time to safely exit from the discharge area prior to system discharge."

However, EPA is also aware that existing OSHA regulations may provide adequate coverage against exposure to toxic levels of gaseous agents and their decomposition products. Section 1910.162 (b)(3) states, "(i) the employer shall assure that employees are not exposed to toxic levels of gaseous agent or its decomposition products," and paragraph (b)(4) states, "(ii) the employer shall provide a distinctive pre-discharge employee alarm * * * when agent design concentrations exceed the maximum safe level for employee exposure." EPA invites comment on the adequacy of 1910.162 (b)(3) to provide workplace protection for agents that differ from Halon 1301.

In those relatively rare instances where explosion suppression or fireball suppression of Class B fires is immediately necessary to protect life, discharge of any suitable agent without an alarm may be necessary. The Agency solicits descriptive comments on such situations and on appropriate use restrictions of agents.

In many occupied areas, total flooding halons can be replaced by improved detection equipment and manually operated extinguishing systems. Improved detection systems, if they detect fires in their early stages, can alert occupants to the existence of a fire so they may extinguish it with handheld extinguishers. In those cases in which a total flooding system is deemed necessary, improved detection systems and the use of cross-zoning can also reduce false alarms that result in the unnecessary discharge of total flooding systems.

The following substitutes are approved by the Agency for use as total flooding agents in occupied areas:

(a) HBFC-22B1

HBFC-22B1 is acceptable as a 1301 substitute only in occupied areas from which personnel can be safely evacuated and egress can occur before concentration of HBFC-22B1 exceeds its cardiotoxic LOEL. The required extinguishing concentration for HBFC-22B1 is estimated at 44,000 ppm (or 4.4 percent) and its design concentration is 5.4%. The LOEL for cardiotoxicity is 1 percent while its NOEL is 0.3%. EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur in 30 to 60 seconds, use is permitted up to a concentration not exceeding the LOEL. All personnel must be evacuated before concentration of HBFC-22B1 exceeds 1

percent. This compound is unlikely to be feasible as a total flooding agent because its design concentration exceeds its cardiotoxic level.

While HBFC-22B1 has an ODP of 0.74 and will be phased out on January 1, 1996, the Agency believes that the substance can serve a useful role in helping users transition away from Halon 1301, which has an ODP estimated at 16. HBFC-22B1 is available immediately and can replace 1301 at a ratio of 1.1 by weight and a ratio of 1.3 by storage volume. Thus, current 1301 total flooding systems can be converted to HBFC-22B1 with only minor increases in storage volume (or losses in efficacy). Other total flooding agents, though having a lower ODP, would require much larger additions of agent weight and storage volume.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40 CFR 721.1296).

(b) HCFC-22

HCFC-22 is acceptable as a total flooding agent in occupied areas from which personnel can be safely evacuated and egress can occur before concentration of HCFC-22 exceeds its cardiotoxic LOAEL.

HCFC-22 has an acute cardiotoxicity with a LOAEL of 5 percent; however its extinguishment concentration of 11.6 percent and its design concentration of 13.9 percent makes this compound unlikely to be used as a single agent because it exceeds its cardiotoxic level. EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur in 30 to 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before the concentration of HCFC-22 exceeds 5 percent. This compound is unlikely to be feasible as a total flooding agent because its design concentration exceeds its cardiotoxic effect level.

The ODP for HCFC-22 is 0.055 and the 100 year GWP is 1500, both of which are higher than other candidate HCFCs. It also requires the highest extinguishing concentration of the candidate HCFCs and is somewhat inferior in terms of weight and storage volume equivalents.

(c) HCFC-124

HCFC-124 is acceptable as a total flooding agent in occupied areas from which personnel can be safely evacuated and egress can occur before concentration of HCFC-124 exceeds its cardiotoxic LOAEL. HCFC-124 demonstrates average performance as a fire extinguishant, has relatively low ODP of .022, and, compared to other candidate 1301 substitutes for which GWP has been estimated, has a relatively low 100 year GWP value of 430. Testing indicates that the substance has a cardiotoxicity LOAEL of 2.5 percent with no effect NOAEL apparent at 1.0 percent. The extinguishing concentration of HCFC-124 is 8.2 percent and its design concentration is 9.8 percent.

EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur in 30 to 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HCFC-124 exceeds 2.5 percent. This compound is unlikely to be feasible as a total flooding agent because its design concentration exceeds its cardiotoxic level.

(d) [HCFC BLEND] A

[HCFC BLEND] A is acceptable alternative to Halon 1301 only in occupied areas from which personnel can be safely evacuated and egress can occur before concentration of [HCFC Blend] A exceeds its cardiotoxic LOAEL. Based on full-scale testing, the extinguishing concentration of this blend has been determined to be approximately 8.6 percent and therefore the design concentration is approximately 10.3 percent. Preliminary reports of test data indicate that the cardiotoxicity NOAEL of the blend is at least 10.0 percent, and therefore the LOAEL is likely to be greater than 10.0 percent. The Agency is awaiting the final report validating this data, but believes the preliminary report represents a conservative assessment of the cardiotoxicity of the blend. The blend has an ODP higher than other proposed HCFC substitutes, but appears somewhat more effective from a weight and storage volume equivalency basis.

EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity.

For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of [HCFC Blend] A exceeds 10.3 percent. This compound is a feasible candidate for use in a normally occupied area.

(e) HFC-23

HFC-23 is an acceptable alternative to Halon 1301 in occupied areas only for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions; and from which personnel can be safely evacuated and egress can occur before concentration of HFC-23 exceeds its cardiotoxic LOAEL.

HFC-23 is attractive for use as a total flooding agent in occupied areas because the draft report on cardiotoxicity indicates that its cardiotoxic NOAEL is over 30% without added oxygen and over 50% with added oxygen, compared to a design concentration of 14.9%. The Agency is awaiting the final report to validate these values, but believes that the draft report adequately represents the likely cardiotoxicity of the agent. Still, in order to ensure safe evacuation, EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-23 exceeds 30 percent.

While this agent has an ODP of zero, it has a relatively high GWP and an atmospheric lifetime of some 300 to 400 years. Until the Agency completes its analysis of its likely effects on global warming, it is listed as acceptable for particular critical uses only.

The weight equivalent of HFC-23 is 2.0 while its storage volume is 4.6.

(f) HFC-134a

The Agency has determined that HFC-134a is an acceptable alternative to Halon 1301 only in occupied areas from which occupants can be safely evacuated and egress can occur before concentration of HFC-134a exceeds its cardiotoxic LOAEL. HFC-134a has a cardiotoxic NOAEL of 4 percent, a LOAEL of 8 percent, and an

extinguishing concentration of 10.5 percent. EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-134a exceeds 8 percent. This compound is unlikely to be feasible as a total flooding agent in occupied areas because its design concentration exceeds its cardiotoxic level.

Like the other HFCs, HFC-134a has an ODP of zero. It also has among the lowest GWP of the candidate 1301 replacements for which GWP has been estimated.

Extinguishment tests conducted with HFC-134a indicate that the substance is considerably less effective than 1301. Systems that use HFC-134a will therefore require approximately 2.5 times more extinguishant by weight and 3.1 times more storage volume than 1301 systems. Such considerations preclude HFC-134a from being used in most existing equipment.

(g) HFC-227ea

HFC-227ea is acceptable for use as a total flooding agent in occupied areas from which occupants can be safely evacuated and egress can occur before concentration of HFC-227ea exceeds its cardiotoxic LOAEL. The preliminary report on the cardiotoxicity of HFC-227ea indicates a cardiotoxic NOAEL of 8.1% and a LOAEL of at least 10.5%. The Agency is awaiting the final report to validate the data, but believes that the draft report represents a conservative estimate of its likely cardiotoxic value. The design concentration for this agent is 7.1%, which provides a sufficient margin of safety for use in an occupied area. EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-227ea exceeds 10.5 percent.

HFC-227ea does not deplete stratospheric ozone. In addition, HFC-227ea is the most effective of the proposed HFC substitutes for Halon 1301. Testing indicates an extinguishing concentration of 5.9 percent. HFC-

227ea can replace Halon 1301 at a ratio of 2.4 by weight and 2.55 by volume which may limit its applicability in existing total flood systems.

(h) FC 3-1-10

FC 3-1-10 is acceptable as a total flooding agent in occupied areas only for those limited applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions. Experimental results indicate that FC 3-1-10 can extinguish fires in a total flood application at concentrations of 5.5 percent. The cardiotoxicity NOAEL of 40% for this agent is well above its extinguishment concentration and therefore is safe for use in occupied areas. In order to ensure safe evacuation, EPA proposes that, for occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the NOAEL for cardiotoxicity. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of FC 3-1-10 exceeds 40 percent.

Due to the long atmospheric lifetime of FC 3-1-10, the Agency urges that the chemical be used only in those limited instances described above in which a viable alternative is not available. In order to reduce emissions of FC 3-1-10 into the atmosphere, the Agency is also proposing to require that FC 3-1-10 not be used in system discharge tests. In addition, the Agency is proposing to require FC 3-1-10 to be recovered from total flooding systems before servicing and recycled for later use. Fire detection should also be cross-zoned to avoid unnecessary discharge and maintained to high reliability. In most total flooding applications, the Agency believes that alternatives to FC 3-1-10 exist. These include the halocarbon replacements identified above. As a result, EPA is proposing to restrict its use only to those applications described above.

(i) [Inert Gas Blend]

[Inert Gas Blend] is approved as a total flooding agent in occupied areas. This agent is a non-reactive, non-halocarbon substance, and thus not carcinogenic, mutagenic, or teratogenic; the toxicity and cardiotoxicity tests normally applied to halon substitutes do not apply here. Rather, this agent is a potential asphyxiant as it is designed to decrease the oxygen to a level at which combustion cannot be supported. This

blend is designed to increase breathing rates, thus making the oxygen deficient atmosphere breathable for short periods of time. Data submitted by the manufacturer was peer-reviewed by pulmonary, cardiac, and stroke specialists. All have agreed that the blend does not pose significant risk to the working population and may even pose less risk than does exposure to halocarbon agents. However, to ensure safety, the Agency proposes to approve this blend under the conditions that the design concentration results in at least 14% oxygen and 4% carbon dioxide. In addition, if the oxygen concentration of the atmosphere falls below 12%, personnel must be evacuated and egress must occur within 30 seconds. Since a fire can be expected to consume oxygen and form decomposition products, personnel should treat any fire situation as an emergency and promptly exit the space.

Concerns have been raised about the decibel level of this system upon discharge. The manufacturer has submitted a report indicating the decibel level to be 117 decibels for 3 seconds followed by a decay in noise level over 5 minutes, compared to 130 decibels for a typical halon system. The Time Weighted Average (TWA) of this system is 57 decibels. These levels are in compliance with the OSHA workplace maximum allowed peak of 140 decibels and a maximum Time Weighted Average (TWA) of 90 decibels.

(j) Carbon Dioxide

Carbon Dioxide is approved as a total flooding agent in occupied areas.

The Agency is not proposing to regulate alternative fire protection agents that are currently in widespread use. However, questions have been raised about the Agency's position on the use of carbon dioxide as a total flooding agent in occupied areas.

Exposure to carbon dioxide poses an imminent threat to life. However, because it displaces oxygen, it is an effective fire protection agent. As a result, both OSHA and the National Fire Protection Association (NFPA) address CO₂ systems for occupied areas. OSHA 1910.162(b)5 requires a pre-discharge alarm for systems with a design concentration of 4 percent or greater. NFPA has written a standard (NFPA 12) that explicitly controls how such CO₂ systems may be safely used in occupied areas. To protect life, it requires a system design such that no personnel may be present upon system discharge. The EPA recognizes both the OSHA regulation and the NFPA standard as industry practice and therefore references them in this rule.

In the review of proposed substitutes, the Agency looks at a variety of health and environmental factors, including whether the agent contributes to global warming. While carbon dioxide is a greenhouse gas, it is a byproduct of many industrial processes. We realize that carbon dioxide is recaptured and reformulated as a fire fighting agent and thus does not require new production. Therefore, the Agency has determined that its status as a greenhouse gas is irrelevant to our review.

(k) Water

Water sprinkler systems are also approved for use as a 1301 substitute in occupied areas. Such systems should not be used on Class C electrical fires or in instances in which secondary damage is considered unacceptable.

(5) Total Flooding: Unoccupied Areas.

In unoccupied areas, human exposure to potentially toxic substitutes or decomposition products are of less concern than in occupied areas. Key criteria in the decision process therefore become agent efficacy and environmental considerations. At the same time, the Agency must ensure that personnel are not exposed to toxic concentrations of fire protection agents or their decomposition products when the substances are vented or leak out from the extinguishment area. Precautions must also be taken to prevent exposures to personnel entering a normally unoccupied area after a discharge. In addition, if there is a possibility that someone must enter a room while an agent is likely to exceed the NOAEL level, Self Contained Breathing Apparatuses (SCBA) must be worn.

Based on these considerations, the Agency has determined that the following agents are acceptable substitutes to Halon 1301 in unoccupied areas:

(a) HBFC-22B1

In unoccupied areas, toxicity concerns are minimal. Thus, for the reasons outlined in the section on occupied areas, HBFC-22B1 is acceptable for use in unoccupied areas. Because of its low storage volume equivalency ratio, HBFC-22B1 can be used in existing total flooding systems to help speed the transition away from Halon 1301.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated

Significant New Use Rule (40 CFR 721.1296).

(b) HCFC-22

HCFC-22 is acceptable as a total flooding agent in unoccupied areas. However, due to the low efficacy of the agent and its high ODP and GWP relative to other proposed substitutes, the Agency believes this is a less attractive replacement than other potential candidates.

(c) HCFC-124

HCFC-124 is acceptable as a total flooding agent in unoccupied areas. This agent is relatively effective for a physical action agent and has lower ODP and GWP values than other substitutes.

(d) [HCFC BLEND] A

[HCFC BLEND] A is acceptable as a substitute for Halon 1301 in unoccupied total flooding applications. [HCFC BLEND] A is not anticipated to result in toxic exposures when used in unoccupied areas. The blend has an ODP higher than other HCFC substitutes, but appears more effective on a weight and storage volume equivalency basis.

(e) HFC-23

HFC-23 is an acceptable alternative to Halon 1301 in unoccupied areas only for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions.

HFC-23 has a design concentration of 14.9%. While this agent has an ODP of 0, it has a relatively high GWP and an atmospheric lifetime of some 300 to 400 years. Until the Agency completes its analysis of its likely effects on global warming, it is listed as acceptable for particular critical uses only.

The weight equivalent of HFC-23 is 2.0 while its storage volume is 4.6.

(f) HFC-125

HFC-125 is acceptable for use as a Halon 1301 substitute in unoccupied areas.

Specific cardiotoxicity information has not been received by the Agency regarding HFC-125. However, in unoccupied areas, it is not expected that human health would be threatened by use of HFC-125. In addition, HFC-125 does not deplete stratospheric ozone.

Despite its zero ODP, HFC-125 has one of the highest calculated GWP (100 year GWP of 2500) of any HFC or HCFC currently planned for production as a halon or CFC substitute.

(g) HFC-134a

In unoccupied areas, toxicity concerns are minimal. Thus, for the reasons outlined in the section on occupied areas, HFC-134a is acceptable for use in unoccupied areas.

(h) HFC-227ea

In unoccupied areas, it is not expected that human health would be threatened by use of HFC-227ea. In addition, HFC-227ea does not deplete stratospheric ozone. HFC-227ea is therefore acceptable for use in unoccupied areas.

HFC-227ea is the most effective of the proposed HFC substitutes for Halon 1301. Testing indicates an extinguishing concentration of 5.9 percent. HFC-227ea can replace Halon 1301 at a ratio of 2.4 by weight and 2.55 by volume which may limit its applicability in existing total flood systems.

(i) FC 3-1-10

FC 3-1-10 is acceptable as a total flood agent in unoccupied areas only for those limited applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; Armored Personnel Vehicles and related vehicles; and for explosion inertion/suppression with flammable liquids and gases. Due to the long atmospheric lifetime of FC 3-1-10 and its global warming potential, the Agency urges fire protection specialists to consider alternatives to FC 3-1-10 in unoccupied areas. Such alternatives would include other halocarbon systems, water sprinkler systems, or manually operated extinguishers in conjunction with improved and well-maintained fire detection and warning devices and the use of cross-zoning to avoid unnecessary discharge.

In those limited cases described above in which FC 3-1-10 is the optimal fire protection choice, care must be taken to limit releases of FC 3-1-10. To this end, the Agency is also proposing to require (1) that systems not be tested using FC 3-1-10, and (2) that during servicing and maintenance all FC 3-1-10 be recovered from the total flood system and recycled for later use.

(j) [Inert Gas Blend]

[Inert Gas Blend] is approved for use as a 1301 substitute in unoccupied areas. This agent would not be considered a "drop in" replacement in a total flooding system due to its high extinguishing concentration.

(k) Carbon Dioxide

Carbon Dioxide is approved for use as a Halon 1301 substitute in unoccupied areas. CO₂ is currently widely used as a total flooding agent. In the past, CO₂ systems were used in many of the applications now served by halons. As a total flooding agent, CO₂ has an extinguishing concentration ten times that of Halon 1301 and requires 1.4 times the storage volume required by 1301 systems; it is also an asphyxiant in the concentrations required for total flooding. Thus, it is most suited for use in unoccupied areas.

In the review of proposed substitutes, the Agency looks at a variety of health and environmental factors, including whether the agent could potentially contribute to global warming. While carbon dioxide is a greenhouse gas, it is a byproduct of many industrial processes. We realize that carbon dioxide is recaptured and reformulated as a fire fighting agent and thus does not require new production. Therefore, the Agency has determined that its status as a potential global warmer is irrelevant to our review.

(l) Water

Water sprinkler systems are also approved for use as a 1301 substitute in unoccupied areas. EPA proposes that such systems should not be used on Class C electrical fires or in instances in which secondary damage is considered unacceptable.

(6) Explosion Inertion

Explosion inertion agents are not currently regulated by OSHA or any other regulatory body. However, design concentrations for systems protecting from explosion of various gases or flammable liquids may expose personnel to cardiotoxic levels of inertion agents. While the Agency is not currently proposing to place conditions for the use of alternatives in occupied areas, it may do so in the final rule subject to public comment as well as further analysis with agencies such as OSHA and OMB. EPA could place a condition for use of alternative agents in occupied areas which would identify the cardiotoxic LOAEL and would prohibit design concentrations that exceed that level.

EPA requests comment on the use of conditions where no regulatory gap, per se, exists, but where the use of an alternative poses risk to the public. By imposing such conditions, EPA would be establishing a new regulatory framework where one did not previously exist.

(a) HBFC-22B1

HBFC-22B1 is acceptable for use as a Halon 1301 replacement in explosion inertion applications in unoccupied areas. HBFC-22B1 is an effective halon substitute for explosion inertion, requiring an inertion concentration of 8 percent. Because this value exceeds the recommended exposure concentrations for short-term exposures to HBFC-22B1, and because it cannot be assumed that occupants would have an opportunity to safely evacuate in the event of an explosion, the Agency considers this substitute safe only for use in unoccupied areas.

HBFC-22B1 appears to be a suitable candidate for replacing Halon 1301 in existing explosion inertion applications. The storage volume equivalent for HBFC-22B1 is 1.6, lower than any other halon substitute. Thus, despite the relatively high ODP of HBFC-22B1 compared to other substitute agents, HBFC-22B1 can accelerate the transition away from Halon 1301.

This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) section 5(e) Consent Order and associated Significant New Use Rule (40 CFR 721.1296).

(b) HFC-23

HFC-23 is acceptable as an explosion inertion agent only for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions. While this agent has an ODP of 0, it has a relatively high Global Warming Potential and an atmospheric lifetime of some 300 to 400 years. The Agency is currently restricting its use until further analysis on this issue is complete. Until then, the Agency urges explosion protection specialists to consider alternatives to HFC-23 in unoccupied areas.

HFC-23 is attractive for use as an explosion inertion agent in occupied areas because the draft report on cardiotoxicity indicates that its cardiotoxic NOAEL is over 30% without added oxygen and over 50% with added oxygen. The Agency is awaiting the final report to validate these values, but believes that the draft report adequately represents the likely cardiotoxicity of the agent.

Explosion inertion requires the rapid discharge of agent, often without providing time for evacuation of personnel. Possible exposure of

occupants to toxic level of the compound must be carefully controlled and balanced against the risk of explosion. While the Agency is not currently imposing conditions on the use of this agent in occupied areas, employers are advised to evaluate this agent in light of the fact that the required design concentrations vary for different atmospheres. The design concentration should not exceed the cardiotoxic LOAEL for HFC-23 of 50% in an occupied area. The Agency also recommends that employers provide an alarm to alert personnel of system discharge, and to evacuate all personnel as soon as possible after system discharge.

(c) HFC-125

HFC-125 is acceptable for use as an explosion inertion agent only in unoccupied areas. At this time sufficient information has not been received by the Agency to allow use of HFC-125 as an explosion protection agent in occupied areas. In applications in which exposures to personnel can be avoided, however, HFC-125 is acceptable.

(d) HFC-227ea

HFC-227ea is acceptable for use as an explosion inertion agent in occupied and unoccupied areas. The preliminary report on the cardiotoxicity of HFC-227ea indicates a cardiotoxic LOAEL of at least 10.5%. The Agency is awaiting the final report to validate the data, but believes that the draft report represents a conservative estimate of its likely cardiotoxic value. Because required design concentrations vary for different atmospheres, explosion protection engineers must ensure that this agent is not used in an occupied area when a concentration greater than the estimated cardiotoxic LOAEL of 10.5% is required.

Explosion inertion requires the rapid discharge of agent, often without providing time for evacuation of personnel. Possible exposure of occupants to toxic level of the compound must be carefully controlled and balanced against the risk of explosion. While the Agency is not currently imposing conditions on the use of this agent in occupied areas, employers are advised to evaluate this agent in light of the fact that the required design concentrations vary for different atmospheres. The design concentration should not exceed the cardiotoxic LOAEL for HFC-227ea of 10.5% in an occupied area. The Agency also recommends use of an alarm to alert personnel of system discharge, and

to evacuate all personnel as soon as possible after system discharge.

This agent is also acceptable for unoccupied areas.

(e) FC 3-1-10

FC 3-1-10 is acceptable as an explosion inertion agent only for those limited applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions. Due to the long atmospheric lifetime of FC 3-1-10 and its potentially large global warming potential, the Agency urges explosion protection specialists to consider alternatives to FC 3-1-10 in unoccupied areas. Explosion inertion studies conducted with methane and propane indicate an inerting concentration of 7.8 percent and 9.5 percent respectively. Additional performance data is being collected for use with other flammable gases. No data has been received by the Agency for explosion suppression applications.

The cardiotoxicity NOAEL of this agent is 40 percent and its LOAEL is greater than 40%, and thus is well suited for use in occupied areas. Explosion inertion requires the rapid discharge of agent, often without providing time for evacuation of personnel. Possible exposure of occupants to toxic level of the compound must be carefully controlled and balanced against the risk of explosion. While the Agency is not currently imposing conditions on the use of this agent in occupied areas, employers are advised to evaluate this agent in light of the fact that the required design concentrations vary for different atmospheres. The design concentration should probably not exceed the cardiotoxic NOAEL for FC 3-1-10 of 40% in an occupied area. The Agency also recommends use of an alarm to alert personnel of system discharge, and to evacuate all personnel as soon as possible after system discharge.

In those limited cases described above in which FC 3-1-10 is determined to be the optimal explosion inertion choice, care must be taken to limit releases of FC 3-1-10. To this end, the Agency is also proposing to require (1) that systems not be tested using FC 3-1-10, and (2) that during servicing and maintenance all FC 3-1-10 be recovered from the inertion system and recycled for later use.

(f) [Inert Gas Blend]

[Inert Gas Blend] is approved for use as a 1301 substitute for explosion

inertion in occupied and unoccupied areas. This agent is a non-reactive, non-halocarbon substance, and thus not carcinogenic, mutagenic, or teratogenic; the toxicity and cardiotoxicity tests normally applied to halon substitutes do not apply here. Rather, this agent is a potential asphyxiant as it is designed to decrease the oxygen to a level at which combustion cannot be supported. This blend is designed to increase breathing rates, thus making the oxygen deficient atmosphere breathable for short periods of time. Data submitted by the manufacturer was peer-reviewed by pulmonary, cardiac, and stroke specialists. All have agreed that the blend does not pose significant risk to the working population and may even pose less risk than does exposure to halocarbon agents.

The inerting concentration for this blend is 44 percent for methane/air mixtures and 50 percent for propane/air mixtures. A 50 percent concentration would result in an atmosphere of only 10.5 percent oxygen content, which is the lower limit at which studies show this agent safe for use with healthy, young people. Explosion inertion requires the rapid discharge of agent, often without providing time for evacuation of personnel. Possible exposure of occupants to a hypoxic, or oxygen reduced, atmosphere must be carefully controlled and balanced against the risk of explosion. The Agency thereby requires an alarm to alert personnel of system discharge, and all personnel must evacuate as soon as possible after system discharge.

Concerns have been raised about the decibel level of this system upon discharge. The manufacturer has submitted a report indicating the decibel level to be 117 decibels for 3 seconds followed by a decay in noise level over 5 minutes, compared to 130 decibels for a typical halon system. The Time Weighted Average (TWA) of this system is 57 decibels. These levels are in compliance with the OSHA workplace maximum allowed peak of 140 decibels and a maximum Time Weighted Average (TWA) of 90 decibels.

b. Proposed Unacceptable Substitutes.

(1) Streaming Agents: Commercial/Industrial Use. (a) CFC-11. CFC-11 is proposed unacceptable in its proposed application as a Halon 2402 substitute or for large outdoor uses. This agent has been proposed as a substitute for Halon 2402, as well as for use in a new niche for large outdoor fires, such as for dropping from helicopters. Halon 2402 is not used in the U.S. and thus does not require a substitute agent. As a new use in the large outdoor sector, such as dropping from helicopters, other non-ozone depleting methods are already in use and thus do not warrant introduction of this substitute.

H. Sterilants

1. Overview

CFC-12 is widely used in combination with ethylene oxide (EtO) to sterilize medical equipment and devices. The most prevalent combination consists of 12 percent EtO mixed with 88 percent CFC-12; the mixture is therefore referred to as "12/88". EtO serves as the actual sterilant in this mixture and can be used alone as a sterilant, but by itself, EtO is highly flammable. CFC-12 acts as a stabilizing agent to reduce the overall flammability of the blend.

Sterilants, including 12/88, are used in a variety of applications. These include hospital sterilization, medical equipment sterilization, pharmaceutical production, spice fumigation, commercial research and development, and contract sterilization. Hospitals are by far the most numerous users of sterilants. Within hospitals, 12/88 is the most popular sterilant. Estimates indicate that in 1989, EtO/CFC-12 was used for over 95 percent of all sterilization in hospitals. Pure EtO systems are also used in hospitals, but typically as small, tabletop models. Few hospitals have large pure EtO systems in-house. Other individual users of sterilant such as contract sterilizers and pharmaceutical producers, while less numerous than hospitals, typically consume more sterilant than the average hospital. They are also more likely to use pure EtO sterilization systems to handle large capacity loads.

Despite the varied end uses of sterilants, the Agency did not divide its analysis and regulation of the sterilants sector into distinct end uses. This is because alternatives to 12/88 are consistent across end uses, and the sterilant sector as a whole represents one of the smallest use sectors for Class I substances which is being considered in the SNAP program. On an ODP-weighted basis, US consumption of

CFC-12 for sterilization represented less than 4 per cent of the total US consumption of ozone depleting substances in 1990.

Several alternatives to 12/88 are currently in widespread use, but each is limited in applicability by material properties of the devices to be sterilized. These currently available alternatives are unlikely to serve as widespread substitutes for 12/88. Steam sterilizers, for example, are used in many applications and are less expensive to purchase and to operate than 12/88 systems. However, steam can only be used to sterilize equipment that can resist high temperatures. Pharmaceutical manufacturers already use steam to the maximum extent possible, but hospitals may be able to shift some of their current 12/88 use to steam by separating heat-resistant devices from heat-sensitive ones. Other alternatives such as radiation, peracetic acid, and glutaraldehyde are also in use, but, like steam, are incompatible with many of the materials now sterilized with 12/88. In fact 30 to 50 per cent of new products are initially sterilized with gamma radiation, but it is not possible to re-sterilize hospital surgical equipment with gamma radiation. Instead, 12/88 must be used.

Other alternatives are currently under development. These include chlorine dioxide, gaseous ozone, vapor phase hydrogen peroxide, and ionized gas plasma. Many of these alternatives are also incompatible with materials currently sterilized with 12/88. Those that may be applicable as partial substitutes for 12/88, such as hydrogen peroxide, are not expected to be commercially available in the near term.

For these reasons, alternatives such as steam and other currently available technologies should be used wherever applicable, but are not specifically addressed in this proposal. Additional information on such alternatives and on specific uses of 12/88 can be found in the supporting documentation retained in the public docket. The proposed determinations in this section are based on the risk screen described in the background document titled "Characterization of Risk from the Use of Substitutes for Class I Ozone-Depleting Substances: Sterilization."

2. Substitutes for Sterilization. a. Halocarbons

A number of halocarbon substitutes have been suggested as viable alternatives to CFC-12 in EtO blends for sterilization. These include HCFC-123, HCFC-124, HFC-125, HCFC-141b, and HFC-134a and HFC-227ea. At present, however, only HCFC-124 and HFC-

227ea have been proposed as near-term candidates. While HCFC-124 has been fully evaluated by the Agency in this rule, a final determination on HFC-227ea will be completed as soon as exposure data are received. Additional research will be required to determine the suitability of the other agents in EtO blends.

Many of the proposed halocarbons offer good potential as EtO diluents. They demonstrate good flame retardation, low ODPs, low GWPs, low toxicity, materials compatibility, acceptable vapor pressures, and good blending properties. Mixtures of halocarbons with EtO would most likely be at ratios similar to 12/88, or with a slightly lower EtO content. HCFC-124 has been tested with 8.6 percent EtO, for example. Such properties would make halocarbon blends virtual drop-in replacements for 12/88 in existing systems. The blends would also be far less damaging to stratospheric ozone than is 12/88.

b. Carbon Dioxide

Carbon dioxide is already in widespread use as a sterilant in blends with EtO. The most common blend contains 10 percent EtO and 90 percent CO₂ and is referred to as "10/90". While 10/90 is compatible with most of the materials now sterilized with 12/88, it must be used at higher operating pressures than 12/88 systems and hence is not a direct drop-in replacement for 12/88. Use of CO₂ blends requires that the sterilizing unit itself be upgraded to handle higher operating pressures in order to prevent excessive leakages of EtO from the system. However, operating costs for CO₂ systems are typically lower than those for 12/88 systems.

CO₂ and EtO tend to separate while stored in pressurized containers. Thus, initial discharges from the canisters during use may contain excessively high amounts of flammable EtO; final discharges from nearly empty canisters may contain pure CO₂ and may not effectively sterilize equipment. To overcome this problem, "unit dose" canisters have been developed for use in conjunction with CO₂ sterilizers. For safe operation, these canisters must be connected and disconnected from the sterilizing unit before and after every use, thereby increasing the risk of accidental exposure. Improved training procedures will be required with such systems.

c. Pure EtO

Pure EtO systems can also be used in place of current 12/88 sterilizers. By itself, EtO is toxic, carcinogenic, and

flammable. Thus, additional precautions must be taken to limit occupational exposures and conflagration. Present OSHA standards and proper engineering controls have demonstrated their ability to provide for safe operation of such systems. Pure EtO systems are currently used by many contract sterilizers, large hospitals, and other large users.

Pure EtO cannot be used in existing 12/88 sterilizing equipment without significant technical changes. Large sterilizers may have to be relocated or rooms modified in order to reduce damage from possible explosions. Both large and small systems require retrofits to provide the capability to properly vent EtO and to prevent explosions. Such conversions are costly, but may produce long-term cost savings. Operating costs for pure EtO systems are lower than those for 12/88 systems.

3. Preliminary Listing Decisions

a. Acceptable. (1) HCFC-124

HCFC-124 is acceptable as a substitute for CFC-12 in EtO blends.—Initial testing in hospital, industrial, and laboratory settings indicates that an EtO/HCFC-124 blend can serve as a virtual drop-in replacement for 12/88, enabling users to transition away from CFC-12 while still using their existing equipment.

Use of HCFC-124 in sterilizers will allow significant reductions in skin cancer cases and deaths resulting from ozone depletion. HCFC-124 has an ODP of only 0.02. Modeling results indicate that even if HCFC-124 replaces all current use of CFC-12 in sterilization, resulting skin cancer deaths in the total US population born before 2030 will total only 600 more than if a zero ODP substitute were available. In addition, the low GWP of HCFC-124 ensures that use of the chemical in sterilizers will have a negligible effect on global warming.

Under Title III of the Clean Air Act Amendments of 1990, the Agency is required to regulate any of the 189 hazardous air pollutants (HAPs). Ethylene oxide is a HAP, and the user is alerted to follow all upcoming regulations concerning the use of ethylene oxide, whether used alone or in a blend. For example, it is likely in the future that Title III will require a system that prevents venting of EtO into the atmosphere, therefore users installing new HCFC-124/EtO systems may choose to take this into consideration.

(2) Carbon Dioxide

Carbon dioxide is acceptable as a substitute for CFC-12 in EtO blends

used for sterilization. Carbon dioxide can effectively reduce the flammability of EtO and does not deplete stratospheric ozone. While CO₂ is considered a greenhouse gas, atmospheric modeling indicates that its use in the sterilants sector will have no measurable impact on global warming. Furthermore, most CO₂ currently used in sterilant mixtures is the recaptured by-product of other chemical processes, so its manufacture for use in sterilizers should not increase emissions to the atmosphere. Carbon dioxide is an asphyxiant in high concentrations, but engineering controls designed to limit occupational exposures from the more toxic EtO will also serve to prevent potentially lethal exposures to CO₂.

Blends of CO₂ and EtO are commercially available at present, and proven process cycles already exist. Blends of CO₂ and EtO have been in widespread use for years and dominated the market before the development of 12/88. Recent flammability tests indicate that the maximum concentration of EtO in CO₂ blends may have to be lowered from its traditional level of 10 per cent to perhaps 8 or 9 per cent to achieve adequate levels of safety. As mentioned above, ethylene oxide is a HAP, and the user is alerted to follow all upcoming regulations concerning the use of ethylene oxide, whether used alone or in a blend.

Carbon dioxide blends will not serve as direct drop-in replacements for 12/88. The higher operating pressures of CO₂/EtO blends will require modifications to existing equipment. The Montreal Protocol's technology assessment report on sterilants estimated that less than one-half of the 12/88 sterilizers currently used in hospitals are certified to operate at the higher pressures necessary for CO₂/EtO blends.

(3) Pure EtO

Pure EtO is acceptable as a substitute for 12/88 in sterilization. By itself, EtO is neither an ozone depleting substance nor a contributor to global warming. However, EtO is toxic, carcinogenic, and flammable. While these factors must be considered in the decision to approve EtO as a substitute for 12/88 and must be considered by users selecting appropriate substitutes for their current use of 12/88, the Agency considers current applicable standards and operating procedures (such as OSHA standards for occupational exposure) sufficient to protect human health and the environment. Thus, pure EtO systems are acceptable substitutes for 12/88. Users are advised to adhere to all existing workplace standards and to

train workers in the proper operation of EtO equipment. Historical experience with pure EtO systems indicates that they can be used safely when operated in accordance with such guidelines. Because of the threat posed by vented EtO to the general population, the Agency also recommends that pure EtO systems be used in conjunction with emission control technologies such as catalytic converters or acid water scrubbers to prevent exposures of the general population to dangerous levels of EtO.

As mentioned above, ethylene oxide is a HAP, and the user is alerted to the probability of future regulations concerning the use of ethylene oxide, whether used alone or in a blend.

Pure EtO should not be considered a drop-in replacement for 12/88. EtO systems operate at atmospheric pressure or below, allowing some current 12/88 equipment to be retrofit for pure EtO through the addition of proper ventilation and control technologies. However, the costs associated with such changes, especially with larger equipment, can be prohibitive. Nevertheless, use of pure EtO can reduce operating costs substantially compared to those achieved with equivalent 12/88 systems.

b. Unacceptable Substitutes [None]

I. Aerosols

1. Overview

To provide perspective on EPA's decisions in the aerosols sector, this section presents first an overview of important related regulations. Subsequent parts of the section describe the substitutes in the aerosols sector and present EPA's decisions on the substitutes. The decisions are summarized in Appendix B at the end of this notice. The proposed decisions presented in this section are based on the risk screen contained in the draft background document entitled "Risk Screen on Use of Substitutes for Class I Ozone-Depleting Substances: Aerosols."

Following scientific concerns raised in 1974 regarding possible ozone depletion from CFCs, EPA and the Food and Drug Administration (FDA) acted on March 17, 1978 (43 FR 11301; 43 FR 11318) to ban the use of CFCs as aerosol propellants in all but "essential applications." During the mid-1970s, use as aerosol propellants constituted over 50 percent of total CFC consumption in the United States. The 1978 ban reduced aerosol use of CFCs in this country by approximately 95 percent, eliminating nearly half of the total U.S. consumption of these chemicals.

Some CFC aerosol products were specifically exempted from the ban based on a determination of "essentiality". (See reference Essential Use Determinations—Revised, 1978.) The other uses of CFCs in aerosol and pressurized dispenser products (e.g., as an active ingredient, a solvent, or as the sole ingredient) were excluded from the ban because they did not fit the narrow definition of "aerosol propellant". Therefore, prior to the 1990 Clean Air Act Amendments, the only aerosol products that still contained CFCs were products exempted from the 1978 ban on CFC propellants or products excluded from the 1978 ban.

The amended Clean Air Act of 1990 includes statutory authorities relevant to use of HCFCs in several sections of Title VI. Title VI divides controlled ozone-depleting substances into two distinct classes. Class I is comprised of CFCs, halons, carbon tetrachloride and MCF. Class II is comprised solely of HCFCs. In addition to mandating the phase out of Class I and Class II substances, section 610 of Title VI also provides for the prohibition of certain products made with Class I and Class II substances. The product bans for Class I substances and Class II substances are distinct from one another and are addressed in subsections 610(b) and 610(d), respectively. In section 610(b), Congress directed EPA to promulgate regulations that prohibit the sale or distribution of certain "nonessential" products that release Class I substances as of November 15, 1992. Under this subsection, Congress specifies particular products as nonessential and directs EPA to identify other nonessential products. In the Notification of Proposed Rulemaking (57 FR 1992, January 16, 1992), EPA proposed regulations that implement the requirements of section 610(b) and ban certain nonessential products that release Class I substances. Under this rule, EPA proposed to ban, among other products, flexible and packaging foam, and aerosols and other pressurized dispensers using CFCs. The use of methyl chloroform, while a Class I substance, is not restricted under this proposed rule.

As directed by Congress, EPA conducted research into the purpose or intended use of products containing Class I substances, the technological availability of substitutes, safety and health considerations, and other relevant factors including the economic impact of banning selected products. EPA then proposed to ban the use of CFCs as propellants and solvents in all aerosol products with the following

specific exemptions (57 FR 1992, January 16, 1992):

- Contraceptive vaginal foams;
- lubricants for pharmaceutical and tablet manufacture;
- metered dose inhalation devices;
- gauze bandage adhesives and adhesive removers;
- commercial products using CFC-11 or CFC-113 as lubricants, coatings, or cleaning fluids for electrical and electronic equipment;
- commercial products using CFC-11 or CFC-113 as lubricants, coatings, or cleaning fluids for aircraft maintenance; and
- release agents for molds using CFC-11 or CFC-113 in the production of plastic or elastomeric materials.

In addition to the first four products listed above, EPA is likely to exempt additional medical products as directed by the CAA. Medical devices, as defined in section 601, include devices, diagnostic products, drugs, and drug delivery systems that (a) utilize a Class I or Class II substance for which no safe and effective alternative has been developed and (b) have been approved and determined to be essential by the FDA Commissioner in consultation with the EPA Administrator. It is important to note that a product being exempted from the Class I ban does not imply exemption from the phase-out requirements under the CAA, which the Agency is examining separately.

Section 610(d) of the CAA prohibits the sale or distribution of certain products that contain or are manufactured with Class II substances. This ban, which is effective January 1, 1994, extends to certain aerosols and pressurized dispensers which contain Class II substances and plastic foam products which contain or are manufactured with a Class II substance. EPA believes that the ban on certain products containing Class II substances is self-executing. Section 610(d)(1) bans the sale of the specified Class II products on its own terms, without any reference to required regulations. Thus, EPA is not required to determine which products will be banned.

However, section 610(d)(2) allows EPA to grant exceptions and exclusions from the ban on aerosol and pressurized dispenser products containing class II substances. Specifically, EPA is authorized to grant exceptions from the prohibition where the use of the aerosol product or pressurized dispenser is determined by the Administrator to be essential as a result of flammability or worker safety, and where the only available alternative to use of a Class II substance is use of a Class I substance

which legally could be substituted for such Class II substance (i.e., use of a Class I substance that is still allowed). In addition to these two criteria for exceptions, aerosol products may be excluded from the ban as a result of a third consideration in section 610 (d)(2); namely, that the ban on products containing Class II substances shall not apply to any medical device. Reflecting the self-executing nature of the CAA ban, any aerosol product or pressurized dispenser containing a Class II substance is banned as of January 1, 1994, unless EPA grants an exception.

HCFCs have current and potential applications as propellants and as solvents in aerosol products. However, until recently, their use has been limited by the aerosol industry because of their high cost relative to traditional options such as CFCs and hydrocarbons. Increased regulation of CFCs, including taxation of these substances and an eventual phase-out, has meant that HCFCs are, for an interim period, economically viable in some applications, particularly where concern about flammability limits the use of cheaper alternatives, such as hydrocarbons.

2. Substitutes for Aerosols

The Class I substances that are currently being used in aerosol applications include CFC-11, CFC-12, CFC-113, CFC-114, and methyl chloroform (MCF). Similarly, the Class II substances that are currently being used are HCFC-22, HCFC-142b, and HCFC-141b. The Agency has elected only to discuss alternatives for the CFC-11, CFC-113, MCF, HCFC-22, HCFC-142b, and HCFC-141b.

The uses for CFC-12 and CFC-114 are as propellants in medical applications and will not be discussed here because the substitutes for these applications are currently being developed and will have to undergo FDA approval. Possible substitutes in this application include HFC-134a and HFC-227ea, which both have low toxicity and zero ozone depletion potential. Regulatory approval for these compounds, however, is contingent on FDA approval, which will likely occur over the next several years.

A variety of chemicals are currently being used or are being considered as substitutes for Class I and II controlled substances used in non-inhalation aerosols and pressurized containers. The suitability of alternatives depends upon the product in which they are used. Each of these alternatives has its own physical and chemical characteristics which make it optimal choice for the product in question, in terms of such factors as solvency

properties, propellant characteristics, performance, cost, and environmental considerations. However, the Agency believes that a majority of the substitutes considered to replace the Class I and II controlled substances used as propellants or solvents in aerosols and pressurized containers are currently available and easily integrated into existing aerosol production facilities.

The primary substitutes for the propellant uses of HCFC-22 and HCFC-142b are as follows:

- Hydrocarbons
- Dimethyl ether
- HFCs
- Compressed Gases
- Alternative Processes

The primary substitutes for the solvent/diluent uses of CFC-11, CFC-113, MCF, and HCFC-141b are as follows:

- Petroleum Distillates
- Ketones, esters, ethers, and alcohols
- HCFC-141b
- Terpenes
- Chlorinated Solvents
- Water-Based Systems

This list of substitutes was compiled with the help of companies that submitted information on substitutes to the Agency in response to the January 16, 1992, Advance Notice of Proposed Rule-Making. Today's decisions on these substitutes are listed in Appendix B. The remainder of the section discusses these substitutes, the decision on each substitute, and the Agency's reasoning behind each determination. Vendors or users of other substitutes not included on the table for the SNAP determinations on aerosols should provide information on the substitutes so that the Agency can complete the determinations.

a. Substitutes for Propellants.—(1) Hydrocarbons. Hydrocarbons are promising replacements for nonessential uses of HCFC-22 as a propellant in aerosols and pressurized containers. These small chain compounds, such as butane, isobutane, and propane, have low boiling points, making them excellent propellants. They are used separately or in mixtures, are inexpensive compared to HCFC-22 (HCFC-22 is four times more expensive than hydrocarbons), and are readily available from most chemical distributors.

The Agency believes that the major area of concern with the replacement of hydrocarbons for HCFC-22 is the high flammability of hydrocarbons. In applications where a nonflammable propellant is needed, a hydrocarbon could not be used. For example, the use of hydrocarbons around electrical

equipment could prove hazardous if sparks from the equipment were to ignite the hydrocarbon propellant.

Hydrocarbons are adequate substitute propellants where flammability is not a concern. To reduce product flammability, hydrocarbons can be used with water-based formulations in products such as insecticides where product quality would not be adversely impacted. Manufacturers are also hindered from selling hydrocarbon propelled aerosols in certain jurisdictions. In California, for example, the use of hydrocarbons is restricted because of their classification as volatile organic compounds which contribute to low level ozone or smog.

(2) Dimethyl Ether. Dimethyl ether (DME) is a medium pressure, flammable, liquified propellant. Because of its chemical properties, it can be used as a combination propellant/solvent, although it is typically classified together with other propellants and is used in combination with other propellants. Practices for manufacture and use of aerosol products formulated with DME parallel practices employed with hydrocarbons.

(3) Hydrofluorocarbons. Hydrofluorocarbons (HFCs) such as HFC-134a and HFC-152a are partially fluorinated hydrocarbons, which have recently been developed. These compounds are less dense than HCFC-22, but with minor reformulation adjustments could function equally well as propellants except in products such as noise horns, which require a more dense gas. Because HFCs have only recently been developed, they are only now becoming readily available and are expected to be priced significantly higher than HCFC-22.

Preliminary studies show that HFCs are nonflammable and have low toxicity, which would make them good replacements for HCFC-22 as a propellant. They also may be used in conjunction with flammable chemicals to reduce the flammability of such mixtures. For example, HFCs are being tested for use with dimethyl ether (DME) in safety sprays and animal repellents. Although DME is flammable, the overall product formulation is not. HFCs are also being tested as replacements for CFCs still used in medical applications because of their nonflammable, nontoxic properties.

(4) Compressed Gases. Compressed Gases such as carbon dioxide, nitrogen, air, and nitrous oxide are common, low molecular weight gases used as propellants in aerosol products but not as drop-in replacements. First, alternative dispensing mechanisms and stronger containers are needed because

these gases are under significantly greater pressure. Containers holding compressed gases are, therefore, larger and bulkier. Second, because these chemicals have low molecular weights, they are inadequate as replacements for HCFC-22 in products requiring a dense gas propellant, such as noise horns, or in products requiring fine dispersion of the product, such as surface lubricants and weld inspection developers. Third, compressed gases disperse material faster because they are under higher pressure, which contributes to wasted product.

Compressed gases are readily available from most chemical distributors and are inexpensive. Compressed gases cool upon expansion. This property could be beneficial when they are used as freezing agents and gum removers and could substitute for some nonessential uses of HCFC-22. Compressed gases are also nonflammable and can serve as propellants in applications where a nonflammable propellant is necessary, but not in applications where a fine even dispersion is required.

(5) Alternative Processes. Alternative processes, such as manually operated pumps and sprays, provide an alternative delivery mechanism in place of the aerosol dispenser. Development of alternative process replacements depends on technological feasibility, but successful implementation of these processes depends on consumer or worker preferences. Some products, such as aerosol foams, cannot now be easily formed with alternative processes, making the replacement of the propellant difficult. In other products, the alternative process may not provide proper dispersion or accurate application of the product, limiting its use. Persons using manual pumps or sprays (in applications where alternative processes function adequately as replacements) on a continuous basis may become fatigued with the constant pumping motion, thus reducing consumer satisfaction. Therefore, alternative processes could not easily replace the use of aerosols in applications where it is not technologically feasible or where the product is used repeatedly. Nonetheless, these substitutes can serve as viable alternatives in certain applications.

b. Substitutes for Solvent/Diluents. (1) Petroleum Distillates. Petroleum distillates are hydrocarbons fractionated from the distillation of petroleum. These compounds are loosely grouped into paraffins (six carbon chains to ten carbon chains—n-hexane, n-heptane, etc.) and light aromatics (toluene and xylene) and come in various grades of purity. These compounds have good

solvent properties, are inexpensive (about half the price of MCF), and are readily available from chemical distributors. When a controlled substance is used only as a diluent, such as in automotive undercoatings, substitution using petroleum distillates is relatively easy with minor reformulation changes. Many of these products containing petroleum distillates even outperform their chlorinated counterpart.

Petroleum distillates are, however, flammable, and thus cannot be used as replacement solvents in applications where the solvent must be nonflammable such as electronic cleaning applications. In addition, pesticide aerosols formulated with certain petroleum distillates must adhere to requirements imposed under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

(2) Oxygen-Containing Hydrocarbons. Oxygen-containing hydrocarbons are compounds based on hydrocarbons containing appendant oxygen (alcohols and ketones), integral oxygens (ethers), or both (esters). These compounds are relatively inexpensive compared to MCF—about half the cost—and are readily available from chemical distributors. These compounds are also flammable and cannot be used as substitute solvents in applications where the solvent must be nonflammable.

These compounds are currently being blended with Class I substances to reduce the amount of Class I substances used in a product formulation. Since the quantity of these compounds is small, the product still remains nonflammable. Some manufacturers, however, are completely reformulating products such as spot removers with ketones, esters, ethers, or alcohols. To continue the use of these convenient products, consumers may have to be educated about the product's increased flammability.

(3) Hydrofluorocarbons (HFCs). HCFC-141b is a potential substitute to replace CFC-11 and CFC-113 used in solvent/diluent applications in aerosols and pressurized dispensers. HCFC-141b's ODP is similar to MCF, making it unlikely that aerosol manufacturers would reformulate their products away from MCF towards HCFC-141b.

HCFC-141b has a number of characteristics which make it a suitable alternative solvent, namely: it is nonconductive, nonflammable, and evaporates quickly. HCFC-141b is expensive compared to the pretax price of CFC-113 (almost three times the cost). However, HCFC-141b is slightly corrosive to plastic parts, and could not

serve as a drop-in replacement for all the uses of CFC-11 and CFC-113 as a solvent.

(4) Terpenes. Terpenes are unsaturated hydrocarbons based on isoprene subunits. They have good solvent properties and could replace ozone-depleting compounds in some solvent cleaning applications. They are flammable, which limits their use in applications that require nonflammable solvents. Some terpenes have a slight citrus scent while others have a more stronger unpleasant odor, thereby making them unpleasing to use over a constant period of time.

(5) Chlorinated Solvents. Chlorinated solvents such as perchloroethylene, trichloroethylene, and methylene chloride can be used to replace CFC-11, CFC-113, and MCF in solvent applications in aerosol and pressurized containers. These chlorinated solvents are extremely effective and can dissolve compounds which are difficult to dissolve in other solvents, such as fluorinated polymers used in water and oil repellents. However, due to toxicity concerns associated with these substances, their application is likely to be limited, especially in products sold to the general public or in products that are used frequently by workers. In addition, pesticide aerosols formulated with these chlorinated solvents must adhere to requirements under FIFRA.

Chlorinated solvents, because they are strong solvents and nonflammable, are promising substitutes in cleaning applications for electronic equipment or electric motors where safeguards could be used to protect workers from the potentially toxic fumes. These compounds are readily available from chemical distributors at prices comparable to MCF.

(6) Water-Based Formulations. Water-based formulations provide a replacement for the use of CFC-11, CFC-113, and MCF as solvents in aerosols and pressurized dispensers. These reformulated products usually contain new components/active-ingredients that are water soluble. The overall function of the reformulated product remains the same, but the product's substituents are changed.

Most formulations are nonflammable, yet may be difficult to use around sources of electricity because they may short out electrical equipment. Such products may also have short shelf-lives because the active ingredient may decompose in an aqueous environment. Also, these products when sprayed do not evaporate quickly, resulting in product accumulation. This may be problematic in certain applications such as where the accumulation of a water-

based product contributes to rust or corrosion. The possibility of reformulating products is product-specific, depending on the feasibility of finding active ingredients that are water soluble.

(7) Monochlorotoluene/chlorobenzotrifluorides. Monochlorotoluene and chlorobenzotrifluorides are of commercial interest as solvent substitutes for aerosols. These compounds can be used either in isolation or in various mixtures, depending on desired chemical properties. The Agency recently received information on these formulations, and it will issue a SNAP determination for these substitutes in the next set of listing decisions.

3. Preliminary Listing Decisions

a. Acceptable Substitutes. (1)

Propellants (a) Hydrocarbons.

Hydrocarbons are acceptable substitutes as propellants in the aerosols sector. Hydrocarbons have several environmental advantages over other substitutes. For example, they have zero ozone-depletion potential, and because of their extremely short atmospheric residence times they are estimated to have insignificant impact on global warming. Yet their reactivity contributes to formation of tropospheric ozone. The Agency has assessed this effect, however, and found that the increase in volatile organic compound emissions (VOCs) from these substitutes will have no significant effect on tropospheric ozone formation.

Hydrocarbons have a long history of use, and the increase due to replacement of CFCs as aerosol propellants represents a fraction of current consumption. Hydrocarbon propellants acquired industrial importance in the U.S. in the early 1950s. By 1978, when the ban on CFC propellants in the U.S. was promulgated, nearly half of all aerosol units being produced in the U.S. were already using hydrocarbon propellants. This percentage grew to nearly 90 percent in 1979.

Most of the hydrocarbon propellants are essentially non-toxic. Very high concentration of hydrocarbons are necessary to alter normal body functions. No temporary or permanent physiological malfunctions are produced by these chemicals. Very high concentrations of hydrocarbons may result in asphyxiation because of lack of oxygen.

Hydrocarbon propellants are flammable. Thus, precautions will need to be taken in receiving, unloading, transferring, storing, and filling

hydrocarbons aerosol products. The listing of these compounds as acceptable substitutes does not exempt producers or users from other regulatory or industrial standards such as those promulgated by OSHA. However, because of the widespread use of these materials, industry is already familiar with the safety precautions necessary in switching from a CFC filling operation to one using hydrocarbons.

(b) HCFC-22

HCFC-22 is an acceptable substitute as a propellant in the aerosols sector. The principal characteristic of HCFC-22 that has resulted in its increased use is non-flammability. However, the use of HCFC-22, either by itself or blended with other compounds, will be prohibited after January 1, 1994 due to the high ozone-depletion potential of this compound. As noted earlier, section 610(d) of the CAA Amendments of 1990 prohibits the sale or distribution of aerosol products or other pressurized dispensers that contain Class II substances (i.e., HCFCs) by January 1, 1994. Section 610(d)(2) allows EPA to grant exceptions where the use of the aerosol product or pressurized dispenser is determined by the Administrator to be essential as a result of flammability or worker safety, and where the only available alternative to the use of a Class II substance is the legally permitted use of a Class I substance.

The Agency is not restricting substitution of HCFC-22 for Class I propellants at this time. However, the Agency advises companies that, under the SNAP program, the Agency will only allow uses of HCFC-22 consistent with the exemptions provided under section 610(d)(2), once these regulations are promulgated in 1994.

(c) HCFC-142b

HCFC-142b is an acceptable substitute as a propellant in the aerosols sector. Although this compound has a comparatively high ODP, it is one of the few non-toxic, non-flammable substitutes. However, as described in the section on HCFC-22, use of HCFC-142b, either by itself or blended with other compounds, will be prohibited after January 1, 1994 under section 610(d)(2). After that date, the SNAP program will only grant exemptions for use of HCFC-142b for essential applications based on worker safety and flammability as classified under section 610.

(d) HFC-152a and HFC-134a

HFC-152a and HFC-134a are acceptable substitutes as propellants in

the aerosols sector. HFC-152a has both zero ozone-depletion potential and a low global warming potential. However, HFC-152a by itself is flammable, and necessary precautions should be taken when using this chemical. HFC-134a also has zero ozone-depletion potential, yet this compound does have a relatively long atmospheric lifetime and could therefore contribute to global warming. Despite these concerns, the Agency has approved these substitutes due to their ability to fill certain niche applications where other substitutes do not exist.

The use of these HFCs by themselves or blended with HCFC-22 or HCFC-142b will be allowed. However, as noted above, the use of HCFC-22 and HCFC-142b, either by itself or blended with other compounds, will be prohibited after January 1, 1994 under section 610(d)(2). Limited exemptions will apply, as discussed above.

(e) Dimethyl Ether

Dimethyl ether is an acceptable substitute propellant in the aerosols sector. The principal environmental concern for use of DME is its ability to contribute to ground-level ozone formation. However, the Agency's screen of effects from increased use of VOCs in aerosol products suggests that increases in ground-level ozone formation from use of DME would be minor.

(f) Compressed Gases

Compressed gases are acceptable substitutes as propellants in the aerosols sector. The Agency believes that although compressed gases such as air, carbon dioxide, nitrogen are presently only used in about 7-9 per cent of the aerosol products, their use will grow in the future. These gases have low toxicity and industrial practices for using these substitutes are well established. Since these gases are under significantly greater pressure, containers holding these gases will have to be larger and bulkier, and safety precautions will have to be undertaken during filling operations. Carbon dioxide and nitrogen are non-flammable and do not require the use of explosion proof gassing equipment. Nitrous oxide, while non-flammable, can create a moderate explosion risk under certain temperature and pressure conditions.

(g) Alternative Processes

Alternative Processes are acceptable as propellants in the aerosols sector. Alternative processes such as finger and trigger pumps, two-compartment aerosol products, mechanical pressure dispenser systems, and non-spray

dispensers (e.g., solid stick dispensers) have found increasing use as replacement for conventional aerosol products. The Agency believes that these products do not pose any significant risks, since they rely on mechanical force to replace the propellant.

(2) Solvents

(a) Petroleum Distillates.—*Petroleum distillates are acceptable substitutes as solvents in the aerosol sector.* Petroleum distillates have had a long history of use, and increases due to replacements for aerosol applications represent a fraction of the current consumption across industries. Concerns for risks from these compounds in possible uses as pesticide aerosol solvents have already been addressed under FIFRA authorities.

(b) HCFC-141b

HCFC-141b, either by itself or blended with other compounds, is an acceptable substitute for aerosol solvent applications. Like HCFC-22, the principal problem with HCFC-141b is that it has a comparatively high ODP—0.11. This is the highest ODP of all HCFCs; in fact, the ODP of HCFC-141b is about twice as high as HCFC-22. Yet in certain cases, such as where flammability is a technical impediment to use of other alternatives, HCFC-141b may be the only alternative to replace other ozone-depleting solvents. Several companies have already contacted the Agency indicating that they have tested alternatives, and that in some cases only HCFC-141b meets performance or safety criteria.

Under the SNAP program, the Agency will allow the use of HCFC-141b as a substitute for CFC-11 or CFC-113 use until January 1994, when regulations under section 610(d)(2) will be promulgated. Key features of section 610 are described under the listing decision for HCFC-22.

(c) Other Chlorinated Solvents

Trichloroethylene (TCE), perchloroethylene (PERC) and methylene chloride (MeCl), are acceptable substitutes as solvents in the aerosols sector. These substitutes have the technical capability to meet a large portion of the needs of the aerosols industry. However, the Agency anticipates that, due to toxicity concerns associated with the past use of these alternatives, the market share for these other chlorinated solvents will not increase substantially.

The toxicity of these three solvents has been subject of extensive analysis. Their use has the potential to pose high

risks to workers as well as to residents in nearby communities or consumers using products containing such chemicals.

Although risks to workers can be reduced by adhering to OSHA standards, residual risks to residents in nearby communities may remain. The Agency is aware of potential for these risks to occur, and it has the authority necessary to address them under Title III of the CAA. This section of the CAA lists three of these solvents as Hazardous Air Pollutants, and authorizes the Agency to establish controls for their use. In addition, any risks through use of these compounds as pesticide aerosols have already been addressed using FIFRA authorities.

The Agency did not explicitly evaluate risks to consumers, since it received no indication that these chlorinated solvents were of commercial interest for use in consumer aerosols. The Agency strongly encourages manufacturers to formulate consumer products based on other compounds with fewer known adverse effects on human health.

(d) Oxygen-Containing Hydrocarbons

Oxygen-containing hydrocarbons (ketones, esters, ethers, and alcohols) are acceptable substitutes as solvents in the aerosols sector. Most of these compounds have a long history of use, and the increase due to replacement as aerosol substitutes represents a fraction of the current consumption across all industries.

(e) Terpenes

Terpene-based products are acceptable substitutes as solvents in the aerosols sector. Terpene-based chemicals have a long history of use as industrial solvents, and the increase due to replacement of ozone-depleting compounds in aerosol applications represents a fraction of current consumption across all industries. Additionally, many of these chemicals are naturally occurring organic hydrocarbons and exhibit significant biodegradability.

The use history of these chemicals does not negate the inherent toxicity of these compounds to aquatic life. However, the Agency does not believe that in this case significant adverse effects are to be expected, since in aerosol applications the terpenes volatilize during use and would consequently not be discharged to surface or ground water where aquatic species are to be found.

(f) Water-Based Formulations

Water-based formulations are acceptable substitutes for propellants in the aerosols sector. The Agency did not identify any significant environmental concerns associated with use of these products. They can contain small amounts of VOCs, but these amounts are minor in comparison to products formulated solely with organic solvents.

b. Proposed Unacceptable Substitutes.

(1) Propellants.

None

(2) Solvents.

None

J. Tobacco Expansion. 1. Overview

Tobacco expansion is the process of puffing leaves of tobacco to increase the volume of tobacco used in cigarette production. Currently, one of the primary technologies used to expand tobacco in the U.S. uses CFC-11. One and one half million pounds annually are used in the U.S. in this application.

In the CFC-11 process, tobacco is saturated with CFC-11 in a stainless steel vessel maintained at 120 degrees Fahrenheit and pressurized to 20 psi. The tobacco is then permeated with hot air (330° F) which expands the tobacco. The CFC-11 is vaporized and recovered by cooling and compressing. The CFC-11 is continually recovered and recycled.

The Agency received information about three potential substitutes: (1) Carbon dioxide technology, an alternative process substitute, (2) HCFC-123, a drop-in replacement, and (3) HFC-227ea. In this action, the Agency is listing carbon dioxide as an acceptable substitute for CFC-11 in tobacco expansion. The decision on HCFC-123 as a substitute for CFC-11 for tobacco expansion is pending completion of the Agency's review of the data. Similarly, HFC-227ea is pending completion of review of the data.

2. Proposed Acceptable Substitutes. a. Carbon Dioxide

The Agency has determined the use of carbon dioxide as a substitute for CFC-11 in tobacco expansion to be acceptable. Carbon dioxide has been successfully used in the tobacco industry for approximately twenty years. It is non-toxic, non-flammable, and it has zero ODP. A permissible exposure level (PEL) has been set at 5,000 ppm, a level that can easily be met during the well contained tobacco expansion process. The carbon dioxide process is similar to the process using CFC-11, though pressure and

temperature parameters are different. For this reason carbon dioxide cannot be used as a retrofit for CFC-11 equipment; new equipment must be purchased in order to use carbon dioxide for tobacco expansion.

Although carbon dioxide is a greenhouse gas, increased use of carbon dioxide for tobacco expansion will not increase global warming because the carbon dioxide used in tobacco expansion is a by-product of the production of other gases. The carbon dioxide is captured from a stream of gas that otherwise would be emitted to the ambient air. Additionally, carbon dioxide recycling equipment is available, which will also help limit emissions of carbon dioxide to the atmosphere.

K. Adhesives, Coatings, and Inks. 1. Overview

Methyl chloroform (MCF) is used as a solvent in adhesives, coatings, and inks because of its favorable properties: high solvency, low flammability, low toxicity, relative high stability, and low boiling point. Unlike a number of other solvents classified as volatile organic compounds (VOCs), MCF does not photochemically degrade in the lower atmosphere to lead to ground-level ozone formation. This key property caused many manufacturers to switch from formulations containing VOC solvents to MCF in the mid 1980s as regulatory pressure increased to reduce VOC emissions in nonattainment areas. Companies achieved compliance by altering their solvent-borne formulations, thereby avoiding costly capital investment in new equipment, changes in operating procedures, and employee retraining. This trend has been reversed as companies have begun to respond to the phase-out of MCF under the stratospheric ozone protection provisions of the Clean Air Act.

This section examines substitutes that can be used in place of MCF in this sector, and presents the Agency's proposed decisions and supporting analysis on acceptability of these substitutes. These determinations are summarized in Appendix B at the end of the sector discussions.

Of the three uses for MCF in this sector, use of MCF is largest in the adhesives subsector. In 1989, manufacturers of adhesives consumed about 28,000 metric tons (MT) of MCF in their formulations, roughly nine per cent of the total MCF produced in the U.S. (HSEA, 1991). Solvent-based adhesive formulations constitute 15 per cent of all adhesive types. MCF is desirable as a solvent for adhesives because it evaporates rapidly, is

nonflammable, performs comparably to or better than VOC-formulated products, and does not photochemically degrade in the lower atmosphere. Current consumption of methyl chloroform as a solvent in the adhesives sector is estimated to be 32,000 MT.

MCF is used in five adhesive types:

- laminate adhesives;
- flexible foam adhesives;
- hardwood floor adhesives;
- metal to rubber adhesives; and
- tire patch adhesives.

MCF is no longer commonly used in the following adhesive applications where its use was once widespread:

- pressure sensitive adhesives (tapes, labels, etc.);
- flexible packaging adhesives;
- aerosol-propelled adhesives; and
- shoe repair glues and other

consumer adhesives. In manufacture of coatings and inks, MCF usage rose steadily throughout the 1980s and began declining in the early 1990s. In 1989, the consumption of MCF used in coatings and inks was 18,480 MT, six percent of the total 310,000 MT of MCF consumed in the U.S. Current consumption in the coatings and inks sector is estimated to be 23,000 MT. MCF is the only ozone-depleting substance currently used in coatings and inks formulations. As with uses in adhesives, MCF has replaced some of the applications in coatings and inks which previously used VOC solvents.

The current use of MCF in coatings and inks applications occurs four use areas:

- flexographic and rotogravure printing inks;
- wood stains;
- metal coatings; and
- aerospace coatings.

2. Substitutes in the Adhesives, Coatings, and Inks Sector

Methyl chloroform-based adhesives, coatings, and inks can be replaced by either substitute solvents or alternative application technologies. In most instances, the alternatives are expected to perform as well as products containing MCF. Factors that determine which particular alternative is best in a given situation include physical and chemical properties, replacement chemical costs, capital investment costs, and product performance.

The primary substitutes to replace methyl chloroform in adhesives, coatings, and inks include:

- petroleum distillates;
- organic solvents (ketones, esters, ethers, alcohols);
- chlorinated solvents;
- terpenes;
- water-based formulations;
- high-solids formulation; and

- alternative process alternatives;
- powder formulations
- hot melts
- thermoplastic plasma spray coatings
- radiation cured
- moisture cured
- chemical cured
- reactive liquids.

These substitutes can be grouped into four basic categories: solvent substitutes, water-based formulations, high-solids formulations, and alternative processes.

a. Solvent Substitutes. Petroleum distillates are hydrocarbons fractionated from the distillation of petroleum. These compounds are loosely grouped into paraffins (six carbon chains to ten carbon chains—hexane, heptane, etc.) and light aromatics (toluene and xylene), and come in various levels of purity. These compounds have good solvent properties, cost about half as much as MCF, and are readily available from chemical distributors.

Organic solvents such as alcohols, ketones, ethers, and esters dissolve a wide range of polar and semi-polar substances. These compounds are relatively inexpensive compared to MCF (about half the cost) and are readily available. They function well as solvents and dissolve most resins and binders used in adhesives, coatings, and inks.

Chlorinated solvents such as perchloroethylene and methylene chloride are chlorinated hydrocarbons. These chemicals can be used to replace MCF used in adhesives, coatings and inks. These solvents are commercially available from chemical distributors at prices comparable to those for methyl chloroform.

Chlorinated solvent compounds are chemically similar to MCF and thus are able to substitute directly for MCF with minor changes in the formulation of the product; product quality is expected to remain unchanged. Manufacturers can use chlorinated solvents in existing equipment with minor changes, resulting in low capital costs.

Terpenes are unsaturated hydrocarbons based on isoprene subunits. They have good solvent properties and could replace MCF in some coating and ink products. Terpenes, such as d-limonene, cost about seven times more than MCF, and are commercially available from chemical distributors. Manufacturers can use terpenes in existing equipment with minor changes.

Monochlorotoluene and chlorobenzotrifluorides are also of commercial interest as solvent substitutes for adhesives, coatings, and

inks. These compounds can be used either in isolation or in various mixtures, depending on desired chemical properties. The Agency recently received information on these formulations, and it will issue a SNAP determination for these substitutes in the next set of listing decisions.

b. Water-Based Formulations. Water-based coatings contain water rather than conventional solvents. Primary uses of these coatings include furniture, aluminum siding, hardboard, metal containers, appliances, structural steel, and heavy equipment. Water-based coatings are priced roughly 20 to 30 per cent more than methyl chloroform-based coatings.

Water-based inks use water and other co-solvents such as alcohols and alkyl acetates to dissolve resins, binders, and pigments instead of conventional solvents. Water-based inks accounted for 55 per cent of the flexographic inks and 15 per cent of the gravure inks used in the U.S. in 1987. Water-based inks are priced roughly 10 per cent less than methyl chloroform-based inks.

Water-based adhesives currently account for about 45 per cent of world adhesive market. Water-based adhesives will likely dominate the market to replace MCF in general consumer uses and in areas where a rigid bond is not needed. Water-based adhesives—especially water-based latexes, which are stable dispersions of solid polymeric material in an essentially aqueous medium—can effectively replace MCF use in the flexible foams sector because of the flexibility of the bond they provide. Water-based latex adhesives have the potential to penetrate 85–90 per cent of the MCF-based adhesive market in flexible foams applications. They still pose a number of problems, however, including:

- long set and dry times;
- deterioration during storage; and
- the production of bacteria-contaminated waste water.

Water-based replacements have not proven effective in binding high density laminates or hardwood flooring. Slow tack, set, and dry times continue to be a problem and trapped moisture enhances the chances of warping. In cases where MCF is used for door assemblies or sealants, water-based urethane adhesives containing polyisocyanates can be used instead.

c. High-Solid Formulations. High-solids coatings resemble conventional coatings in appearance and use, except high-solids coatings contain less solvent and a greater percentage of resin. High-solids coatings are currently used on appliances, metal furniture, and farm and road construction equipment. High-

solids coatings are priced 20 to 30 percent higher than methyl chloroform-based coatings, yet the buyer receives more usable paint because the coatings contain less solvent reducing their volume.

High-solids adhesives can reduce the amount of solvent used in adhesives by increasing the percentage of solids in the formulation. Adhesives formerly containing 30–50 percent solids after reformulation. High-solids adhesives have good performance characteristics, including initial bond strength, and can be applied using existing equipment at normal line speeds with minimal modification. For bonding rubber assemblies, high solid adhesive films are often too thick, resulting in limited versatility and generally poor performance. High-solids formulations, however, are already used widely in the flexible foams, hardwood flooring, and high-pressure laminates industries. The solvent of choice in these industries remains MCF, but with a decreased portion of solvent in the formulations, less solvent is consumed overall. High solids formulations are only a transitional replacement until adequate substitutes are found that do not contain MCF.

d. Alternative Process Substitutes. Powder adhesives, the first category of alternative process substitutes, are composed of one-part epoxies, urethanes, and natural resins. These adhesives are often supplied as powders that require heat to cure. They are generally applied in one of three ways: by sifting the powder onto preheated substrates, by dipping a preheated substrate into the powder, and by melting the powder into a paste or liquid and applying it by conventional means. Since high temperatures are required to activate and thermoset powder adhesives, their ability to replace MCF-based formulations will depend on the characteristics substrates being bonded: if the materials being bonded are heat sensitive, heat-activated powder adhesives can not be used.

Powder coatings have no solvent, containing only resins and pigments in powder form. Typically, the coated object is heated above the powder's melting point, so that the resin fuses into a continuous film. Powder coatings have been used on various types of metal products such as appliances, concrete reinforced bars, automobiles, steel shelving, lawn and farm equipment, and some furniture. The elevated temperatures necessary to melt the coatings, however, restrict the use of powder coatings on plastic and wood products. Powder coatings are priced

comparably to methyl chloroform-based coatings.

Hot melt adhesives are 100 percent solid thermoplastic binders that can be used to replace MCF formulations in applications that require a rigid bond. Hot melts currently account for about 20 percent of the adhesives market, and they, along with water-based adhesives, will likely benefit most from the move away from MCF-based adhesive formulations. Hot melts are now used instead of MCF formulations in laminating applications, especially those involving the lamination of flexible foam products. They can also replace MCF-based adhesive formulations in OEM production of high-pressure laminates and possibly in the installation of hardwood flooring. The potential ability of hot melt adhesives to replace MCF-based formulations in the flexible foams sector is limited to 10–15 percent penetration because of the need for flexible bonds in most furniture and bedding applications.

Thermoplastic plasma spray coatings are powder coatings that melt in transit towards the object to be coated propelled by a pressurized inert gas, such as Argon. An electric arc strips electrons from the plastic particles fusing them together as they move through the applicator gun. Thermoplastic plasma spray coatings can be used to coat large and small objects of metal, wood, plastic, or fiberglass.

Radiation curing is a production technique for drying and curing adhesives with radiant energy in the form of ultraviolet (UV) or infrared (IR) light, electron beams (EB), and gamma or x-rays. The binding agents that can be cured with radiant energy are acrylics, epoxies, urethanes, anaerobic adhesives, and polyester resins. In many cases, if the materials are either heat sensitive or opaque, radiation curing cannot be employed.

Radiation-dried coatings are applied as either a powder or as a high-solids form and dried using the same radiant energy forms as used in radiation-cured adhesives. The binder systems that can be dried with radiant energy are also similar. In cases where the radiant energy is harmful to a component, such as sensitive electronic equipment, radiant-dried coating cannot be employed.

Moisture-cured, chemical-cured, and reactive liquid adhesives are still not widely used because they are still being developed or because performance or application problems still have to be addressed. They will not be widely commercially available for several years.

3. Preliminary Listing Decisions. a. Acceptable Substitutes

(1) Solvent Substitutes. (a) Petroleum Distillates

Petroleum distillates are acceptable substitutes for adhesives, coatings, and inks. The principal concern with these substitutes is over risk to workers during manufacture and use of the alternative solvent. However, the Agency's analysis of these alternatives indicated that risks from use of petroleum distillates are well understood and, as a consequence, already subject to necessary controls. For instance, although these solvents are flammable, industry has a good record of safe use of these substitutes. Additionally, certain of the petroleum distillates have low Permissible Exposure Limits (PELs), for example n-hexane, but the Agency's survey of exposures in the workplace found that these levels can successfully be attained if adequate ventilation and appropriate work practices are implemented.

The Agency's analysis of the potential for risks to residents in nearby communities did indicate the potential for adverse effects near a site with industrial use of petroleum distillates if a relatively toxic petroleum distillate is used. However, the Agency does not believe that the risk screen describes the true risk presented by these chemicals. First, it is unlikely that solvents as toxic as the chemical chosen for the purpose of the risk screen—n-hexane—are in wide-spread use. Second, the screen used as past MCF emissions as a proxy for emissions of n-hexane. This approach does not account for other regulatory controls, such as VOC controls, that limit emissions of petroleum distillates from industrial sites, and would consequently also serve to lower any other health risks to the general population from these chemicals.

For this reason, the Agency believes that petroleum distillates merit use as substitutes, although it encourages manufacturers to formulate products where possible with compounds with lowest inherent toxicity.

(b) Alcohols, Ketones, Ethers and Esters

Alcohols, Ketones, Ethers and Esters are acceptable substitutes for adhesives, coatings, and inks. The concerns for use of these solvents parallel the concerns associated with petroleum distillates. In this case, two of the typical hydrocarbons examined in the Agency's risk screen, methyl ethyl ketone and methyl isobutyl ketone, also have comparatively low toxicity. For the same reasons described in the section

on petroleum distillates, the Agency is approving these compounds as substitutes for MCF. This approval also includes the same guidance to manufacturers—to select chemicals for product formulations with lowest inherent toxicity.

(c) Chlorinated Solvents

Perchloroethylene, methylene chloride and trichloroethylene are acceptable substitutes for adhesives, coatings, and inks. Uses of these solvents merit special caution, since they are suspected human carcinogens. However, as with other solvents, the Agency's risk screen indicates that proper workplace practices significantly reduce risks in occupational settings. The Agency's examination of risks to the general population determined the highest potential for adverse effects to be associated with use of trichloroethylene, since it has the greatest cancer potency. The screen pointed to the need for further assessment of the hazards from use of this chemical, and the Agency notes that authorities exist to address any risks determined from such analyses under Title III of the Clean Air Act. Title III lists all three of the chlorinated solvents as Hazardous Air Pollutants, and mandates development of Maximum Achievable Control Technology to control emissions of these chemicals in various industrial settings.

(d) Terpenes

Terpenes are acceptable substitutes for adhesives, coatings, and inks. The principal environmental concern with terpenes is their toxicity to aquatic life. In applications for terpenes in adhesives, coatings, and inks, however, the terpenes are both used and bound in the product formulation, meaning that there are no discharges of wastewater effluent that could present a risk. Other potential environmental hazards associated with these compounds arise from their flammability and unpleasant odors, but these can be controlled by good workplace practices.

(2) Water-Based Formulations/High-Solid Formulations

Water-based formulations and high-solid formulations are acceptable substitutes for adhesives, coatings, and inks. The Agency did not identify any environmental or health concerns associated with use of these products. These formulations do contain small amounts of VOCs, but the increase in VOC loadings from these products is expected to be extremely small in comparison to VOC contributions from other sources.

(3) Alternative Processes

Alternative processes, including powder formulations, hot melt, thermoplastic plasma spray, radiation-based formulations, and moisture-cured, chemical-cured, and reactive liquid alternatives, are all acceptable substitutes for adhesives, coatings, and inks. The Agency did not identify any health or environmental concerns associated with use of these substitutes. Since this grouping includes such a wide variety of products for which it is difficult to complete an in-depth risk screen, the Agency solicits additional detail on any potential environmental or health effects that merit further investigation.

X. Additional Information

A. Executive Order 12291

Executive Order (EO) 12291 requires the preparation of a regulatory impact analysis for major rules, defined by the order as those likely to result in: (1) An annual effect on the economy of \$100 million or more; (2) a major increase in costs or prices for consumers, individual industries, Federal, state or local government agencies; (3) significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic or export markets.

EPA has determined that this proposed regulation does not meet the definition of a major rule under EO 12291 and therefore has not prepared a formal regulatory impact analysis. EPA has instead prepared an economic analysis which estimated potential costs of the proposed regulation, using the reductions of production and consumption under the CFC phase-out as a baseline. This analysis showed that the SNAP program was not likely to impose costs of greater than \$100 million on industry, and in fact, to the extent the program established by this rule helps spread the word about available, economically viable substitutes for Class I and II ozone-depleting compounds, this rule provides solid benefits to industry in their effort to move away from prohibited compounds. The economic analysis summarized in the foregoing discussion has been placed in the record for this rulemaking.

B. Regulatory Flexibility Act

The Regulatory Flexibility Act, 5 U.S.C. 601-602, requires that Federal agencies examine the effects of their regulations on small entities. Under 5

U.S.C. 604(a), whenever an agency is required to publish a general notice of proposed rule-making, it must prepare and make available for public comment an initial regulatory flexibility analysis (RFA). Such an analysis is not required if the head of the Agency certifies that a rule will not have a significant economic effect on a substantial number of small entities, pursuant to 5 U.S.C. 605(b).

The Agency believes that today's proposed regulation, if promulgated, will not have a significant effect on a substantial number of small entities and has therefore concluded that a formal RFA is unnecessary. Because costs of the requirements as a whole are expected to be minor, the rule is unlikely to adversely affect small businesses, particularly as the rule exempts small sectors and end-uses from reporting requirements and formal Agency review. In fact, to the extent that information gathering is more expensive and time-consuming for small companies, this rule may well provide benefits for small businesses anxious to examine potential substitutes to any ozone-depleting Class I and II substances they may be using, by requiring manufacturers to make information on such substitutes available.

C. Paperwork Reduction Act

The information collection requirements in this proposed rule have been submitted for approval to the Office of Management and Budget (OMB) under the *Paperwork Reduction Act*, 44 U.S.C. 3501 et seq. An Information Collection Request document has been prepared by EPA (ICR No. 1596.02) and a copy may be obtained from Sandy Farmer, Information Policy Branch, EPA, 401 M St., SW. (PM-223Y), Washington, DC 20460 or by calling (202) 260-2740.

Public reporting burden for this collection of information is estimated to vary from 4 to 166 hours per response with total estimated reporting burden on the industry of 8,772 hours. This estimate includes time for initial contact with the Agency, reviewing instructions, searching existing data sources, gathering and maintaining the data needed, completing the collection and presentation of information, and responding to any additional requests for missing data.

Send comments regarding the burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Chief, Information Policy Branch, EPA, 401 M St., S.W. (PM-223Y), Washington, DC 20460, and to the

Office of Information and Regulatory Affairs, Office of Management and Budget, Washington, DC 20503, marked "Attention: Desk Officer for EPA." The final rule will respond to any public comments on the information collection requirements contained in this proposal.

XI. References

1. United Nations Environment Programme, World Meteorological Organization, et al. *Scientific Assessment of Stratospheric Ozone: 1991* (17 December 1991).
2. Intergovernmental Panel on Climate Change, World Meteorological Organization, United Nations Environment Programme. *Climate Change: The IPCC Scientific Assessment* (1990).
3. Halogenated Solvents Industry Alliance (HSIA), 1,1,1-Trichloroethane (Methyl Chloroform) White Paper (May 1991).

List of Subjects in 40 CFR Part 82

Administrative practice and procedure, Air pollution control, Reporting and recordkeeping requirements.

Dated: April 23, 1993.

Carol M. Browner,
Administrator.

Appendix A to the Preamble—Class I and Class II Ozone Depleting Substances

Class I and Class II Ozone-Depleting Substances

CLASS I

Group I:

Chlorofluorocarbon-11
CFC-11 (CF₃Cl)
Trichlorofluoromethane
Chlorofluorocarbon-12
CFC-12 (CF₂Cl₂)
Dichlorodifluoromethane
Chlorofluorocarbon-113
CFC-113 (C₂F₃Cl₃)
Trichlorotrifluoroethane
Chlorofluorocarbon-114
CFC-114 (C₂F₄Cl₂)
Dichlorotetrafluoroethane
Chlorofluorocarbon-115
CFC-115 (C₂F₅Cl)
Monochloropentafluoroethane

Group II:

Halon—1211
(CF₂ClBr)
Bromochlorodifluoromethane
Halon—1301
(CF₃Br)
Bromotrifluoromethane
Halon—2402
(C₂F₄Br₂)
Dibromotetrafluoroethane

Group III:

Chlorofluorocarbon-13
CFC-13 (CF₃Cl)
Chlorotrifluoromethane
Chlorofluorocarbon-111

CFC—111 (C ₂ FCF ₃)	HCFC—22 (CHF ₂ Cl)	Hydrochlorofluorocarbon-226 HCFC—226 (C ₂ HF ₂ Cl) Monochlorohexafluoropropane
Pentachlorofluoroethane	Monochlorodifluoromethane	Hydrochlorofluorocarbon-231 HCFC—231 (C ₃ H ₂ F ₃ Cl ₃) Pentachlorofluoropropane
Chlorofluorocarbon-112	Hydrochlorofluorocarbon-31	Hydrochlorofluorocarbon-232 HCFC—232 (C ₃ H ₂ F ₂ Cl ₄) Tetrachlorodifluoropropane
CFC—112 (C ₂ F ₂ Cl ₄)	HCFC—31 (CH ₂ FCF ₃)	Hydrochlorofluorocarbon-233 HCFC—233 (C ₃ H ₂ F ₃ Cl ₃) Trichlorotrifluoropropane
Tetrachlorodifluoroethane	Monochlorofluoromethane	Hydrochlorofluorocarbon-234 HCFC—234 (C ₃ H ₂ F ₄ Cl ₂) Dichlorotetrafluoropropane
Chlorofluorocarbon-211	Hydrochlorofluorocarbon-121 HCFC—121 (C ₂ HFCl ₂) Tetrachlorofluoroethane	Hydrochlorofluorocarbon-235 HCFC—235 (C ₃ H ₂ F ₃ Cl ₃) Monochloropentafluoropropane
CFC—211 (C ₃ FCF ₃)	Hydrochlorofluorocarbon-122 HCFC—122 (C ₂ HF ₂ Cl ₃) Trichlorodifluoroethane	Hydrochlorofluorocarbon-241 HCFC—241 (C ₃ H ₃ FCF ₂ Cl) Tetrachlorofluoropropane
Heptachlorofluoropropane	Hydrochlorofluorocarbon-123 HCFC—123 (C ₂ HF ₃ Cl ₂) Dichlorotrifluoroethane	Hydrochlorofluorocarbon-242 HCFC—242 (C ₃ H ₃ F ₂ Cl ₃) Trichlorodifluoropropane
Chlorofluorocarbon-212	Hydrochlorofluorocarbon-124 HCFC—124 (C ₂ HF ₄ Cl) Monochlorotetrafluoroethane	Hydrochlorofluorocarbon-243 HCFC—243 (C ₃ H ₃ F ₃ Cl ₂) Dichlorotrifluoropropane
CFC—212 (C ₃ F ₂ Cl ₆)	Hydrochlorofluorocarbon-131 HCFC—131 (C ₂ H ₂ FCF ₃) Trichlorofluoroethane	Hydrochlorofluorocarbon-244 HCFC—244 (C ₃ H ₃ F ₄ Cl) Monochlorotetrafluoropropane
Hexachlorodifluoropropane	Hydrochlorofluorocarbon-132B HCFC—132B (C ₂ H ₂ F ₂ Cl ₂) Dichlorodifluoroethane	Hydrochlorofluorocarbon-251 HCFC—251 (C ₃ H ₄ FCF ₃) Trichlorofluoropropane
Chlorofluorocarbon-213	Hydrochlorofluorocarbon-133A HCFC—133A (C ₂ H ₂ F ₃ Cl) Monochlorotrifluoroethane	Hydrochlorofluorocarbon-252 HCFC—252 (C ₃ H ₄ F ₂ Cl ₂) Dichlorodifluoropropane
CFC—213 (C ₃ F ₃ Cl ₃)	Hydrochlorofluorocarbon-141B HCFC—141B (C ₂ H ₃ FCF ₂) Dichlorofluoroethane	Hydrochlorofluorocarbon-253 HCFC—253 (C ₃ H ₄ F ₃ Cl) Monochlorotrifluoropentane
Pentachlorotrifluoropropane	Hydrochlorofluorocarbon-142B HCFC—142B (C ₂ H ₃ F ₂ Cl) Monochlorodifluoroethane	Hydrochlorofluorocarbon-261 HCFC—261 (C ₃ H ₃ F ₂ Cl ₂) Dichlorofluoropropane
Chlorofluorocarbon-214	Hydrochlorofluorocarbon-221 HCFC—221 (C ₃ HFCl ₆) Hexachlorofluoropropane	Hydrochlorofluorocarbon-262 HCFC—262 (C ₃ H ₃ F ₂ Cl) Monochlorodifluoropropane
CFC—214 (C ₃ F ₄ Cl ₄)	Hydrochlorofluorocarbon-222 HCFC—222 (C ₃ HF ₂ Cl ₃) Pentachlorodifluoropropane	Hydrochlorofluorocarbon-271 HCFC—271 (C ₃ H ₃ FCl) Monochlorofluoropropane
Tetrachlorotetrafluoropropane	Hydrochlorofluorocarbon-223 HCFC—223 (C ₃ HF ₃ Cl ₄) Tetrachlorotrifluoropropane	Appendix B to the Preamble—Preliminary Listing Decisions
Chlorofluorocarbon-215	Hydrochlorofluorocarbon-224 HCFC—224 (C ₃ HF ₄ Cl ₃) Trichlorotetrafluoropropane	
CFC—215 (C ₃ F ₅ Cl ₃)	Hydrochlorofluorocarbon-225CA HCFC—225CA (C ₃ HF ₅ Cl ₂) Dichloropentafluoropropane	
Trichloropentafluoropropane	Hydrochlorofluorocarbon-225CB HCFC—225CB (C ₃ HF ₃ Cl ₂) Dichloropentafluoropropane	
Chlorofluorocarbon-216		
CFC—216 (C ₃ F ₆ Cl ₂)		
Dichlorohexafluoropropane		
Chlorofluorocarbon-217		
CFC—217 (C ₃ F ₇ Cl)		
Monochloroheptafluoropropane		
Group IV:		
Carbon Tetrachloride (CCl ₄)		
Group V:		
Methyl Chloroform (C ₂ H ₃ Cl ₃)		
1,1,1 Trichloroethane		
CLASS II		
Hydrochlorofluorocarbon-21		
HCFC—21 (CHFCl ₂)		
Dichlorofluoromethane		
Hydrochlorofluorocarbon-22		

REFRIGERANTS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC—11 Centrifugal Chillers (Retrofits)	¹ HCFC—123 ...	Acceptable		EPA worker-monitoring studies of 123 show that 8-hour TWA can be kept within 1 ppm (less than the OEL of 10 ppm) when recycling and ASHRAE standards are followed. 123 is the only available retrofit for low-pressure systems; it also has (1) the lowest ODP of all available HCFCs and (2) lowest GWP of all available HCFCs and HFCs.
CFC—11 Centrifugal Chillers (New Equipment/ Alternative Substances).	¹ HCFC—123 ...	Acceptable		EPA worker-monitoring studies of 123 show that 8-hour TWA can be kept within 1ppm (less than the OEL of 10ppm) when recycling and ASHRAE standards are followed. 123 is the only replacement for low-pressure systems; it also has (1) the lowest ODP of all available HCFCs, and (2) lowest GWP of all available HCFCs and HFCs.
	¹ HCFC—22	Acceptable		Alternative Substance replacement that will allow early transition out of CFCs in some uses.
	² HFC—134a	Acceptable		Alternative Substance replacement that may be appropriate in some applications.
	Ammonia Vapor Compression.	Acceptable		
	Lithium/bromide/water absorption.	Acceptable		Alternative Substance equipment commercially available; can be operated using waste heat (e.g. steam); can be source of heated water supply; (heat recovery).

REFRIGERANTS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-12 Centrifugal Chillers (Retrofits) CFC-12 Centrifugal Chillers (New Equipment/ Alternative Substances).	Ammonia-water absorption.	Acceptable		Alternative Substance equipment commercially available for many years.
	² HFC-134a	Acceptable		
	² HFC-134a	Acceptable		
	¹ HCFC-123 ...	Acceptable		EPA worker-monitoring studies of 123 show that 8-hour TWA can be kept within 1ppm (less than the OEL of 10ppm) when recycling and ASHRAE standards are followed. 123 is the only replacement for low-pressure systems; it also has (1) the lowest ODP of all available HCFCs, and (2) lowest GWP of all available HCFCs and HFCs.
CFC-12 Reciprocating Chillers (Retrofits). CFC-12 Reciprocating Chillers (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Alternative Substance replacement that will allow early transition out of CFCs in some uses.
	Ammonia Vapor Compression.	Acceptable		
	Ammonia/water absorption.	Acceptable		Alternative Substance equipment commercially available.
	Lithium/bromide/water absorption.	Acceptable		Alternative Substance equipment commercially available; can be operated using waste heat (e.g. steam); can be source of heated water supply, (heat recovery).
CFC-12 Household Refrigerators, Single Evaporator (Retrofits). CFC-12 Household Refrigerators, Single Evaporator (New Equipment/Alternative Substances).	² HFC-134a	Acceptable		Can be retrofitted if system is flushed.
	¹ HCFC-22	Acceptable		HCFC-22 systems account for majority (>98%) of reciprocating chiller market. Readily available, proven reliability. Extensive research underway to identify zero-ODP, energy-efficient substitutes for HCFC-22—as retrofits and in new systems.
	² HFC-134a	Acceptable		To be used as a service refrigerant. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Leading candidate as replacement of CFC-12, but testing still underway.
CFC-12 Cold Storage Warehouses (Retrofits).	² HFC-134a	Acceptable		Flammability concerns believed to be minor [see ADL/UL reference (#64123); potential for significant energy efficiency.
	¹ HCFC-22	Acceptable		Currently more widely available than 134a, which will allow early transition from CFC-12.
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Users may experience flammability and/or energy efficiency problems due to potential differential fractionation of this blend in shellside applications. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	² HFC-134a	Acceptable		
CFC-12 Cold Storage Warehouses (New Equipment/Alternative Substances).	Ammonia	Acceptable		Widely available and practical for some (i.e. very large) applications.
	² HFC-134a	Acceptable		Expected to be available for higher temperatures near the middle of the decade.
	¹ HCFC-22	Acceptable		Currently, more widely available than HFC-134a, which will allow early transition from CFC-12.
	High to Low Pressure Stepdown Process.	Acceptable		
CFC-12 Residential Residential Dehumidifiers (Retrofits).	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	² HFC-134a	Acceptable		
	¹ HCFC-22	Acceptable		
	² HFC-134a	Acceptable		

REFRIGERANTS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-12 Residential Freezers (Retrofits).	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Residential Freezers (New Equipment/ Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-152a	Acceptable		
	² HFC-134a	Acceptable		
CFC-12 Commercial Ice Machines (Retrofits).	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Commercial Ice Machines (New Equipment/ Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		
	Ammonia	Acceptable		
	Vapor Compression.			
CFC-12 Industrial Process Refrigeration (Retrofits).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		User may experience flammability and/or energy efficiency problems due to potential differential fractionation of this blend in shellside applications. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Industrial Process (New Equipment/ Alternative Substances).	¹ HCFC-22	Acceptable		Currently more energy efficient and more widely available than HFC-134a, which will allow early transition from CFC-12. Technology is available.
	² HFC-134a	Acceptable		
	Ammonia	Acceptable		
	Vapor Compression.			
	Chlorine	Acceptable		EPA suggests, but does not require, that this substitute only be used at industrial facilities which manufacture or use chlorine in the process stream.
	Propane	Acceptable		EPA suggests, but does not require, that this substitute only be used at industrial facilities which manufacture or use hydrocarbons in the process stream.
	Butane	Acceptable		EPA suggests, but does not require, that this substitute only be used at industrial facilities which manufacture or use hydrocarbons in the process stream.
CFC-12 Refrigerated Transport (Retrofits).	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	² HFC-134a	Acceptable		Not yet commercially available.
CFC-12 Refrigerated Transport (New Equipment/ Alternative Substances).	¹ HCFC-22	Acceptable		
	² HFC-134a	Acceptable		
CFC-12 Retail Food (Retrofits)	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Users may experience flammability and/or energy efficiency problems due to potential differential fractionation of this blend in shellside applications. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Retail Food (New Equipment/ Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		
	Ammonia	Acceptable		
	Vapor Compression.			
CFC-12 Vending Machines (Retrofits)	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		

REFRIGERANTS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Users may experience flammability and/or energy efficiency problems due to potential differential fractionation of this blend in shellside applications. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Vending Machines (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
CFC-12 Water Coolers (Retrofits)	² HFC-134a ¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Water Coolers (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
CFC-12 Mobile Air Conditioners (Retrofits).	² HFC-134a ² HFC-134a	Acceptable Acceptable		
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		To be used as a service refrigerant. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Mobile Air Conditioners (New Equipment/Alternative Substances).	² HFC-134a	Acceptable		
CFC-114 Centrifugal Chillers (Retrofits).	¹ HCFC-124 ...	Acceptable		
CFC-114 Centrifugal Chillers (New Equipment/Alternative Substances).	¹ HCFC-124 ...	Acceptable		
CFC-500 Centrifugal Chillers (Retrofits).	¹ HCFC-142b .. ² HFC-134a	Acceptable Acceptable		
	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Users may experience flammability and/or energy efficiency problems due to potential differential fractionation of this blend in shellside applications. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-500 Centrifugal Chillers (New Equipment/Alternative Substances).	² HFC-134	Acceptable		
	¹ HCFC-22 ¹ HCFC-123 ...	Acceptable Acceptable		EPA worker-monitoring studies of 123 show that 8-hour TWA can be kept within 1ppm (less than the OEL of 10ppm) when recycling and ASHRAE standards are followed. 123 is the only replacement for low-pressure systems; it also has (1) the lowest ODP of all available HCFCs, and (2) lowest GWP of all available HCFCs and HFCs.
	Ammonia Vapor Compression.	Acceptable		
	Lithium/bromide/water absorption.	Acceptable		Alternative Substance equipment commercially available; can be operated using waste heat (e.g. steam); can be source of heated water supply, (heat recovery).
CFC-500 Residential Dehumidifiers (Retrofits).	¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-500 Residential Dehumidifiers (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
CFC-500 Refrigerated Transport (Retrofits).	² HFC-134a ¹ HCFC-22/ HFC-152a/ HCFC-124.	Acceptable Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	² HFC-134a ¹ HCFC-22/ Propane/ HFC-125.	Acceptable Acceptable		Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-500 Refrigerated Transport (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
	² HFC-134a	Acceptable		

REFRIGERANTS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-502 Cold Storage Warehouses (Retrofits).	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	¹ HCFC-22	Acceptable		
CFC-502 Cold Storage Warehouses (New Equipment/Alternative Substances).	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	¹ HCFC-22	Acceptable		Currently more widely available than 125, which will allow early transition from CFC-12.
CFC-502 Residential Freezers (New Equipment/Alternative Substances).	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	Ammonia Vapor Com- pression.	Acceptable		
CFC-502 Commercial Ice Machines (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		
CFC-502 Industrial Process Refrigeration (Retrofits).	Ammonia Vapor Com- pression.	Acceptable		
	¹ HCFC-22	Acceptable		Currently more widely available than HFC-134a, which will allow early transition from CFC-12.
CFC-502 Industrial Process Refrigeration (New Equipment/Alternative Substances).	² HFC-134a	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Currently more efficient and more widely available than HFC-134a, which will allow early transition from CFC-12.
CFC-502 Industrial Process Refrigeration (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		
	² HFC-134a	Acceptable		
CFC-502 Refrigerated Transport (Retrofits).	Ammonia Vapor Com- pression.	Acceptable		EPA suggests, but does not require, that this substitute only be used at industrial facilities which manufacture or use chlorine in the process stream.
	Chlorine	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Refrigerated Transport (New Equipment/Alternative Substances).	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		
	¹ HCFC-22	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Refrigerated Transport (New Equipment/Alternative Substances).	² HFC-134a	Acceptable		
	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Retail Food (Retrofit)	¹ HCFC-22	Acceptable		
	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Retail Food (New Equipment/Alternative Substances).	¹ HCFC-22	Acceptable		Currently more widely available than 125, which will allow early transition from CFC-12.
	¹ HCFC-22/ Propane/ HFC-125.	Acceptable		Flammability is a concern. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	Ammonia	Acceptable		

REFRIGERANTS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
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¹ Use of HCFCs is subject to (1) no venting during servicing prohibition under section 608, which was effective July 1, 1992, (2) recycling requirements under section 608 once they are promulgated, (3) section 609 motor vehicle air conditioning regulations, (4) the phaseout schedule for all Class II chemicals under section 605, which is currently being revised under EPA's efforts to accelerate the phaseout of all ozone-depleting chemicals, and (5) mandatory recycling.

² Use of HFCs is subject to the no venting prohibition under section 608(c)(2), which takes effect November 15, 1995, at the latest.

REFRIGERANTS UNACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Comments
CFC-11 Centrifugal Chillers (New Equipment/Alternative Substances).	HCFC-141b	Proposed Unacceptable.	Flammability may be an issue. Has a high ODP and is not generally available in new equipment.
CFC-12 Centrifugal Chillers (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Centrifugal Chillers (New Equipment/Alternative Substances).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Reciprocating Chillers (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Reciprocating Chillers (New Equipment/Alternative Substances).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Household Refrigerators, Single Evaporator (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Cold Storage Warehouses (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Cold Storage Warehouses (New Equipment/Alternative Substances).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II alone.
CFC-12 Residential Freezers (Retrofits).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses higher risk to ozone depletion than use of Class II chemicals alone.
CFC-12 Residential Freezers (New Equipment/Alternative Substances).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
CFC-12 Industrial Process (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
CFC-12 Retail Food (Retrofit)	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
CFC-12 Mobile Air Conditioners (Retrofits).	HCFC-22/HCFC-142b/Isobutane.	Proposed Unacceptable.	Flammability may be a serious issue. Data on flammability, fractionation and hose permeability is required for full evaluation.
	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
CFC-12 Mobile Air Conditioners (New Equipment/Alternative Substances).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
All CFC-12 Refrigeration Uses	Hydrocarbon Blend A	Proposed Unacceptable.	Flammability may be a serious issue. Data on flammability, materials compatibility and hose permeability is required for full evaluation.
CFC-500 Centrifugal Chillers (Retrofit).	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses a higher risk of ozone depletion than use of Class II chemicals alone.
All HCFC-22 Refrigeration Uses ..	HCFC-22/HCFC-142b/CFC-12.	Proposed Unacceptable.	As a blend of both Class I and Class II chemicals, it poses higher risk to ozone depletion than use of Class II chemicals alone.

REFRIGERANTS—PENDING DECISIONS

Application	Substitute	Comments
CFC-12 Household Refrigerators, Single Evaporator (Retrofit).	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
	HCFC-22/HCFC-142b.	EPA has not yet concluded review of the data.
CFC-12 Household Refrigerators, Single Evaporator (New Equipment/Alternative Substances).	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
	HCFC-22/HCFC-142b.	EPA has not yet concluded review of the data.
CFC-12 Residential Freezers (Retrofits).	R200b	EPA has not yet concluded review of the data.
	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
CFC-12 Residential Freezers (New Equipment/Alternative Substances).	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
CFC-12 Commercial Ice Machines (New Equipment/Alternative Substances).	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Refrigerated Transport (New Equipment/Alternative Substances).	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-12 Cold Storage	R200a	EPA has not yet concluded review of the data.
CFC-12 Mobile Air Conditioners (Retrofits).	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
CFC-12 Mobile Air Conditioners (New Equipment/Alternative Substances).	HCFC/HFC/fluoroalkane Blend A.	As discussed earlier, EPA is concerned about the potential wide use of perfluorinated compounds, particularly in situations where containment may be difficult to assure. As a result, EPA will be reviewing perfluorinated compound uses to assess the aggregate quantity likely to be used and to determine any necessary emission control.
CFC-12 Chillers, Heat Pumps and Commercial Refrigeration Systems.	HFC-227ea	EPA has not yet concluded review of the data.
CFC-12 Refrigerant	HCFC-142b	EPA has not yet concluded review of the data.
CFC-13 Refrigerant	HFC-23	EPA requests additional data on the use of this substitute.
CFC-114 Centrifugal Chillers (New Equipment/Alternative Substances).	R200b	EPA has not yet concluded review of the data.
	R200c	EPA has not yet concluded review of the data.
	R200d	EPA has not yet concluded review of the data.
	R200e	EPA has not yet concluded review of the data.
	R200f	EPA has not yet concluded review of the data.
	R200g	EPA has not yet concluded review of the data.
	R200j	EPA has not yet concluded review of the data.
	R200l	EPA has not yet concluded review of the data.
CFC-114 Chillers, Heat Pumps and Commercial Refrigeration Systems.	HFC-227ea	EPA has not yet concluded review of the data.
CFC-502 Air Conditioning, Heat Pumps, and Chillers.	HFC-143a	EPA has not yet concluded review of the data.
CFC-502 Cold Storage Warehouses (New Equipment/Alternative Substances).	HFC-125	Final decision pending data addressing efficiency concerns. Can be used as a component in mixtures. Not yet widely available.
	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Cold Storage	R200a	EPA has not yet concluded review of the data.
CFC-502 Commercial Ice Machines (New Equipment/Alternative Substances).	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Industrial Process Refrigeration (New Equipment/Alternative Substances).	HFC-143a	Pending receipt of data on flammability. Material has high potential GWP.
	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.

REFRIGERANTS—PENDING DECISIONS—Continued

Application	Substitute	Comments
CFC-502 Refrigerated Transport (New Equipment/Alternative Substances).	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
CFC-502 Retail Food (New Equipment/Alternative Substances).	HFC-125	HFC-125 can be used as a component in mixtures. Data on efficiency is needed to fully evaluate.
Heat Pumps	HFC-125/ HFC-143a/ HFC-134a.	Final decision pending receipt of data on flammability controls and constituent toxicity of HFC-143a. Precautions must be taken during recycling of blends to avoid mixing with other refrigerants.
	HFC-143a	Pending receipt of data on flammability. Material has high potential GWP.
	HFC-134a	EPA has not yet concluded review of the data.
	HFC-152a	EPA has not yet concluded review of the data.
	HFC-32	EPA has not yet concluded review of the data.
	HFC-125/ HFC-134a/ HFC-32.	EPA has not yet concluded review of the data.
	R200a	EPA has not yet concluded review of the data.
Mobile Air Conditioning	CO2	EPA has not yet concluded review of the data.
Commercial and Residential Air Conditioners, Cold Storage Warehouses, Industrial Cooling, Mobile Air Conditioning.	Evaporative Cooling.	EPA has not yet concluded review of the data.
Conventional Air Conditioning	Dessicant-based Dehumidification.	EPA has not yet concluded review of the data.
	Dessicant-based Natural Gas.	EPA has not yet concluded review of the data.
	HFC-125/ HFC-134a/ HFC-32.	EPA has not yet concluded review of the data.
	R200a	EPA has not yet concluded review of the data.

FOAMS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-11 Polyurethane, Rigid Laminated Boardstock.	HCFC-123	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with increased ventilation, where needed. Very easy to use as a retrofit; energy efficiency close to CFC-11. Current availability is limited.
	HCFC-141b	Acceptable		Only chemical alternative that is or soon will be available in sufficient quantities to meet demand of industry. Has highest ODP of HCFCs. Will allow virtually immediate transition out of CFC-11. Fairly good energy efficiency properties.
	HCFC-142b	Acceptable		Technology not yet available in most applications to allow near-term use. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22	Acceptable		Technology under development.
	HCFC-22/ HCFC-141b.	Acceptable		Technology under development. HCFC-141b is only chemical alternative that is currently available in sufficient quantities to meet demand of industry and has fairly good energy efficiency properties.
	HCFC-141b/ HCFC-123.	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with increased ventilation, where needed. Fairly good energy efficiency properties.
	HCFC-22/ HCFC-142b.	Acceptable		Technology not yet available in most applications to allow near-term use. Increases in thermal conductivity may reduce energy efficiency.

FOAMS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-11 Polyurethane, Rigid Appliance	HFC-134a	Acceptable		Technology not yet available in most applications to allow near-term use. Potentially large increases in thermal conductivity which will reduce energy efficiency.
	HFC-152a	Acceptable		Technology not yet available in most applications to allow near-term use. Potentially large increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers.
	Hydrocarbons (Pentane etc.).	Acceptable		Technology not yet available in most applications to allow near-term use. Potentially large increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers. Major sources of VOC emissions are subject to the New Source Review (NSR) program.
	2-Chloro-propane.	Acceptable		Technology under development. Flammability may be an issue for workers and consumers.
	Carbon Dioxide HCFC-22	Acceptable Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-123	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with increased ventilation, where needed. Easy to use as a retrofit; energy efficiency close to CFC-11. Current availability is limited.
	HCFC-141b	Acceptable		Only chemical alternative that is or will soon be available in sufficient quantities to meet demand of industry. Has highest ODP of HCFCs. Will allow virtually immediate transition out of CFC-11. Fairly good energy efficiency properties.
	HCFC-142b	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22/ HCFC-141b.	Acceptable		Technology under development. HCFC-141b is only chemical alternative that is currently available in sufficient quantities to meet demand of industry and has fairly good energy efficiency properties.
	HCFC-22/ HCFC-142b.	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-123/ HCFC-141b.	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with increased ventilation, where needed. Fairly good energy efficiency properties.
	HFC-134a	Acceptable		Technology not yet available in most applications to allow near-term use. Potential increases in thermal conductivity which will reduce energy efficiency.
	HFC-152a	Acceptable		Technology not yet available in most applications to allow near-term use. Potential increases in thermal conductivity will reduce energy efficiency. Flammability may be an issue for workers and consumers.
	Hydrocarbons (Pentane, Isopentane, Hexane etc.).	Acceptable		Technology not yet available in most applications to allow near-term use. Potentially large increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers. Major sources of VOC emissions are subject to the New Source Review (NSR) program.
	Carbon Dioxide	Acceptable.		

FOAMS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-11 Polyurethane, Rigid Commercial Refrigeration Foams, Spray Foams and Sandwich Panel Foams.	HCFC-22	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-123	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with use of increased ventilation, where needed. Easy to use as a retrofit; energy efficiency close to CFC-11. Current availability is limited.
	HCFC-141b	Acceptable		Only chemical alternative currently or soon to be available in sufficient quantities to meet demand of industry. Has highest ODP of the HCFCs. Will allow virtually immediate transition out of CFC-11. Fairly good energy efficiency properties.
CFC-11 Polyurethane, Rigid Commercial Refrigeration Foams, etc. (continued).	HCFC-142b	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency.
	HCFC-22/142b	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency.
	HFC-134a	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency.
	HFC-152a	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers.
	Hydrocarbons (Pentane, Isopentane, Hexane etc.)	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers. Major sources of VOC emissions are subject to the New Source Review (NSR) program.
	Carbon Dioxide	Acceptable		
CFC-11 Polyurethane, Rigid Slabstock and Other.	HCFC-22	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-141b	Acceptable for use in insulating and flotation foams only.		Only chemical alternative that is or soon will be available in sufficient quantities to meet demand of industry. Will allow virtually immediate transition out of CFC-11. Fairly good energy efficiency properties. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that, with the exception of flotation applications, there are other non-ODP alternatives, or alternatives with lower ODPs, available for use in packaging, decorative, and other noninsulating applications. Use of HCFC-141b for flotation foams may be restricted further under section 610 Non-Essential Use Ban. See HCFC discussion in Preamble for detail.

FOAMS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-12 Poly-styrene, Extruded Boardstock.	HCFC-123	Acceptable		Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved increased ventilation, where needed. Easy to use as a retrofit; energy efficiency close to CFC-11. Current availability is limited.
	Hydrocarbons (Pentane, Isopentane, Butane, Isobutane etc.).	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers. Major sources of VOC emissions are subject to the New Source Review (NSR) program.
	Carbon Dioxide . HCFC-22	Acceptable. Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-142b	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22/142b .	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HFC-134a	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency.
	HFC-152a	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers.
CFC-11, CFC-113 Phenolic, Insulation Board.	Hydrocarbons (Pentane, Isopentane, Butane, Isobutane etc.).	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers. Major sources of VOC emissions are subject to the New Source Review (NSR) program.
	HCFC-22/Hydrocarbons (Isopentane etc.).	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency. Flammability may be an issue for workers and consumers.
	Carbon Dioxide . HCFC-141b	Acceptable. Acceptable		Only chemical alternative that is or soon will be available in sufficient quantities to meet demand of industry. Has highest OPD of HCFCs. Will allow virtually immediate transition out of CFC-11. Fairly good energy efficiency properties.
	HCFC-142b	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22/142b .	Acceptable		Technology under development. Increases in thermal conductivity may reduce energy efficiency.
	HCFC-22/Hydrocarbons (Isopentane etc.).	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Flammability may be an issue for workers and consumers.
	Hydrocarbons (Pentane, Isopentane etc.).	Acceptable		Technology under development. Potential increases in thermal conductivity which will reduce energy efficiency. Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.

FOAMS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-11 Polyurethane, Flexible.	2-Chloropropane	Acceptable		Proprietary technology. Flammability may be an issue for workers and consumers.
	Carbon Dioxide	Acceptable		
	HCFC-123	Acceptable		Current availability is extremely limited. Recent worker monitoring studies indicate OEL for 123 (10 ppm) can be achieved with increased ventilation, where needed. Subject to section 610 Non-essential Use Ban.
	HFC-134a	Acceptable		Technology under development.
	HFC-152a	Acceptable		Technology under development. Flammability may be an issue for workers and consumers.
	Methylene Chloride	Acceptable		Revised OSHA PELs have been proposed at 25 ppm (TWA) for methylene chloride (Nov. 7, 1991). Subject to meeting all future ambient air controls for hazardous air pollutants under Title III of the 1990 CAAA.
CFC-11 Polyurethane, Integral Skin.	Acetone	Acceptable		Regulated as a VOC under Title I of the Clean Air Act. Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.
	AB Technology	Acceptable		AB generates more carbon monoxide (CO) than other blowing agents. OSHA has set a PEL for CO at 35 ppm TWA with a ceiling of 200 ppm.
	Carbon Dioxide	Acceptable		
	HCFC-22	Acceptable		Technology not yet available in most applications to allow near-term use. Subject to section 610 Non-essential Use Ban.
	HCFC-123	Acceptable		Recent worker monitoring studies indicates OEL for HCFC-123 (10 ppm) can be achieved with increased ventilation, where needed. Very easy to use as a retrofit; energy efficiency close to CFC-11. Current availability is extremely limited. Subject to section 610 Non-essential Use Ban.
CFC-11 Polyurethane, Integral Skin (continued).	HCFC-141b	Acceptable only for uses which provide for motor vehicle safety in accordance with Federal Motor Vehicle Safety Standards.		Only chemical alternative that is currently available in sufficient quantities to meet demand of industry. Will allow virtually immediate transition out of CFC-11. HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that, with the exception of motor vehicle safety foams, there are other non-ODP alternatives, or alternatives with lower ODPs, available for use in integral skin foams. See HCFC discussion in Preamble for detail on section 610 Non-Essential Use Ban and motor vehicle safety foams exemption.
	HCFC-22/HCFC-141b	Acceptable only for uses which provide for motor vehicle safety in accordance with Federal Motor Vehicle Safety Standards.		HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that, with the exception of motor vehicle safety foams, there are other non-ODP alternatives, or alternatives with lower ODPs, available for use in integral skin foams. See HCFC discussion in Preamble for detail on section 610 Non-Essential Use Ban and motor vehicle safety foams exemption.
	HFC-134a	Acceptable		Technology under development.
	HFC-152a	Acceptable		Technology under development. Flammability may be an issue for workers and consumers.

FOAMS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-12 Poly-styrene, Extruded Sheet.	Hydrocarbons (Pentane, Isopentane, Butane etc.).	Acceptable		Technology under development. Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.
	Methylene Chloride.	Acceptable		Revised OSHA PELs have been proposed at 25 ppm (TWA) for methylene chloride (Nov. 7, 1991). Subject to meeting all future ambient air controls for hazardous air pollutant under Title III of the 1990 CAAA.
	Carbon Dioxide . HFC-134a	Acceptable. Acceptable		Technology not yet available in most applications to allow near-term use.
	HFC-152a	Acceptable		Technology not yet available in most applications to allow near-term use. Flammability may be an issue for workers and consumers.
CFC-12, CFC-114, CFC-11 Polyolefin.	Hydrocarbons (Pentane, Isopentane, Butane, Isobutane etc.).	Acceptable		Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.
	Carbon Dioxide . HCFC-22	Acceptable. Acceptable		Technology not yet available in most applications to allow near-term use.
	HCFC-142b	Acceptable		Technology not yet available in most applications to allow near-term use.
	HCFC-22/ HCFC-142b.	Acceptable		Technology not yet available in most applications to allow near-term use.
	HCFC-22/Hydrocarbons (Isopentane etc.).	Acceptable		Technology under development. Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.
	HFC-134a	Acceptable		Technology not yet available in most applications to allow near-term use.
	HFC-152a	Acceptable		Technology not yet available in most applications to allow near-term use. Flammability may be an issue for workers and consumers.
	Hydrocarbons (Butane, Isopentane etc.).	Acceptable		Technology under development. Major sources of VOC emissions are subject to the New Source Review (NSR) program. Flammability may be an issue for workers and consumers.
	Carbon Dioxide .	Acceptable.		

FOAMS.—UNACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decisions	Comments
CFC-11 polyurethane, rigid slabstock and other.	HCFC-141b (or blends thereof).	Proposed unacceptable except for insulation and flotation foams.	HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that, with the exception of flotation applications, there are other non-ODP alternatives, or alternatives with lower ODPs, available for use in packaging, decorative, and other noninsulating applications. Use of HCFC-141b may be restricted further under section 610 Non-Essential Use Ban. See HCFC discussion in Preamble for details.
CFC-11 polyurethane, flexible.	HCFC-141b (or blends thereof).	Proposed unacceptable.	HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives are sufficiently available to render the use of HCFC-141b unnecessary in flexible polyurethane foams.

FOAMS.—UNACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decisions	Comments
CFC-11 polyurethane, integral skin.	HCFC-141b (or blends thereof).	Proposed unacceptable except for use in motor vehicle safety foams.	HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that, with the exception of motor vehicle safety foams, there are other non-ODP alternatives, or alternatives with lower ODPs, available for use in integral skin foams. See HCFC discussion in Preamble for details on section 610 Non-Essential Use Ban and motor vehicle safety foams.
CFC-114, CFC-12, CFC-11 polyolefin.	HCFC-141b (or blends thereof).	Proposed unacceptable.	HCFC-141b has an ODP of 0.11, almost equivalent to that of methyl chloroform, a Class I substance. The Agency believes that non-ODP alternatives, or alternatives with lower ODPs, are sufficiently available to render the use of HCFC-141b unnecessary in polyolefin foams. See HCFC discussion in Preamble for details on section 610 Non-Essential Use Ban and motor vehicle safety foams.

FOAMS.—PENDING SUBSTITUTES

Application	Substitute	Comments
CFC-11, CFC-113 polyurethane, rigid laminated boardstock.	Alternative products: expanded polystyrene, fiberboard, fiberglass.	Agency has not completed review of data.
CFC-11, CFC-113 rigid polyurethane, appliance foams.	Alternative products: fiberglass, vacuum panels	Agency has not completed review of data.
CFC-11 polyurethane, rigid slabstock and other.	Alternative products: fiberglass, expanded polystyrene.	Agency has not completed review of data.
CFC-11 polyurethane, rigid spray and commercial refrigeration foams, and sandwich panels.	Alternative products: fiberglass, expanded polystyrene.	Agency has not completed review of data.
CFC-11, CFC-113 phenolic	HFC-143a	Pending receipt of additional data.
	Alternative products: fiberglass, expanded polystyrene.	Agency has not completed review of data.
CFC-11 polyurethane, flexible	Alternative technologies: new polyol technologies ...	Agency has not completed review of data.
	Enviro-Cure Process	Agency has not completed review of data.
	Alternative products: fiberfill, natural latex foams, polyester batting.	Agency has not completed review of data.
Foams, alternative process	Electroset process	Insufficient data. Also need information on proposed end-use.
CFC-12, CFC-114 polystyrene, extruded.	HCFC-22/isopentane blend	Agency has not completed review of data. Also need more data on proposed end use: sheet and/or boardstock.
	HFC-124	Insufficient data. Also need information of proposed end-use: sheet and/or boardstock.
	HFC-125	Insufficient data. Also need information of proposed end-use: sheet and/or boardstock.
	HFC-143a	Insufficient data. Also need information of proposed end-use: sheet and/or boardstock.
CFC-12, CFC-114 polystyrene, extruded boardstock.	Alternative products: expanded polystyrene, fiberboard.	Agency has not completed review of data.
CFC-12, CFC-114 polyolefin	HFC-143a	Agency has not completed review of data.
	Alternative products: paper, cardboard, expanded polystyrene.	Agency has not completed review of data.
Polyurethane, rigid/frothing process	HFC-143a	Insufficient data.
Polyurethane, rigid	HFC-356	Insufficient data. Also need information on proposed end-use.
Blowing Agent.	HFC-227ea/pentane	Insufficient data. Also need information on proposed end-uses.
	HFC-227ea/2-methylpropane	Insufficient data. Also need information on proposed end-uses.
	Nitrogen gas	Insufficient data. Also need information on proposed end-uses.

SOLVENT CLEANING—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed condition	Comments
Metals cleaning w/ CFC-113, MCF.	Aqueous cleaners	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.

SOLVENT CLEANING—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed condition	Comments
Electronics cleaning w/CFC-113, MCF.	Semi-aqueous cleaners (terpenes/surfactants).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (alcohols).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (petroleum-based).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Organic solvents (esters, ketones, ethers, etc.).	Acceptable		OSHA standards must be met, if applicable. EPA investigating workplace exposures where no OSHA standards exist.
	Trichloro-ethylene, perchloro-ethylene, methylene chloride.	Acceptable		OSHA standards must be met. EPA expects to issue Maximum Achievable Control Technology requirements under the Clean Air Act for this application by 1994.
	Supercritical fluids, plasma cleaning, UV/Ozone cleaning.	Acceptable		OSHA standards for ozone must be met.
	Aqueous cleaners	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (terpenes/surfactants).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (alcohols).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (petroleum-based).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Organic solvents (esters, ketones, ethers, etc.).	Acceptable		OSHA standards must be met, if applicable.
	Trichloro-ethylene, perchloro-ethylene, methylene chloride.	Acceptable		OSHA standards must be met. EPA expects to issue Maximum Achievable Control Technology requirements under the Clean Air Act for this application by 1994.
	No-clean alternatives	Acceptable		Approval covers low solids fluxes and inert gas soldering.
	Supercritical fluids, plasma cleaning, UV/Ozone cleaning.	Acceptable		OSHA standards for ozone must be met.
Precision cleaning w/CFC-113, MCF.	Perfluoro-carbons	Acceptable for spot-free cleaning and drying of high-performance computer components where no other alternative exists.		Under SNAP, EPA has reviewed and found acceptable only certain narrowly defined uses of perfluorinated compounds. Wider use of perfluorinated compounds (e.g., basic metal cleaning or circuit board defluxing) is of concern due to long atmospheric lifetimes, and potential to contribute to global warming.
	Aqueous cleaners	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (terpenes/surfactants).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Semi-aqueous cleaners (alcohols).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.

SOLVENT CLEANING—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed condition	Comments
	Semi-aqueous cleaners (petroleum-based).	Acceptable		EPA expects to issue effluent guidelines for this industry under the Clean Water Act by 1994. Constituents should be drawn from the Agency's list of cleaner components, available from the SNAP Coordinator.
	Organic solvents (esters, ketones, ethers, etc.).	Acceptable		OSHA standards must be met, if applicable. EPA investigating workplace exposures where no OSHA standards exist.
	Trichloro-ethylene, perchloro-ethylene, methylene chloride.	Acceptable		OSHA standards must be met. EPA expects to issue Maximum Achievable Control Technology requirements for this application by 1994.
	Supercritical fluids, plasma cleaning, UV/Ozone cleaning.	Acceptable		OSHA standards for ozone must be met.
	Perfluoro-carbons	Acceptable for spot-free cleaning and drying of high-performance computer components where no other alternative exists.		Under SNAP, EPA has reviewed and found acceptable only certain narrowly defined uses of perfluorinated compounds. Wider use of perfluorinated compounds (e.g., circuit board defluxing or basic metal cleaning) is of concern due to long atmospheric lifetimes, and potential to contribute to global warming.

SOLVENT CLEANING—UNACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Comments
Metals cleaning w/ CFC-113.	HCFC 141b and blends with alcohols.	Proposed unacceptable with limited critical use exemptions.	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment. EPA will grant limited critical use exemptions where all other substitutes fail to meet safety or performance standards.
Metals cleaning w/ MCF.	HCFC 141b blends with alcohols.	Proposed unacceptable	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment.
Electronics cleaning w/CFC-113.	HCFC 141b and blends with alcohols.	Proposed unacceptable with limited critical use exemptions.	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment. EPA will grant limited critical use exemptions where all other substitutes fail to meet safety or performance standards.
Electronics cleaning w/MCF.	HCFC 141b blends with alcohols.	Proposed unacceptable	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment.
Precision cleaning w/CFC-113.	HCFC 141b and blends with alcohols.	Proposed unacceptable with limited critical use exemptions.	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment. EPA will grant limited critical use exemptions where all other substitutes fail to meet safety or performance standards.
Precision cleaning w/MCF.	HCFC 141b blends with alcohols.	Proposed unacceptable	High ODP; other alternatives exist. Effective date: As of 30 days after final rule for new equipment; as of January 1, 1996 for existing equipment.

SOLVENT CLEANING—PENDING DECISIONS

Application	Substitute	Comments
Metals cleaning w/ CFC-113, MCF.	Monochloro-toluene/benzo-trifluorides	Agency has not completed review of data.
	Brominated hydrocarbons	Agency has not completed review of data.
	Volatile methyl siloxanes	Agency has not completed review of data. Preliminary indications are that this substitute merits approval.
Electronics Cleaning w/ CFC-113, MCF.	Brominated hydrocarbons	Agency has not completed review of data.
Precision cleaning w/ CFC-113, MCF.	Brominated hydrocarbons	Agency has not completed review of data.

SOLVENT CLEANING—PENDING DECISIONS—Continued

Application	Substitute	Comments
	HCFC-123	More information needed on feasibility of achieving OEL. EPA investigating toxicity concerns.
	HCFC-225	Toxicity data yet to be completed. HCFC-225cb isomer is of commercial interest, but toxicity concerns may limit interest in the isomer.

HALONS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
Halon 1211 Streaming Agents—Consumer Applications	HBFC-22B1	Acceptable in non-residential uses only.		ODP of compound (.74) precludes acceptability of widespread use in consumer applications. Will be phased out (except for essential uses) January 1, 1996. Anticipated exposure levels in consumer applications exceed toxic levels. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Consent Order.
	HCFC-123	Acceptable.		Contains small percentage of PFC which has an unusually long atmospheric lifetime, and could potentially contribute to global climate change. EPA suggests but does not require that users minimize emissions by minimizing use during training, and by recovery and recycling during maintenance and servicing. Not commercialized for residential use. [CFC Blend] can help transition away from halon 1211 in applications requiring a highly effective fire extinguishant with low toxicity. Because CFCs are a Class I substance, production will be phased out by January 1, 1996. The manufacturer notes that this agent is not suitable for Class B fires involving escaping gases. Not rated for use against Class A fires. Can result in temporary loss of visibility if discharged in confined areas. Not suitable for use against electrical fires (Class C). Effective against flammable liquids. Can also be used against Class A fires. Not suitable for discharge onto live electrical equipment.
	[HCFC Blend] B	Acceptable		
	[CFC Blend]	Acceptable in non-residential uses only.		
	Carbon Dioxide	Acceptable		Proper procedures regarding the operation of the extinguisher and ventilation following dispensing the extinguishant is recommended. Worker exposure may be a concern in small office areas. Acceptability in commercial applications will accelerate the transition away from Halon 1211 which has a significantly higher ODP. HBFC-22B1 is considered an interim substitute for Halon 1211. Because the HBFC-22B1 has an ODP of .74, production will be phased out (except for essential uses) on January 1, 1996. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Consent Order.
	Dry Chemical	Acceptable		
	Water	Acceptable		
Halon 1211 Streaming Agents—Commercial/Industrial Applications	Foam	Acceptable		
	HBFC-22B1	Acceptable		

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
Halon 1211 Streaming Agents—Military Applications	HCFC-123	Acceptable		Contains small percentage of PFC which has an unusually long atmospheric life-time, and could potentially contribute to global climate change. EPA suggests but does not require that users minimize emissions by minimizing use during training, and by recovery and recycling during maintenance and servicing.
	[HCFC Blend] B	Acceptable		
	[CFC Blend]	Acceptable		
	Dry Chemical	Acceptable		[CFC Blend] can help transition away from halon 1211 in applications requiring a highly effective fire extinguishant with low toxicity.
	Carbon Dioxide	Acceptable		Because CFCs are a Class I substance, production will be phased out by January 1, 1996.
	Water	Acceptable		The manufacturer notes that this agent is not suitable for Class B fires involving escaping gases.
	Foam	Acceptable		Can result in temporary loss of visibility if discharged in confined areas.
	HBFC-22B1	Acceptable		Not rated for use against Class A fires.
	HCFC-123	Acceptable		Not suitable for use against electrical fires (Class C).
	[HCFC Blend] B	Acceptable		Effective against flammable liquids. Can also be used against Class A fires.
	FC 5-1-14	Acceptable for use in military flightlines, inside military aircraft, and in military computer and telecommunication facilities.	FC 5-1-14 shall not be used during training exercises. FC 5-1-14 must be recovered from the fire protection system prior to servicing and recycled for later use.	Not suitable for discharge onto live electrical equipment.
	[CFC Blend]	Acceptable		Acceptability in commercial applications will accelerate the transition away from Halon 1211 which has a significantly higher ODP.
	Dry Chemical	Acceptable		HBFC-22B1 is considered an interim substitute for Halon 1211. Because the HBFC-22B1 has an ODP of .74, production will be phased out on January 1, 1996.
	Carbon Dioxide	Acceptable		This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Consent Order.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
Halon 1301 Total Flooding—Occupied Areas	Water	Acceptable		Not suitable for use against electrical fires (Class C).
	Foam	Acceptable		Effective against flammable liquids. Can also be used against Class A fires. Not suitable for discharge onto live electrical equipment.
	HBFC-22B1	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HBFC-22B1 exceeds 1%	HBFC-22B1 can be utilized in existing equipment with only minor modifications and can thus facilitate a more rapid transition away from Halon 1301. The design concentration is approximately 5.3% while its cardiotoxic LOAEL is 1%. Evacuation must be complete before 1% concentration is reached. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area. HBFC-22B1 can be considered only an interim substitute for Halon 1301. HBFC-22B1 has an ODP of .74; thus, production will be phased out on January 1, 1996. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substances Control Act (TSCA) Consent Order.
	HCFC-22	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HCFC-22 exceeds 5%	The design concentration is approximately 13.9% while its cardiotoxic NOAEL is 2.5% and the LOAEL is 5%. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
	HCFC-124	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HCFC-124 exceeds 2.5%	The design concentration is approximately 9.8% while its cardiotoxic NOAEL is 1.0% and its LOAEL is 2.5%. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area.
	[HCFC BLEND] A	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of [HCFC BLEND] A exceeds the design concentration of 10.3%	The design concentration is approximately 10.3%. Preliminary data indicates that the NOAEL is at least 10.0%, and therefore the LOAEL is likely to be higher. Until the Agency receives the LOAEL data, this agent is approved to the design concentration of 10.3%. Evacuation must be complete before 10.3% concentration is exceeded. EPA awaits the final report on cardiotoxicity test data. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
	HFC-23	Acceptable for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions.	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-23 exceeds 30%	The design concentration is approximately 14.9% while preliminary data indicates that its cardiotoxic NOAEL is 30% without added oxygen and 50% with added oxygen. Its LOAEL is likely to exceed 50%. Evacuation must be complete before 30% concentration is reached. EPA awaits the final report on cardiotoxicity test data. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area. Due to concerns about this agent's Global Warming Potential, the agency is currently restricting its use until further analysis is complete. Required extinguishing concentration and storage volume ratio are the highest of all potential candidates, but weight ratio is only 2.0.
	HFC-134a	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-134a exceeds 8.0%.	The design concentration is approximately 12.6% while its cardiotoxic LOAEL is approximately 8.0%. Evacuation must be complete before 8.0% concentration is reached. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area.
	HFC-227ea	Acceptable	For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL.	The design concentration is approximately 7.1% while preliminary data indicates that its cardiotoxic NOAEL is 8.1% and its LOAEL is greater than 10.5%. Evacuation must be complete before a concentration of 10.5% is exceeded. EPA awaits the final report on cardiotoxicity test data.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
			For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of HFC-227ea exceeds 10.5%.	Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area. This agent was submitted to the Agency as a Premanufacture Notice (PMN) agent and is presently subject to requirements contained in a Toxic Substances Control Act (TSCA) Significant New Use Rule (SNUR).
FC 3-1-10	Acceptable for applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; or life support functions.		For occupied areas from which personnel cannot be evacuated in one minute, use is permitted only up to concentrations not exceeding the cardiotoxic NOAEL. For occupied areas from which personnel can be evacuated or egress can occur between 30 and 60 seconds, use is permitted up to a concentration not exceeding the LOAEL. All personnel must be evacuated before concentration of FC 3-1-10 exceeds 40% FC 3-1-10 shall not be used to test total flooding systems unless captured and recycled or destroyed. Fire detection should be cross-zoned to avoid unnecessary discharge and maintained to high reliability. FC 3-1-10 must be recovered from the fire protection system prior to servicing and must be recycled for later use.	The design concentration is approximately 6.6% while its cardiotoxic NOAEL is 40% and its LOAEL is over 40%. Must conform with OSHA 29 CFR 1910 Subpart L Section 1910.160 of the U.S. Code. This section requires that employees be alerted to impending system discharge by suitable alarms and provided with sufficient time to safely exit the area prior to system discharge. Per OSHA requirements, protective gear (SCBA) must be available in the event personnel must reenter the area. Under SNAP, EPA has reviewed and found acceptable only certain narrowly defined uses of perfluorinated compounds. Wider use of perfluorinated compounds is of concern due to long atmospheric lifetimes, and potential to contribute to global warming.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments *
Halon 1301 Total Flooding—Unoccupied Areas	[Inert Gas Blend]	Acceptable	The design concentration must result in at least 14% oxygen and 4% CO ₂ . If the oxygen concentration of the atmosphere falls below 12%, personnel must be evacuated and egress must occur within 30 seconds	Studies have shown that healthy, young individuals can remain in a 12% to 14% oxygen atmosphere for 30 to 40 minutes without impairment. However, in a fire emergency, the oxygen level may be reduced below safe levels, and the decomposition products formed by the fire are likely to cause harm. Thus, the Agency does not contemplate personnel remaining in the space after system discharge during a fire without Self Contained Breathing Apparatus (SCBA) as required by OSHA. System design must adhere to OSHA 1910.162(b)5 and NFPA Standard 12.
	CO ₂	Acceptable		
	Water	Acceptable		
	HBFC-22B1	Acceptable		HBFC-22B1 can be considered only an interim substitute for Halon 1301. HBFC-22B1 has an ODP of .74; thus, production will be phased out January 1, 1996. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Consent Order. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	HCFC-22	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	HCFC-124	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	[HCFC BLEND] A	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	HFC-23	Acceptable for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; Life support functions such as Armored Personnel Vehicles and related vehicles; and for explosion inertion/suppression with flammable liquids and gases.		Due to concerns about this agent's Global Warming Potential, its use is restricted pending further review by the Agency. Required extinguishing concentration and storage volume ratio are the highest of all potential candidates, but weight ratio is only 2.0.
	HFC-125	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
Halon 1301 Explosion Inertion	HFC-134a	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	HFC-227ea	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Significant New Use Rule (SNUR).
	FC 3-1-10	Acceptable for applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; Life support functions such as Armored Personnel Vehicles and related vehicles; and for explosion inertion/suppression with flammable liquids and gases.	FC 3-1-10 may not be used for training exercises. Detection should be cross-zoned to avoid unnecessary discharge and maintained to high reliability. Recycling/recovery equipment must be used during servicing of fire protection system	Under SNAP, EPA has reviewed and found acceptable only certain narrowly defined uses of perfluorinated compounds. Wider use of perfluorinated compounds is of concern due to long atmospheric lifetimes, and potential to contribute to global warming. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	[Inert Gas Blend]	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	Carbon Dioxide	Acceptable		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	Water	Acceptable		
	HBFC-22B1	Acceptable only in normally unoccupied areas.		HBFC-22B1 can be considered only an interim substitute for Halon 1301. HBFC-22B1 has an ODP of .74; thus, production will be phased out on January 1, 1996. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is presently subject to requirements contained in a Toxic Substance Control Act (TSCA) Consent Order. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.

HALONS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
	HFC-23	Acceptable for high value applications such as those involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; life support functions; and for explosion inertion/suppression with flammable liquids and gases.		Preliminary analysis of cardiotoxicity tests indicates that the no effect level for cardiac sensitization exceeds 50%. Design concentrations vary for different atmospheres. The design concentration should not exceed the cardiotoxic LOAEL of 50% in an occupied area. Due to concerns about this agent's Global Warming Potential, its use is restricted pending further Agency review. Required extinguishing concentration and storage volume ratio are the highest of all potential candidates, but weight ratio is only 2.0.
	HFC-125	Acceptable only in normally unoccupied areas.		OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	HFC-227ea	Acceptable		Design concentrations vary for different atmospheres. The design concentration must not exceed the cardiotoxic LOAEL of 10.5% in an occupied area. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits. This agent was submitted to the Agency as a Premanufacture Notice (PMN) and is subject to requirements contained in a Toxic Substance Control Act (TSCA) Significant New Use Rule (SNUR).
	FC 3-1-10	Acceptable for applications involving the protection of public safety or national security; telecommunication or computer equipment related to public safety or national security; life support functions; and for explosion inertion/suppression with flammable liquids and gases.	FC 3-1-10 shall not be used to test explosion inertion systems unless captured and recycled or destroyed. FC 3-1-10 must be recovered from the explosion inertion system prior to servicing and must be recycled for later use.	Design concentrations vary for different atmospheres. The design concentration must not exceed the cardiotoxic LOAEL of 40% in an occupied area. Under SNAP, EPA has reviewed and found acceptable only certain narrowly defined uses of perfluorinated compounds. Wider use of perfluorinated compounds is of concern due to long atmospheric lifetimes, and potential to contribute to global warming. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.
	[Inert Gas Blend]	Acceptable		Efficacy data required for acceptance in normally occupied areas. OSHA requires that protective gear (SCBA) be worn by personnel entering the space until oxygen levels return to 19.5% and relevant decomposition products decrease to OSHA limits.

HALONS—UNACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Comments
Halon 1211 Streaming Agents—Commer- cial/Industrial Applications.	[CFC-11]	Proposed Un- acceptable.	This agent has been proposed for large outdoor fires for which non-ozone depleting alternatives are currently used.

HALONS—PENDING DECISIONS

Application	Substitute	Comments
Halon 1211 Streaming Agents—Consumer Applications	HFC-227ea	Cardiotoxicity and personnel monitoring data required.
Halon 1211 Streaming Agents—Commercial/ Industrial Applications.	HFC-227ea HBFC-22B1/ HFC-227ea Blend.	Cardiotoxicity and personnel monitoring data required. Cardiotoxicity, decomposition product, and personnel monitoring data required. HBFC-22B1 is considered an interim substitute for Halon 1211. Because the HBFC-22B1 has an ODP of .74, production will be phased out (except for essential uses) on January 1, 1996.
Halon 1211 Streaming Agents—Military Ap- plications.	HFC-227ea HBFC-22B1/ HFC-227ea Blend.	Cardiotoxicity and personnel monitoring data required. Cardiotoxicity, decomposition product, and personnel monitoring data required. HBFC-22B1 is considered an interim substitute for Halon 1211. Because the HBFC-22B1 has an ODP of .74, production will be phased out (except for essential uses) on January 1, 1996.
Halon 1301	HBFC-22B1/ HFC-227ea Blend.	Cardiotoxicity and decomposition product data required.
Total Flooding—Occupied Areas	HBFC-22B1 HFC-32	HBFC-22B1 is considered an interim substitute for halon. Because the HBFC-22B1 has an ODP of .74, production will be phased out (except for essential uses) on January 1, 1996. Need additional information on potential flammability. Cardiotoxicity data is required.
	Water Mist/Fog	No company has proposed commercialization of this agent as a halon substitute. Due to its potential flammability, this agent may require blending with another agent. This newly developing technology for use on Class A, B and C fires is of high interest. The Agency has not yet received a formal submission in order to complete its evaluation.
	HFC-125	Need additional information on cardiotoxicity.
	SF6	This agent has been proposed as an alternative for discharge testing of halon systems.
Halon 1301 Total Flooding—Unoccupied Areas	Water Mist/Fog	This newly developing technology for use on Class A, B, and C fires is of high interest. The Agency has not yet received a formal submission in order to complete its evaluation.
Halon 1301	[HCFC BLEND] A	Explosion Inertion test data on blend required.
Explosion Inertion	SF6	This agent has been proposed as an alternative for discharge testing of halon systems.

STERILANTS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial deci- sion	Proposed con- ditions	Comments
12/88 Blend of EtO/CFC-12.	CO ₂ /EtO	Acceptable		CO ₂ /EtO blends can serve as drop-in replacements to 12/88 in some but not in all existing equipment because they require a higher operat- ing pressure.
Sterilant	HCFC-124/ETO	Acceptable		Maximum EtO concentration in a CO ₂ /EtO blend may have to be re- duced to 8-9 percent to reduce flammability. In a blend with EtO, HCFC-124 is the only available drop-in replace- ment for about half of the equipment now using 12/88. However, HCFC-124 is an ozone depleting substance; it should be use to steri- lize only that equipment that cannot be sterilized using other alter- natives such as steam or CO ₂ /EtO blends. Because HCFC-124 is a Class II substance, its use may be subject to future regulation promulgated under Section 608 of the Clean Air Act Amendments of 1990. As a HAP, use of EtO must comply with Title III of the CAA.

STERILANTS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial decision	Proposed conditions	Comments
12/88 Blend of EtO/CFC-12.	Pure EtO	Acceptable		EtO is a toxic, carcinogenic substance and is considered a hazardous air pollutant. Potential exposures of the general population to EtO releases can be limited either through the use of catalytic converters which convert waste EtO into CO ₂ and water, or through the use of acid water scrubbers which convert waste EtO into ethylene glycol.
Sterilant				Must be used in accordance with manufacturer recommendations to address flammability concerns. Must be used in accordance with OSHA standards to limit occupational exposures.
	Steam	Acceptable		Applicable only to devices resistant to heat and moisture.

STERILANTS—PENDING DECISIONS

Application	Substitute	Comments
12/88 blend of EtO/CFC-12 sterilant	[HCFC Blend] A	Agency has not completed review of data.
	HFC-125/EtO	Agency has not completed review of data.
	HFC-227ea/EtO	Need exposure data.

AEROSOLS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial Decision	Proposed Conditions	Comments
CFC-11, HCFC-22, HCFC-142b as aerosol propellants.	Hydrocarbons (Propane, Isobutane, n-butane).	Acceptable		Hydrocarbons are flammable materials and must be used with the necessary precautions.
	Dimethyl ether	Acceptable		DME is flammable and must be used with the necessary precautions. Blends of DME with HCFCs would be subject to section 610 restrictions.
	HFC-152a, HFC-134a.	Acceptable		Expense of these compounds is likely to limit widespread use.
	Alternative processes (pumps, mechanical pressure dispensers, non-spray dispensers).	Acceptable.		
	Compressed Gases (Carbon dioxide, air, nitrogen, nitrous oxide).	Acceptable.		
CFC-11 as aerosol propellant.	HCFC-142b	Acceptable		Use of HCFC-142b, either by itself or blended with other compounds will be prohibited January 1, 1994 under section 610 (d).
	HCFC-22	Acceptable		Use of HCFC-22, either by itself or blended with other compounds will be prohibited January 1, 1994 under section 610 (d).
CFC-11, CFC-113, MCF, HCFC-141b as aerosol solvents.	Petroleum Distillates (C-6 to C-10 paraffins and light aromatics).	Acceptable		Petroleum distillates are flammable materials and must be used with the necessary precautions. Pesticide aerosols must adhere to FIFRA standards.
	Chlorinated solvents (trichloroethylene, perchloroethylene, methylene chloride).	Acceptable		EPA expects to issue control technology requirements under Title III of the Clean Air Act. Pesticide aerosols must adhere to FIFRA standards. Not suitable for use in consumer products.
	Organic solvents (e.g., methanol, ethanol, isopropanol, acetone).	Acceptable		These substitutes are flammable materials and must be used with the necessary precautions.
	Terpenes	Acceptable		These substitutes are flammable materials and must be used with the necessary precautions.

AEROSOLS—ACCEPTABLE SUBSTITUTES—Continued

Application	Substitute	Initial Decision	Proposed Conditions	Comments
CFC-11, CFC-113, MCF as aerosol solvents.	Water-Based Formulations. HCFC-141b	Acceptable. Acceptable		Use of HCFC-141b, either by itself or blended with other compounds will be prohibited January 1, 1994 under Section 610 (d).

AEROSOLS—PENDING DECISIONS

Application	Substitute	Comments
CFC-12 as aerosol propellant	HFC-227	FDA approval still required in metered dose inhalers. Likely to have low environmental impacts.
CFC-11, CFC-113, MCF, HCFC-141b as aerosol solvents.	Monochloro/toluene/benzo-trifluorides.	

TOBACCO EXPANSION—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
CFC-11 Tobacco expansion.	Carbon dioxide	Acceptable		Carbon dioxide cannot be used as a drop-in or a retrofit, but requires new equipment.

TOBACCO EXPANSION—PENDING SUBSTITUTES

Application	Substitute	Comments
CFC-11 Tobacco expansion	HCFC-123	Agency has not completed review of data. Potential drop-in replacement.
	HFC-227ea	Agency has not completed review of data.

ADHESIVES, COATINGS, AND INKS—ACCEPTABLE SUBSTITUTES

Application	Substitute	Initial decision	Proposed conditions	Comments
Methyl Chloroform, Adhesives, Coatings, and Inks.	Petroleum distillates	Acceptable		OSHA standards exist for many of these chemicals. Formulators should use chemicals with lowest toxicity, where possible.
	Organic solvents (Alcohols, Ketones, Ethers, and Esters).	Acceptable		OSHA standards exist for many of these chemicals. Formulators should use chemicals with lowest toxicity, where possible.
	Chlorinated solvents (methylene chloride, trichloro-ethylene, perchloro-ethylene).	Acceptable		High inherent toxicity. Use only when necessary.
	Terpenes	Acceptable.		
	Water-based formulations	Acceptable.		
	High-solid formulations	Acceptable.		
	Alternative technologies (e.g., powder, hot melt, thermoplastic plasma spray, radiation-cured, moisture-cured, chemical-cured, and reactive liquid).	Acceptable.		

ADHESIVES, COATING, AND INKS—PENDING DECISIONS

Application	Substitute	Comments
Methyl Chloroform Adhesives, Coatings and Inks.	Monochloro-toluene/benzo-trifluorides	Agency has not completed review of data.

Appendix C to the Preamble—Data Confidentiality Claims

Data Confidentiality Claims

1. Special Requirements for Submitting Data to the Docket

Data submissions must be provided in three copies. If information is claimed as confidential, all CBI must be deleted from the third copy which will become part of the public docket. If no claims of confidentiality are made for the submission, the third copy should be identical to the other two. When portions of the submission are claimed as CBI, the first two copies will include the CBI material as provided in section V of this notice. The following special preparation is required for the third copy:

- Remove the "Supplemental Statement of Data Confidentiality Claims." (see Appendix C, 2)
- Excise from the body of the study any information you claim as confidential. Replace with generic information if it is available.
- Mark the third copy plainly on both its cover and its title page with the phrase "Public Docket Material—contains no information claimed as confidential."

2. Supplemental Statement of Data Confidentiality Claims

For any portion of a submission that is claimed as confidential, the following information must be included within a Supplementary Statement of Data Confidentiality Claims:

- Identify specifically by page and line number(s) each portion of the study for which you claim confidentiality.
- Give the reasons why the cited passage qualifies for confidential treatment.
- Indicate the length of time—until a specific date or event, or permanently—for which the information should be treated as confidential.
- Identify the measures taken to guard against undesired disclosure of this information.
- Describe the extent to which the information has been disclosed, and what precautions have been taken in connection with these disclosures.
- Enclose copies of any determinations of confidentiality made by EPA, other Federal agencies, or courts concerning this information.
- If you assert that disclosure of this information would be likely to result in substantial harmful effects to you, describe those harmful effects and explain why they should be viewed as substantial.
- If you assert that the information is voluntarily submitted, indicate whether you believe disclosure of this information might tend to lessen the availability to EPA of similar information in the future, and if so, how.

If required substantiation is not provided along with the submission of information claimed as confidential, EPA may make the complete submitted information available to the public without further notice to the submitter.

For the reasons set out in the preamble, EPA is hereby proposing to amend 40 CFR Part 82 as follows:

PART 82—PROTECTION OF STRATOSPHERIC OZONE

1. **Authority:** The authority citation for part 82 continues to read as follows: 42 U.S.C. 7414, 7601, 7671—7671q.

2. Part 82 is proposed to be amended by adding Subpart G to read as follows:

Subpart G—Significant New Alternatives Policy Program

Sec.

- 82.170 Purpose and scope.
- 82.172 Definitions.
- 82.174 Prohibitions.
- 82.176 Applicability.
- 82.178 Information required to be submitted.
- 82.180 Agency review of SNAP submissions.
- 82.182 Confidentiality of data.
- 82.184 Petitions.

§ 82.170 Purpose and scope.

(a) The purpose of the regulations in this subpart is to implement section 612 of the Clean Air Act, as amended, regarding the safe alternatives policy on acceptability of substitutes for ozone-depleting compounds. This program will henceforth be referred to as the "Significant New Alternatives Policy" (SNAP) program. The objective of this program is to identify substitutes for ozone-depleting compounds, to evaluate the acceptability of those substitutes, and to promote the use of those substitutes believed to present lower overall risks to human health and the environment.

(b) The regulations in this subpart describe persons and substitutes subject to reporting requirements under the SNAP program and explain preparation and submission of notices and petitions on substitutes. The regulations also establish Agency procedures for reviewing, processing, and for making public EPA's notices and petitions on substitutes. Finally, the regulations prohibit the use of alternatives which EPA has determined may have adverse effects on human health or the environment where EPA has identified alternatives that on an overall basis, reduce risk to human health and the environment and are currently or potentially available.

§ 82.172 Definitions.

(a) *Act* means the Clean Air Act, as amended, 42 U.S.C. 7401 *et seq.*

Agency means the U.S. Environmental Protection Agency.

Class I or II means the specific ozone-depleting compounds described in section 602 of the Act.

Commerce means trade, traffic, transportation, or other commerce that could potentially occur between a place in a state of the United States and any place outside of such state.

Critical use means uses of a substitute where no other substitute exists that meets existing performance or technical standards.

Decision means any final determination made by the Agency under section 612 of the Act on the acceptability or unacceptability of a substitute for a Class I or II compound.

EPA means the U.S. Environmental Protection Agency.

Formulator means any person engaged in the preparation or formulation of a substitute, after chemical manufacture of the substitute or its components, for distribution or use in commerce.

Health and safety study or *study* means any study of any effect of a substitute or its components on health or the environment or on both, including underlying data and epidemiological studies, studies of occupational, ambient, and consumer exposure to a substitute, toxicological, clinical, and ecological, or other studies of a substitute and its components, and any other pertinent test. Chemical identity is always part of a health and safety study.

(1) Information which arises as a result of a formal, disciplined study is included in the definition. Also included is information relating to the effects of a substitute or its components on health or the environment. Any available data that bear on the effects of a substitute or its components on health or the environment would be included.

(2) Examples include:

(i) Long- and short-term tests of mutagenicity, carcinogenicity, or teratogenicity; data on behavioral disorders; dermatotoxicity; pharmacological effects; mammalian absorption, distribution, metabolism, and excretion; cumulative, additive, and synergistic effects; acute, subchronic, and chronic effects; and structure/activity analyses;

(ii) Tests for ecological or other environmental effects on invertebrates, fish, or other animals, and plants, including: acute toxicity tests, chronic toxicity tests, critical life stage tests, behavioral tests, algal growth tests, seed germination tests, microbial function tests, bioconcentration or bioaccumulation tests, and model ecosystem (microcosm) studies;

(iii) Assessments of human and environmental exposure, including workplace exposure, and effects of a particular substitute on the

environment, including surveys, tests, and studies of: biological, photochemical, and chemical degradation; air, water and soil transport; biomagnification and bioconcentration; and chemical and physical properties, e.g., boiling point, vapor pressure, evaporation rates from soil and water, octanol/water partition coefficient, and water solubility;

(iv) Monitoring data, when they have been aggregated and analyzed to measure the exposure of humans or the environment to a substitute;

(v) Any assessments of risk to health or the environment resulting from the manufacture, processing, distribution in commerce, use, or disposal of the substitute or its components.

Importer means any person who imports a chemical substitute into the United States. "Importer" includes the person primarily liable for the payment of any duties on the merchandise or an authorized agent acting on his or her behalf. The term also includes, as appropriate:

- (1) The consignee;
- (2) The importer of record;
- (3) The actual owner if an actual owner's declaration and superseding bond has been filed; or
- (4) The transferee, if the right to draw merchandise in a bonded warehouse has been transferred.

Major industrial use sector means a sector which EPA has reviewed under the SNAP program with consumption patterns of ozone-depleting substances comparable to those for refrigeration, foam-blowing, fire extinguishing, solvent cleaning, aerosols, sterilants, tobacco puffing, pesticides, or adhesives, coatings and inks.

Manufacturer means any person engaged in the direct chemical manufacture of a substitute.

Mixture means any mixture or blend of two or more individual chemical compounds.

Person means any natural person, 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, and any department, agency or instrumentality of the Federal government.

Pesticide has the meaning contained in the Federal Insecticide, Fungicide, and Rodenticide Act, 7 U.S.C. Section 136 *et seq.* and the regulations issued under it.

Premanufacture Notice Program has the meaning described in 40 CFR part 720 subpart A under the Toxic Substances Control Act, 15 U.S.C. Section 2601 *et seq.*

Producer means any person who manufactures or formulates a substitute for distribution or use in commerce.

Research and development means quantities of a substitute manufactured, imported, or processed or proposed to be manufactured, imported, or processed solely for research and development.

Significant new use means use of a substitute in a major industrial use sector as a result of the phase-out of ozone-depleting compounds.

Small uses means uses of a substitute outside of a major industrial use sector (see definition of *major industrial use sector* in this section) or uses of a substitute of less than 10,000 lbs per year within a major industrial use sector or any other sector.

Substitute means any chemical, product substitute, or alternative manufacturing process, whether existing or new, that could replace a Class I or II compound.

Test marketing means the distribution in commerce of a substitute to no more than a defined number of potential customers to explore market capability in a competitive situation during a limited testing period prior to the broader distribution of that substitute in commerce.

Use means any application of a substitute, whether for use in a manufacturing process or product, consumption by the end-user, or in intermediate uses such as formulation or packaging for other subsequent uses.

§ 82.174 Prohibitions.

(a) No person may use a substitute before the expiration of 90 days after a notice is submitted to EPA under § 82.176(a).

(b) No person may use a substitute which a person knew or has reason to know was manufactured, processed, or imported in violation of the regulations in this subpart or in violation of any condition in the acceptability determination.

(c) No person may use a substitute without adhering to the conditions set by the acceptability decision.

(d) No person may use a substitute after the effective date of any rulemaking adding such substitute to the list of unacceptable substitutes.

§ 82.175 Applicability.

(a) Any producer of a substitute must submit a notice of intent to introduce a substitute into commerce 90 days prior to such introduction. Any producer or formulator of a substitute already in commerce must submit a notice as of 90 days after [THE EFFECTIVE DATE OF THE FINAL RULE], if such substitute

has not already been reviewed and approved by the Agency.

(b) Substitutes exempt from reporting requirements under the SNAP program are listed in paragraph (c) of this section.

(c) The following substitutes are exempt from notification requirements:

(1) **Substitutes already listed as acceptable.** Producers of substitutes need not resubmit notices of a substitute if the substitute has already been listed under existing Agency decisions as acceptable.

(2) **Small use.** Substitutes covered by the Agency's definition of small uses in § 82.172 are exempt from notification requirements. However, the Agency may evaluate a substitute classified as a small use if it has reason to believe the substitute could present a risk of significant adverse effects on human health and the environment, and require submissions to support such evaluations. EPA will announce the obligation to make such submissions through the quarterly *Federal Register* notifications or to individual affected parties.

(3) **Test marketing.** Production of substitutes for the sole purpose of test marketing is exempt from reporting requirements. Persons taking advantage of this exemption are, however, required to notify the Agency in writing.

(4) **Research and development.** Production of substitutes for the sole purpose of research and development is exempt from reporting requirements. Persons taking advantage of this exemption are, however, required to notify the Agency in writing.

(5) **Second-generation substitutes.** Substitutes that replace first-generation substitutes that are not ozone-depleting chemicals are exempt from reporting. However, if the second generation substitute is replacing a compound that contributes to stratospheric ozone depletion, information must be submitted to EPA for review under SNAP.

(6) **Formulation changes.** In cases where substitution of Class I or II compounds causes formulators to change other components in a product, these auxiliary formulation changes are exempt from reporting.

(7) **Substitutes for export only.** Substitutes entirely produced for export only are not subject to reporting.

(8) **Substitutes used as feedstocks.** Substitutes used as feedstocks which are largely or entirely consumed, transformed or destroyed in the manufacturing or use process are exempt from reporting.

§ 82.178 Information required to be submitted.

(a) Persons whose substitutes are subject to reporting requirements pursuant to § 82.176 must provide the following information:

(1) *Name and description of the substitute.* The substitute should be identified by its (i) Commercial name; (ii) Chemical name; (iii) Trade name(s); (iv) identification numbers (e.g., Chemical Abstract Service (CAS) registry, National Institutes of Occupational Safety and Health Registry of Toxic Effects of Chemical Substances (NIOSH RTECS), EPA hazardous waste identification number, OHM-TADS, DOT/UN/NA/IMCO shipping, HSDB, NCI); (v) Chemical formula; and (vi) Chemical structure.

(2) *Physical and chemical information.* Key properties to EPA will use to characterize the substitute include: molecular weight; physical state; melting point; boiling point; density; taste and/or odor threshold; solubility; partition coefficients (Log K_{ow} , Log K_{oc}); vapor pressure; and Henry's Law Constant.

(3) *Substitute applications.* Identification of the applications in which the substitutes are likely to be used.

(4) *Process description.* For each application identified, descriptive data on processing, including in-place pollution controls.

(5) *Ozone depletion potential.* The predicted ozone depletion potential (ODP) of substitute chemicals. The submitter must also provide supporting documentation.

(6) *Global warming potential.* Submitters must provide data on the total global warming potential of the substitute, including information on direct and indirect contributions to global warming caused by the production or use of the substitute (e.g., energy changes).

(7) *Toxicity data.* Health and safety studies on the effects of a substitute, its components, its impurities, and its degradation products on any organism (e.g., humans, mammals, fish, wildlife, and plants). For tests on mammals, the Agency requires a minimum submission of the following tests to characterize substitute risks: A range-finding study that considers the appropriate exposure pathway for the specific use (e.g., oral ingestion, inhalation, etc.), and a 90-day subchronic repeated dose study in an appropriate rodent species. For substitutes being evaluated as fire suppressants, a cardiotoxicity study is also required. Additional mammalian toxicity tests may be identified based on the substitute and application in

question. To sufficiently characterize aquatic toxicity concerns, both acute and chronic toxicity data for a variety of species are required. For this purpose, the Agency requires a minimum data set as described in "Guidelines for Deriving Numerical National Water Quality Criteria for the Protection of Aquatic Organisms and their Uses," which is available through the National Technical Information Service (#PB-85-227049).

Other relevant information and data summaries, such as the Material Safety Data Sheets, should also be submitted. To assist in locating any studies referred to but not included in a submission, the submitter must provide citations for the date and type of submission to ensure that these studies can be located quickly.

(8) *Environmental fate and transport.* Where available, EPA requests information on the environmental fate and transport of substitutes. Such data shall include information on bioaccumulation, biodegradation, adsorption, volatility, transformation, and other data necessary to characterize movement and reaction of substitutes in the environment.

(9) *Flammability.* Data on the flammability of a substitute chemical or mixture. Specifically, data on flash point and flammability limits must be submitted, as well as information on the procedures used for determining the flammability limits. For substitutes that will be used in consumer applications, documentation of testing results conducted by independent laboratories should be submitted where appropriate. Detail on any suggested abatement techniques to minimize the risks associated with the use of flammable substances or blends should also be provided.

(10) *Exposure data.* Modeling or monitoring data on exposures associated with the manufacture, formulation, transport, and use of a substitute. Descriptive process information for each substitute application, as described in this section, will be used to develop exposure estimates where exposure data are not readily available. Depending on the application, exposure profiles will be needed for workers, consumers, and the general population.

(11) *Environmental release data.* Data on emissions from the substitute application and equipment, as well as pollutant releases or discharge to all environmental media (ambient air, surface and groundwater, hazardous/solid waste). Submitters should provide information on release locations. Any information on any pollution controls used or that could be used in

association with the substitute (e.g., emissions reduction technologies, wastewater treatment, treatment of hazardous waste) and the costs of such technology is also requested.

(12) *Replacement ratio for a chemical substitute.* The Agency must receive information on the replacement ratio for a chemical substitute versus the Class I or II substances being replaced. The term "replacement ratio" means how much of a substitute must be used to replace a given quantity of Class I or II substance being replaced.

(13) *Required changes in use technology.* Detail on the changes in technology needed to use the alternative is required. Such information should include a description of whether the substitute can be used in existing equipment—with or without some retrofit—or only in new equipment. Data on the cost (capital and operating expenditures) and estimated life of the technology modifications should also be submitted.

(14) *Cost of substitute.* Data on the expected average cost of the alternative. In addition, information is needed on the expected equipment lifetime for an alternative technology. Other critical cost considerations should be identified, as appropriate.

(15) *Availability of substitute.* If the substitute is not currently available, the timing of availability of a substitute.

(16) *Anticipated market share.* Data on the anticipated near-term and long-term nationwide substitute sales.

(17) *Applicable regulations under other environmental statutes.* Information on whether the substitute(s) is (are) regulated under other statutory authorities, in particular the Clean Water Act, Safe Drinking Water Act, the Resource Conservation and Recovery Act, the Federal Insecticide, Fungicide, and Rodenticide Act, the Toxic Substances Control Act, the Comprehensive Environmental Response, Compensation and Liability Act, the Emergency Planning and Community Right-to-Know Act, or other titles under the Clean Air Act (CAA).

(18) *Information already submitted to the Agency.* Information requested in the SNAP program notice that has been previously submitted to the Agency as part of past regulatory and information-gathering activities may be referenced. Submitters that cannot provide references to data sent previously to the Agency should include all requested information in the SNAP notice.

(19) *Information already available in the literature.* If any of the data needed to complete the SNAP program notice are available in the literature, complete

references for such information should be provided.

(b) The Significant New Alternatives Policy (SNAP) form is designed to provide the Agency with the information necessary to reach a decision on the acceptability of a substitute.

(1) Submitters requesting review under the SNAP program only should send the SNAP form to the address for the SNAP coordinator provided on the form.

(2) Submitters filing jointly under SNAP and PMN should send the SNAP addendum along with the PMN form to the PMN coordinator identified on the SNAP form. Submitters must also send both documents to the SNAP coordinator, with a reference to indicate the notice has been furnished to the Agency under the PMN program. Submitters providing information on new chemicals for joint review under the Premanufacture Notice program and SNAP must adhere to the TSCA minimum testing requirements described in TSCA section 4.

(3) Submitters filing jointly under SNAP and under the Federal Insecticide, Fungicide, and Rodenticide Act should send the SNAP form to the Office of Pesticide Programs, Registration Division, as well as to the SNAP coordinator.

§ 82.180 Agency review of SNAP submissions.

(a) Processing of SNAP Notices.

(1) *90-day review process.* The 90-day review process will begin once EPA receives a submission and determines that such submission includes data on the substitute that are complete and adequate, as described in § 82.178. The Agency may suspend or extend the review period to allow for submission of additional data needed to complete the review of the notice.

(2) *Letter of receipt.* The SNAP coordinator will send a letter of receipt to the submitter once the Agency receives the SNAP notice. The SNAP coordinator will also assign the SNAP notice a tracking number, which will be identified in the letter of receipt.

(3) *Initial review of notice.* The SNAP coordinator will review the notice to ensure that basic information necessary to process the submission is present (i.e., name of company, identification of substitute, etc.). The SNAP coordinator will also review substantiation of any claim of confidentiality.

(4) *Determination of data adequacy.* Upon receipt of the SNAP submission, the Agency will review the completeness of the information supporting the application. If additional

data are needed, the submitter will be contacted following completion of this review. The 90-day review period will not commence until EPA has received data it judges adequate to support analysis of the submission.

(5) *Availability of new information during review period.* If critical new information becomes available during the review period that may influence the Agency's evaluation of a substitute, the submitter must notify the Agency about the existence of such information within 10 days of learning of such data. The submitter must also inform the Agency of new studies underway, even if the results will not be available within the 90-day review period. The Agency may contact the submitter to explore extending or suspending the review period depending on the type of information received and the stage of review.

(6) *Completion of detailed review.* Once the preliminary data review steps have been completed, the Agency will complete a detailed evaluation of the notice. If during any time the Agency perceives a lack of information necessary to reach a SNAP determination, it will contact the submitter and request the missing data.

(7) *Criteria for review.* To determine whether a substitute is acceptable or unacceptable as a replacement for Class I or II compounds, the Agency will evaluate:

- (i) Atmospheric effects and related health impacts;
- (ii) General population risks from ambient exposure to compounds with direct toxicity and to increased ground-level ozone;
- (iii) Ecosystem risks;
- (iv) Occupational risks;
- (v) Consumer risks; and
- (vi) Cost and availability of the substitute.

(8) Communication of decision.

(i) *Communication of decision to the submitter.* Once the SNAP program notice review has been completed, the Agency will notify the submitter in writing of the decision. Sale or manufacture may continue if the Agency fails to reach a decision within 90 days or fails to communicate that decision or the need for additional data to the submitter.

(ii) *Communication of decision to the public.* The Agency will publish in the *Federal Register* every three months a complete list of the acceptable and unacceptable alternatives that have been reviewed to date. In the case of substitutes proposed for placement on the unacceptable list or for removal from either list, a formal rule-making process will ensue.

(b) *Types of listing decisions.* When reviewing and listing substitutes, the Agency will place substitutes in one of 5 categories:

(1) *General acceptance.* Where the Agency has reviewed a substitute and found no reason to prohibit its use, it will list the alternative as acceptable for the applications listed in the notice.

(2) *Approval subject to use limitations.* After reviewing a notice, the Agency may make a determination that a substitute is acceptable if certain conditions are met to minimize risks to human health and the environment.

(3) *General prohibition.* This designation will apply to substitutes where the Agency's review indicates that the substitute poses risk of adverse effects to human health and the environment and that alternatives exist that reduce overall risk.

(4) *Prohibition with limited exemptions for critical use.* Even though the Agency can restrict the use of a substitute based on the potential for adverse effects, it may be necessary to grant a limited number of exemptions because of the lack of alternatives for specialized uses within the application. The Agency will refer to such exemptions as "critical use exemptions." Critical use exemptions will be granted only for the time period necessary to develop and implement alternatives not yet available. These exemptions are discussed further in § 82.184.

(5) *Substitutes pending completion of review.* Submissions for which the Agency has not reached a determination will be described as pending. For all substitutes in this category, the Agency will work with the submitter to obtain any missing information and to determine a schedule for providing the missing information if the Agency wishes to extend the 90-day review period. EPA will use the authority under section 114 of the Clean Air Act to gather this information, if necessary. In some instances, the Agency may also explore using additional statutory provisions (e.g., section 4 of TSCA) to collect the needed data.

(c) *Outreach.* The Agency will publish the SNAP determinations and any revisions four times a year in the *Federal Register*. In addition to the quarterly publications, the Agency will communicate decisions through a clearinghouse and its outreach program. The outreach program includes a hotline and presentations at conferences and in trade journals. The Agency will maintain a list of vendors that sell substitutes that EPA has determined present lower environmental risks than the Class I and II compounds.

(d) *Joint processing under SNAP and FIFRA.* The Agency will coordinate reviews of substitutes submitted for evaluation under both FIFRA and the CAA.

(e) *Joint processing under SNAP and TSCA.* The Agency will coordinate reviews of substitutes submitted for evaluation under both the TSCA PMN program and the CAA.

§ 82.182 Confidentiality of data.

(a) *Clean Air Act provisions.* Anyone submitting information must assert a claim of confidentiality at the time of submission for any data they wish to have treated as confidential business information (CBI) under 40 CFR part 2, subpart B. Failure to assert a claim of confidentiality at the time of submission may result in disclosure of the information by the Agency without further notice. The submitter should also be aware that under section 114(c) of the Clean Air Act, emissions data may not be claimed as confidential.

(b) *Substantiation of confidentiality claims.* At the time of submission, EPA requires a substantiation of any confidentiality claims made. Moreover, under 40 CFR part 2, subpart B, confidentiality assertions may later be reviewed even when confidentiality claims are received. The submitter will also be contacted as part of this evaluation process.

(c) *Confidential provisions for toxicity data.* In the event that toxicity or health and safety studies are listed as confidential, this information cannot be maintained as confidential where such data is also submitted under TSCA or FIFRA because of specific disclosure provisions in those statutes. However, information contained in the toxicity study that is not relevant to the effects of a substance on human health and the environment (e.g., discussion of process information, proprietary blends) can be maintained as confidential subject to 40 CFR part 2, subpart B.

(d) *Joint submissions under other statutes.* Information submitted as part of a joint submission to either SNAP/TSCA or SNAP/FIFRA must adhere to CBI practices under those statutes. For such submissions, the SNAP handling of such notices will follow CBI requirements under those statutes.

§ 82.184 Petitions.

(a) *Who may petition.* Any person may petition the Agency to amend existing listing decisions under the SNAP program, or to add a new substance to the SNAP lists.

(b) *Types of petitions.* Four types of petitions exist:

(1) Petitions to add a substitute not previously reviewed under the SNAP program to the approved list. This type of petition is comparable to the 90-day notifications, except that it would only be initiated by entities other than the companies that manufacture, formulate, or use the substitute. Companies that manufacture, formulate, or use substitutes that want to have their substitutes added to the approved list must submit information on the substitute under the 90-day review program;

(2) Petitions to add a substitute not previously reviewed under the SNAP program to the prohibited list;

(3) Petitions to delete a substitute from the approved list and add it to the prohibited list;

(4) Petitions to delete a substitute from the prohibited list and add it to the approved list.

(c) *Content of the petition.* A petition must contain the information described in § 82.178, which lists the items to be submitted in a 90-day notification. The Agency also requires that the petitioner submit information on the type of action requested and the rationale for the petition. For petitions that request approval for substitutes on "critical use" grounds, the Agency requires the information described in paragraph (e) in this section on critical uses. For petitions that request a re-examination of a substitute previously reviewed under the SNAP program, the submitter must reference the prior submittal.

(d) *Petition process.*

(1) *Notification of affected companies.* If the petition concerns a substitute previously either approved or restricted under the SNAP program, the Agency will contact the manufacturer(s) of that substitute.

(2) *Review for data adequacy.* The Agency will review the petition for adequacy of data. As with the 90-day notices, the Agency may suspend review until the petitioner submits the information necessary to evaluate the petition. To reach a timely decision on

substitutes, EPA may use collection authorities such as those contained in section 114 of the Clean Air Act as well as information collection provisions of other environmental statutes.

(3) *Review procedures.* To evaluate the petition, the Agency may submit the petition for review to appropriate experts.

(4) *Timing of determinations.* If data are adequate, as described in § 82.180, the Agency will respond to the petition within 90 days of receiving a complete petition. If the petition is inadequately supported, the Agency will query the petitioner to fill any data gaps before the 90-day review period begins, or may deny the petition because data are inadequate.

(5) *Rulemaking procedures.* EPA will initiate rulemaking whenever EPA grants a petition to add a substance to the list of unacceptable substitutes, remove a substance from either list, approve an alternative with conditions that are not otherwise required, or grant a critical use exemption.

(6) *Communication of decision.* The Agency will inform petitioners within 90 days whether their request has been granted or denied. If a petition is denied, the Agency will publish in the *Federal Register* an explanation of the determination. If a petition is granted, the Agency will publish the revised SNAP list incorporating the final petition decision within 6 months of reaching a determination or in the next scheduled update, if sooner.

(e) *Critical use petitioners.* Petitioners may request the Agency, based on technology or safety concerns, to allow limited exemptions for specialized uses of a substitute that has previously been placed on the prohibited list. For such petitions, the Agency requires that the petitioner provide documentation on the critical use in question. This documentation shall include descriptions of substitutes examined and rejected, process or product in which the critical use substitute is needed, reason for rejection of other alternatives, e.g., performance, technical or safety standards, and anticipated date other substitutes will be available and projected time for switching.

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Federal Register

**Wednesday
May 12, 1993**

Part III

Department of Health and Human Services

Food and Drug Administration

**21 CFR Part 352 et al.
Sunscreen Drug Products for Over-the-
Counter Human Use; Tentative Final
Monograph; Proposed Rule**

DEPARTMENT OF HEALTH AND HUMAN SERVICES**Food and Drug Administration****21 CFR Parts 352, 700, and 740**

[Docket No. 78N-0038]

RIN 0905-AA06

Sunscreen Drug Products for Over-the-Counter Human Use; Tentative Final Monograph**AGENCY:** Food and Drug Administration, HHS.**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) sunscreen 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 Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products, public comments on an advance notice of proposed rulemaking that was based on those recommendations, public comments submitted in response to a notice of public meeting to discuss appropriate testing procedures for OTC sunscreen drug products, presentations made at the public meeting, and public comments submitted in response to the meeting. 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 November 8, 1993. New data by May 12, 1994. Comments on the new data by July 12, 1994. Written comments on the agency's economic impact determination by November 8, 1993.

ADDRESSES: Written comments, objections, new data, or requests for oral hearing to the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD-810), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-295-8000.

SUPPLEMENTARY INFORMATION: In the Federal Register of August 25, 1978 (43 FR 38206), 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 sunscreen drug products, together with the recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (Topical Analgesic Panel), 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 November 24, 1978. In a notice published in the Federal Register of December 1, 1978 (43 FR 56249), FDA extended the period for comments to December 15, 1978, to allow more time for the collection and assessment of data to provide for more meaningful comments on the advance notice of proposed rulemaking. Reply comments in response to comments filed in the initial comment period could be submitted by December 26, 1978.

In a notice published in the Federal Register of March 21, 1980 (45 FR 18403), the agency advised that it had reopened the administrative record for OTC sunscreen 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 a notice of public meeting and reopening of the administrative record published in the Federal Register of September 4, 1987 (52 FR 33598), the agency announced that a public meeting would be held to discuss recommendations of the Topical Analgesic Panel regarding final product testing and related claims of OTC sunscreen drug products. The meeting was held on January 26, 1988, and minutes of the meeting are on public display in the Dockets Management Branch (Ref. 1). Interested persons were given until April 26, 1988, to submit comments in response to the meeting. In a notice published in the Federal Register of May 4, 1988 (53 FR 15853), FDA extended the period for submission of comments on the testing procedures and related claims for OTC sunscreen drug products to May 26, 1988, to allow full opportunity for informed comments on the testing procedures.

The agency has received four petitions and one comment requesting that it reopen the administrative record for sunscreen drug products to admit

several OTC sunscreen ingredients that have been marketed in Europe but not in the United States. Although no decision has been reached regarding these petitions, they are discussed in this tentative final monograph. All data and information on other subjects that have been submitted to the agency while the rulemaking was closed will be considered after the tentative final monograph is published.

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 (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, 27 manufacturers, 2 manufacturers' associations, 31 consumers, 6 universities, 1 health care professional, and 1 health care professional society submitted comments. Two manufacturers, one manufacturer's association, and one university submitted reply comments. In response to the notice of public meeting and the public meeting, 13 manufacturers, 2 manufacturers' associations, 1 foreign manufacturer's association, 1 foreign professional association, 2 universities, 1 foreign government, 2 testing laboratories, 1 health care research institute, and 5 health care professionals 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 August 25, 1978 (43 FR 38206), 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 352 (21 CFR part 352), FDA states for the first time its position on the establishment of a monograph for OTC sunscreen 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 sunscreen drug products.

This proposal constitutes FDA's tentative adoption of the Panel's conclusions and recommendations on OTC sunscreen 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 drug procedural regulations (21 CFR 330.10) 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. Accordingly, 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 product that is subject to the monograph and that contains a nonmonograph condition, i.e., a condition 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 it is the subject of an approved application. Further, any OTC drug product subject to this monograph that is 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 sunscreen drug

products (43 FR 38206), 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 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 these 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.

If the agency determines that any labeling for a condition included in the final monograph should be implemented sooner than the 12-month effective date, 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 December 12, 1972 (37 FR 26156) 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 (address above).

Reference

(1) Comment No. TR1, Docket No. 78N0038, Dockets Management Branch.

I. Introduction

In section 201(g) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(g)(1)), a "drug" is defined as (A) articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them, (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals, (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals, and (D) articles intended for use as a component of any articles specified in (A), (B), or (C) above. Sunscreen products are marketed with various intended uses, such as (1) beach products for occasional use to protect consumers from extreme sunlight conditions, (2) tanning products to aid consumers in acquiring a tan, and (3) non-beach products for daily use to protect consumers from chronic exposure to sunlight (e.g., make-up preparations and lipsticks). Although these intended uses are different, the agency considers each one a drug use.

Beach products are considered drugs because they prevent sunburn, protect the skin against harm from the sun, and prevent skin damage through overexposure to the sun. In addition, consumers equate these products with mitigating harmful effects of the sun. For these reasons, sunscreen beach products are drugs under section 201(g)(1)(B). Such products are also drugs under section 201(g)(1)(C) because they affect the body's physiological response to solar radiation (i.e., they lessen the erythema reaction). Tanning products that contain sunscreens are drugs because they prevent a sunburn (section 201(g)(1)(B)) and affect melanogenesis (section 201(g)(1)(C)). Non-beach sunscreen products are drugs because they prevent lip or skin damage (section 201(g)(1)(B)) as well as freckling and uneven skin coloration (section 201(g)(1)(C)). The drug/cosmetic distinction of products containing sunscreens is discussed further in comment 27.

Throughout this tentative final monograph, the agency makes extensive use of acronyms. For the reader's convenience, the agency is including in one easily accessible place a chart containing the most commonly used acronyms in this document.

Acronym	Definition
AAD	American Academy of Dermatology.
CIE	Commission International De L'Eclairage.
CTFA	Cosmetic, Toiletory and Fragrance Association.
DIN	Deutsches Institut fuer Normung.
IR	Infrared.
MED	Minimal Erythema Dose.
MED(PS) ..	Minimal Erythema Dose on Protected Skin.
MED(US) ..	Minimal Erythema Dose on Unprotected Skin.
NDA	New Drug Application.
NDMA	Nonprescription Drug Manufacturers Association.
PCD	Product Category Designation.
SPF	Sun Protection Factor.
U.S.P.	United States Pharmacopoeia.
UV	Ultraviolet.
UVA	Ultraviolet A.
UVB	Ultraviolet B.
UVC	Ultraviolet C.

II. The Agency's Tentative Conclusions on the Comments

A. General Comments on Sunscreen Drug Products

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 comment incorporated by reference previous comments dated March 4, 1972 on the proposed procedural regulations governing the OTC drug review and comments dated June 4, 1973 on the proposed antacid monograph.

The agency addressed this issue in paragraphs 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 at 9471 to 9472) and in paragraph 3 of the preamble to the tentative final monograph for OTC antacid drug products, published in the *Federal Register* of November 12, 1973 (38 FR 31260). FDA reaffirms the conclusions stated in those documents. 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 recommended that the term "ultraviolet light" should be replaced throughout the Panel's report by the term "ultraviolet radiation." The comment stated that light is the part of the electromagnetic spectrum that can be seen by the eye, and because UV radiation is by definition invisible, the use of the word "light" is inappropriate.

The agency agrees with the comment that the use of the term "ultraviolet light" is inappropriate. Because the term "light" refers to the waveband detectable by the human eye (i.e., visible light of approximately 400 to 760 nanometers (nm)), the term "ultraviolet radiation" is preferred when speaking of the wavelength region of approximately 100 to 400 nm (Refs. 1 and 2). Therefore, the agency is using the term "ultraviolet radiation" throughout this tentative final monograph. The agency is also using the following terminology for 3 wavelength ranges in the UV radiation portion of the spectrum: UVA for the range from 320 to 400 nm, UVB for the range from 290 to 320 nm, and UVC for the range from 200 to 290 nm.

References

- (1) Magnus, I. A., "An Introduction to the Basic Physics of Electromagnetic Radiation," in *Dermatological Photobiology*, Blackwell Scientific Publications, London, p. 5, 1976.
- (2) "Dermatology in General Medicine," 3d Ed., edited by T. B. Fitzpatrick, et al., McGraw-Hill Book Company, New York, p. 1443, 1987.

3. Referring to the Panel's discussion of the types of solar radiation (43 FR 38206 at 38209), one comment stated that the reference cited for the statement that the solar spectrum at the earth's surface consists of wavelengths between 295 and 1,800 nm is not authoritative. The comment stated that Bener (Ref. 1), Johnson (Ref. 2), and Schulze and Grafe (Ref. 3) should be credited for that statement.

Referring to the Panel's discussion at 43 FR 38214, the comment stated that reference 2 had been incorrectly quoted. The comment provided the correct reference as "Pathak, M. A., et al., 'Sunlight and Melanin Pigmentation,' in 'Photochemical and Photobiological Reviews,' Vol. I, edited by K. C. Smith, Plenum Press, New York, pp. 211-239, 1976" (Ref. 4).

The agency agrees with the comment and is including the above information in the administrative record for this rulemaking.

References

- (1) Bener, P., "Spectral Intensity of Natural Ultraviolet Radiation and its Dependence on Various Parameters," in *The Biologic Effects*

of Ultraviolet Radiation (with Emphasis on the Skin)," edited by F. Urbach, Pergamon Press, London, pp. 351-358, 1969.

(2) Johnson, F. S., "The Solar Constant," *Journal of Meteorology*, 11:431-439, 1954.

(3) Schulze, R., and K. Grafe, "Consideration of Sky Ultraviolet Radiation in the Measurement of Solar Ultraviolet Radiation," in *The Biologic Effects of Ultraviolet Radiation*, edited by F. Urbach, Pergamon Press, London, pp. 359-372, 1969.

(4) Pathak, M. A., et al., "Sunlight and Melanin Pigmentation," in *Photochemical and Photobiological Reviews*, Vol. I, edited by K. C. Smith, Plenum Press, New York, pp. 211-239, 1976.

4. One comment recommended that a general discussion on the radiation in "artificial sunlight" or "natural sunlight" should be added to the Panel's discussion of the types of solar radiation (43 FR 38206 at 38209). The comment stated that, in addition to UV radiation, visible sunlight and IR light play an important role in solar radiation. (The comment apparently is referring to the fact that an artificial light source ("artificial sunlight") emits mainly UV radiation, whereas the sun's spectrum ("natural sunlight") includes UV radiation and also visible light and IR radiation.)

The Panel's discussion focused on the UV radiation emitted by an artificial light source ("artificial sunlight") and by the sun. Although agreeing with the comment's observation that visible and IR radiations are also important components of natural sunlight, the agency believes that these radiations (400 nm and beyond) are not within the scope of the OTC drug review of sunscreens. It is the UV portion (290 to 400 nm) of the sun's spectrum ("natural sunlight") that reaches the earth's surface and the UV radiation from artificial light sources ("artificial sunlight") that can produce skin erythema, melanogenesis, and cancer (Ref. 1) (43 FR 38206 at 38210 and 38211). The majority of OTC sunscreen ingredients primarily protect the skin from UVB radiation (290 to 320 nm) (43 FR 38219 to 38253). Therefore, the Panel did not discuss solar radiation of longer wavelengths, i.e., visible and IR radiations. Accordingly, the agency does not believe that it is necessary to add a discussion of the visible and IR radiation present in "natural sunlight" in this tentative final monograph.

References

- (1) Parrish, J. A., H. A. D. White, and M. A. Pathak, "Photomedicine," in *Dermatology in General Medicine*, 2d Ed., edited by T. P. Fitzpatrick, et al., McGraw-Hill Book Company, New York, pp. 942-994, 1979.

5. One comment asserted that the Panel's statement, "The sun's rays

associated with diseases are related to the light sensitivity range from 290 to 800 nm," at 43 FR 38206 at 38209 is inconsistent with statements made at 43 FR 38210 to 38212 about the harmful effects of sunlight on the skin. The comment stated that the Panel's discussion on disease resulting from exposure to the sun's rays referred only to effects caused by rays in the range of 290 to 400 nm. Therefore, according to the comment, it was inappropriate to generalize and refer to the effects of solar radiation from 290 to 800 nm.

The Panel's reference to solar radiation in the range of 290 to 800 nm was background information to identify the range of wavelengths associated with diseases related to light sensitivity, i.e., photosensitivity reactions (Ref. 1). The Panel's discussion of photosensitization appears at 43 FR 38219. The Panel's discussion at 43 FR 38210 to 38212 describes in detail the more serious and common harmful effects, i.e., skin cancer and premature skin aging, that may be induced by the UV radiation from the sun. It was not intended to be a discussion of all light sensitivity diseases. Therefore, the agency finds no inconsistency in the statements referred to by the comment.

Reference

(1) Kesten, B. M., and M. Slatkin, "Diseases Related to Light Sensitivity," *Archives of Dermatology and Syphilology*, 67:284-301, 1953.

6. Referring to the Panel's statement that "UV-C is not effective in stimulating pigmentation (tanning)" (43 FR 38206 at 38209 and 38210), one comment contended that this statement is incorrect and should have read "UV-C is much less effective in producing pigmentation than UV-B."

The agency has reviewed the scientific literature regarding the types of solar radiation involved in tanning and agrees with the Panel's statement. As the Panel pointed out, UVC radiation from sunlight does not reach the earth's surface (43 FR 38209). Tanning involves two distinct photobiological processes: immediate tanning and delayed tanning (Refs. 1 and 2). Immediate tanning can be induced by UVA radiation (320 to 400 nm) and visible light (400 to 700 nm). It is an immediate darkening reaction that occurs 1 to 2 hours after exposure to sunlight. It does not involve melanogenesis but is due to the darkening of preformed pigment in the skin. Delayed tanning is a process that occurs 48 to 72 hours after exposure to UVB radiation (290 to 320 nm) and involves the synthesis of new melanin pigment. The agency is unaware of any data showing that solar UVC radiation

(200 to 290 nm) stimulates pigmentation through either of the two tanning processes.

References

- (1) Jimbow, K., M. A. Pathak, G. Szabo, and T. B. Fitzpatrick, "Ultrastructural Changes in Human Melanocytes after Ultraviolet Radiation," in "Sunlight and Man," edited by M. A. Pathak, et al., University of Tokyo Press, Tokyo, pp. 195-215, 1974.
- (2) Pathak, M. A., and K. Stratton, "Effects of Ultraviolet and Visible Radiation and the Production of Free Radicals in Skin," in "The Biological Effects of Ultraviolet Radiation (with emphasis on the skin)," edited by F. Urbach, Pergamon Press, London, pp. 207-222, 1969.

7. One comment argued that the Panel's statement that the maximum UVB effect is reached at 296.7 nm (43 FR 38206 at 38209) is incorrect and that the maximum effectiveness of the UVB erythema action spectrum is between 292 and 295 nm.

For many years, 296.7 or 297 nm was accepted as the most erythemogenic UVB wavelength in the standard erythema curve. At the time the Panel conducted its review, various sources reported different wavelengths of UVB radiation as producing the maximum erythemogenic skin response: 296 nm (Ref. 1), 296.7 nm (Ref. 2), and 297 nm (Ref. 3). However, other sources have reported slightly lower wavelengths as producing this response. For example, the results of a study on the maximum erythemogenic response of the skin of the abdomen using a high pressure xenon arc grating monochromator showed 292 nm as the most erythemogenic UVB wavelength (Ref. 4). Another investigation of the effect of UVB radiation on the skin on the back of the trunk utilizing a high intensity prism grating monochromator resulted in values of 292.5 and 294 nm for the maximum erythemogenic response (Refs. 5 and 6). Such discrepancies may be the result of improvements in the integrity of monochromatic light sources that have caused the erythema action spectrum to be reassessed. Furthermore, because the area of the body exposed to the radiation and the method for assessing the erythemogenic response may vary from laboratory to laboratory, slight differences in values may be reported for the most erythemogenic UVB wavelength. The agency invites the submission of more recent data and comment on a proposed action spectrum appropriate for sunscreen drug product testing. (See comment 84.)

References

- (1) Berger, D. S., "The Theory of Sunscreens and Suntanning," in "The Chemistry and Manufacture of Cosmetics,"

2d Ed., Vol. III, edited by M. G. de Navarre, Continental Press, Orlando, FL, pp. 159-172, 1975.

(2) Schulze, R., "Effectiveness of UV Absorbers and Commercially Available Sunscreens (Wirksamkeit von UV-Absorbern und Handelsueblicher Sonnenschutzmittel)," *Journal of the Society of Cosmetic Chemists*, 14:544-565, 1963.

(3) Hausser, K. W., and W. Vahle, "Sunburn and Suntanning," in "The Biologic Effects of Ultraviolet Radiation," edited by F. Urbach, Pergamon Press, Oxford, United Kingdom, 1969, pp. 3-21.

(4) Freeman, R. G., et al., "Relative Energy Requirements for an Erythema Response of Skin to Monochromatic Wavelengths of Ultraviolet Present in the Solar Spectrum," *Journal of Investigative Dermatology*, 47:586-592, 1966.

(5) Cripps, D. J., and C. A. Ramsay, "Ultraviolet Action Spectrum with a Prism-Grating Monochromator," *British Journal of Dermatology*, 82:584-592, 1970.

(6) Cripps, D. J., "Instrumentation and Action Spectra in Light-associated Diseases," *Journal of Investigative Dermatology*, 77:20-31, 1981.

8. One comment disagreed with the Panel's statement, "At 307.4 nm the maximal amount of energy to cause sunburn is delivered by the sun to the skin" (43 FR 38206 at 38209). The comment noted that the integration of the action spectrum for erythema and the emission spectrum for UVB in the summer at noon in Davos, Switzerland, shows the peak of the effectiveness spectrum to lie in the vicinity of 305 to 308 nm. Therefore, the comment contended that "the maximal amount of sunburn causing energy" is not delivered at 307.4 nm, but rather that the "maximal effectiveness" of noon sunlight UV radiation is located near 306 nm rather than 295 nm.

The agency has reviewed the study by Schulze (Ref. 1), which the Panel cited as the basis for its statement that the maximal amount of energy to cause sunburn is delivered at 307.4 nm. The agency agrees with the comment that the statement is incorrect. Schulze combined data from a 1935 study by the CIE, which determined the relative erythema efficiency of various wavelengths of UV radiation, with data from a study by Bener conducted in Davos, Switzerland, which determined the irradiation intensity of sunlight (see Table 1 and Fig. 2 in Ref. 1). Schulze combined the data from the two studies to obtain an efficiency curve for global radiation, i.e., the relative erythema efficiency of various wavelengths of UV radiation multiplied by the intensity of the irradiation of those wavelengths. This produced an efficiency curve for natural sunlight with a peak at 307.4 nm. Because 307.4 nm is the peak of the curve resulting from the combination of

the erythema action spectrum (CIE values) and the solar spectrum, the value actually represents an erythema effectiveness maximum. (See comment 84 for a discussion of the erythema effectiveness spectrum.) Therefore, the Panel's statement should have read, "The maximal effectiveness of ultraviolet radiation from noon sunlight occurs at about 307 nm."

Reference

(1) Schulze, R., "Effectiveness of UV Absorbers and Commercially Available Sunscreens (Wirksamkeit von UV-Absorbern und Handelsüblicher Sonnenschutzmitteln)," *Journal of the Society of Cosmetic Chemists*, 14:544-565, 1963.

9. Three comments disagreed with the Panel's statement that the erythema reaction is maximal in intensity at 6 to 20 hours after exposure to UVB radiation (43 FR 38206 at 38209). Two of the comments stated that the postexposure time for the maximum intensity of the erythema reaction to UVB radiation is 12 to 24 hours, and the third comment reported it as 18 to 24 hours. One comment added that if postexposure redness is maximum in 6 to 8 hours, the radiation source contained significant UVC radiation (wavelengths less than "280 nm"), and provided a reference for this statement (Ref. 1). One of the comments also disagreed with the Panel's statement that the erythema reaction to UVA radiation is maximal in intensity about 72 hours after exposure (43 FR 38209). The comment maintained that the erythema reaction to UVA radiation is maximal in intensity at 12 to 24 hours following exposure and is only maximum at 72 hours when photosensitizing agents such as methoxypsoralen (8-MOP) are applied topically or given orally.

The information on solar energy provided by the Panel at 43 FR 38209 was intended as background information and is not included in the tentative final monograph. Because UVC radiation from the sun is strongly absorbed by the earth's ozone layer and, thus, largely prevented from reaching the earth's surface (Ref. 2), the agency believes that it is not necessary to consider UVC radiation in the tentative final monograph on OTC sunscreen drug products.

The Panel recommended postexposure time limits of 16 to 24 hours for the evaluation of an erythema reaction to UV radiation under the testing procedures described in §§ 352.42(h), 352.43, and 352.46. Although the comments differed on the lower time limit for the occurrence of the maximum intensity of an erythema

reaction following UVB radiation exposure, there appears to be general agreement on 24 hours as the upper time limit. Investigators assessing the effects of UVA and UVB radiations generally use 24 hours postexposure as the time period to determine the skin's erythema reaction to these radiations. The agency believes that the disagreement concerning the lower postexposure time limit for the maximum intensity of the erythemogenic response is a result of differences in methodology between laboratories, i.e., differences in light source, skin types, area and location of skin exposed, and variations in the judgment of the maximum response.

Moreover, the agency believes that immediate pigmentation may interfere with an investigator's perception of the MED if the evaluation is done at 16 hours' postexposure. The agency believes that sunscreen testing results will be more accurate if the MED is determined at 22 to 24 hours post irradiation rather than 16 to 24 hours post irradiation. Therefore, the agency is proposing those time frames in §§ 352.72(h) and 352.73 of this tentative final monograph. (See comment 95.)

References

(1) Pathak, M.A., and J.H. Epstein, "Normal and Abnormal Reactions of Man to Light," in "Dermatology in General Medicine," edited by T.B. Fitzpatrick, et al., McGraw Hill Book Company, New York, pp. 977-1036, 1971.
(2) Pathak, M.A., T.B. Fitzpatrick, and J.A. Parrish, "Topical and Systemic Approaches to Protection of Human Skin Against Harmful Effects of Solar Radiation," in "The Science of Photomedicine," edited by J.D. Regan and J.A. Parrish, Plenum Press, New York, pp. 441-473, 1982.

10. Referring to the Panel's statement that "approximately 20 to 50 millijoules per centimeter squared (mJ/cm²) of UVB energy is required to produce one MED * * * (43 FR 38206 at 38209), one comment stated that this number is approximately correct, provided it is specified that all the UVB energy has been converted by means of an action spectrum to the effectiveness of UV radiation of a wavelength of approximately 297 nm. The comment added that the statement is untrue if it is integrated energy from 290 to 320 nm.

The agency agrees with the comment. In its report, the Panel stated the approximate amount of energy required for each of the bands of the UV spectrum (UVA, UVB, and UVC) to induce one MED. This statement illustrated the relative amounts of energy required for each of these bands to produce one MED. The agency notes that the determination of an MED is highly variable. The MED varies among

individuals and for different sites of the body, mainly, because of varying degrees of pigmentation and thickness of the stratum corneum layer of the skin (Ref. 1). Other variables affecting MED measurements are the wavelengths and irradiance of the optical source, the distance of the test subject from the source, the size of the exposed test area, the angle of incidence of the radiation on the test area, heat, humidity, wind, previous light exposure, definition of the end point, and the time the response is read (Ref. 1). In a study where these variables were controlled and the MED of one individual measured for UVB and UVA radiations, the amount of energy of UVB radiation required to cause 1 MED was 19 mJ/cm² (Ref. 2). The agency notes that this value correlates reasonably well with the range cited by the Panel (43 FR 38206 at 38209).

The agency agrees that UV energy should be converted to erythema effective radiation before determining MEDs. The agency discusses the use of an appropriate action spectrum for the OTC sunscreen testing procedures in comment 84.

References

(1) Parrish, J.A., H.A.D. White, and M.A. Pathak, "Photomedicine," in "Dermatology in General Medicine," 2d ed., edited by T.B. Fitzpatrick, et al., McGraw-Hill Book Company, New York, pp. 952 and 953, 1979.
(2) Ying, C.Y., J.A. Parrish, and M.A. Pathak, "Additive Erythemogenic Effects of Middle (280-320 nm) and Long (320-400 nm) Wave Ultraviolet Light," *Journal of Investigative Dermatology*, 63:273-278, 1974.

11. Two comments disagreed with the Panel's statement "In the long run, suntanning is not good for the skin," (43 FR 38206 at 38209). One comment felt that the term "suntanning" is not accurate in this context and that the term "prolonged sunbathing" would be preferred. The other comment stated that the term "suntanning" is erroneous and anecdotal and that the resulting tan is protective against subsequent actinic damage. This comment stated that the terms "prolonged sunbathing" or "excessive sun exposure" should have been used.

The Panel felt that overexposure to sunlight damages the skin and can lead to various skin lesions, and that the cumulative exposure to sunlight from childhood into adulthood can lead to skin cancer (43 FR 38209). When the Panel stated that "suntanning is not good for the skin," it was expressing a general opinion on the cumulative effects of exposure to sunlight. The use of the term "suntanning," as opposed to "excessive sun exposure" or "prolonged sunbathing," was the Panel's choice of words. The use of any of these terms

would be acceptable; however, changing the Panel's statement would not affect the substance of the Panel's report or the tentative final monograph. Therefore, the agency sees no basis for revising the Panel's statement.

12. One comment stated that the investigators (Refs. 1 and 2) who were cited in the Panel's discussion of the types of solar radiation (43 FR 38206 at 38210) did not evaluate the energy requirements for the induction of an erythema reaction by UVA, UVB, or UVC radiation. The comment stated that the Panel should have referred to investigators who reported the energy required to produce the MED reaction (i.e., UVA radiation requires about 20 to 50 J/cm², UVB radiation requires approximately 20 to 50 mJ/cm², and UVC radiation requires about 5 to 20 mJ/cm²) (43 FR 38209 to 38210). The comment argued that a literature citation of this important information is essential.

The agency is not aware of the specific source used by the Panel for the data on energy requirements for the induction of an erythema reaction as a result of UVA, UVB, or UVC radiation. The agency notes, however, that the figures used at 43 FR 38209 are comparable to those appearing generally in the literature (Refs. 3 and 4).

References

- (1) Kesten, B.M., and M. Slatkin, "Diseases Related to Light Sensitivity," *A.M.A. Archives of Dermatology and Syphilology*, 67:284-301, 1953.
- (2) Schulze, R., "Effectiveness of UV Absorbers and Commercially Available Sunscreens (Wirksamkeit von UV-Absorbern und Handelsüblicher Sonnenschutzmittel)," *Journal of the Society of Cosmetic Chemists*, 14:544-565, 1963.
- (3) Cripps, D.J., and C.A. Ramsay, "Ultraviolet Action Spectrum with a Prism-Grating Monochromator," *British Journal of Dermatology*, 82:584-592, 1970.
- (4) Freeman, R.G., et al., "Relative Energy Requirements for an Erythematous Response of Skin to Monochromatic Wave Lengths of Ultraviolet Present in the Solar Spectrum," *The Journal of Investigative Dermatology*, 47:586-592, 1966.

13. Referring to the Panel's discussion of factors affecting the amount of sunlight exposure (43 FR 38206 at 38210), one comment stated that the UV energy of sunlight is greatest between 10 a.m. and 2 p.m. at all times of the year, rather than (just) in midsummer as stated by the Panel. The comment added that while the amount of radiation received varies with the seasons, relative intensity does not. The comment said that, in the Panel's discussion of morning and late afternoon sun angle, the phrase "reducing the ultraviolet radiation

component of sunlight by as much as 75 percent" is an appropriate statement, rather than the phrase "reducing the sunlight's intensity by 75 percent."

The agency agrees with the comment. On any day of the year, the intensity of the UV energy of sunlight is greatest between 10 a.m. and 2 p.m. (Ref. 1); the intensity of the UV sunburning component of sunlight is reduced 75 percent when the sun is at an angle of about 45 degrees (e.g., in the late afternoon) (Ref. 2). The amount or intensity of UVB radiation received at the earth's surface is reduced in proportion to the angle of incidence of the radiation. At lower angles of incidence UVB radiation is attenuated by a longer passage through the ozone layer, which absorbs UVB radiation.

References

- (1) Kreps, S.I., "Sun Burn Protection and Sun Tan Preparations," *American Perfumer and Cosmetics*, 78:73-77, 1963.
- (2) Fitzpatrick, T.B., M.A. Pathak, and J.A. Parrish, "Protection of the Human Skin Against the Effects of the Sunburn Ultraviolet (290-320 nm)," in "Sunlight and Man," edited by M.A. Pathak et al., University of Tokyo Press, Tokyo, pp. 751-765, 1974.

14. One comment contended that the table "Guide for Fair-Skinned People" (43 FR 38206 at 38210) is confusing. The comment stated that it is not apparent why 4 times the MED should produce a painful sunburn in New Jersey, but 5 times the MED should do so in Florida, or why 8 times the MED should produce a blistering sunburn in New Jersey and 12 times the MED should do so in Florida. The comment argued that these data are incompatible with each other and should be verified with the authors (Ref. 1).

The agency has determined that the cited reference (Ref. 1) in the Panel's report is not the source of the information that appears in the "Guide for Fair-Skinned People" (43 FR 38210). Further, the agency is not aware of the source of this information. Because the information in the "Guide" has no bearing on the content of the tentative final monograph, it will not be discussed further.

Reference

- (1) Fitzpatrick, T.B., M.A. Pathak, and J.A. Parrish, "Protection of the Human Skin Against the Effects of the Sunburn Ultraviolet (290-320 nm)," in "Sunlight and Man," edited by M.A. Pathak, et al., University of Tokyo Press, pp. 751-765, 1974.

15. Referring to the Panel's discussion of the harmful effects of sunlight on the skin (43 FR 38206 at 38210), one comment stated that "light is only one of the parameters inducing skin cancer." The comment added that "other

environmental parameters are responsible for a less resistant cell, e.g., nutrition, lack of exercise, alcohol, drugs, smoking."

The agency recognizes that UV radiation is not the only parameter believed to be responsible for inducing skin cancer. However, parameters such as those named by the comment are unrelated to the use of OTC sunscreen drug products and are beyond the scope of this rulemaking.

16. One comment stated that the word "would" appearing at 43 FR 38206 at 38210, third column, line 6 should be replaced by "could," and that at 43 FR 38211, second column, line 23, the words "lower wavelength limit of cancer-producing radiation" should be replaced by "upper wavelength limit."

The word "would" referred to by the comment is part of a quote by Cleary (Ref. 1). The agency has reviewed this reference and found that it is correctly quoted. Therefore, the comment's suggested change would be incorrect.

The words at 43 FR 38211 referring to the wavelength limits of cancer-producing radiation were cited by the Panel as being supported by Blum (Ref. 2). The agency has reviewed this reference and agrees with the comment that the words "lower wavelength limit" are incorrect; however, the agency believes that the sentence in the Panel's report could have been clearer if it had stated " * * * because the wavelengths that cause cancer of the skin of experimental animals are those 320 nm and shorter, i.e., the same spectral range that produces sunburn in human skin * * * ." This wording would be more consistent with the statement made by Blum.

References

- (1) Cleary, D. M., "Is There Too Much Sunshine in Your Life?," *The Sunday Bulletin/Discoverer*, Philadelphia, pp. 12-16, May 15, 1977.
- (2) Blum, H. F., "Carcinogenesis by UV Light," Princeton University Press, Princeton, NJ, pp. 285-305, 1959.

17. Referring to the Panel's definition of "sunscreen sunburn preventive agent" (43 FR 38206 at 38213), one comment recommended that the Panel make a statement that "the sunscreen may remove the sunburning rays, but it may or may not transmit long-wavelength ultraviolet radiation of 320-400 nm." The comment mentioned that PABA may absorb radiation from 290 to 320 nm but will transmit radiation greater than 320 nm, whereas a benzophenone derivative may absorb UV radiation from 290 to 380 nm.

In discussing the types of solar radiation, the Panel noted that

"sunburn" radiation has a wavelength in the 290 to 320 nm region and not the 320 to 400 nm region (43 FR 38209). Therefore, the Panel defined a sunscreen sunburn preventive agent as an active ingredient that absorbs 95 percent or more of the light in the UV range at wavelengths from 290 to 320 nm and thereby removes the sunburning rays (43 FR 38213). The Panel did not include this definition for a "sunscreen sunburn preventive agent" in its recommended monograph, but included a definition for a "sunscreen active ingredient" (in § 352.3(b)) as follows: "An active ingredient that absorbs at least 85 percent of the light in the UV range at wavelengths from 290 to 320 nanometers, but transmits UV light at wavelengths longer than 320 nanometers. Such agents permit tanning in the average individual and also permit some reddening (erythema) without pain." This definition contains part of the statement requested by the comment concerning the transmittance of the longer wavelengths of UV radiation, i.e., "transmits UV light at wavelengths longer than 320 nm." However, the definition would not apply to ingredients which absorb UV radiation longer than 320 nm, e.g., dioxybenzone, a benzophenone derivative. Therefore, the agency is replacing the word "transmits" with the phrase "may or may not transmit" in the definition and is including the revised definition in § 352.3(c) of this tentative final monograph. The definition will be applicable to sunscreen active ingredients that absorb and transmit UV radiation in the 320 to 400 nm range. The agency is also proposing to replace the term "UV light" with "UV radiation." (See comment 2.) Regarding the last sentence in the Panel's recommended definition, the agency does not believe that this sentence is necessary to define a sunscreen active ingredient. Therefore, the last sentence in the Panel's recommended definition is not being retained. The proposed definition in § 352.3(c) for a sunscreen active ingredient now reads as follows: "An active ingredient that absorbs at least 85 percent of the radiation in the UV range at wavelengths from 290 to 320 nanometers, but may or may not transmit radiation at wavelengths longer than 320 nanometers."

18. Referring to the Panel's definitions of a sunscreen sunburn preventive agent and a sunscreen suntanning agent (43 FR 38206 at 38213), one comment suggested that these definitions should mention "the measuring conditions because of the correlation between layer thickness and transmission."

The Panel realized that its definitions are based on the UV-absorbing properties of a single active ingredient of a sunscreen product, not on how the ingredient might perform in a final formulation or in combination with other active ingredients (48 FR 38213). Therefore, the Panel included final formulation testing, with specific measuring conditions, in its recommended monograph. The Panel, however, did not include definitions of a sunscreen sunburn preventive agent or a sunscreen suntanning agent in its recommended monograph. The agency also does not propose to include definitions in the tentative final monograph. Thus, it is not necessary to revise the Panel's definitions.

19. One comment noted that the Panel stated that sunscreen active ingredients may be combined with other active ingredients such as skin protectants (43 FR 38206 at 38217). The comment added that the Panel did not define the term "skin protectant" and asked the meaning of the term.

The term "skin protectant" was defined in proposed § 347.3(a) of the tentative final monograph for OTC skin protectant drug products, published in the Federal Register of February 15, 1983 (48 FR 6832), as follows: "A drug which protects injured or exposed skin or mucous membrane surface from harmful or annoying stimuli." A final definition will appear in the final monograph for OTC skin protectant drug products in a future issue of the Federal Register.

20. Referring to the Panel's general discussion on sunscreens (43 FR 38206 at 38218), one comment questioned the source of the Panel's description of an ideal sunscreen vehicle. The comment stated that every person has his or her own ideas about an ideal vehicle, depending on skin constitution and the environment, and added that a certain content of emollients is important, especially in a dry climate and in water.

The Panel described the characteristics of an ideal sunscreen vehicle at 43 FR 38218 as follows: "An ideal sunscreen vehicle would be stable, neutral, nongreasy, nondegreasing, nonirritant, nondehydrating, nondrying, odorless, efficient on all kinds of human skin, hold at least 50 percent water, be easily compounded of known chemicals, and have infinite stability during storage." The Panel pointed out that there is no ideal vehicle and that the vehicles in common use represent a compromise of advantages against disadvantages. Vehicles for topical delivery of active ingredients are complex mixtures of substances involved in physical and chemical

interactions with the outer layer of human skin. The effects of abrasion, sweating, and washing on the physical and chemical properties of the active ingredients often depend upon the vehicle.

The agency believes that the Panel based its description of an ideal sunscreen vehicle on the experience of its members with various dermatological preparations and on information found in standard references, textbooks, and the scientific literature concerning the anatomy and physiology of the skin (43 FR 38217). The Panel did not make any recommendations concerning sunscreen vehicles for inclusion in the monograph. However, it did state in its definition of SPF value in § 352.3(d) that this determination is to be made on the "final formulation of the sunscreen product," which includes the vehicle. Also, the water resistant tests proposed by the Panel in § 352.46 are to be conducted with the final-formulated sunscreen product. (The agency is not proposing the Panel's recommended sweat resistance test. See comment 100.)

The agency acknowledges that there are different ideas about what constitutes an ideal vehicle for a sunscreen drug product. The Panel's general discussion of an ideal vehicle provides useful guidance to manufacturers of these products.

21. Referring to the Panel's general discussion on sunscreens (43 FR 38206 at 38219), one comment stated that the Panel's definition of the term phototoxicity is inaccurate and incomplete. The comment recommended careful rewording and revision of the definition. The comment argued that (1) Phototoxicity is a dose-related response ("usually an exaggerated sunburn reaction of all individuals to adequate simultaneous exposure to a photoreactive chemical and radiation of appropriate wavelengths"), (2) the exposure of skin to radiation alone may not produce any reaction in skin or may produce a minimal reaction which is not pathologic, (3) the topical application of the product or the chemical ingredient of the product may not produce any reaction, (4) in phototoxic reactions, simultaneous exposure of the skin to the chemical and the radiation of appropriate wavelength will result in an abnormal pathologic reaction manifested by erythema, edema, and even a blistering response, (5) the fluorescence property of a molecule has nothing to do with phototoxicity because there are hundreds of molecules that are fluorescent and yet are not photosensitizing, and (6) skin

photosensitization can occur when the absorbed energy by the chemical leads to the formation of either free radicals, singlet oxygen, covalent conjugation with DNA, ribonucleic acid, and protein, or damage of the cell membrane and lysosomes.

The Panel's report was not intended to be an in-depth discussion of phototoxicity. Rather, the Panel defined phototoxicity as it relates to the general discussion of sunscreens and the effects of exposure to sunlight. The agency is not including a definition of phototoxicity in this tentative final monograph. However, the agency discusses its position on sunscreen protection from phototoxic and photoallergic reactions in comment 33.

22. One comment recommended that FDA "advertise" the most effective sunscreen products and the recommended percentage of the ingredients in sunscreen preparations.

The agency is proposing in this tentative final monograph explicit and detailed labeling that manufacturers may use for all Category I sunscreen drug products. This includes SPF values, which are required in sunscreen labeling as a guide as to how a product will act on a consumer's skin, and five optional labeling claims (under "Product Category Designation") that are related to the SPF values of sunscreen ingredients (e.g., minimal (SPF 2 to under 4), moderate (SPF 4 to under 8), high (SPF 8 to under 12), very high (SPF 12 to under 20), and ultra high (SPF 20 to 30)). (See comment 45 for a discussion of new terminology for PCD's.) In addition, the monograph will provide the effective dosage limits (on a percentage basis) for each Category I sunscreen ingredient. (See comment 37.)

After publication of the final monograph, all sunscreen drug products marketed OTC will have to comply with the standards of safety and effectiveness established by the agency and be labeled accordingly. This labeling will enable consumers to select the product that is appropriate for their use.

23. One comment suggested that the agency formulate specific guidelines for providing safe, effective sunscreen lotions, creams, and gels for use on children. The comment stated that the AAD and the Skin Cancer Foundation are committed to educating parents on the importance of protecting their children against the potential harmful effects of solar radiation. The comment contended that, although the skin of children is more sensitive to the effects of sunlight than is the skin of adults, specific sunscreens for children have not been marketed. Also, specific guidelines for evaluating the safety and

effectiveness of sunscreens for children are not available. However, the comment also stated that children are more sensitive to contact irritation reactions and delayed hypersensitivity reactions to chemicals that may be present in a sunscreen product. The comment added that recently some manufacturers are claiming effectiveness of their product for children's skin, but that tests performed to support such a claim were unsatisfactory.

A second comment disagreed with the comment above regarding the need for special guidelines on SPF values of sunscreens designed especially for children. This comment stated that, as with all sunscreen products, appropriate safety and effectiveness testing should be conducted prior to marketing. This comment cited the transcript of the January 26, 1988 FDA meeting on OTC sunscreen drug products at page 37 (Ref. 1) where one participant contended that " * * * there is a great need for high SPF sunscreens in children. They are the ones who get the most sunlight." In addition, the participant stated that " * * * two-thirds of all the radiation you are going to get is before age 15 or 20 and it is there that the greatest protection has to be given."

The Topical Analgesic Panel discussed "adult skin" and "infant skin" in its report on OTC external analgesic drug products, published in the Federal Register of December 4, 1979 (44 FR 69773), and in its report on OTC sunscreen drug products (43 FR 38206 at 38217). The Panel was concerned with possible differences in percutaneous absorption between infant skin and adult skin. The Panel thoroughly discussed the absorptive characteristics of infant and adult skin and defined adult human skin to be that of individuals older than 6 months of age. The Panel stated that the skin of infants under 6 months may have different absorptive characteristics. In order to provide an added margin of safety, the Panel stated that sunscreen ingredients which it reviewed are not to be used on children under the age of 6 months (44 FR 69773). The Panel considered this margin of safety important because biologic systems which metabolize and excrete drugs absorbed through the skin may not be fully developed in children under the age of 6 months (43 FR 38217). The Panel recommended, and the agency agrees, that only sunscreen drug products providing a minimum SPF value of 4 should be used on children between 6 months and 2 years of age. All sunscreen products, regardless of their SPF value, may be used on

children 2 years of age and older. The agency is proposing to include these requirements in the directions for use. (See comments 61 and 66.)

In addition, the agency notes that the first comment did not submit data to support its contention that the skin of children is more sensitive than is the skin of adults to sunlight, contact dermatitis, or delayed sensitivity reactions; nor did the comment submit results to substantiate its claim that "tests performed * * * were unsatisfactory."

The agency agrees that the use of sunscreens with high SPF values may be advantageous to adults and children. (See comment 46.) The agency believes, however, that the need for special guidelines for the use of sunscreen drug products designed especially for children, as suggested by the first comment, has not been established.

Reference

(1) Transcript of meeting between the public and FDA to discuss appropriate testing procedures for OTC sunscreen drug products, January 26, 1988, Rockville, MD, page 37, comment no. TR, Docket No. 78N-0038, Dockets Management Branch.

B. Comments on Drug/Cosmetic Status of Sunscreen Drug Products

24. Four comments maintained cosmetic companies were not afforded the opportunity to participate in the sunscreen products rulemaking process because they were not given adequate notice. One comment stated that the fact that a cosmetic trade association and certain cosmetic manufacturers participated in these proceedings does not alter this reasoning because many cosmetic companies also sell drug products. Two comments emphasized that although a notice was published in the Federal Register of December 12, 1972 (37 FR 26456), this notice gave no indication that FDA might attempt to reclassify, as drugs, articles historically regulated as cosmetics or otherwise to establish any requirements for cosmetics. The comments stated that (1) The notice invited submissions with respect to "sunburn prevention and treatment drug products" and (2) that there was no indication that manufacturers of cosmetic products containing sunscreens might be subject to the same compositional or labeling requirements as sunburn prevention products. The comments added that there were factors that could have led the cosmetic industry, including manufacturers of suntan products, to conclude that there was no need to submit data and information to the Topical Analgesic Panel concerning

products traditionally regarded solely as cosmetics. These factors included FDA's statement in the *Federal Register* of May 11, 1972 (37 FR 9473) in the procedural regulations governing the OTC drug review that it would not review products for which only cosmetic claims were made, FDA's Trade Correspondence (Ref. 1), and FDA's cosmetic product regulations. The comments stated that if FDA intends to regulate cosmetic products under the OTC drug regulations, the current proposal should be withdrawn and the Panel reconvened to consider submissions from cosmetic manufacturers, pursuant to a new and sufficient notice and request for information.

The agency does not agree with the comments. Both the public and the cosmetic industry have had and will continue to have the opportunity to participate fully in the process for developing the sunscreen monograph. The agency regularly published notices in the *Federal Register* announcing the dates of the Topical Analgesic Panel's meetings. A part of each meeting was open to the public, and minutes of the meetings were available to the public. One of the industry liaison members on the Panel was nominated by the CTFA, the principal cosmetic industry trade association. Thus, adequate notice was provided for all parties, including cosmetic manufacturers, to present their positions to the Panel during its deliberations. Interested persons had a similar opportunity to comment and submit information to the agency following publication of the Panel's report. Furthermore, in the *Federal Register* of September 4, 1987 (52 FR 33598), the agency announced that a public meeting to discuss sunscreen testing procedures would be held on January 26, 1988, and that the administrative record for sunscreen drug products would be reopened until April 2, 1988. Several cosmetic companies and the CTFA participated in that meeting and submitted written comments to the agency. Finally, the present tentative final monograph is a proposed regulation. Once again, all interested parties have an opportunity to participate and to make their views known before a final regulation (monograph) is issued.

The agency emphasizes that this rulemaking for OTC sunscreen products applies only to drug products that contain sunscreen ingredients, display labeling that identifies those active ingredients as sunscreens, or display labeling claims that allude to the sun-blocking or sun-protection properties of those active ingredients. The distinction

between sunscreen-containing products that are drugs and those that are cosmetics is discussed in comment 27.

Reference

(1) "FD & C Act Trade Correspondence," United States Department of Agriculture, Food and Drug Administration, TC-61, February 15, 1940.

25. Several comments stated that many cosmetics are currently "represented" as aids in acquiring an even tan or as useful in screening the sun, but are not "represented" for the treatment or prevention of sunburn. The comments maintained that the proposed monograph should be clarified to eliminate ambiguity and to exclude cosmetic products (e.g., moisturizers, make-up, and lipsticks) more explicitly by revising the monograph to state that cosmetics are excluded. The comments stated that the proposed rule can have no application to cosmetic products as they are defined in the Federal Food, Drug, and Cosmetic Act (the act), and that the mandate of the OTC drug review is to evaluate the safety and effectiveness of acknowledged drugs, not to provide a means for the reclassification of products. Consequently, some comments suggested that proposed § 352.1 "Scope" be amended by: (1) Changing the term "sunscreen product" to read "drug represented for use in prevention of sunburn" and (2) adding at the end of § 352.1 the sentence "This part does not apply to an article represented for use as a sunscreen or containing an ingredient with sunscreen properties if the article is intended for use solely as a cosmetic as defined in section 201(i) of the act, 21 U.S.C. 321(i)." One comment suggested rewording § 352.1 to read "An Over-the-Counter sunscreen drug product in a form suitable for topical administration * * *." This comment also suggested adding the following to the end of § 352.1: "a product otherwise a cosmetic shall not be considered a 'drug' because it contains a sunscreen agent and such fact is recognized in product labeling or promotion as 'contains sunscreen.'"

Conversely, one comment contended that the word "sunscreen" in § 352.1 should be clearly defined to include all products that consumers consider within the meaning of the term suntan lotion, i.e., any product sold for use on the skin in connection with sunbathing, swimming, or other outdoor activity.

The agency agrees with the comments that stated that the monograph for OTC sunscreen products applies only to drugs. However, the agency has tentatively concluded that any product containing sunscreen active ingredients

and displaying sunscreen labeling claims is a drug even if the product is not labeled for the prevention or treatment of sunburn (see comment 27). In order to clarify that the scope of this monograph extends only to drug products, and to be consistent with the format of monographs for other OTC drug product categories, the word "drug" is being added to § 352.1 to read: "An over-the-counter sunscreen drug product in a form suitable for topical administration * * *." Because this section, as revised, clearly applies only to drug products, the agency believes that it would be redundant to add a sentence to the end of § 352.1 emphasizing that the proposed rule does not apply to cosmetics.

The agency disagrees with the comments that products which are primarily designed to be used as cosmetics but which contain a sunscreen active ingredient are outside the scope of the monograph. However, the agency recognizes that products such as lipsticks and make-up preparations containing sunscreen active ingredients and displaying sunscreen labeling claims may require separate consideration. Accordingly, the agency is proposing appropriate labeling for such products. (See comments 27 and 52.)

The agency does not agree with the comment that suggested that the word "sunscreen" should be defined as pertaining to all products sold for use on the skin in connection with sunbathing, swimming, or other outdoor activity. The agency recognizes that many OTC products sold for use on the skin in connection with sunbathing, swimming, or other outdoor activity contain no sunscreen active ingredients, provide no sunscreensing protection, and do not have drug labeling. In addition, as discussed in comment 27, some products such as shampoos, hair conditioners, or nail polishes may contain a sunscreen and bear only cosmetic labeling. These products are cosmetics and, therefore, are not within the scope of this monograph.

The agency believes that the revised "Scope" language being proposed in § 352.1 of this tentative final monograph will adequately define the coverage of this class of drugs.

26. Four comments suggested revising the statement of identity in § 352.50(a) to read "sunburn prevention product" (instead of "sunscreen") in order to distinguish between sunscreen-containing products that make a specific "representation" regarding usefulness in the prevention of sunburn (i.e., sunscreen drug products) and sunscreen-containing products that refer

to suntanning or to screening or blocking the sun (i.e., sunscreen cosmetic products). The comments recommended using the term "sunburn prevention product" throughout the monograph instead of the term "sunscreen" to describe the regulated class of drug products. Another comment suggested that the term "sun prevention product" be used in the monograph in lieu of "sunscreen."

One of the comments stated that FDA should adopt a statement of identity for cosmetic products containing a sunscreen ingredient intended for everyday nonbeach use that is different from the statement adopted for beach products containing a sunscreen ingredient. The comment suggested "skin shield," "UV light block," "UV light filter," or any other such similar statement. The comment recommended that this statement of identity appear on the label of an everyday use, nonbeach cosmetic product along with any other statement of identity required for such a product in 21 CFR 701.11 (e.g., "Brand X Facial Cream and (or with) Skin Shield").

The comment also suggested that FDA define products for which this new statement of identity would be applicable as "Drug products containing one of the active ingredients set forth in § 352.10 and bearing labeling limited to the chronic exposure representations in § 352.50(b)(1)(iv) or (b)(1)(v), and not represented for use in the prevention or treatment of sunburn." The comment maintained that "adoption of such a definition is a necessary recognition of the distinctive nature of everyday use, nonbeach beauty products that contain a sunscreen ingredient and are represented as useful in the prevention of skin cancer and/or premature aging of the skin, but are not represented for the prevention or treatment of sunburn."

The agency does not agree with the comments that the statement of identity in § 352.50(a) of this tentative final monograph should be changed to read "sunburn prevention product" or "sun prevention product" instead of "sunscreen," or that these terms should replace "sunscreen" throughout the monograph. The agency believes that the term "sunscreen" appropriately identifies a product that reduces the amount of harmful UV radiation from sunlight impinging on the skin. Sunscreen active ingredients absorb specific segments of the UV spectrum, or they reflect or scatter UV radiation and thereby prevent it from reaching the skin. Sunscreens only extend the amount of time necessary for the sun to produce a sunburn. To classify these products as "sunburn prevention

products" or "sun prevention products" would mislead the consumer; these products only moderate the erythema reaction of the exposed skin, and the possibility of sunburn still remains. The agency tentatively concludes that the term "sunscreen" appropriately describes the principal intended action of these drug products, and that this term is well understood by consumers. Therefore, in this tentative final monograph, the agency is proposing that the labeling of the product identifies the product as a "sunscreen."

The agency does not believe that separate statements of identity or separate definitions are necessary to distinguish "nonbeach" products that contain sunscreens but are not indicated for the prevention or treatment of sunburn from "beach" products containing sunscreens. The agency is aware that some products, such as lipsticks and make-ups, contain sunscreen active ingredients and display Category I sunscreen labeling claims other than for the prevention or treatment of sunburn. These products are primarily intended for use as cosmetics. Nevertheless, these products are also drugs and cannot be regarded solely as cosmetics because the sunscreen added to the product is intended to provide protection from the sun. Some of the labeling recommended by the Panel for sunscreen drug products may not be appropriate for these products. Therefore, the agency is proposing alternative labeling, including specific warnings and directions, for products such as lipsticks and make-ups. (See comments 27 and 52.) The agency believes that these regulations will adequately distinguish between "beach" and "nonbeach" sunscreen-containing drug products.

27. Several cosmetic manufacturers and a cosmetic trade association submitted comments stating that certain cosmetic products are not subject to regulation under an OTC drug monograph. Such products include makeups, lipsticks, and suntanning preparations containing a sunscreen ingredient and displaying labeling that refers to the sun-shielding or sun-blocking properties of the product, but not claiming to prevent sunburn. The comments maintained that when an ingredient can be used for either drug or cosmetic purposes, its status as a drug or a cosmetic, or both, is determined by the representations made by the manufacturer or distributor in the labeling or advertising for the product. Many comments emphasized that mere inclusion of an ingredient in a product does not cause the product to become a drug if the finished product is intended

for use only as a cosmetic. To support their contentions, some of the comments cited the definitions of "drug" and "cosmetic" in sections 201(g) and (i) of the act (21 U.S.C. 321(g) and (i)) and prior case law. The comments also maintained that, according to an "FDA FD & C Act Trade Correspondence of 1940 (TC-61)" (Ref. 1), a product containing a sunscreen ingredient and represented as an aid to acquiring an even tan (but not for the prevention or treatment of sunburn) is a cosmetic and not a drug. Some comments added that FDA regulations in 21 CFR 720.4(c), which establish cosmetic product categories, include "suntan and sunscreen preparations."

Several comments stated that the mere use of the term "sunscreen" or of a truthful reference to blocking the rays of the sun or protection against the sun does not cause a product to be a drug. These comments asserted that only a product explicitly offered for use in preventing sunburn or other diseases may be categorized as a drug. The comments maintained that many products such as lipsticks, make-up preparations, and suntanning lotions that contain sunscreens have traditionally been regulated as cosmetics. The comments added that consumers use such products to avoid freckling, redness, or uneven coloration resulting from exposure to the sun. According to the comments, such uses are cosmetic. Many comments implied that if a reference to sunscreen ingredients and sunscreen properties in the labeling of a cosmetic would cause the product to be a drug, then cosmetic manufacturers would exclude sunscreen active ingredients from their products. The comments added that FDA should encourage the use of sunscreen ingredients in cosmetic skin products because of the favorable impact of the use of such products on the incidence of skin cancer and premature aging of the skin.

One comment stated that the inclusion of sunscreens can be rationalized as contributing to tanning rather than preventing sunburn. The comment added that sunscreens allow the consumer to stay in the sun longer, which is necessary for a deep, long-lasting tan; consumers can use these products to plan a tan and to increase the time in the sun. According to the comment, consumers can thereby obtain an even tan and one that does not readily fade.

The Panel was charged with evaluating the safety, effectiveness, and labeling of OTC active ingredients intended to prevent injury from exposure to the sun. It concluded that

overexposure to the sun results in various kinds of skin damage including sunburn, premature aging of the skin, and skin cancer (43 FR 38206 at 38211). The Panel stated that the use of sunscreens may mitigate the harmful effects of UV radiation from the sun on the exposed skin of susceptible individuals. The Panel recognized that many suntanning products had been traditionally regarded by FDA as cosmetics. However, the Panel believed that "regardless of the claims, products intended to be used for the prevention of sunburn or any other such similar condition should be regarded as drugs" (43 FR 38209). As discussed below, the agency concurs with this view.

After evaluating the active ingredients in the products submitted for review, the Panel stated:

(T)hese preparations reduce by varying amounts the solar radiation absorbed by the skin and thereby affect the physiological response and extent of the erythema reaction (redness) produced. Indeed, these products affect the structure and function of the body by screening, reflecting, or scattering the harmful, burning rays of the sun. This is a desirable alteration to a normal physiological response to solar radiation for individuals with sensitive and extra sensitive skin (43 FR 38209).

The Panel classified products intended to be used for preventing sunburn and similar conditions as drugs regardless of claims that were made for the products.

In a 1940 advisory opinion referred to as Trade Correspondence (TC)-61 (Ref. 1), the agency stated its policy regarding the drug/cosmetic status of sunburn and suntan preparations. TC-61 holds that a product promoted for prevention of damage from the sun is a drug, and a product that is promoted solely for the purpose of acquiring an even tan can be considered a cosmetic. Overexposure to the sun was not generally perceived to be harmful in 1940, and most of the products currently on the market were not available then. Since 1940, however, there has been a significant body of information developed on the harmful effects of the sun on human health and a significant change has occurred in consumer perception of the purpose of suntanning products. Today, consumers expect protection from a product that is promoted for suntanning. A letter from FDA to industry counsel, dated June 17, 1976 (Ref. 2), stated that the agency had changed the position set out in TC-61. FDA's present policy, as expressed in the 1976 letter, is that a product containing a sunscreen ingredient, even when labeled solely as a tanning aid, is both intended and understood to be a

sunburn preventive. Such a product, therefore, is a drug under the act.

Sunscreen active ingredients affect the structure and function of the body by screening, reflecting, or scattering the harmful, burning rays of the sun, thereby altering the normal physiological response to solar radiation. Use of these ingredients helps to prevent diseases such as sunburn and may help to reduce the chance of skin lesions and skin cancer. When used in a suntan product, sunscreen active ingredients may help to obtain a tan by permitting the user to remain in the sun for a longer time without burning. Their primary intended use, however, is as a drug: to screen out UV radiation during the extended time of exposure so as to prevent skin damage through overexposure. Further, the agency believes that consumers expect protection from a tanning product that contains a sunscreen, irrespective of the claims for which the product is promoted.

The agency finds that TC-61 is out of date with current scientific knowledge and is no longer applicable. The agency intends to revoke TC-61 in accordance with 21 CFR 10.85(g). A notice of revocation and the final monograph for OTC sunscreen drug products will be published concurrently.

When an ingredient can be used for either drug or cosmetic purposes, its regulatory status as a drug or cosmetic, or both, is determined by objective evidence of the distributor's intent. As suggested by the comments, this includes, but is not limited to, the representations made by the manufacturer or distributor in the labeling or promotion of the product. The agency believes that the inclusion of a sunscreen active ingredient in a product that is intended or promoted to protect the consumer's skin from the harmful effects of the sun brings the product within the statutory definition of a "drug." A "drug" is defined in the act as an article "intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" or "intended to affect the structure or any function of the body." (21 U.S.C. 321(g)). It is, of course, settled law that in determining whether an article is a drug, FDA is not bound by the manufacturer's subjective claims, but can find actual therapeutic intent on the basis of objective evidence. *National Nutritional Foods Association v. Matthews*, 557 F.2d 325 (2d Cir. 1977). Such intent may be derived from labeling, promotional material, advertising, and any other relevant source. *Id.* Such "relevant source" can be the consumer's intent in using the

product. *Action on Smoking and Health v. Harris*, 655 F.2d 236 (D.C. Cir. 1980).

Also, when consumers see on the label of a product the term "sunscreen" or similar terms that could be interpreted as claiming that the product functions as a sunscreen, such as "sun shield" or "UVA/UVB filter," they quite rightly expect the product to protect them in some way from the harmful effects of the sun, irrespective of other labeling statements. The agency believes that consumers equate the term "sunscreen" or similar terms with the mitigation of the harmful effects of the sun, such as sunburn, premature aging of the skin (or skin aging due to the sun), and skin cancer.

Accordingly, the agency tentatively concludes, and is proposing in this tentative final monograph, that the use of the term "sunscreen" or a similar term on the label of a product causes that product to be a drug, except for specific nontherapeutic uses as discussed below. Likewise, similar claims, such as "shields from the sun," "blocks out the rays of the sun," "protects from the sun," "protects against UV rays," "prevents freckling," "prevents redness," or "prevents uneven coloration" are drug claims. Such claims imply that exposure to the sun is harmful, and that blocking it will provide benefits. These claims also imply that the product affects a physiological function of the body. The agency also considers that the use of the term "SPF" or the use of any SPF value in the labeling of a product as a basis for the product to be considered a drug. An SPF value provides assurance that the product will protect the skin from sun damage and, thus, will help to prevent disease and will affect the structure and function of the body.

The agency agrees with one of the comments that the inclusion of sunscreen ingredients in some cosmetic skin products is of benefit to the consumer. However, long-term use of products containing ineffective (or less than fully effective) sunscreen ingredients could result in a consumer being exposed to more UV radiation than the consumer would expect. Such use could have serious effects (e.g., increase the chance of skin lesions and skin cancer). The agency believes that all products containing a sunscreen active ingredient and claiming to protect the consumer from the sun or to enhance the consumer's ability to obtain an effect from sun exposure (i.e., a tan) must be regulated as drugs in order to ensure the effectiveness of the sunscreen ingredient. Therefore, FDA tentatively concludes that, except for a few select exceptions discussed below,

all products that contain sunscreen active ingredients and bear labeling identifying these active ingredients as sunscreens are drugs. Likewise, sunscreen containing-products that bear claims alluding to the sun-blocking or sun-shielding properties of the products or claims promoting a product's ability to help the consumer stay in the sun longer without harmful effects are drugs. Such products may also be regulated, but not solely, as cosmetics. Regarding the statement made by some comments that FDA regulations in 21 CFR 720.4(c) include suntan and sunscreen preparations, in the *Federal Register* of January 28, 1992 (57 FR 3128 at 3129), the agency revised § 720(c)(13) to delete sunscreen preparations.

Regarding one comment's statement that sunscreens may be added to a product to contribute to the tanning process and not to prevent sunburn, the agency agrees that sunscreens may indirectly aid the tanning process by allowing a person to remain in the sun for a longer period of time without burning. However, the agency believes that tanning products that contain sunscreens are drugs because the inclusion of a sunscreen in a tanning product implies that the product will protect against harm from the sun while the user is tanning. For a further discussion of tanning products and claims, see comments 29 and 58.

The agency is aware that there are many skin products such as lipsticks and make-up preparations on the market that contain sunscreens, and whose primary intended use is as a cosmetic. Nevertheless, under this tentative final monograph, such products are also drugs if they contain any of the following anywhere in their labeling or promotional material:

- (1) The terms "sunscreen" (or a similar term as discussed above) or "SPF,"
- (2) An SPF value, or
- (3) Any other claims referring to the therapeutic attributes of sunscreen ingredients.

The agency acknowledges that a product may contain a sunscreen ingredient and be a cosmetic and not a drug. For example, a sunscreen ingredient may be included in a cosmetic product without making it a drug if: (1) It is a color additive (e.g., titanium dioxide in a lipstick), (2) it is used to protect the color of the product (e.g., sulisobenzene in a cologne, or (3) it is not intended to function as a drug, and no claims are made about the ingredient. In these cases, the term sunscreen is not used, no SPF value is given, and the sunscreen ingredient is only mentioned in the product's

labeling by its cosmetic name in the ingredient list in accordance with agency regulations in § 701.3. There are several specific conditions described below where additional information about the sunscreen may be provided.

In order to provide guidance regarding appropriate labeling for cosmetic products containing sunscreen ingredients, the agency is providing in this document some examples of labeling that would cause a product to be a drug. Any labeling on a cosmetic product that implies that the product has a therapeutic benefit or affects the structure or function of the body is unacceptable. The agency tentatively concludes that the following labeling is unacceptable for cosmetic products that contain a sunscreen:

- (1) The word "sunscreen" or similar terms anywhere in the labeling (except for the specific instances described below)
- (2) "shields from the sun"
- (3) "blocks out the rays of the sun"
- (4) "protects from the sun"
- (5) "prevent or protect against freckling"
- (6) "prevent or protect against wrinkling"
- (7) "prevent or protect against redness or uneven coloration of the skin"
- (8) "protects against UVA/UVB"
- (9) "shields the skin against specific factors that accelerate the signs of skin aging"
- (10) "helps to acquire an even tan"
- (11) "permits tanning"
- (12) "protects against premature aging, skin aging, skin lesions, and skin cancer" with or without stating "due to the sun" in the labeling of the product.

Such labeling would cause sunscreen-containing products to be considered drugs as well as cosmetics under the act.

As discussed in comment 52, the agency does not believe that all of the labeling recommendations made by the Panel are applicable to drug/cosmetic products that contain sunscreens. Therefore, the agency is proposing specific directions and other labeling appropriate for this type of product.

As stated above, in most situations, the use of the word "sunscreen" or similar terms in the labeling of a product would cause the product to be considered a drug. The agency recognizes, however, that there are a few situations in which the term "sunscreen" could be used in the labeling of a strictly cosmetic product for which there is no therapeutic use. For example, a sunscreen ingredient may be included in a product to protect hair from sun damage (e.g., padimate O in a hair conditioner or hair spray).

Also, a sunscreen ingredient may be used in a nail polish to protect the color of the polish after application on the fingernails. If there are other instances where the nontherapeutic use of a sunscreen should be included in the labeling of the product, manufacturers should inform the agency in comments to this notice.

In the example cited above, the sunscreen ingredient is not being used to protect the skin from sunburn or other adverse effects of the sun; therefore, it would be misleading to represent anywhere in the product's labeling that the sunscreen has any therapeutic purpose. However, the labeling could state that the product contains a sunscreen to inform consumers why the product would protect the hair. For example, the labeling might state "contains a sunscreen to protect the hair from the damaging effects of sunning." It would be misleading to consumers to only use the term "contains a sunscreen" in such labeling without clarifying the purpose of the ingredient. Without such qualification, consumers might believe the product offered skin protection. Therefore, the product would be misbranded under section 201(n) and 602(a) of the act (21 U.S.C. 321(n) and 362(a)).

The agency is proposing to amend 21 CFR part 700 in subpart B, *Requirements for Specific Cosmetic Products*, by adding new § 700.35, as follows:

(a) A product that includes a sunscreen active ingredient and the term "sunscreen" in its labeling or in any other way represents or suggests that it is intended to prevent, cure, treat, or mitigate disease or to affect a structure or function of the body comes within the definition of a drug in § 201(g)(1) of the Federal Food, Drug, and Cosmetic Act. Sunscreen active ingredients affect the structure or function of the body by screening, reflecting, or scattering the harmful, burning rays of the sun, thereby altering the normal physiological response to solar radiation. These ingredients also help to prevent diseases such as sunburn and reduce the chance of premature skin aging or skin cancer due to the sun. Moreover, when consumers see the term "sunscreen" on the label of a product, they expect the product to protect them in some way from the harmful effects of the sun, irrespective of other labeling statements. Consequently, the use of the term "sunscreen" in a product's labeling normally makes that product a drug. However, sunscreen ingredients may also be used in some cosmetic products

for nontherapeutic uses. In order to avoid consumer misunderstanding, if a cosmetic product uses the term "sunscreen" anywhere in its labeling, the term "sunscreen" must be qualified by describing the cosmetic benefit provided by the sunscreen. For example: "This product contains a sunscreen that assists in protecting the hair from damage by the sun."

(b) Any information describing the purpose of the sunscreen in the product shall appear in direct conjunction with the term "sunscreen."

The final monograph will cover only the drug use of the active ingredients listed therein. The concentration ranges, limitations, warnings, and directions established for these ingredients in the monograph will not apply to the use of the same ingredients in products intended solely for use as cosmetics. Those products intended for both drug and cosmetic use will be required to conform to the requirements of the final monograph. However, such products, in addition to bearing the indications allowed for sunscreen drug products, may also be labeled for cosmetic use, in conformity with section 602 of the act (21 U.S.C. 362) and the provisions of 21 CFR parts 701 and 740.

In accordance with the revised labeling requirements for OTC drug products, it is the agency's view that cosmetic claims may not appear within the boxed area designated "APPROVED USES." As discussed in the final rule on the agency's "exclusivity policy" (51 FR 16258 at 16264 (paragraph 14)), cosmetic terminology is not reviewed and approved by FDA in the OTC drug monographs and therefore could not be placed in the box. Cosmetic claims may appear elsewhere in the labeling, should manufacturers choose the labeling alternative provided in § 330.1(c)(2)(i) or (c)(2)(iii) for labeling drug/cosmetic products. Although the agency does not specifically prohibit commingled drug and cosmetic labeling in other than the indications section, such claims should be appropriately described so that consumers will more readily be able to differentiate the drug aspects from the cosmetic aspects of such labeling. If commingled drug and cosmetic labeling claims are confusing or misleading, the product's labeling could be misleading within the meaning of the act and misbranded under sections 502(a) and 602(a) of the act (21 U.S.C. 352(a) and 362(a)).

References

(1) "FD & C Act Trade Correspondence," United States Department of Agriculture, Food and Drug Administration, TC-61, February 15, 1940.

(2) Letter from S. Fine, FDA, to R. Kingham, Covington and Burling, dated June 17, 1978, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

28. Three comments, referring to the cosmetic portion of the labeling of a drug/cosmetic product, argued that the limitations set by the Panel for ingredients for drug use do not establish an inference with respect to the use of the same ingredient as a cosmetic. For example, § 352.10 of the Panel's proposed monograph (43 FR 38206 at 38264) restricts red petrolatum to use at a level of 30 percent or more in a sunscreen drug product, yet that same ingredient may be used properly at any safe level in a cosmetic. The comments also asserted that the warnings in proposed § 352.50(c) (43 FR 38268) do not establish any need for warnings on cosmetic products. Citing the Comptroller General's "Report to the Congress" concerning cosmetics, HRD-78-139, August 8, 1978, page 132, the comments added that FDA has recognized that a warning required for a particular ingredient in a drug product may not be appropriate when that ingredient is used in a cosmetic product. The comments maintained that FDA may not prohibit truthful and nonmisleading labeling concerning cosmetic aspects of a cosmetic that is also a drug, and that such labeling is subject to regulation by FDA under its cosmetic authority, not under its drug authority.

The agency agrees that this monograph applies only to sunscreen products that fall within the statutory definition of "drugs." In order to make it clear that the scope of the monograph extends only to drug products, the agency is proposing that the word "drug" be added to § 352.1 ("Scope"), to read "An over-the-counter sunscreen drug product * * *." (See comment 25.)

29. Stating that tanning is in the cosmetic area, one comment opposed any requirement that a cosmetic suntan product contain a sunscreen agent at any concentration level. Conversely, a number of comments contended that allowing "tanning" products to be marketed without sunscreens is misleading because consumers would believe that they have protection against sunburn when in fact they do not. The comments maintained that such products would actually promote sunburn and its subsequent, serious side effects. The comments asserted that allowing a tanning claim for products without sun protective factors would be contrary to the best interest of the public. Expressing concern that products making "tanning only" claims

would be exempt from the proposed OTC sunscreen standards, one comment contended that these regulations are designed to provide protection from the acute effects of UV radiation in the 290 to 320 nm range (UVB), and that tanning is a direct response to that radiation. The comment stated that for products to influence tanning, they can either accelerate, diminish, or have no effect on UVB radiation. The comment argued that "tanning only" products should either diminish the amount of "UV-B flux" or should be labeled "sunburn, then tan." The comment contended that the term "tanning only" should not be allowed if those products allow normal or accelerated sunburn.

One comment was opposed to the sale of "tanning" products, but felt that the government cannot restrict the sale of such products. The comment, therefore, suggested that tanning products be required to carry warning labels. Another comment acknowledged that tanning products do not make a claim for sunburn protection, but suggested that, because of the consumer's perception that such products will reduce the risk of sunburn, all tanning products should contain a sunscreen agent with a minimum SPF value of 4.

Another comment urged that any product that claims to promote or permit tanning be required to contain a sunscreen and have a minimum SPF value of 2 or be deemed adulterated and/or misbranded. The comment argued that suntanning products without a minimum SPF value of 2 are dangerous and pose serious health hazards. The comment stated that the agency banned the use of chlorofluorocarbon propellants because chlorofluorocarbons cause a decrease in the ozone layer which can result in an increase in UV radiation to the earth and increased skin damage. The comment contended that, from a public health viewpoint, a requirement of a minimum SPF value of 2 for suntanning products is as necessary to protect the skin as the ban of chlorofluorocarbon propellants. The comment cited research indicating that the use of certain suntanning products without sunscreens may increase the amount of UV radiation penetrating the skin by as much as 10 percent (Ref. 1). The comment added that the health hazards attributable to long-term overexposure to the sun have been proven conclusively, and that it is less than responsible to market products that promote tanning but afford no protection from overexposure to UV radiation. The comment further contended that a sunscreen-containing product with an SPF value of 2 will

afford 50 percent more protection from long-term and short-term harm induced by overexposure to the sun than products without sunscreens.

The comment claimed that a survey that it conducted (Ref. 2) involving 903 consumers (age 35 and under) who purchase products for use in the sun demonstrated that 92 percent felt that protection from sunburning, as well as tanning, are expected attributes of a tanning product whether or not the label claims protection. From the results of the survey, the comment concluded that consumers believe and expect that a product that promotes or permits tanning will also provide protection from sunburn and other harmful effects of the sun.

Although the comment felt that the Panel recognized that suntanning products should contain a sunscreen with a minimum SPF value of 2, the comment did not agree that suntanning products need to be regulated as drugs. The comment recommended an addition to the cosmetic regulations in 21 CFR part 700 that would define suntanning cosmetic products as articles making suntanning claims and formulated with a minimum SPF value of 2. The comment cited the following examples as precedent for such a regulation: (1) The banning of hexachlorophene in cosmetics except as a preservative at levels not higher than 0.1 percent, (2) the banning of halogenated salicylanilides in cosmetics, and (3) the defining of the term "egg" as a name in cosmetic products containing not less than 2 percent egg. The comment contended that failure to enact such a regulation will force manufacturers of sunscreen products to market more tanning products without sunscreens in order to compete with products making only tanning claims. The comment stated further that this action would increase consumer use of tanning only products (without sunscreens) and increase the number of consumers placed in danger from overexposure to the sun. The comment concluded that, if the agency does not promulgate the comment's recommended cosmetic regulation, suntanning products should be included within the scope of the proposed rule for OTC sunscreen drug products.

The agency recognizes that tanning products have traditionally been used for cosmetic purposes to help an individual acquire a tan. These products are of two basic types: those that contain sunscreen ingredients and those that do not. Suntanning products that contain sunscreen ingredients are designed to minimize the burning effects of the sun. They permit the user to stay in the sun

longer without receiving a painful sunburn and still acquire the desired tan. Tanning products without sunscreen ingredients are designed primarily to condition the skin while sunbathing to acquire a tan. Although the agency does not believe that all suntanning products should be required to contain a sunscreen ingredient, it believes that all suntanning products should be labeled so that the consumer can use them safely.

The agency believes that, as the data cited in the comments suggest, there has been a change in consumer perception regarding the purpose of suntanning products, and that the consumer expects a certain amount of protection from the sun from a product that is marketed for suntanning. The agency has tentatively determined that any tanning product that contains a sunscreen ingredient should be regulated as a drug product regardless of its claims because the inclusion of a sunscreen ingredient in a tanning product implies that the product will protect against harm from the sun while the user is tanning. Moreover, these products have a drug effect by reducing by varying amounts the UV radiation absorbed by the skin and affecting the physiological response and extent of the erythema reaction produced. Therefore, any tanning product that contains a sunscreen ingredient must comply with the monograph for OTC sunscreen drug products and must provide a minimal SPF of 2. A suntanning product that does not contain a sunscreen may be considered a cosmetic.

The agency is aware that some tanning products containing no sunscreen ingredient are labeled with SPF 0 and SPF 1. The use of SPF values in the labeling of a tanning product may lead the consumer to assume that the product contains a sunscreen ingredient when, in fact, it does not. Such labeling, especially SPF 1, could cause consumers to expect the product to provide some protection against the adverse effects of the sun. The agency considers such labeling on a tanning product that contains no sunscreen ingredient to be false and misleading and causes the product to be misbranded under section 602 of the act (21 U.S.C. 362).

In addition, because suntanning products are marketed specifically for use in the sun or at commercial tanning facilities, the agency is concerned about the health hazards associated with using such products if they do not contain sunscreen ingredients. The agency believes that in the absence of labeling statements that inform the consumer of the amount of protection that can

reasonably be expected from the use of these products, such products could be potentially dangerous. The agency tentatively finds that the majority of consumers expect sunburn protection from suntanning products, whether the product contains a sunscreen ingredient or not. Because of the serious consequences of overexposure to the sun, the agency believes that it is important for the consumer to know whether a suntanning product contains a sunscreen ingredient or not. Failure to contain such information would constitute a failure to reveal facts material in light of the representations that are made (e.g., "suntanning") and with respect to the consequences that may result from the use of the article. Therefore, in conjunction with this tentative final monograph, the agency is proposing, under 21 U.S.C. 321(n), 362(a), and 371(a), to amend the cosmetic regulations in 21 CFR Part 700 by adding § 740.19 as follows: "*Suntanning preparations.* The labeling of suntanning preparations that do not contain a sunscreen ingredient must display the following warning: 'Warning—This product does not contain a sunscreen and does not protect against sunburn.'"

References

- (1) White, H., et al., "Enhancement of Transmission of Optical Radiation Through Human Epidermis by Topical Applications," 1978, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (2) Comment No. C00048, Docket No. 78N-0038, Dockets Management Branch.

C. Comments on Specific Sunscreen Active Ingredients

30. One comment recommended the use or creation of simpler names for many of the sunscreen active ingredients because simpler names would be more easily recognized by the public. Maintaining that sunscreens with simpler names have a marketing advantage over other sunscreen ingredients with more complex names, the comment contended that the variety of sunscreens available to the public will tend to become limited if some sunscreen ingredients have very complex names. The comment added that the variety of sunscreens available is very important to consumers with specific allergies or sensitivities. Stating that section 508 of the act (21 U.S.C. 358) clearly authorizes the assigning of simple names, the comment suggested establishing simple names for all approved ingredients by using CTFA names or abbreviations where available and by creating simple names using CTFA guidelines for the remaining compounds. The comment claimed that

the following names are unduly complex: diethanolamine p-methoxycinnamate, ethyl 4-[bis(hydroxypropyl)] aminobenzoate; 2-ethylhexyl 2-cyano-3,3-diphenylacrylate; and ethylhexyl p-methoxycinnamate. The comment added that the CTFA name PABA for aminobenzoic acid is very widely recognized, and that elimination of this name would confuse many consumers. The comment argued that use of the name aminobenzoic acid for chemical accuracy seems ludicrous when proprietary names such as Padimate A are allowed.

Another comment urged that the name PABA or p-aminobenzoic acid be used rather than the chemical name aminobenzoic acid recommended by the Topical Analgesic Panel at 43 FR 38206 at 38219. The comment stated that the name PABA designates the para position of the amino group to the carboxyl group, that the U.S.P. uses the name PABA, and that other pharmacopeias list the ingredient as a para derivative. The comment contended that this designation distinguishes the para-derivative from the ortho- and meta-amino derivatives of benzoic acid, which is a desirable distinction because the ortho derivative is potentially a photosensitizing agent.

Under section 502(e) of the act (21 U.S.C. 352(e)), any drug, including any sunscreen drug product, is deemed misbranded unless its label bears, to the exclusion of any other nonproprietary name, the established name of the active ingredient, if the active ingredient has an established name. Agency regulations in 21 CFR 299.4(b) relating to official names and established names for drugs provide that the established name of an active ingredient is defined as (1) an official name designated pursuant to section 508 of the act (21 U.S.C. 358); (2) if no such official name has been designated for the active ingredient and the active ingredient is a chemical entity that is recognized in an official compendium, then the established name of the active ingredient will be the name recognized in such compendium; and (3) if neither paragraphs (1) or (2) applies, then the common or usual name for the active ingredient will be the established name.

In the Federal Register of September 25, 1984 (49 FR 37575), the agency revoked the existing list of official names of drugs designated by the agency in § 299.20 (21 CFR 299.20) and stated that the agency will not routinely designate official names under section 508 of the act. As stated in paragraph (e) of § 299.4 (21 CFR 299.4(e)), the established name of an active ingredient

under section 502(e) of the act will ordinarily be either the compendial name of the active ingredient or, if there is no compendial name, the common and usual name of the active ingredient. Interested persons are advised, in the absence of the designation of an official name, to rely on the nonproprietary name listed in the publication entitled *USAN and the USP Dictionary of Drug Names* (Ref. 1) as the established name for any drug.

As the Panel pointed out, aminobenzoic acid has been the official name for this compound since the publication of the National Formulary XII in 1965 (43 FR 38206 at 38219). Prior to that, the official name was PABA (p-aminobenzoic acid). The Panel noted that this obsolete designation occasionally appears in the published literature (43 FR 38219). Aminobenzoic acid is the name used in U.S.P. XXI for para-aminobenzoic acid (Ref. 2). Therefore, aminobenzoic acid is the established name used by FDA for this ingredient and is the name that must appear in the labeling of sunscreen drug products. The agency does not believe that it is necessary to distinguish the para-derivative from the ortho- and meta-amino derivatives of benzoic acid because, as the Panel pointed out, the ortho and meta isomers have little, if any, use in human therapeutics (43 FR 38219), and these isomers are neither included in this tentative final monograph nor in the U.S.P. Therefore, in § 352.10(a) of this tentative final monograph, the agency is using the name "aminobenzoic acid."

Although padimate A is an established name (Ref. 3), it does not appear in this tentative final monograph because FDA has determined that there are insufficient data to support the safety of this ingredient. The agency is reclassifying padimate A in Category III. (See comment 35.)

Regarding 2-ethylhexyl 2-cyano-3,3-diphenylacrylate, one of the examples of long and confusing ingredient names given by the first comment, the agency notes that the established name for this ingredient is octocrylene (Ref. 4). Therefore, in § 352.10(k) of this tentative final monograph, the agency is proposing the name "octocrylene" in place of the name "2-ethylhexyl 2-cyano-3,3-diphenylacrylate" used by the Topical Analgesic Panel.

The following sunscreen active ingredients listed in § 352.10 of the Panel's recommended monograph do not currently have names established in official compendia or in *USAN and the U.S.P. Dictionary of Drug Names*: (1) Diethanolamine p-methoxycinnamate, (2) ethyl 4[bis(hydroxypropyl)]

aminobenzoate, (3) ethylhexyl p-methoxycinnamate, (4) 2-ethylhexyl salicylate, (5) glyceryl aminobenzoate, (6) lawsone with dihydroxyacetone, (7) menthyl anthranilate, (8) 2-phenylbenzimidazole-5-sulfonic acid, and (9) red petrolatum. Several of these ingredients have names that have been used for many years in cosmetic labeling (Ref. 5). The agency believes that these names can be accepted as the common and usual names for these ingredients unless names are established in official compendia or in *USAN and the U.S.P. Dictionary of Drug Names*. Therefore, in this tentative final monograph, the agency is proposing, for these ingredients, that the following names should be accepted as the common or usual names: (1) Diethanolamine methoxycinnamate for diethanolamine p-methoxycinnamate, (2) octyl methoxycinnamate for ethylhexyl p-methoxycinnamate, (3) octyl salicylate for 2-ethylhexyl salicylate, (4) lawsone with dihydroxyacetone, as proposed by the Panel, (5) menthyl anthranilate, as proposed by the Panel, (6) phenyl benzimidazole sulfonic acid for 2-phenylbenzimidazole-5-sulfonic acid, and (7) red petrolatum, as proposed by the Panel.

The names used in cosmetic labeling for ethyl 4[bis(hydroxypropyl)] aminobenzoate and glyceryl aminobenzoate are ethyl dihydroxypropyl PABA and glyceryl PABA, respectively (Ref. 5). As explained above in the discussion of aminobenzoic acid, the use of PABA as part of established names for sunscreen ingredients is obsolete. In correspondence with USAN (Ref. 6), the agency requested USAN names for ethyl 4-[bis(hydroxypropyl)] aminobenzoate and glyceryl aminobenzoate. USAN provided USAN Council Members two names for each ingredient and asked them to select the preferable names (Ref. 7). For ethyl 4-[bis(hydroxypropyl)] aminobenzoate, USAN suggested either ethyl dihydroxypropyl aminobenzoate or roxadimate. For the other ingredient, USAN suggested either glyceryl aminobenzoate or lisadimate. Currently, no final decision has been made regarding USAN names for these two ingredients. Therefore, in this tentative final monograph, the agency is using the names recommended by the Panel. When USAN designates new names for these ingredients, the agency will include these new names in the monograph for OTC sunscreen drug products.

References

(1) "USAN and the USP Dictionary of Drug Names," United States Pharmacopoeial Convention, Inc., Rockville, MD, 1989.

(2) "United States Pharmacopoeia XXI-National Formulary XVI," United States Pharmacopoeial Convention, Inc., Rockville, MD, pp. 63, 1989.

(3) "USAN and the USP Dictionary of Drug Names," United States Pharmacopoeial Convention, Inc., Rockville, MD, p. 419, 1989.

(4) "USAN and the USP Dictionary of Drug Names," United States Pharmacopoeial Convention, Inc., Rockville, MD, p. 404, 1989.

(5) "CIPA Cosmetic Ingredient Handbook, First Edition," The Cosmetic, Toilet and Fragrance Association, Inc., Washington, pp. 86-87, 1988.

(6) Letter from C. S. Kumkumian, FDA, to D. O. Shiffman, USAN, dated May 25, 1989, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(7) Letters from S. V. Fuerst, USAN, to USAN Council Members, dated August 16, 1989, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

31. One comment contended that the Panel did not use the appropriate terminology in expressing the UV absorbance values for cinoxate (43 FR 38206 at 38222). The comment stated that absorbance values should be expressed in optical density units or as extinction coefficients, not as a percentage as done by the Panel.

In its discussion of the effectiveness of cinoxate, the Panel made the following statement: "The UV absorbance of cinoxate at 1 percent concentration in isopropyl myristate is less than 10 percent at 270 and 338 nm, but total between 280 to 320 nm with the maximum at 310 nm." (43 FR 38222). The agency has reviewed the data (Ref. 1) and agrees with the comment that the appropriate terminology for expressing absorbance values was not used in this statement. The agency also notes that the maximum wavelength of 310 nm was incorrectly reported; based on the data, the wavelength for maximum absorption should have been 308 nm. In addition, the cited data do not demonstrate total absorbance between 280 and 320 nm; they only demonstrate that the absorbance is nearly total. Therefore, the agency concludes that the relevant data can be summarized with the following statement: "The UV absorbance of cinoxate at 1 percent concentration in isopropyl myristate is nearly total between 280 to 320 nm with the maximum absorbance at 308 nm."

Reference

(1) OTC Vol. 060002.

32. One comment submitted data in support of the safety and effectiveness of 5-(3,3-dimethyl-2-norbornylidene)-3-

penten-2-one and requested that it be reclassified from Category III to Category I as an OTC sunscreen drug product ingredient. The data included one effectiveness study and several safety studies, i.e., skin irritation, phototoxicity, photosensitization, acute oral toxicity, and eye irritation tests (Ref. 1).

"Borrelone" is currently the official title for this ingredient in the *USAN and the USP Dictionary of Drug Names* (Ref. 2). The Panel found borrelone safe in the dosage range used as a sunscreen ingredient (43 FR 38257). The agency concurs with the Panel's evaluation and also finds that the additional safety data submitted by the comment further support the Panel's recommendation. The agency has reviewed the efficacy study submitted by the comment and determined that the data are inadequate to support the reclassification of borrelone from Category III to Category I. The test protocol used was deficient because it failed to specify the experimental conditions, i.e., the emittance specifications of the light source, the film thickness of the test material (amount applied per skin area), the distance between the light source and the exposure surface, and the skin types of the test subjects. In addition, the study lacked a control standard sunscreen to validate the experimental data. As a result, the data are insufficient to establish the effectiveness of borrelone as an OTC sunscreen drug ingredient. Based on the data reviewed, the agency is proposing to classify borrelone in Category III for effectiveness as a sunscreen ingredient. The agency's detailed comments and evaluation of the data are on file in the Dockets Management Branch (Ref. 3).

References

(1) Comment No. C00066, Docket No. 78N-0038, Dockets Management Branch.

(2) "USAN and the USP Dictionary of Drug Names," United States Pharmacopoeial Convention, Inc., Rockville, MD, p. 82, 1989.

(3) Letter from W. E. Gilbertson, FDA, to E. R. Yuhas, Dragoco, Inc., coded LET016, Docket No. 78N-0038, Dockets Management Branch.

33. One comment questioned the effectiveness of lawsone with dihydroxyacetone against UVA radiation (320 to 400 nm), especially when photoprotection against a photosensitization reaction induced by UVA radiation plus orally administered drugs such as dechloromycin or psoralen is investigated. The comment stated that the Panel should have investigated photoprotection against drug-induced photosensitivity reactions, which are usually caused by UVA radiation. The comment contended that the Panel

should not have approved a claim of photoprotection against UVA radiation until the product is tested and the data are submitted for evaluation and approval. The comment stated that, although people with Skin Types I and II can normally tolerate up to 30 to 40 J/cm² of UVA radiation, if such a person has ingested or applied a photosensitizing agent, he or she may not tolerate 3 to 5 J/cm² of UVA radiation. Contending that in such situations only careful testing can demonstrate whether a product protects against UVA, the comment concluded that a testing procedure for a claim of UVA photoprotection should be included in the Panel's recommendations.

In its discussion of Category I sunscreen ingredients (43 FR 38206 at 38235), the Panel referred to a report (Ref. 1) that the use of lawsone with dihydroxyacetone is effective against both UVB radiation (290-320 nm) and UVA radiation (320-400 nm). In evaluating the effectiveness of Category I sunscreens, the Panel determined whether the individual sunscreen ingredients absorbed UV radiation in the UVB band, the range between 290 and 320 nm (43 FR 38218). This spectrum is most likely to cause sunburn in normal individuals (43 FR 38209). The Panel did not evaluate sunscreen ingredients for protection against photosensitization reactions, which are normally induced by radiation in the UVA band (i.e., 320-400 nm) (Ref. 2). Accordingly, the Panel did not include in § 352.50(b) a claim of photoprotection against UVA radiation for lawsone with dihydroxyacetone or for any other Category I sunscreen drug product. However, as stated in comment 53, the agency believes that claims related to UVA protection are important information for consumers because UVA radiation has been shown to be harmful to the skin in that it contributes to both acute and chronic skin damage. Therefore, the agency is proposing in this tentative final monograph that a product may, in certain circumstances, include UVA protection claims in its labeling. The ingredient(s) used in such products must have an absorption spectrum that extends to 360 nm or above in the UVA range, and the product must demonstrate UVA protection using appropriate testing procedures that the agency is proposing be developed and included in the monograph for OTC sunscreen drug products. (See comments 53 and 73.) Therefore, the combination of lawsone with dihydroxyacetone could display

UVA protection claims if it fulfills the above requirements.

The agency acknowledges that some Category I sunscreen ingredients may protect the user from drug-induced photosensitization reactions caused by UVA radiation (43 FR 38206 at 38235, 38239, 38249, and 38250). However, the agency is aware that numerous chemicals, including ingredients in soaps and perfumes as well as therapeutic drugs, can induce photosensitivity reactions in a person exposed to UVA radiation (Refs. 2 and 3). Furthermore, depending upon the absorption spectrum of the photosensitizing compound, the photosensitivity reaction may be elicited by different wavelengths (Ref. 3). If a sunscreen ingredient does not protect against the appropriate wavelength for a specific ingredient, it will not protect against a photosensitivity reaction to that ingredient. Many variables are involved in the relationship between the photosensitizing chemicals, the UV radiation, and the host, and the consumer is often unaware of these relationships (Ref. 3). Factors related to the chemical include the route of administration, ability to penetrate the skin, formulation, interaction with skin, metabolism and elimination, absorption spectrum, and quantum yield of the parent chemical and its metabolites. The radiation variables include the spectral irradiance of the source, dose and rate of delivery, number and frequency of exposures, the timing of the radiation relative to the presence of the chemical, and optics of the skin. Host factors include thickness and hydration of stratum corneum, melanization of the epidermis, integrity of the skin, and immune status (Ref. 3). Even when a patient reports a skin eruption to a physician, the etiologic role of sunlight may not be immediately apparent to the physician. Therefore, the agency concludes that claims for protection against drug-induced photosensitization reactions induced by UVA radiation should only be made in professional labeling; such information should not be included in labeling directed to the general public. The Panel did not include professional labeling in its proposed monograph, and at present the agency does not have adequate data for developing such labeling in this tentative final monograph. The agency invites comment on this matter and will consider professional labeling for claims of protection against photosensitization reactions in the final monograph for OTC sunscreen drug products, if adequate data are submitted in response

to the tentative final monograph. (See comment 69.)

References

- (1) "Proposed Physicians Only Professional Literature," draft of unpublished study in OTC Vol. 060069.
- (2) Fitzpatrick, et al., "Sunlight and Man," edited by M.A. Pathak et al., University of Tokyo Press, Tokyo, pp. 8-11, 1974.
- (3) Parrish, J.A., H.A.D. White, and M.A. Pathak, "Photomedicine," in "Dermatology in General Medicine," 2d Ed., edited by T.B. Fitzpatrick, et al., McGraw Hill Book Company, New York, pp. 952, 966, 969, and 977-978, 1979.

34. One comment requested that 3-(4-methylbenzylidene)-camphor be included in the monograph as a Category I sunscreen. The comment stated that it had submitted data (Ref. 1) on this ingredient to the Panel, and, at its fourteenth meeting, the Panel had classified the ingredient in Category III based on a lack of in vivo data to demonstrate effectiveness in man or animals (Ref. 2). The manufacturer submitted additional data that included controlled studies in seventy subjects performed in three independent investigations (Ref. 3). Based on these data, the Panel reclassified 3-(4-methylbenzylidene)-camphor 0.1 to 2.5 percent to Category I at its twenty-first meeting (Ref. 4). The comment explained that it assumed from the minutes of that meeting (Ref. 4) that this classification was settled. The comment stated it was surprised when the advance notice of proposed rulemaking stated that the ingredient 3-(4-methylbenzylidene)-camphor was not generally recognized as safe and effective for OTC use, based on a lack of clinical and marketing data, and the ingredient was classified in Category II (43 FR 38206 at 38255).

The comment stated that 3-(4-methylbenzylidene)-camphor had been marketed in the United States and throughout the world under the trade name Eusolex 6300 since December 1973. The manufacturer also indicated that approximately 350,000 units of an OTC sunscreen product containing 3 percent Eusolex 6300 were sold at retail in the United States during 1974 to 1978 (Ref. 5). The comment provided letters from distributors and manufacturers of OTC sunscreen drug products who used 3-(4-methylbenzylidene)-camphor as a sunfilter in their products. One manufacturer stated that some sunscreen drug products containing 3-(4-methylbenzylidene)-camphor were distributed in Europe as well as marketed in North America under different trademarks.

The comment contended that general recognition of the safety of a product

could, in fact, be based in part or in whole upon foreign experience, and that the relevance of foreign experience would depend not upon geography alone, but upon a scientific and medical determination. The comment cited the case of *FMALI Herb, Inc. v. Heckler*, 715 F.2d 1385 (9th Cir. 1983) as support for its argument.

The comment subsequently provided additional marketing history information for 3-(4-methylbenzylidene)-camphor (Ref. 6). However, the manufacturer was unable to provide documentation to substantiate the dates of the labeling presented at the meeting. Therefore, the agency concluded that no decision could be made until the manufacturer was able to document the marketing history of 3-(4-methylbenzylidene)-camphor. To date, no new data or information has been submitted to support the reclassification of 3-(4-methylbenzylidene)-camphor from Category II to Category I.

Three similar petitions have requested the agency to reopen the administrative record for this rulemaking to include additional ingredients. One petition (Ref. 7) requests that the agency include the ingredient ethoxylated ethyl-4-aminobenzoate (PEG-25 PABA) as Category I in the monograph for OTC sunscreen drug products. The petition contends that the extensive marketing experience of ethoxylated ethyl-4-aminobenzoate in Europe as an OTC sunscreen ingredient since the early 1950's and the available data supporting the safety and effectiveness of this ingredient satisfy the statutory and regulatory criteria for inclusion of this ingredient in the OTC drug review.

The second petition (Ref. 8) requests that the agency include the ingredient isoamyl-p-methoxycinnamate in Category I. The petition states that isoamyl-p-methoxycinnamate has been marketed in Europe since 1976 and is not a new drug because there is general recognition among experts that the drug is safe and effective for its intended use. The petition contends that the available data for this ingredient conform to the standards for safety and effectiveness set forth in the agency's review of OTC sunscreens.

The third petition (Ref. 9) requests that the agency include the ingredient avobenzene (Parsol 1789), a UVA absorber, in Category I. The petition states that since avobenzene was introduced in 1981, it has been continuously used throughout the world, including Europe, Africa, Asia, Australia, South America, and Canada. The petition noted, however, that the United States is the only country in

which avobenzone is not freely available for use in sunscreen formulations. The petition mentioned that avobenzone is available in the United States in one product, "Photoplex," approved under an NDA. The petition mentioned that avobenzone is the only available sunscreen ingredient that affords broad spectrum UVA protection and that including avobenzone in the monograph for OTC sunscreen drug products would provide United States consumers with broader access to an important UVA sunscreen that is currently available to other consumers around the world.

The agency is currently considering these petitions, but has not yet reached a decision concerning the use of foreign marketing data as the sole basis to support the inclusion of an ingredient in the OTC drug review. The agency's decisions on these petitions will have an impact on any decisions it makes concerning whether 3-(4-methylbenzylidene)-camphor can be included in the OTC drug review unless documentation of the marketing of this ingredient in the United States prior to December 4, 1975 is provided.

The agency has determined that it would not be in the public interest to unduly delay publication of the tentative final monograph for OTC sunscreen drug products while this matter is being resolved. Therefore, at this time the agency is deferring a decision concerning whether any of these ingredients should be considered for inclusion in the OTC sunscreen monograph. A decision will be announced in a future issue of the Federal Register.

References

- (1) OTC Volumes 060086 and 060090.
- (2) Summary Minutes of the 14th Meeting of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Treatment and Prevention Products, October 22-23, 1974, OTC Vol. 060181.
- (3) OTC Vol. 060115.
- (4) Summary Minutes of the 21st Meeting of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Treatment and Prevention Products, September 30 and October 1, 1975, OTC Vol. 060181.
- (5) Comment No. SUP5, Docket No. 78N-0038, Dockets Management Branch.
- (6) Memorandum of Meeting between FDA and E. Merck Industries, Inc., Rona Pearl, and Covington and Burling, coded MM1, Docket No. 78N-0038, Dockets Management Branch.
- (7) Comment No. CP2, Docket No. 78N-0038, Dockets Management Branch.
- (8) Comment No. CP3, Docket No. 78N-0038, Dockets Management Branch.
- (9) Comment No. CP4, Docket No. 78N-0038, Dockets Management Branch.

35. Two comments contended that padimate A is phototoxic and is inappropriate for use as a Category I sunscreen ingredient. One comment cited a study by Kaidbey and Kligman (Ref. 1) as evidence that padimate A is phototoxic to humans. The comment strongly urged that padimate A be removed from the list of safe and effective sunscreen active ingredients. The other comment noted that the Panel was apparently unaware, at the time of its deliberations, of subsequently published reports by Kaidbey and Kligman (Ref. 1) and by Emmett, Taphorn, and Kominsky (Ref. 2) which document the phototoxic properties of padimate A. The comment stated that these reports should be fully considered by the Commissioner prior to final categorization of this sunscreen ingredient as safe for use in drug products. The comment concluded it is inappropriate to permit any active ingredient that has been demonstrated to be phototoxic to be used in products intended for use in direct sunlight.

Stating that padimate A is safe at concentrations up to 3 percent, another comment contended that it is an irritant, especially on the face, at the maximum 5-percent concentration recommended by the Panel. Remarking that 5 percent padimate A can be an irritant to 70 percent of users who swim in chlorinated pools, the comment stated that several published studies (not identified in the comment) indicate that 5 percent padimate A causes burning, itching, and contact and photocontact irritation reactions. The comment claimed that many manufacturers have reduced the concentration or discontinued the use of padimate A because of its irritating effect. Noting that the Panel determined that padimate A is a dose-related irritant, the comment stated that a safe concentration needed to be resolved.

A reply comment stated that studies done in its own laboratories, as well as a review of the raw data for the study conducted by Kaidbey and Kligman (Ref. 1) and discussion of that study with the authors, supported its belief that padimate A is not a phototoxic agent in the concentrations in which it is used in sunscreen products. A second reply comment referred to the submitted reports (Refs. 1 and 2) and stated that the ingredient referred to in the Emmett, Taphorn, and Kominsky study is not padimate A, but a mixture of the para and ortho isomers of amyl dimethylaminobenzoate containing a substantial quantity of the ortho isomer. The reply comment explained that padimate A is the para isomer, while the ortho isomer is phototoxic and is not

used in sunscreen products. The reply comment submitted a report on a padimate A phototoxicity test on mice and swine by Forbes (Ref. 3) and contended that the test results refute the claim that padimate A is a phototoxic material. The comment added that 12 years of marketing over 250 million packages also support the evidence against phototoxicity.

The Panel classified 1 to 5 percent padimate A in Category I as a sunscreen ingredient. The agency has reviewed the literature submitted by the comments and believes that there is sufficient evidence that padimate A at a 5-percent concentration is a weak phototoxic agent. Further studies are necessary to determine the drug's phototoxic potential at lesser concentrations.

Kaidbey and Kligman (Ref. 1) tested various sunscreen agents to determine their potential for provoking phototoxicity. The test agents included aminobenzoic acid and its esters (glyceryl aminobenzoate, padimate A, padimate O) obtained from a commercial source, and the purified isomeric forms of amyl dimethylaminobenzoate (amyl ortho-dimethylaminobenzoate and amyl paradimethylaminobenzoate (padimate A)). A 5-percent solution of each sunscreen dissolved in 95 percent ethanol was used. Additionally, proprietary sunscreens containing sulisobenzene, aminobenzoic acid, and esters of aminobenzoic acid (identified above) were tested. The number of subjects varied between 8 and 17 per test agent. Each preparation was applied to the subjects' backs and covered with patches of nonwoven cotton cloth. Six hours later the sites were uncovered and irradiated with UVA and visible light. Responses were evaluated 24 hours later.

In the tests comparing aminobenzoic acid and its esters, only sites treated with padimate A (5 percent) exhibited phototoxicity after exposure to 30 J/cm² of UVA radiation over a period of 14 minutes; 12 out of 17 subjects experienced reactions. In the tests comparing ortho and para isomers of amyl dimethylaminobenzoate, in which subjects were exposed to 15 J/cm² of UVA radiation over a period of 7 minutes, the ortho isomer was a far more potent photosensitizer with 10 out of 10 positive responders; the para isomer (padimate A) produced 2 out of 10 positive responders. In the tests comparing proprietary sunscreens containing sulisobenzene, aminobenzoic acid, and esters of aminobenzoic acid, in which subjects were exposed to 30 J/cm² of UVA radiation over a period of 14 minutes,

only products containing padimate A exhibited a phototoxic reaction. In this test, 4 out of 9 subjects responded positively to one product containing padimate A alone; 9 out of 13 subjects responded positively to another product containing padimate A alone; and 6 out of 10 subjects responded positively to a product containing a combination of aminobenzoic acid and padimate A. Products containing aminobenzoic acid alone, padimate O alone, glyceryl aminobenzoic acid alone, and sulisobenzonolone did not cause a positive response.

The solar simulator used in the study by Kaidbey and Kligman (Ref. 1) did not emit a spectrum with the same proportions of UVA, visible, and infrared radiation as present in natural sunlight. The wavelength range of most importance when considering the question of phototoxicity is the UVA range. The UVA radiation emitted by the light source used in these studies is sufficiently comparable to natural UVA to make the use of this source valid. The amount of UVA used was approximately 30 J/cm², which is a very large amount, equal to several hours of UVA from sunlight on a sunny summer day in the northeastern U.S., and approaches the MED for UVA in some light-skinned individuals (43 FR 38206 at 38209). This dose, however, did not elicit erythema in the sites used as controls or in the sites to which other sunscreen agents had been applied.

In the Kaidbey and Kligman study (Ref. 1), the test materials were applied and occluded for 6 hours prior to radiation exposure. Occlusion enhances penetration and would tend to maximize the responsiveness to the applied agent. In practice, sunscreen products are rarely occluded; therefore, the phototoxicity resulting from occlusive test methods may be more severe than that obtained during normal use patterns. However, the Kaidbey and Kligman study shows that it is possible to elicit human cutaneous phototoxicity with 5 percent padimate A at UVA doses that may be encountered by individuals during prolonged, intense sunlight exposure. Therefore, the agency believes that this study does indicate that 5 percent padimate A is a phototoxic agent, although a weak one.

The Emmett, Taphorn, and Kominsky study (Ref. 2) used mixed para and ortho isomers of amyl dimethylaminobenzoate, as stated by the second reply comment. However, the investigators also tested the phototoxicity of the amyl paradimethylaminobenzoate isomer, which is known as padimate A. In this study, an in vitro test of padimate A using Ehrlich ascites

cells showed phototoxicity. In the human photopatch testing, patches containing the test agents were applied to the skin of four normal subjects (i.e., subjects free of photosensitivity) for 24 hours. Subsequently, the subjects were exposed to clear noonday sunlight for 30 minutes. The reactions observed 24 hours later showed that the mixed ortho and para isomers of amyl dimethylaminobenzoate resulted in a phototoxic response (marked erythema and/or erythema with edema) in three of four subjects, and one subject experienced mild erythema in reaction to the purified amyl dimethylaminobenzoate. The authors concluded that the phototoxic reaction on human skin with pure amyl paradimethylaminobenzoate was less marked than with the mixed isomer preparations, suggesting that ortho isomers may be the most important phototoxic agents.

The testing of mice and swine by Forbes (Ref. 3) showed that padimate A was not phototoxic to those animals. However, the agency does not believe that the Forbes study demonstrates that padimate A is not a phototoxic agent at concentrations and light exposures that may be encountered by humans using padimate A in the concentrations recommended by the Panel. From the information submitted, it is not possible to determine what concentrations of the active ingredients were applied to the mice and swine used in these experiments. The dose of UVA radiation used (36×10^3 J/M² = 3.6 J/cm²) is much less than that used in the Kaidbey and Kligman study (Ref. 1). Also, it is not easy to quantitatively relate dose/response from animal models to human skin, except in a general sense.

The weight of these studies suggests that padimate A is phototoxic in humans at concentrations in the 5-percent range if sufficient UVA exposure occurs, particularly if the test is maximized by occlusive techniques. However, lesser concentrations and/or lesser UVA exposures may not produce sufficient damage to be appreciable at a clinical threshold. There is no evidence to indicate that phototoxicity is truly absent at any specific concentration, because an increased UVA dose may be able to elicit such reactions. For example, if 5 percent padimate A and a 5- to 10-J/cm² UVA dose produces no visible reaction, but 5 percent padimate A and a 30-J/cm² UVA dose produces visible phototoxicity, will 3 percent padimate A and a 40-J/cm² UVA dose be phototoxic? Although these higher doses of UVA approach the minimal erythema dose for UVA in some individuals, one can conceive of

circumstances in which individuals could encounter such levels from natural sunlight (e.g., lifeguards, equatorial vacationers, etc.).

From the information available, the agency cannot determine a "safe" level of padimate A. The agency believes the available evidence shows that 5 percent padimate A is a weak phototoxic agent. Large but obtainable doses of UVA in human subjects are required in order to elicit clinically-evident effects from padimate A, particularly if maximization factors are present (such as occlusion, multiple applications during sunbathing, or hydration of skin after bathing but before application). The agency is not aware of any padimate A phototoxicity studies more recent than the 1978 Kaidbey and Kligman study (Refs. 1 and 4). Furthermore, the agency has been informed that manufacturers in the U.S. no longer use padimate A in sunscreen drug products and that the ingredient has been banned from use by the European Economic Community (Ref. 5).

Therefore, in this tentative final monograph, the agency is classifying padimate A at 5 percent and higher concentrations in Category II and in concentrations less than 5 percent in Category III. Further studies are required to determine the phototoxic potential of padimate A at less than 5 percent concentrations. Human studies should be designed to test these lower concentrations, using maximization as well as "normal use" procedures. The Kaidbey and Kligman study (Ref. 1) can be used as a suitable model of a maximization study. Reproducibly negative tests done with a statistically sufficient number of light-skinned individuals would tend to indicate levels of padimate A that would be "safe," as defined by a lack of clinically observable toxicity. The agency's detailed comments on the data are on file in the Dockets Management Branch (Ref. 6).

References

- (1) Kaidbey, K.H., and A.M. Kligman, "Phototoxicity to a Sunscreen Ingredient, Padimate A," *Archives of Dermatology*, 114:547-549, 1978.
- (2) Emmett, E.A., B.R. Taphorn, and J.R. Kominsky, "Phototoxicity Occurring During the Manufacture of Ultraviolet-Cured Ink," *Archives of Dermatology*, 113:770-775, 1977.
- (3) Forbes, P.D., "Phototoxicity Test," unpublished report in C00058, Docket No. 78N-0038, Dockets Management Branch.
- (4) Memorandum of telephone conversation between J. Rippers, FDA, and K. Kaidbey, Ivy Laboratories, dated May 6, 1988, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(5) Memorandum of telephone conversation between J. Rippers, FDA, and M. Gardner, The Cosmetic, Toiletry and Fragrance Association, dated March 3, 1989, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(6) Letters from W.E. Gilbertson, FDA, to J.M. Clayton, Plough, Inc.; Howard Iserman, Van Dyk & Company, Inc.; and A.M. Kligman and K.H. Kaidbey, University of Pennsylvania, coded LET026, LET027, and LET028, respectively, Docket No. 78N-0038, Dockets Management Branch.

36. One comment noted that zinc oxide had been present in earlier lists of sunscreen ingredients, but was not included in the final list of active sunscreen ingredients recommended by the Panel in § 352.10. Stating that zinc oxide ointments and creams have a long history of use as a sunblock, as well as a skin protectant, the comment requested that the original data on the drug be reviewed and that zinc oxide be listed as a sunscreen active ingredient in the monograph.

FDA listed zinc oxide as an active sunscreen ingredient in its request for data on OTC topical analgesic drug products, which included antirheumatic, otic, burn, sunburn prevention and treatment drug products (37 FR 26456). Zinc oxide was a labeled ingredient in marketed products submitted for review to the Panel (Refs. 1 through 4). The Panel that reviewed these drug products evaluated both sunscreen and skin protectant drug products. After reviewing the submitted data, the Panel classified zinc oxide at concentrations of 1 to 25 percent as a Category I skin protectant (43 FR 34628 at 34648). Although zinc oxide was a labeled ingredient in a marketed sunscreen product (Ref. 3), the Panel classified zinc oxide as an inactive ingredient in the advance notice of proposed rulemaking for OTC sunscreen drug products (43 FR 38206 at 38208).

The comment did not present any data or information to support the use of zinc oxide as a sunblock, i.e., sunscreen opaque sunblock ingredient. The agency has reviewed the data in a study by Luckiesh et al. (Ref. 5), which had been submitted to the Panel (Ref. 3), in which zinc oxide was used alone and in combination with phenyl salicylate, another sunscreen ingredient. The study was designed to measure the ability of zinc oxide at concentration levels from 15 to 33.3 percent, as well as other ingredients, to absorb UV radiation over a broad range of wavelengths. Zinc oxide (33.3 percent) was the only test preparation that was studied as a single ingredient.

All subjects in the study developed skin erythema after 15 seconds of exposure to a lamp that was a source of

UV radiation intensity equivalent to sixty times the most intense sunlight measured in Cleveland, Ohio over a 4-year period. One minute exposure to the lamp was determined to be equivalent to 1 hour of exposure to that sunlight. The subjects were then treated on the upper arm with a thin coating of the various sunscreen test preparations. A thin coating was defined as one which was rubbed out quite well, corresponding to the thinnest coating which is likely to be applied on the skin. The sunscreen properties of zinc oxide at 33.3 percent in white petrolatum were tested in only one subject. Although the test product demonstrated sunscreen properties, results from one subject alone are insufficient to support effectiveness of this ingredient as a sunblock.

Using a thin-film spectrophotometric method, Luckiesh et al. (Ref. 5) recorded the UV radiation transmitted by the test ingredients at wavelengths from 296.7 to 365 nm. The study revealed that with a 0.03 millimeter (mm) thickness coat of 33.3 percent zinc oxide in combination with 10 percent phenyl salicylate in white petrolatum there was zero transmission of UV energy at various wavelengths between 296.7 and 313 nm, and 0.8 and 3 percent transmission at 334.2 and 365 nm, respectively. When the concentration of zinc oxide was reduced to 15 percent in a combination product with 10 percent phenyl salicylate, the UV energy transmission of the 0.03 mm coat was then 0.02, 0.04, 0.1, 6, and 44 percent at 296.7, 302.2, 313, 334.2, and 365 nm, respectively. When the coat of this test preparation was increased to 0.06 mm there was zero transmission of UV energy at the four lower wavelengths (296.7 to 334.2 nm) and 0.3 percent at 365 nm. With a 0.03 mm coat of a 33.3 percent zinc oxide in white petrolatum test preparation, there was 2.2, 3.0, 5, 7.8, and 8.5 percent transmission of UV energy at wavelengths 296.7, 302.2, 313, 334.2, and 365 nm, respectively. When the coat of zinc oxide was increased to 0.06mm, the UV energy transmission was reduced to 0.18, 0.3, 0.75, 2.2, and 2.4 percent at the respective wavelengths. The investigators concluded from this study that "Undoubtedly, zinc oxide is not to be ignored as an ultraviolet light filter," and "zinc oxide is of definite value in preventing sunburn."

The agency recognizes that the range of UV radiation absorbance reported in this limited study is similar to the UV radiation range reported for other sunscreen products reviewed by the Panel. The agency is aware that for many years zinc oxide has been used by

consumers as a sunblock (Refs. 6 through 10). However, the agency concludes that the data submitted on zinc oxide to this rulemaking are insufficient to support its effectiveness as a Category I sunscreen as a sunblock because the effectiveness data for this ingredient when used alone are limited to one subject. Studies to demonstrate the effectiveness of zinc oxide as a Category I sunscreen should follow the requirements of the testing procedures in Subpart D of this tentative final monograph.

Therefore, because the available data are insufficient to demonstrate the effectiveness of zinc oxide as a sunscreen active ingredient, the agency is proposing to classify zinc oxide in Category III.

References

- (1) OTC Vol. 060007.
- (2) OTC Vol. 060137.
- (3) OTC Vol. 060154.
- (4) OTC Vol. 060001.
- (5) Luckiesh, M., et al., "Protective Skin Coatings for the Prevention of Sunburn," *Journal of the American Medical Association*, 130:1-6, 1946.
- (6) Harber, L. C., "Photosensitivity and Sunburn," in "Current Therapy," edited by H. F. Conn, W. B. Saunders Co., Philadelphia and London, pp. 571-572, 1968.
- (7) Wilkinson, D. S., "Treatment," in "Textbook of Dermatology," edited by A. Rook, D. S. Wilkinson, and F. J. G. Ebling, F. A. Davis Co., Philadelphia, pp. 1810 and 1820, 1968.
- (8) Arndt, K. A., "Manual of Dermatologic Therapeutics with Essentials of Diagnosis," Little, Brown, and Co., Boston, p. 329, 1978.
- (9) "Drug Evaluations," 6th Ed., American Medical Association, Chicago, pp. 1025-1026, 1986.
- (10) Lysne, J. M., "Prevention and Treatment of Sunburn," insert from *Drug Store News*, (4) 1956, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

D. Comments on Dosages for Sunscreen Drug Products

37. One comment contended that the minimum dosage requirement for sunscreen active ingredients in § 352.10 is unnecessary and should be deleted. The comment proposed that a manufacturer be permitted to use an ingredient at any lower concentration which provides an SPF of at least 2. The comment provided an example where a manufacturer may wish to combine two or more active sunscreen ingredients in a formulation that would provide an acceptable SPF value of 2, but would be unable to do so because using the minimum allowable concentrations of the active ingredients would result in a preparation with an SPF value greater than 2. The comment added that such

a restriction would be arbitrary and not in the best interest of the consumer.

A second comment also questioned the necessity of the lower dosage limits because all sunscreen products must be tested for effectiveness. The comment pointed out that the recommended lower dosage limits would not allow 1 percent aminobenzoic acid preparations even though the products may show an SPF value well above the minimal requirement (Ref. 1). The comment concluded that if the product is effective, then the dosage is not low.

Another comment recommended that the concentration range for aminobenzoic acid in the Panel's monograph be changed from a range of 5 to 15 percent to a range of 2 to 15 percent or that the lower limit be eliminated. The comment asserted that although the Panel stated that 2 percent aminobenzoic acid has been found to be an effective sunscreen (43 FR 38206 at 38221), it set the minimum concentration of aminobenzoic acid at 5 percent for any sunscreen product. The comment stated that the effectiveness of aminobenzoic acid as a sunscreen is dependent on the vehicle used and not just on the concentration of the active ingredient. As an example, the comment stated that aminobenzoic acid is less effective in certain creams or oils even if the product contains 20 percent aminobenzoic acid. The comment added that the range of concentrations given in § 352.10 of the Panel's monograph does not ensure effectiveness, but that determination of SPF values for individual products will ensure effectiveness.

A reply comment supported the position that the effectiveness of sunscreen products, not the amount of sunscreen in the products, is the standard by which performance efficacy is measured. The comment recommended that the minimum dosage requirement be deleted because it will not affect product safety or efficacy.

Two comments, submitted in response to the public meeting held on January 26, 1988, to discuss appropriate sunscreen testing methods, also requested that no minimum dosages be required for sunscreen ingredients. These comments urged FDA in determining effectiveness to rely solely on the product's performance as established by appropriate SPF testing. One comment stated that the requirement to meet a minimum dosage level can have an impact on formula flexibility and safety and is not scientifically sound because a specific product's performance is dependent upon the formulation rather than simply on the amount of active ingredient.

Stating that the SPF value is a better and more accurate measure of the effectiveness of a sunscreen drug product, the comment recommended that §§ 352.10 and 352.20 be amended to eliminate the lower dosage range for each of the listed active sunscreen ingredients.

The Panel recommended minimum concentrations for all Category I sunscreen ingredients based on effectiveness data submitted for its review. The agency, however, agrees with the comments that a sunscreen active ingredient's performance is not totally dependent upon the concentration of the active ingredient in the product. Because the formulation of a sunscreen drug product influences the effectiveness of the active ingredient in the product, the Panel recommended final product testing of each formulation to determine the SPF and to assure proper use (43 FR 38206 at 38213). The agency is aware that the presence of a required minimum amount of a sunscreen ingredient in a drug product does not guarantee effectiveness; final product testing can ensure effectiveness. Therefore, the agency agrees with the comments that the effectiveness requirements, i.e., the determination of an SPF value for a sunscreen product, make the use of minimum concentration requirements unnecessary for single ingredient products.

However, the agency is concerned that each ingredient in a sunscreen combination product contributes to the overall effectiveness of the product. To require no minimum contribution at all could allow the use of amounts so small as to be misleading and deceptive to the consumer and could permit the inclusion of ingredients solely for promotional purposes. In addition, this could result in the consumer's exposure to an additional ingredient or ingredients with minimal additional benefit being provided. The agency believes that a minimum amount of each sunscreen ingredient should be present in a combination sunscreen product. The agency has looked for similar situations in other OTC drug monographs and notes that OTC antacid ingredients have no minimum dose stated for the individual ingredients in the final monograph. (See 21 CFR 331.11.) One or more antacid active ingredients may be combined within any maximum daily dosage limit established provided each ingredient is included at a level that contributes at least 25 percent of the total acid neutralizing capacity of the product. The antacid monograph also provides a test for determining the percent contribution of an antacid ingredient in

the combination product. (See 21 CFR 331.21.) The agency believes that sunscreen manufacturers who wish to market a combination sunscreen product should be required to determine that each ingredient in the sunscreen combination contributes in some way to the effectiveness of the product, e.g., that the combination of ingredients produces a higher SPF value than any of the ingredients alone used at monograph concentrations in a single ingredient product or that the combination product protects against a wider range of UV radiation than any of the ingredients alone. Such a requirement is consistent with Part 3 of the agency's "General Guidelines for OTC Combination Products," which states: "Category I active ingredients from the same therapeutic category that have the same mechanism of action * * * may be combined in selected circumstances * * * if the combination meets the OTC combination policy in all respects, the combination offers some advantage over the active ingredients used alone, and the combination is, on a benefit-risk basis, equal to or better than each of the active ingredients used alone at its therapeutic dose" (Ref. 2).

Because the agency agrees with the deletion of the minimum strength requirements for sunscreen ingredients, only maximum concentrations for individual active ingredients are being proposed in § 352.10. However, because of its concern that each ingredient in a combination drug product contributes to the overall effectiveness of the product, the agency concludes that a method must be developed that demonstrates the contribution of each ingredient in a combination sunscreen product before the minimum doses for sunscreen ingredients in combination can be deleted from the monograph. At this time, the agency is unaware of any existing method for determining the contribution of each sunscreen ingredient in a combination sunscreen product. Therefore, although the agency is not including minimum doses for individual sunscreens in proposed § 352.10, it is including minimum doses for sunscreens used in combination with one another in § 352.20(d). The agency invites manufacturers and sunscreen testing laboratories to comment on this matter and to propose an appropriate test method for determining the contribution of each sunscreen ingredient in a combination sunscreen product.

References

- (1) Willis, I., and A.M. Kligman, "Aminobenzoic Acid and Its Esters: The

Quest for More Effective Sunscreens," *Archives of Dermatology*, 102:405-417, 1970.
 (2) Food and Drug Administration, "General Guidelines for OTC Combination Products," September 1978, Docket No. 78D-0322, Dockets Management Branch.

38. One comment stated that the dosage limits for sunscreen active ingredients in the Panel's recommended monograph do not provide protection from ineffective products. The comment explained that the vehicle can have a tremendous effect on product efficacy and that some of the approved sunscreens are used primarily in combinations because they are not sufficiently effective when used alone in the currently recommended lower dosage.

The agency concludes that the lower dosage limits recommended by the Panel for sunscreen active ingredients are effective when properly formulated in a product that provides an SPF of at least 2. As the Panel pointed out, the effectiveness of all Category I sunscreens has been demonstrated by appropriate studies. The UV absorbance of the individual sunscreen between 290 and 320 nm was established and, in most instances, data were available from studies on human subjects treated either with artificial sunlight or with natural sunlight (43 FR 38206 at 38218).

The agency agrees that the vehicle can have a significant effect on the product's effectiveness. However, the influence of the vehicle on the effectiveness of a sunscreen drug product is accounted for in the SPF testing procedure because the test is done on the final formulation of a sunscreen product. As provided in § 352.10, a final sunscreen drug product must have an SPF value of not less than 2. Any product that can demonstrate that it meets the labeled SPF value is considered to be effective.

E. General Comments on Labeling for Sunscreen Drug Products

39. One comment contended that FDA does not have the authority to legislate the exact wording of OTC labeling claims. The comment objected to the agency limiting the labeling claims to the exact terminology of the monograph and rejecting all other terminology, regardless of accuracy. The comment requested that more flexibility in labeling be permitted by adding to the approved indications a statement as follows: " * * * or similar indication statements which are in keeping with the Panel's report."

In the *Federal Register* of May 1, 1986 (51 FR 16258), the agency published a final rule changing its labeling policy for stating the indications for use of OTC drug products. Under 21 CFR

330.1(c)(2), the label and labeling of OTC drug products are required to contain in a prominent and conspicuous location, either (1) the specific wording on indications for use established under an OTC drug monograph, which may appear within a boxed area designated "APPROVED USES"; (2) other wording describing such indications for use that meets the statutory prohibitions against false or misleading labeling, which shall neither appear within a boxed area nor be designated "APPROVED USES"; or (3) the approved monograph language on indications, which may appear within a boxed area designated "APPROVED USES," plus alternative language describing indications for use that is not false or misleading, which shall appear elsewhere in the labeling. All other OTC drug labeling required by a monograph or other regulation (e.g., statement of identity, warnings, and other regulations (e.g., statement of identity, warnings, and directions) must appear in the specific wording established under the OTC drug monograph or other regulation where exact language has been established and identified by quotation marks, e.g., 21 CFR 201.63 or 330.1(g). The proposed rule in this document is subject to the labeling provisions in § 330.1(c)(2); the wording in § 352.52 is consistent with these regulations.

40. A number of comments requested that the labeling of sunscreen products contain more information for using these products. The requests included the following: information on the effectiveness of sunscreens when used for different skin types, or on different parts of the body, or with moisturizers, makeup, or cola drinks, or when used in water, chlorine, or sea spray; more information concerning safe and effective use; labeling which would permit consumers to choose a sunscreen product appropriate for their skin sensitivity; and labeling products with the names and percentage composition of ingredients.

The Panel considered some of the above factors in making its labeling recommendations, e.g., use in water and skin type. The Panel recommended labeling concerning a sunscreen's resistance to its removal by water, i.e., sweat resistance, water resistance, and waterproof properties (43 FR 38206 at 38268). The Panel also recommended that the labeling contain a guide that relates skin types and product category designations to the type of sunscreen product needed for protection (43 FR 38269). The agency agrees that the labeling for sunscreen products should contain such information to aid consumers in choosing the most suitable

sunscreen for their needs. Therefore, the agency is proposing these labeling recommendations. The Panel did not discuss the impact of all the factors mentioned by the comments that may interfere with a sunscreen's effectiveness; factors such as beverages ingested, sea spray, and chlorine were among those not considered. The agency is only proposing those factors in the Panel's recommended labeling that directly relate to the safe and effective use of sunscreen drug products. The agency recognizes that information about other factors may be useful in product selection. However, the agency does not believe that it is practical or necessary to include all of these possible factors in the monograph. Statements and terms outside the scope of the monograph may be included elsewhere in the labeling, provided they are not false or misleading. 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. Even though it is truthful and not misleading, any statement or term that is outside the scope of the monograph may not appear in any portion of the labeling required by the monograph and may not detract from such required information.

Other OTC advisory review panels have recommended, as did the Topical Analgesic Panel, that manufacturers list all inactive ingredients in the labeling of OTC drug products. However, the act does not require the identification of all inactive ingredients in the labeling of OTC drug products.

The act specifies the requirements for ingredient labeling of OTC drug products. Section 502(e) of the act (21 U.S.C. 352(e)) requires that all active ingredients and certain other ingredients, whether included as active or inactive, be disclosed in the labeling. The act also limits the requirement for stating quantity of ingredients in OTC drug products to those specifically mentioned in section 502(e). Although the act does not provide for full labeling of ingredients, as requested by the comment, the SPF value of a sunscreen drug product does provide a quantification of the protection afforded by the active ingredient(s).

Although the act does not require the disclosure of all inactive ingredients in the labeling of OTC drug products, the agency agrees with the Panel that listing of inactive ingredients in OTC drug product labeling would be in the public interest. Consumers with known allergies or intolerances to certain ingredients would then be able to

identify substances that they may wish to avoid.

The NDMA (formerly "The Proprietary Association"), the trade association that represents approximately 85 OTC drug manufacturers who reportedly market between 90 and 95 percent of the volume of all OTC drug products sold in the United States, has announced that its member companies would voluntarily begin to list inactive ingredients in the labeling of OTC drug products under guidelines established by the Association (Ref. 1). Under another voluntary program begun in 1974, the member companies of NDMA have been including the quantities of active ingredients on OTC drug labels. The agency commends these voluntary efforts and urges all other OTC drug manufacturers to voluntarily label their products in accordance with NDMA's guidelines.

Reference

(1) "Voluntary Codes and Guidelines of the OTC Medicines Industry," Nonprescription Drug Manufacturers Association, Washington, DC, pp. 18 and 19, copy included in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

41. One comment contended that a package insert is essential for OTC sunscreen drug products. The comment stated that because uncontrolled exposure to the sun leads to premature aging of the skin and skin cancer, all sunscreen drug products should have "danger signs" about solar radiation and artificial UV light sources, instructions for regular use of sunscreens, and guidelines to create public awareness about the ways to prevent the effects of the sun's damaging rays. The comment felt that substantial information about solar radiation and UV radiation should be provided to consumers and that precautions such as the following should be included in a package insert for sunscreen drug products: "apply sunscreens uniformly and liberally before every sun exposure," "reapply after swimming or perspiration," "wear * * * lightly [tightly] woven clothing," "protect the eyes with ultraviolet opaque sun goggles," "beware of reflective surfaces (sand, snow, water, etc.)," "use sunscreens even on cloudy or hazy days," "avoid tanning parlors." The comment added that OTC drugs such as aspirin, antihistamines, nasal decongestants, and antifungal agents have package inserts. A second comment opposed the requirement of a package insert because it would single out sunscreens as the only OTC drugs requiring this extraordinary labeling.

The agency agrees that educating the public about the dangers of excessive sun or UV radiation exposure is important. However, a number of the items that the comment suggested for inclusion in a package insert, while useful, go beyond the necessary information required for the safe and effective use of these drug products. Examples include the statements about wearing certain types of clothing and avoiding tanning parlors. After evaluating the comment's other suggestions for information to be contained in a package insert, the agency believes that the labeling proposed in this tentative final monograph addresses many of these items and it is not necessary specifically to require a package insert for these products. One example is the "alert" statement being proposed in this document, which states: "SUN ALERT: The sun causes skin damage. Regular use of sunscreens over the years may reduce the chance of skin damage, some types of skin cancer, and other harmful effects due to the sun." (See comment 56.) A statement similar to this currently appears in the labeling of many marketed sunscreen drug products. In addition, the directions for use being proposed in this tentative final monograph advise the consumer to apply the sunscreen liberally, generously, smoothly, or evenly before exposure to the sun and after swimming, excessive sweating, or towel drying. (See comment 66.)

The agency encourages manufacturers to provide consumers useful information and does not oppose the inclusion of a package insert containing additional information. As noted in comment 40, other statements may be included in labeling provided they are not false or misleading.

Although package inserts are not essential for OTC sunscreen drug products, there may be cases where it is necessary for the manufacturer to use a package insert or other mechanism to provide the required monograph labeling for an OTC drug product. For example, when an OTC drug product is packaged in a container that is too small to contain the required labeling, it should be enclosed in a carton or be accompanied by a package insert that provides the labeling required by the monograph. This type of packaging is likely to be necessary for sunscreen drug products marketed specifically for application to the lips or nose.

42. One comment stated that the labeling requirements for sunscreen drug products do not include provisions for small packages, and that alternatives should be developed because all of the

required statements will not fit on small packages. A reply comment added that sunscreen-containing products are often marketed in sizes too small to accommodate the full product performance statement (recommended by the Panel in § 352.50(e)) on the principal display panel. This comment objected to the Panel's requirement that product performance statements be placed on the principal display panel, arguing that these statements are quite long and that it is repetitious to require them in addition to the indications in § 352.50(b). The reply comment suggested that the information on the principal display panel be limited to the product's PCD and SPF designations, e.g., "extra protection-SPF 6," with the remainder of the performance statement permitted to appear elsewhere in labeling.

The agency has reviewed the Panel's recommended labeling and, wherever possible, has revised and clarified the labeling so that only essential information is required. The product performance statements proposed in this tentative final monograph (§ 352.52(e)) cover the following four areas: (1) a statement of the PCD, e.g., "Minimal Sun Protection Product," (2) a statement of the product's resistance to removal by sweat or water, e.g., "sweat resistant," (3) a compilation of skin types and recommended PCD's, e.g., "Rarely burns; tans profusely * * * Minimal," and (4) a statement for sunscreens that contain an opaque sunscreen, i.e., "Sunblock." The agency concludes that the labeling information in § 352.52 (e)(1), (e)(2), (e)(3), and (e)(5) is useful but not essential; therefore, the agency is proposing that this information be optional and may be used in labeling if a manufacturer wishes. The information in § 352.52(e)(4) is essential and must be displayed on a sunscreen drug product, but it does not need to be on the principal display panel of the product. The indications in § 352.52(b)(1) include a series of statements concerning sunburn and protection from the harmful effects of the sun. The manufacturer must use any one or more of these indications in the labeling of sunscreen drug products. The indications in § 352.52(b)(2) are "Additional Indications" that are optional statements which may be used on a sunscreen drug product in addition to any of the statements in § 352.52(b)(1).

The agency does not consider the proposed product performance statements in § 352.52(e) to be repetitions of the required indications in § 352.52 (b)(1) and (b)(2). The proposed

indications in § 352.52 (b)(1) and (b)(2) provide the consumer with a variety of indications. The product performance statements in § 352.52(e) include information on the product's water resistance capability and a compilation of skin types and PCD's; the indications do not include similar information.

The Panel concluded that informative labeling should be provided to consumers to aid in the selection of the most appropriate sunscreen product. The Panel recommended that such labeling be placed on the principal display panel of a product where it is most likely to be read. The agency is proposing labeling for the principal display panel of sunscreen drug products in § 352.50 of this tentative final monograph that includes SPF values and water resistance information. PCD information is not required to be placed on the principal display panel. (See comments 45 and 51.)

The labeling provisions in part 201 (e.g., §§ 201.10(i), 201.15, 201.60, 201.61, and 201.62) address various requirements for labeling drugs including drugs packaged in containers too small to accommodate a label with sufficient space to bear all the information required for compliance with various regulations. In those instances where an OTC sunscreen drug product is packaged in a container that is too small or otherwise unable to include all of the required labeling, the product can be enclosed in a carton or be accompanied by a package insert that contains the information complying with the monograph. Manufacturers are also encouraged to print a statement on the product container label, carton, or package insert suggesting that the consumer retain the carton or package insert for complete information about the use of the product when all the required labeling does not appear on the product container label. However, the principal display panel must contain certain information, e.g., statement of identity (§ 201.61) and SPF and water resistance information (proposed § 352.50).

The NDMA has recently promulgated guidelines for industry to consider when examining product labels for readability and legibility (Ref. 1). These guidelines are designed to assist manufacturers in making the labels of OTC drug products as legible as possible. The agency commends this voluntary effort and urges all OTC drug manufacturers to examine their product labels for legibility.

Reference

(1) "Label Readability Guidelines," The Nonprescription Drug Manufacturers

Association, Washington, copy included in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

43. Two comments objected to the Panel's list of skin types (43 FR 38206 at 38213) and to the recommended labeling of sunscreen products according to these skin types. Another comment requested that the Roman numeral designation for skin types be replaced by Arabic numbers. One of the comments suggested that the numbering of skin types should relate directly to the numbered grades of sunscreen protection, i.e., the most sensitive skin, Type I, requiring the "number 1" or highest protection sunscreen and that the skin type list should be shortened so that the information could be presented in large print on the sunscreen label. The comment also felt that skin type VI ("Never burns; deeply pigmented (insensitive)") is unnecessary and offered the following list for sunscreen labeling:

"I for those who burn easily and never tan. Grades 1-2 sunscreen."

"II for those who burn easily and tan minimally. Use grades 3-4."

"III for those who burn when first exposed and tan gradually. Use grades 5-6, etc. for the rest."

Stating that the SPF is more useful for the research and development of sunscreen products than for the labeling of sunscreen products, another comment argued that the consumer would be confused when confronted with a choice of five protection levels and five skin types on a sunscreen label. The comment suggested that skin types be classified in relation to a standardized sunscreen formulation (e.g., the formulation given at 43 FR 38259) as follows:

Very Sensitive Skin—Skin that needs more protection than that provided by the standardized sunscreen formula.

Moderately Pigmented—Skin burns moderately during the first exposures to sun (before skin becomes tan); after tan, skin doesn't burn unless exposed to very intense sun.

Insensitive Skin—Rarely or never burns.

In this suggested system, the protection afforded by each sunscreen product would also be in reference to the standard formulation, e.g., a product offering twice the protection of the standard formulation would be labeled 2X standard. The comment felt that this approach would provide the consumer with a better method for choosing a sunscreen as well as a measure of a sunscreen product's bioequivalence to a well-studied standard formulation.

The agency notes that the Roman numeral designation of skin types found

objectionable by some comments is not included in the Panel's recommendations for sunscreen labeling. These skin type designations were only included in the Panel's report (43 FR 38206 at 38213) for completeness of information as part of a table which relates skin types to recommended sunscreen products. The Roman numeral skin type designations are also found in the selection of test subjects under the general testing procedures (43 FR 38265). The Panel did recommend that information on skin types and PCD statements be included in sunscreen labeling as a guide to the consumer (43 FR 38214). The agency agrees with the Panel that such information aids the consumer in choosing an appropriate product. However, in this tentative final monograph, the agency is proposing that PCD labeling be optional, and therefore, PCD labeling might not be included in the labeling of all products. (See comment 44.) The agency is proposing that an SPF value be displayed on the principal display panel of all sunscreen drug products. (See comment 45.) The agency has determined that the product guide recommended by the Panel would be more useful in aiding consumers to choose an appropriate product if the guide included SPF ranges rather than PCD categories. Furthermore, the agency is proposing to replace the Panel's recommended word "never" in "always burns easily; never tans" with the word "rarely" because "never" is an absolute term, and such an absolute condition is unlikely to be fulfilled. In addition, the agency is adjusting the proposed SPF ranges to more accurately reflect the protection potential of currently marketed sunscreen drug products and the amount of protection needed by the various skin types.

The agency believes that the information in the product guide should be presented in a manner that catches consumers' attention and allows them to quickly ascertain which type of product is appropriate for their skin types. Therefore, the agency is proposing in § 352.52(e)(4) that the following recommended Sunscreen Product Guide appear in the labeling of all sunscreen drug products:

RECOMMENDED SUNSCREEN PRODUCT GUIDE

Sunburn and tanning history	Recommended sun protection product
Always burns easily; rarely tans.	SPF 20 to 30.
Always burns easily; tans minimally.	SPF 12 to under 20.

RECOMMENDED SUNSCREEN PRODUCT GUIDE—Continued

Sunburn and tanning history	Recommended sun protection product
Burns moderately; tans gradually.	SPF 8 to under 12.
Burns minimally; always tans well.	SPF 4 to under 8.
Rarely burns; tans profusely.	SPF 2 to under 4.

The agency points out that the sunburn and tanning history of skin type VI ("Never burns; deeply pigmented (insensitive)") is not included in the proposed guide. The Panel stated that no sunscreen use was indicated for this skin type (43 FR 38206 at 23213); thus it did not include skin type VI in its Recommended Sunscreen Product Guide (43 FR 38269). The agency requests comment on whether such information should be added to the guide.

The alternative statements offered by one comment as shorter than the Panel's recommended statements actually contain more words, e.g., "For those who burn easily and never tan" to replace "Always burns easily; never tans." In addition, in this comment's alternative statements, the PCD statements (maximal, ultra, etc.) are replaced with undefined numerical grades of sunscreen protection level. The alternative statements offered by another comment only included three skin types that would be defined according to a standardized sunscreen formulation. The agency believes that the consumer requires information on more than three skin types and that the proposed suggested compilation of five skin types based on sunburn and tanning history and five SPF ranges offers more thorough and more useful information than the alternatives suggested by the comments.

Furthermore, since 1980, the labeling of most sunscreen products in the United States has voluntarily included SPF values and sometimes has also included PCD statements. (For a discussion of SPF values and PCD statements, see comment 44.) For over a decade, consumers have used and become accustomed to choosing sunscreen products based on this system. The agency believes that consumers are familiar with choosing sunscreen products according to this system and that it would be confusing and unnecessary to introduce an entirely new system for grading protection as suggested by the comments without additional

justification. In addition to required SPF values and optional PCD statements proposed in this tentative final monograph for OTC sunscreen drug product labeling, the agency believes that the required Recommended Sunscreen Product Guide, which relates skin type to the amount of protection needed (i.e., SPF value), will provide consumers with the necessary information from which to choose the sunscreen product best suited for their skin type.

F. Comments on SPF and PCD Labeling for Sunscreen Drug Products

44. In response to the Panel's report, numerous comments "fully supported" the proposed SPF numerical rating system in sunscreen product labeling, indicating that such information will be most helpful to consumers, especially those with fair and sensitive skin. One comment emphasized the necessity for a numerical rating system of no less than 4 categories of protection if the proposed plan of 6 to 15 ratings was unacceptable. Several comments believed that a numerical rating system should be correlated with both efficacy and skin types. Two comments stated that there are too many number categories for the sun protection factor. Another comment suggested alternative labeling based on a numerical rating or a comparison of sunscreen products by reference to a FDA standard sunscreen formula, adding that this approach recognizes the validity of the agency's emphasis on bioequivalence. The comment maintained that the SPF values are more related to research than to practical approaches for labeling. Two comments suggested that, to avoid confusion by the consumer, SPF values should be included in the labeling on sunscreen products and one comment provided the following examples:

"I—Always burns easily, never tans. Use sunscreens grade 8–14."

"II—Always burns easily, tans minimally. Use grades 6–7."

"III—Burns moderately, tans gradually. Use grades 4–5 * * * etc."

Two comments opposed the system recommended by the Panel because they believed it was confusing and unnecessary. One comment felt that there is no need for a double scale to exist, i.e., a numerical rating system with SPF values and a classification system, composed of PCD statements.

In response to the notice of public meeting to discuss appropriate testing procedures for OTC sunscreen drug products, published in the *Federal Register* of September 4, 1987 (52 FR 33598), several comments discussed the relative merits of using PCD's and/or

SPF values in the labeling of sunscreen drug products. Many of the comments supported the use of the PCD on the label, either alone or in addition to the SPF number. One comment maintained that use of the PCD in the labeling of sunscreen products is more useful to the consumer than the SPF, which the comment contended is information used by less than 10 percent of the consumers. Acknowledging that the PCD's are not as widely recognized by consumers as is the SPF numbering system, another comment maintained that PCD's are, nevertheless, useful for standardizing product claims and SPF values and should be retained. One comment contended that numerical SPF values are more meaningful to the consumer than PCD's, but supported retaining the PCD as an optional label statement because these "descriptives" are currently used on some products and have been for many years.

Another comment maintained that the agency should continue to permit the use of both SPF values and PCD's in the labeling of sunscreen drug products because each has meaning and usefulness to both consumer and industry. The comment recognized the need to ensure that sunscreen products are classified into some type of category system that is meaningful to the consumer and that adequately protects the public health. However, the comment argued that SPF values help best to accomplish these goals because they are used (1) to compare the effectiveness of existing products, (2) to monitor product performance over time, and (3) during product development to distinguish the best available formulation. The comment added that SPF values have been in use for 10 years, and the consumer has become accustomed to using these values when selecting products. The comment mentioned data from a consumer survey (Ref. 1) that shows that SPF values are a major factor in a consumer's selection of a sunscreen product. The comment asserted that a review of educational literature published by organizations such as The Skin Cancer Foundation, American Institute for Cancer Research, American Cancer Society, and others indicates that the SPF is discussed more often than the PCD.

One comment maintained that the PCD labeling serves no useful purpose and may be confusing and misleading. In place of the PCD's, the comment recommended that manufacturers continue to use SPF values to provide the sun protection value of a sunscreen formulation. The comment maintained that this would be the simplest and most straightforward manner of

describing a product so that consumers can choose the product appropriate for their needs by comparing the protection offered by one product with another. Stating that consumers are aware of SPF values and base their purchase decisions on these factors, another comment maintained that consumers are largely unaware of PCD's, that PCD's are redundant and less informative than SPF values, and that nothing would be lost by dropping them. Two other comments proposed eliminating the PCD's because they serve no useful purpose and may be misleading and confusing. One comment maintained that manufacturers should continue to use SPF values as the sole means of disclosing the sun protection value of a product. The comment stated that sunscreen testing procedures provide an accurate and reproducible measure of the erythema protection performance of the products tested and that the consumer is familiar with the SPF as a measure of the relative protection offered by various products. The comment added that the consumer has been exposed to the SPF concept for 10 years or more and is well acquainted with the degrees of protection provided by products with different SPF values. Maintaining that the terms (e.g., "ultra," "maximal," and "extra") applied to the different PCD's have no intrinsic meaning that would allow the consumer to make an educated comparison between products, the comment recommended that SPF values alone be used to convey the sun protection performance of a sunscreen product. The comment felt that consumers were sufficiently well-educated regarding SPF values of sunscreens so that PCD's are redundant.

The agency agrees with many comments that the SPF provides consumers with important information. The SPF value is based on a numerical index designed to tell consumers how much protection from the sun a product will provide. The SPF value is defined as the ratio of the amount of energy required to produce a MED or minimal sunburn through a film of a sunscreen drug product to the amount of energy required to produce the same MED without any treatment (43 FR 38206 at 38213). The SPF values are correlated to the efficacy of the sunscreen product and thus are helpful to consumers in identifying the proper product for their needs. This information is especially important to consumers with fair or sensitive skin. The Panel's recommended SPF system contains an SPF scale with values of 2 to 15, i.e., products providing a minimal amount

of protection to products providing the maximum amount of protection. The agency has further determined for the reasons more fully described below that an SPF scale with values up to and including SPF 30 is appropriate. (See comments 46 and 47.)

The agency believes that PCD's are useful for descriptive terms for standardizing the labeling of sunscreen drug products but should not be mandatory labeling. Although PCD labeling may provide useful information to the consumer, it is not necessary for the safe and/or effective use of the product provided an SPF value is included in the products labeling. A single PCD is established for each product after determining the product's SPF value. The five PCD statements being proposed by the agency in this tentative final monograph are as follows: Minimal (SPF 2 to under 4), moderate (SPF 4 to under 8), high (SPF 8 to under 12), very high (SPF 12 to under 20), and ultra high (SPF 20 to 30). (See comment 45.) The PCD and SPF of a sunscreen drug product determines which of the additional indications proposed by the agency in § 352.52(b)(2)(i) to (b)(2)(v) of this tentative final monograph are appropriate for use in the labeling of the product. For example, products whose SPF value (i.e., 8 to under 12) places them within the PCD of "high" may display the indication in § 352.52(b)(2)(iii)(F) "High protection against sunburn for blondes, redheads, and fair skinned people." Products whose SPF value (i.e., 2 to under 4) places them within a PCD of "minimal" may display the indication in § 352.52(b)(2)(i)(B) "Prolongs exposure time before sunburn occurs."

In § 352.52(e)(1) of this tentative final monograph, as with the additional optional indications, the agency is proposing that PCD labeling statements be optional (included by the manufacturer if desired), and not required as recommended by the Panel. This approach is consistent with the many comments that stated that PCD labeling is less important than SPF labeling.

The agency believes that the two comments opposed to the system of SPF values and PCD statements are examples of the misunderstanding by some consumers regarding what information will appear on the labeling of marketed sunscreen drug products. The Panel recommended that the labeling of all sunscreen drug products include a sunscreen drug product guide that lists five skin types and five PCD's with each PCD corresponding to the appropriate skin type (43 FR 38206 at 38268 and

38269). The agency is proposing to revise the Panel's recommended sunscreen drug product guide to include SPF ranges instead of PCD's. (See comment 43.) By using this sunscreen product guide, the consumer may select the proper sunscreen drug product, i.e., the product with the SPF value that conforms with the consumer's skin type and sunburn and suntanning history. Each sunscreen drug product must be labeled with an SPF value and may display an optional specific PCD claim if the manufacturer wishes to include such information in its product's labeling.

The PCD's and the SPF numerical rating system are designed to assist manufacturers and consumers in determining how effective a sunscreen drug product is in protecting a person from the sun's harmful rays and, thus, how effective the product will be in preventing sunburn or skin damage. However, safe use can only be achieved by also including in labeling a Recommended Sunscreen Product Guide so that consumers can select the most appropriate sunscreen drug product based on skin type (sensitivity) and the expected length of exposure time to direct sunlight. The agency concludes that sunscreen drug product labeling based on such a system will make it easier for consumers to select the proper sunscreen drug product. Accordingly, the agency is including the SPF rating system and the Recommended Sunscreen Product Guide in the required labeling for sunscreen drug products in proposed §§ 352.50 and 352.52(e)(4), respectively, and is proposing the PCD statements as optional labeling in § 352.52(e)(1).

Reference

(1) C00083, Docket No. 78N-0038, Dockets Management Branch.

45. In the notice of public meeting to discuss appropriate testing procedures for OTC sunscreen drug products (52 FR 33598 at 33602), the agency noted that the Panel's recommended PCD's may not adequately accommodate sunscreen drug products with high SPF values of 25 or 30. The agency requested comment on how the PCD's might be modified to include higher SPF values.

Several comments supported retaining the five PCD's that were recommended by the Panel. One comment suggested that products with SPF values of 15 or higher should continue to be designated as "ultra." One comment recommended that for those products that have SPF values over 15, the monograph should be changed to read "15 and above" for the "ultra" PCD.

One comment suggested that the ultra category should be comprised of sunscreens with SPF values between 15 and 30+. The comment maintained that retaining the currently proposed designations has a significant benefit in that current products would not need to be relabeled with the category designation and consumer reeducation would not be necessary. It added that the PCD's as currently proposed do encompass all SPF ranges without the necessity for a change. One comment suggested the addition of an SPF 25+ value to the ultra protection category.

Several comments suggested revisions to the PCD's that were recommended by the Panel. One comment maintained that the system found in Australian Standard AS2604 is readily understood by consumers, precludes ambiguity, and is compatible with SPF labeling in excess of 15. It recommended the following categories: (1) Minimal (SPF 2 to less than 4); (2) Moderate (SPF 4 to less than 8); (3) High (SPF 8 to less than 15); and (4) Maximum (SPF 15 and over). Another comment suggested revised wording for the PCD's as follows: (1) low (SPF 2 to under 4); (2) medium (SPF 4 to under 6); (3) high (SPF 6 to under 9); (4) very high (SPF 9 to under 15); and (5) maximal (SPF 15 and above). The comment maintained that this revised wording would be more comprehensible to the consumer than the descriptive terms recommended by the Panel. A third comment stated that PCD's should be divided as follows: (1) minimal (SPF 2 to under 5); (2) moderate (SPF 5 to under 10); (3) extra (SPF 10 to under 15); (4) maximal (SPF 15 to under 25); and (5) ultra (SPF 25 and above).

Noting that the suggested category designations in the September 4, 1987 notice (52 FR 33602) had deleted the SPF 15 category, one comment strongly recommended that the SPF 15 category be retained. The comment cited a survey of pediatricians and dermatologists (Ref. 1) that indicates that they usually recommend SPF 15 sunscreens to their patients. The comment favored retaining the current PCD ranges to maintain continuity, suggested two additional categories, and suggested revising the SPF 15 or greater category to accommodate currently marketed products as follows: for the PCD comprising SPF 15 to under 25, the labeled SPF should be 15; for the PCD comprising SPF 25 to under 30, the labeled SPF should be 25; and for the PCD comprising SPF values of 30 or greater, the labeled SPF should be 30+. However, the comment did not provide any names to be used for its additional PCD's.

One comment recommended that the following classes be used to designate categories rather than the Panel's recommended PCD's: (1) Class 1 (SPF 15 and more); (2) Class 2 (SPF below 15 to SPF 8); (3) Class 3 (SPF 8 to 6); (4) Class 4 (SPF 6 to 4); and (5) Class 5 (SPF below 4). The comment further suggested that each class could be given a specific name which may represent the sensitivity of the skin (e.g., Class 1 would be for very sensitive skin and/or extreme solar conditions; Class 2 would be for sensitive skin and/or moderate solar conditions; Class 3 would be for low sensitive or tanned skin; Class 4 would be for low sensitive or unsensitive skin; and Class 5 would be for minimal sun protection). Adding that Classes 3, 4, and 5 only protect in mild solar intensity, the comment further defined extreme solar conditions as those corresponding to 15 to 25 MED per day for sensitive skin, moderate solar conditions as those equal to about 10 MED per day for sensitive skin, and low solar conditions as those corresponding to about 5 MED per day for sensitive skin.

Some comments argued that the PCD descriptive terms recommended by the Panel (i.e., "minimal," "moderate," "extra," "maximal," and "ultra") are confusing, misleading, and ambiguous, and should not be included in the labeling of sunscreen drug products. Two comments contended that, by definition, the word "maximal" should be the highest rating category, but it falls in the middle of the Panel's recommended SPF range. The comments added that consumers have been educated to purchase products based upon SPF values. Another comment stated that the Panel's report permits a product with an "ultra" PCD to characterize itself as providing the "most protection against sunburn," the "greatest protection against sunburn," or the "highest degree of sunburn protection." The comment stated that these claims are potentially confusing because the product may provide less total sunscreen protection than a higher SPF product or a product with more UVA protection. The comment added that consumers cannot distinguish the true value or degree of protection suggested by these terms because it is not clear whether a "maximal" sunscreen provides greater or less protection than either an "extra" or "ultra" protection product. Another comment maintained that "maximal" and "ultra" each imply the most possible.

One comment maintained that labeling with SPF numbers using the fixed values set forth in the PCD

labeling recommended by the Panel in its proposed monograph is appropriate. Another comment favored the restriction of labeled SPF values to the lowest value of the PCD range. The comment felt that allowing the actual intermediate SPF values within a category to be displayed on the principal display panel becomes a marketing ploy that would unnecessarily confuse the consumer. Stating that it is unlikely that meaningful differences in protection exist between products with SPF 9 and 11, for example, the comment stated that labeling the products as such would be misleading and that labeling both products with SPF 8 would be a more appropriate and conservative approach. A third comment recommended that for all PCD's, either the actual SPF value, as determined by testing, or the lowest SPF number in the PCD would be appropriate for label claims. The comment added that a cap should be set at SPF 30 and any tested value higher than 30 should be expressed on the label only as 30+. One comment maintained that the PCD's recommended by the Panel are not adequate to allow consumers to evaluate sunscreen drug products for effectiveness. Stating that consumers have a good basic knowledge of the SPF system, the comment suggested that actual SPF ratings, in whole number increments, should be allowed on all sunscreens so that accurate comparisons can be made. Another comment maintained that the consumer relies more on the actual SPF of a product than the PCD. The comment stated that providing the actual SPF on the label along with the appropriate PCD is in the best interest of the consumer.

The agency believes that the Panel's recommended PCD's should be revised slightly in order to better accommodate SPF values above 15. The agency believes that a modification of the PCD ranges will ensure that the protective qualities of a sunscreen drug product will be more accurately described. For example, the Panel recommended that SPF 15 sunscreens should be allowed to display the claim "Affords the most protection against sunburn." As stated in comment 46, the agency believes that SPF values above 15 are justified in part because an SPF 15 sunscreen drug product may not provide "the most protection against sunburn" for some fair-skinned persons or under certain circumstances. In the 12 years since the Panel's report on OTC sunscreen drug products was published, advances in technology have produced dramatic improvements in the effectiveness of

sunscreen preparations. Such products have become integral features in public health statements. The National Institutes of Health (NIH) Consensus Development Conference Statement and the AAD both recommend the use of sunscreens with SPF ratings of 15 or higher (Refs. 2 and 3). The Panel recommended that products providing an SPF value of 8 to under 15 could state "Affords maximal protection against sunburn" and that products providing an SPF value of 15 or greater could state "Affords the most protection against sunburn." Because the agency is proposing a revised SPF system in this tentative final monograph, it is also proposing to revise the PCD ranges and to use several different descriptive terms in place of those recommended by the Panel.

Regarding the terms used for PCD categories, the agency agrees with the comments and believes that some of the comparative terms recommended by the Panel (i.e., such as "+", "extra", "maximal," and "ultra") to identify PCD's are confusing and may be misleading to the consumer. It should be noted that the Panel was proposing a new labeling concept, and at the time of its deliberations, such terms were not commonly found in the labeling of sunscreen products. The agency agrees that it is especially difficult to distinguish between the term "maximal" and "ultra" because both would seem to indicate that the sunscreen drug product offers the most protection possible. The agency believes that the terms "minimal" and "moderate" recommended by the Panel are clear and that these terms properly indicate the performance that consumers may expect from a sunscreen drug product in these SPF ranges. The agency is, therefore, proposing that the terms "minimal," and "moderate" be retained. However, the agency proposes that the higher PCD's be identified as "high," "very high," and "ultra high." These terms should assist consumers in making a more informed comparison between sunscreen drug products. The agency invites specific comment on this issue. As mentioned above, the agency does not consider these terms as essential as SPF values and is proposing that the PCD labeling recommended by the Panel in § 352.50(e) of its monograph, as revised above, be optional. (See comment 44.)

In § 352.50(e) of its recommended monograph, the Panel proposed that sunscreen drug products be categorized into PCD's according to their tested SPF and that these products use the lowest SPF value in the applicable PCD as their labeled SPF number. For example, if a

product's test SPF value were 14, the product was categorized into the maximal PCD (i.e., SPF 8 to under 15) and used SPF 8 in its labeling. The agency now believes that the product may display instead its tested SPF value up to SPF 30. (In this tentative final monograph, the agency is proposing that SPF values up to and including SPF 30 are justified. See comments 46 and 47.) A water resistant or very water resistant product must display both its static SPF value (up to SPF 30) and its SPF value that has been determined after the appropriate water immersion test. (See comment 51.) Such labeling will more accurately inform the consumer of the protection offered by a sunscreen drug product, especially for those products in the higher PCD categories, such as "very high", where SPF values may range from SPF 12 to under 20, or "ultra high", where SPF values range from 20 to 30.

Although PCD statements are proposed as optional in this tentative final monograph, the agency believes that SPF values need to be displayed on the principal display panel of OTC sunscreen drug products. Therefore, the agency is proposing a new § 352.50 entitled "Principal display panel of all sunscreen drug products" to include labeling that is required to appear on the principal display panel of all OTC sunscreen drug products as follows: "For products that do not satisfy the water resistant or very water resistant sunscreen test procedures in § 352.76. 'SPF (insert tested SPF value of the product up to 30).'" (For labeling required for the principal display panel of OTC sunscreen drug products that satisfy the water resistant and very water resistant testing procedures in § 352.76, see comment 51.)

Because of the addition of this new labeling section, the agency is proposing to renumber the Panel's recommended § 352.50 "Labeling of sunscreen products" as § 352.52.

In addition, in this tentative final monograph the agency is revising the Panel's recommended PCD labeling in § 352.50(e) and including it in § 352.52(e), as follows:

"(1) For products containing any ingredient identified in § 352.10, the following PCD labeling claims may be used: (i) For products containing active ingredient(s) that provide an SPF value of 2 to under 4. 'Minimal Sun Protection Product.'

(ii) For products containing active ingredient(s) that provide an SPF value of 4 to under 8. 'Moderate Sun Protection Product.'

(iii) For products containing active ingredient(s) that provide an SPF value

of 8 to under 12. 'High Sun Protection Product.'

(iv) For products containing active ingredient(s) that provide an SPF value of 12 to under 20. 'Very High Sun Protection Product.'

(v) For products containing active ingredient(s) that provide an SPF value of 20 to 30. 'Ultra High Sun Protection Product.'"

References

- (1) Comment No. C00083, Docket No. 78N-0038, Dockets Management Branch.
- (2) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference Statement, Vol. 7, Number 8, May 8-10, 1989.
- (3) "Cancer of the Skin," edited by the Task Force on Pamphlets, American Academy of Dermatology, Evanston, IL, 1986.

46. In the notice of public meeting to discuss sunscreen testing procedures (52 FR 33598 at 33599), the agency noted the proliferation of OTC sunscreen drug products that display SPF values greater than 15, which was the Panel's highest recommended classification. Stating that consideration should be given to modifying the Panel's recommended monograph to address these higher SPF values, the agency asked the following: "What benefit is provided to the consumer by sunscreen drug products claiming to have SPF values greatly in excess of 15 (i.e., 23 or even 30) if, as the Panel claims, SPF 15 offers the maximum possible protection?" (See 52 FR 33602.)

Most comments submitted in response to the public meeting maintained that sunscreen drug products with SPF values above 15 are beneficial and justified. One comment asserted that such products provide better protection against the deleterious effects of the sun than do sunscreen drug products with lower SPF values. Two comments noted that, at the time the Panel made its recommendations, SPF 15 was the highest value commercially available. Since that time, newer research and formulation techniques have made it possible to formulate sunscreen products with proven efficacy at SPF levels well above 15. One comment added that these newer products are more protective than those initially contemplated or reviewed by the Panel in the 1970's. Another comment remarked that because of advances in technology, the Panel's proposed labeling that "SPF 15 provides the highest degree of sunscreen protection" is now inaccurate and needs to be corrected.

Several comments pointed out that sunscreen drug products with an SPF of 15 will not offer maximal protection to

a person with extremely sensitive skin (i.e., an individual with Skin Type I who always burns and never tans) and noted that American consumers may be exposed to increased doses of sunlight when on vacation in sites like Hawaii, the Caribbean, and Mexico. One comment added that not only is the intensity of the sun greater in such areas, but persons on vacation in such places may stay out in the sun longer. Another comment stated that the potential for sunburn cannot be avoided completely by using a product with a lower SPF value and reapplying it frequently, and that products with SPF values higher than 15 provide an extra measure of protection for people who either do not want to be or who should not be exposed to the sun. One comment stated that although a product with an SPF of 15 provides significant protection from sunburn, the extra margin of protection afforded by a product with an SPF value in excess of 15 is useful to those sun-sensitive individuals desirous of all-day protection.

One comment stated that products with the higher SPF values screen out more of the sun's total UV radiation spectra responsible for both immediate burning and long-term damage such as photoaging and skin cancers. Another comment submitted several published scientific studies purporting to indicate the benefits of sunscreens in terms of skin cancer protection (Refs. 1 through 4), protection against photoaging (Refs. 5 and 6), and protection of the cutaneous immune functions (Ref. 7). Another comment added that the medical community has continued to stress the importance of adequate sun protection throughout one's lifetime to reduce the risk of skin cancer and premature aging of the skin, and that products with an SPF above 15 would better provide this protection.

One comment maintained that there is ample documentation to indicate that an SPF value of 15 is not adequate protection for a sizeable proportion of the United States' population (Refs. 8 through 11). Based on these data, the comment maintained that the average midsummer MED available per day range from 19 in Bismark, North Dakota, to 44 in El Paso, Texas, for skin Type II individuals. The comment pointed out that although these are sunrise to sunset measurements, 75 percent of the sunburning radiation dose is delivered between 9 a.m. to 3 p.m. During that time period individuals are most active outdoors, and there is a potential exposure in the 30-MED range. The comment also submitted 1980 Census Bureau data that indicate that 39.3

percent of the United States' population is of Celtic origin and would be classified into the lower skin type categories (i.e., Skin Types I or II) (Ref. 12). One comment stated that it had conducted an attitude and use survey in 1987 among 585 sunscreen consumers who were asked, "How important is an SPF of 15 or greater to you in a sunscreen?" The comment stated that 75 percent of the subjects responded positively by selecting either "extremely important" (48 percent) or "very important" (29 percent).

One comment maintained that the AAD and other scientific organizations recognize the need for high SPF products. The comment stated that the German sunscreen standard (DIN 607501) and the Australian standard (AS 2604) recognize that products need to be formulated to meet the needs of consumers with varying skin types. The comment added that, in addition to normal variations in skin type and susceptibility to sunburn, a substantial segment of the population appears to be sun sensitive (Ref. 13) and needs high SPF products to provide adequate protection.

One comment submitted the results of a nationwide random survey of 101 pediatricians and 99 dermatologists to determine their sunscreen recommendations to patients (Ref. 14). The survey found that 21 percent of pediatricians and 49 percent of dermatologists usually recommend products with SPF values higher than 15, and that 75 percent of dermatologists sometimes recommend products with SPF values higher than 15. Only 11 percent of pediatricians and 20 percent of dermatologists felt that sunscreens with SPF values higher than 15 were not medically necessary. The comment maintained that these results indicate that the majority of these medical specialists recognize that products with SPF values above 15 are valuable. Another comment submitted a study (Ref. 15) that investigated the risk reduction for nonmelanoma skin cancers associated with the childhood use of sunscreens. Using a mathematical model based on epidemiological data, the authors quantified the potential benefits of using an SPF 15 sunscreen and estimated that the regular use of such a sunscreen during the first 18 years of life reduced the lifetime incidence of nonmelanoma skin cancer by 78 percent.

Conversely, two comments were opposed to the availability of sunscreen drug products with SPF values higher than 15. One comment questioned the need for sunscreen drug products with high SPF values (i.e., 25 to 30) when

people are not exposed to greater than 15 MED's in a day. The comment maintained that waterproof sunscreen drug products with an SPF of 15 are adequate for the average needs of all people. The comment felt that people with highly sun-sensitive skin are given a false sense of protection when the industry recommends sunscreen drug products with SPF values of 25 or 30, and this action endorses increased sunbathing. Such sun-sensitive persons are at greatest risk of developing acute and chronic skin changes and should not indulge in prolonged sunbathing or remain outdoors for long periods of time. The comment asserted that prolonged sunbathing should be discouraged and the regular use of sunscreen drug products should be encouraged in order to control the increasing trend of actinic keratoses, skin cancer, and the early onset of photoaging. Another comment submitted in response to the Panel's report contended that sunscreens with SPF values greater than 10 are not necessary because people with very sensitive skins with a "disposition to light disease" should use opaque sunscreens.

The agency agrees with the majority of comments that SPF values higher than 15 are justified. The agency notes that in the United States there are enormous variations both in skin type in the population and in the amount of UV radiation to which a person may be exposed, because of differences in geography. Many of the comments submitted to the agency cited varying average daily doses of UV radiation ranging from approximately 9 to 44 MED's depending upon location, altitude, and season. The agency believes that there are situations where consumers routinely are exposed to sufficient UV radiation may require sunscreen drug products with SPF values greater than 15.

Since the Panel's report on OTC sunscreen drug products was published, advances in technology have produced dramatic improvements in the effectiveness of sunscreen preparations. Several elements have contributed to these advances, e.g., development of solar simulators, more knowledge of the optical properties of the skin, greater skills in formulating sunscreen drug products, and greater awareness of the importance of the vehicle in such products (Ref. 16).

The agency believes that sunscreen preparations with SPF values above 15 are important from a public health standpoint. According to an NIH Consensus Development Conference Statement (Ref. 17), the average

American's exposure to UVB radiation has increased considerably over the past several decades due to changing lifestyles, i.e., more outdoor recreational activities, more emphasis on tanning, scantier clothing, and a population shift to the sunbelt. In addition, recent satellite measurements indicate a worldwide decrease in stratospheric ozone over the last decade. This reduction increases the amount of UV radiation that reaches the earth's surface. If the ozone layer continues to be depleted, human exposure to UV radiation will increase correspondingly.

There are serious risks involved with increased exposure to UV radiation. Sunscreen preparations with SPF values higher than 15 are necessary to provide fair-skinned individuals with maximum protection. A large proportion of the United States' population is of Celtic origin (Ref. 12). Such fair-skinned people burn very easily (i.e., in as little as 10 minutes (43 FR 38206 at 38210)) and are most susceptible to the adverse effects of sunlight, such as skin cancer and premature aging of the skin. Therefore, the agency believes that many people in the United States need more protection than that provided by an SPF 15 sunscreen. This need is especially important when people are being exposed to intense sunlight, such as that found in the southern portion of the United States and in many popular vacation areas where consumers normally receive even greater amounts of UV radiation. The NIH Consensus Development Conference Statement recommends the use of sunscreens with SPF ratings of 15 or higher (Ref. 17). It also recommends daily use of these products during appropriate times of the year and states that sunscreens should be applied before exposure, with frequent reapplications thereafter. The agency agrees that sunscreens should be applied frequently and is proposing such in the directions included in § 352.52(d) of this tentative final monograph. (See comment 66.) The AAD also recommends the use of sunscreens with SPF factors of at least 15 to protect against premature aging of the skin and skin cancer (Ref. 18).

The agency also believes that sunscreen drug products with SPF values above 15 may offer better protection to consumers who may not apply a sunscreen as liberally as they should or who do not always reapply a sunscreen as frequently as they should. For such consumers, a sunscreen with an SPF of 20 or 25 may offer an important extra margin of safety. The agency concludes that OTC sunscreen drug products with SPF values higher than 15 are beneficial to consumers and

is proposing that the upper limit for SPF values be 30. (See discussion of proposed SPF 30 upper limit in comment 47.)

In regard to the one comment's concerns about individuals with a "disposition to light diseases," the agency has discussed such photosensitization reactions in comments 33 and 69.

References

- (1) Klugman, L.H., F.J. Akin, and A.M. Klugman, "Sunscreens Promote Repair of Ultraviolet Radiation-Induced Dermal Damage," *The Journal of Investigative Dermatology*, 81:98-102, 1983.
- (2) Forbes, P.D., et al., "Inhibition of Solar U.V.R. Induced Skin Tumors in Hairless Mice Using 2-Ethylhexyl-p-Methoxycinnamate," *Cosmetics, Aerosols & Toiletries in Australia*, 1:27-30, 1986.
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47. Several comments discussed whether or not there should be an upper limit to SPF values. The Standards Association of Australia submitted a copy of its revised standard for sunscreen products (Ref. 1) and stated that it has deliberately restricted SPF factor claims to a maximum of "15+" to prevent the "inevitable number chasing" that is "now occurring in the USA." The comment stated that this restriction prevents products from being "loaded" with sunscreen ingredients for which chronic dermal toxicology data are often lacking.

Two comments believed that SPF values should be capped at 20. One comment stated that the most that it had measured with a Robertson-Berger meter in the tropics on Mauna Loa (19° North latitude, 12,000 feet elevation) was 27 MED's, on a flat surface, from sunrise to sunset. The comment maintained that because a human in the upright position receives at most 60 percent of the ambient UV radiation, a full day's dose would not exceed 16 MED's for a Skin Type I individual. The comment contended that sunscreen drug products with SPF values greater than 20 will only increase cost and make the possibility of irritation from multiple sunscreen ingredients and their photobreakdown products more likely. Another comment maintained that unless one is at a high altitude (e.g., 15,000 to 20,000 feet), one is unlikely to receive UV radiation flux exceeding 15 MED on a clear, bright day. The comment asserted that an average person rarely stays out in the sun for more than 4.5 hours and thus would only receive a maximum dose of 10 to 12 MED. The comment urged the agency to adopt a maximum SPF value of 20, contending that it is not necessary to have "extra potent" sunscreens with SPF values of 25, 30, or 35 and to subject the consumer's skin to potentially toxic effects of high concentrations of chemicals.

Another comment stated that an upper limit of SPF "25+" should be established to ensure adequate sunscreen protection for highly sun-sensitive skin types without exposing consumers to unnecessarily high levels of sunscreen active ingredients. The comment expressed concern that many companies manufacturing sunscreen drug products have embarked upon an SPF "numbers game," leaving consumers with the impression that the higher the SPF number the better the product. The comment felt that such marketing strategies are not rational and expose consumers to excessive levels of sunscreen ingredients that may potentially cause more problems (e.g., invisible dermatitis) than are justified by the benefits. The comment added that placing the upper SPF limit at "25+" would provide industry with an opportunity to reasonably protect the consumer from UV radiation while restricting the current industry marketing movement toward very high SPF values, which needlessly confuse the user.

Several comments believed that SPF claims should be capped at 30. Stating that the trend toward higher SPF values has reached unjustifiable levels, one comment stated that the benefits derived from very high SPF values by the vast majority of consumers are negligible, and that many consumers think that they are getting much more protection than they actually are. Another comment suggested that products with SPF values greater than 30 cannot be justified on a risk/benefit basis because achieving SPF values higher than 30 requires unnecessary exposure to increased levels of sunscreens agents, while increasing overall protection by an insignificant degree. As an example, the comment noted that an SPF 30 sunscreen drug product blocks 96.7 percent of the incident UVB energy whereas an SPF 40 sunscreen drug product only increases this level of protection to 97.5 percent, and the amount of additional sunscreen ingredient "load" in the product to increase the SPF to 40 could realistically increase by up to 25 percent. The comment added that, in the extreme, an SPF 70 would block 98.6 percent of the UV energy versus 96.7 percent blocked by an SPF of 30. The comment maintained that such extra protection is not necessary and that sunscreen drug products with SPF values higher than 30 represent unnecessary and ill-advised exposure to increased sunscreen ingredients at a time when dermatologists and skin cancer groups are recommending that

sunscreens be applied daily to minimize the adverse effects of the sun. The comment concluded that this additional unnecessary exposure to more sunscreen ingredients is ill advised.

One comment stated that a reasonable basis for selecting an SPF cap is the level of protection required for an average consumer who spends an entire day in the sun in a sub-tropical region of the United States such as Florida or Hawaii. The comment maintained that measurements of UV radiation taken in these areas have found that the average consumer can be exposed to as much as 20 MED's. The comment recommended an SPF cap of 30 because this is the maximum amount needed to protect the vast majority of consumers (including Skin Type I individuals) from sunburn under stress conditions of UV exposure.

One comment stated that proponents of high SPF values often cite as justification the needs of people with Skin Type I and people prone to skin cancer. The comment maintained that a sunscreen drug product with an SPF of 30 can adequately protect most of these individuals and added that it is not good public policy to expose most of the population to unnecessarily high levels of sunscreens to protect a very few. The comment contended that people can be misled into a false sense of security when told that a single application of a very high SPF product will protect them all day. In reality, the comment asserted these products are subject to washing or rubbing off, thus reducing their effective level of protection. The comment stated that the needs of special groups would be better served if they were encouraged to reapply their sunscreen products because two applications of an SPF 30 sunscreen drug product will provide more protection under real usage conditions than a single application of a higher SPF product. Another comment stated that individuals who are so sensitive as to need higher than SPF 30 protection should be encouraged to severely limit their sunlight exposure and to use a product with an SPF of 30 when they are necessarily exposed to sunlight. The comment concluded that SPF 30 should be sufficient for all-day sunburn protection for the vast majority of the population under maximum sun exposure conditions.

One comment argued there are data (Ref. 2) demonstrating that enough sunlight exists on many days during the summer months in various locations to permit exposure in excess of 25 MED's for the average Skin Type II and III individual. By extrapolation, the comment maintained that a Skin Type I individual could be exposed to approximately 30 MED's during this

same time frame. The comment acknowledged that these calculations are based upon exposure of an individual lying in a quiet, prone position from sunup to sundown, and may be somewhat inflated. Nevertheless, the comment maintained that these data provide a convincing rationale for an SPF 30 sunscreen drug product that would permit even a Skin Type I to achieve all-day protection as well as allowing for an extra margin of protection to accommodate weather conditions that cannot be factored into SPF testing.

Several comments advocated that no upper limit be set on SPF values. One comment maintained that scientific information is not available to demonstrate a "no-effect" level of sun exposure, especially when considering the sun's contribution to photoaging and to the risk of skin cancer. The comment provided a pamphlet from the AAD (Ref. 3) to substantiate its position. The comment suggested that, in the absence of a demonstrable safety risk, it would be contrary to public policy and to consumers' best interest to preclude manufacturers from offering truthfully labeled sunscreen formulations with as much sun protection as is technologically feasible.

Citing an article by Urbach and Berger (Ref. 2) and stating that a person with average, untanned, Caucasian skin may receive 22 MED's of UV radiation in one day in El Paso, Texas, another comment supported an open-ended numbering system for SPF values, or as an alternative, an upper limit of not less than 40. The comment maintained that limiting the highest allowed SPF number would prevent those consumers who want and need a high level of protection from making valid comparisons among the highest SPF products available.

A comment from an institute that deals with systemic lupus erythematosus and discoid lupus research (diseases associated with photosensitivity) mentioned the need for a sunscreen drug product with an SPF value of up to 40. The comment maintained that the use of such sunscreen drug products would prevent the triggering of the onset of these diseases. The comment included abstracts of scientific publications that include information on the relationship between photosensitivity and lupus and that suggest that sunblocks may be essential for sensitive lupus patients (Ref. 4).

Although the agency has concluded that the available scientific data demonstrate that sunscreen drug products with SPF values above 15 are

reasonable and justified (see comment 46), it finds that SPF values above 30 are not necessary because the available data clearly indicate that a sunscreen drug product with an SPF of 30 assures adequate protection for the majority of consumers even under extreme conditions. As pointed out by one comment, an SPF 30 sunscreen drug product blocks 96.7 percent of the incident UVA energy, whereas an SPF 40 sunscreen drug product only increases this level to 97.5 percent. Further, data compiled by Berger and Urbach in 1982 (Ref. 2) demonstrated that approximately 25 MED's is the highest dose of UVB radiation that an individual with average Caucasian skin can expect to receive in Mauna Loa, Hawaii. In the southern states of the continental United States, an individual can be exposed to approximately 22 MED's in the hottest part of the summer. A sunscreen drug product with an SPF 30 provides all-day protection for all skin types. Such a product also provides an extra margin of protection that allows for the possibility that the product may be inadequately applied and accommodates weather conditions that cannot be factored into the SPF testing procedures that are done with artificial light sources.

Scientific evidence shows a point of diminishing returns at levels above SPF 30; any benefits that might be derived from using sunscreens with SPF values higher than 30 are negligible. The agency does not believe that an "open-ended" approach to SPF values is beneficial to consumers. The difference in protection provided by a sunscreen drug product with an SPF 40 or 50 compared to the protection offered by a product with an SPF 30 is so small as to be nonexistent, especially when one considers the biological variability inherent in an individual's response to the protective quality of sunscreen drug products. (See also discussion in comment 48.)

Regarding the use of high SPF sunscreen drug products to protect consumers with photosensitivity diseases, the agency notes that the exact etiology of these light-related diseases is not known. (See comment 69.) The fact that a sunscreen has a high SPF may not be as important to the consumer with a photosensitivity disease as the UV wavelengths that are absorbed or reflected by the sunscreen ingredient in the product. The agency does not believe that, apart from whatever ingredients may be in the formulation, an SPF 40 sunscreen drug product provides significant benefits that are not also provided by an SPF 30 sunscreen drug product. Unless such benefits can

be shown, the agency believes that an SPF 30 sunscreen drug product provides adequate protection for a consumer with a photosensitivity disease provided that the appropriate wavelength is absorbed or reflected.

Based upon the above, the agency is proposing an upper limit of 30 for SPF values and is proposing to revise the Panel's recommended § 352.50(b) to reflect this maximum SPF value. (See comments 45 and 57.)

Several comments questioned the safety aspect of sunscreen drug products with extremely high SPF values (e.g., 25, 30, or higher). This issue is discussed in comment 48.

References

- (1) Comment No. C00082, Docket No. 78N-0038, Dockets Management Branch.
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48. In response to the notice of public meeting to discuss appropriate testing methods for OTC sunscreen drug products (52 FR 33598), some comments expressed concern regarding the possible toxicity of OTC sunscreen drug products with high SPF values. Maintaining that there is no safety or toxicological data pertaining to "these new sunscreens with high SPF values that contain high concentrations of UV-absorbing and UV-reflecting chemicals," one comment expressed concern about the long-term effects of these preparations. The comment specifically mentioned that little is known about the long-term effects of the small concentration of lead in zinc oxide and titanium dioxide and stated that this may be especially harmful to children. Stating that the constant presence of chemicals on skin is potentially harmful, the comment questioned how many fair-skinned individuals might develop photoallergic reactions by using potent, high SPF sunscreen drug products. The comment suggested that the agency recommend certain test procedures in an animal model system to ensure the safety of high SPF sunscreen drug products when used on a long-term basis.

One comment stated that, at the January 26, 1988 public meeting, some of the discussion of possible safety issues relating to high SPF sunscreen drug products missed the point of the relevant benefit-risk analysis. The comment stated that, although products with SPF values greater than 15 utilize

Category I ingredients within approved concentration ranges, the total sunscreen load tends to increase significantly. For example, in comparing similar lotion formulations, a sunscreen with an SPF of 15 may utilize 11.5 percent total sunscreen ingredients while a sunscreen with an SPF of 40 may require over 22 percent total sunscreen load. The comment stated that the consumer is therefore exposed to greater total levels of active ingredients. Conversely, the incremental difference in protection from UVB rays becomes increasingly smaller. For example, a sunscreen with an SPF of 15 screens 93 percent of UVB rays, a sunscreen with an SPF of 25 screens 96 percent of UVB rays, while a sunscreen with an SPF of 39 screens 97.44 percent of UVB rays. The comment stated that the obvious benefit-risk issue is whether the extremely modest increased protection from sunburn justifies the increased exposure to sunscreen ingredients that may cause skin irritation.

One comment pointed out that the level of sunscreen active ingredients allowed in a sunscreen drug product is now regulated by the advance notice of proposed rulemaking published in 1978 (43 FR 38206) and that all sunscreen drug products, even those with very high SPF values, are limited by these proposed rules. The comment maintained that advances in formulation technology have allowed manufacturers to develop products with relatively low levels of sunscreen active ingredients and still maintain high SPF values. The comment stated that responsible manufacturers test finished products to establish safety prior to marketing, in addition to adhering to the limits established in the proposed rules. The comment added that, although product safety is a very important consideration, limiting the SPF claim on sunscreen drug products will not have a substantial effect on the overall safety of these products.

The comment noted that three speakers at the public meeting suggested that skin irritation might result from use of sunscreen drug products with high SPF values. The comment cited the following three specific statements: (1) "the use of larger numbers and more sunscreen probably will only lead to trouble with photochemical reactions, * * * irritancy * * *"; (2) "[in work with] patients who experience either skin cancer or melanoma, [he] recommend[s] the use of 15 SPF and more, but at least 10 percent of [the subjects] have an irritation with this type of product;" and (3) "[he] recommended SPF-15 sunscreens and

* * * without sunlight exposure * * * [the subjects] had contact irritational reaction, no sensitization," (Ref. 1). The comment stated that no data were submitted to support these statements. The comment added that the patients to whom the last two statements applied had skin diseases and, thus, had compromised skin integrity. The comment maintained that, even if valid and documented scientific studies showed skin irritation in such subjects, there is no reason to believe that any significant irritation would result from the intended use of sunscreens by individuals with healthy skin.

The comment asserted that some of the reactions discussed at the public meeting were described as "some" irritation, "minor to some discomfort," "some burning sensation, a little bit of redness," and "discomfort, a little bit of redness" (Ref. 1). The comment contended that these reactions do not demonstrate a significant irritation problem with sunscreen drug products. The comment added that, in one case, the sunscreen preparations were European formulas, the active ingredients may not have been Category I ingredients, and the concentrations of the active ingredients in the products used were not provided (Ref. 1). The comment added that, as with any dermatological product, the irritation may have been caused by the inactive ingredients and not necessarily by the active sunscreen ingredients. The comment concluded that these speculative comments, by themselves, do not raise any significant safety concerns nor do they warrant any kind of additional warnings on OTC sunscreen drug products.

The comment stated that the Topical Analgesic Panel carefully evaluated the safety of the Category I ingredients included in the OTC drug review. The comment maintained that in the data base considered by the Panel no studies raised any serious concerns about skin irritation with these ingredients. The comment added that two commentators at the public meeting had said the following: (1) "We have not seen any problems in either human or animal safety testing," and (2) "in our experience with many, many customers and many cosmetic houses which use sunscreens, there is a negligible risk of exposure to the standard consumer, which actually is so small that it cannot be measured statistically" (Ref. 1). Maintaining that all drug products cause some type of adverse reaction in particular individuals, the comment added that the question is whether, when balanced against the benefit of the drug product, an adverse reaction is

significant, taking into account the size of the affected population. The comment stated that sunscreen drug products provide not only protection against sunburn but also against development of skin cancer and other kinds of damage to the skin. The comment argued that these benefits greatly outweigh instances of minor, transitory skin reactions that may occur.

The comment stated that manufacturers report a low incidence of consumer complaints about significant skin irritation resulting from the use of OTC sunscreen drug products. The comment maintained that, if there were significant problems with skin irritation, industry and the agency would have heard of them. The comment added that the Panel's recommended monograph requires the label of a sunscreen drug product to display the following warning: "Discontinue use if signs of irritation or rash appear" (43 FR 38206 at 38268). The comment concluded that there are no valid data in the record that sunscreen drug products currently marketed in the United States pose a risk of significant skin irritation.

One comment submitted data purporting to demonstrate that sunscreen drug products with an SPF above 15 are no more irritating than products with an SPF below 15 (Ref. 2). A 21-day cumulative patch-test procedure was used to determine if there is a correlation between the SPF of a sunscreen and its irritation potential. Five pairs of sunscreens were tested, each pair (from a different manufacturer) consisting of a high and a low SPF product in identical or almost identical vehicles. The study demonstrated that the degree of irritation was sometimes slightly greater in the higher SPF product and sometimes slightly greater in the lower SPF product. The investigator concluded, therefore, that the SPF and the irritation potential have no correlation.

The agency has extensively reviewed the available data and does not believe that sunscreens with SPF values higher than 15 (up to SPF 30) pose any significant safety problems. None of the comments that expressed concern regarding the safety of high SPF products submitted any data or information to substantiate their concerns or to show that higher SPF sunscreen drug products pose a greater safety risk.

In § 352.20 of its recommended monograph, the Panel established no upper limit to the number of sunscreen active ingredients that a product may contain. In the absence of any data to the contrary, the agency agrees with the

Panel that any number of sunscreen active ingredients may be combined in a product and is so proposing in § 352.20(a) of this tentative final monograph. Combining various sunscreen ingredients in a product can result in a product that provides protection against a wider spectrum of UV radiation than does a product containing a single sunscreen ingredient. Combinations of sunscreen ingredients, along with improved formulations, also result in products with higher SPF values and afford consumers more protection. However, because the agency requires that each ingredient in a product contribute to the effectiveness of the product, it is proposing in § 352.20(c) of this tentative final monograph that each ingredient in a combination sunscreen drug product should have a minimum concentration. (See comment 37.)

The agency agrees that advances in formulation technology have allowed manufacturers to develop products with relatively low levels of sunscreen active ingredients and still achieve high SPF values. The agency is aware of studies demonstrating the importance of the vehicle on the final performance of a sunscreen drug product. There is a lack of data showing a significant relationship between sunscreen ingredient concentration and the final SPF of a product. In one study (Ref. 3), designed to update performance data of a number of "high potency" sunscreens, the SPF and substantivity of several sunscreens were evaluated according to the testing procedures recommended by the Panel in its report on OTC sunscreen drug products (43 FR 38206 at 38267). The study demonstrated that formulation and vehicle design have a profound effect on SPF values. This was especially evident in the case of three sunscreens, each containing 8 percent padimate O (octyl dimethyl (PABA)) and 6 percent oxybenzone, that were found to have SPF values of 7.85, 15.85, and 18.43. Another sunscreen with a lower total concentration of the same active ingredients (i.e., 8 percent padimate O and 3 percent oxybenzone) had an SPF of 21.

The agency does not believe that increasing the concentration of active ingredients in a sunscreen drug product will necessarily make the product more irritating. The addition of another active ingredient to a drug product always has the potential to increase the risk of increased adverse effects. However, based on the study above (Ref. 3), there may not be any more of a problem in products with SPF values over 15 (up to SPF 30) than there is in products with

lower SPF values. The other study (Ref. 2) also supports this position.

The agency believes that the benefits derived from using a sunscreen drug product with an SPF value up to 30 outweigh any risk that may be present (see comment 46). As stated in comment 47, the agency believes that SPF values should be capped at 30, that any benefits that might be derived from using sunscreen drug products with SPF values higher than 30 are negligible, and that above SPF 30 the risk of added ingredients begins to outweigh the benefit of added protection.

The agency notes that many experts recommended the use of sunscreens with higher SPF values. As stated in comment 46, the NIH Consensus Development Conference Statement recommends the daily use of sunscreens with SPF ratings of 15 or higher (Ref. 4). Over the past several decades, the average consumer's exposure to UVB radiation has increased considerably due to changing lifestyles (e.g., more outdoor recreational activities, more emphasis on tanning, scantier clothing, and a population shift to the sunbelt. Along with increased exposure to UV radiation comes an increased occurrence of adverse effects from UV radiation. For example, the number of office visits for nonmelanoma skin cancer has increased more than 50 percent in the past decade while the overall increase in office visits has been only 11 percent. Therefore, it is imperative to consider ways to minimize the deleterious effects of UV radiation. Use of sunscreens with SPF values of 15 or higher will help to protect susceptible consumers from excessive exposure to UV radiation (Ref. 4).

The AAD also recommends the use of sunscreens with SPF factors of at least 15 to protect against premature aging of the skin and skin cancer (Ref. 5). Cancer of the skin occurs more frequently than any other form of cancer, with close to 400,000 new cases reported each year in the United States. As the human body's largest organ and chief protector against environmental onslaught, the skin is vulnerable to cancer-causing attacks. The principal cause is exposure to the UV rays of the sun. The majority of cancers develop on the unprotected parts of the face, neck, ears, forearms, and hands of persons constantly exposed to sunlight. For optimum protection against developing skin cancer, people should avoid constant exposure to the sun from infancy to adulthood. The use of sunscreens with SPF values of at least 15 are preferred for protection (Ref. 5). The agency agrees with these experts and believes

that sunscreens with SPF values higher than 15 are beneficial to the consumer and are not safety hazards.

The agency agrees with one comment that stated that the warning recommended by the Panel in § 352.50(c)(1)(iii) protects consumers by informing them to discontinue using a sunscreen drug product if signs of irritation or a rash appears. The agency is proposing in this tentative final monograph to expand the Panel's recommended warning by adding a sentence that informs consumers to consult a doctor if the irritation or rash persists. (See comment 63.)

References

- (1) Transcript of the Public Meeting to Discuss Appropriate Testing Methods for OTC Sunscreen Drug Products, pp. 10, 71, 76-77, 84-85, and 87-89, coded TR in Docket No. 78N-0038, Dockets Management Branch.
- (2) Comment No. C00096, Docket No. 78N-0038, Dockets Management Branch.
- (3) Kaidbey, K. H., and A. M. Kligman, "An Appraisal of the Efficacy and Substantivity of the New High-Potency Sunscreens," *Journal of the American Academy of Dermatology*, 4:566-570, 1981.
- (4) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference Statement, Vol. 7, Number 8, May 8-10, 1989.
- (5) "Cancer of the Skin," edited by the Task Force on Pamphlets, American Academy of Dermatology, Evanston, IL, 1986.

G. Comments on Water Resistant Labeling for Sunscreen Drug Products

49. Referring to recommended § 352.50 "Labeling of sunscreen products," one comment recommended allowing use of the word "perspiration" for "sweat" and the word "perspiring" for "sweating." The comment maintained that because the alternative words are synonymous and are well understood by consumers, they will not mislead or confuse consumers.

The agency concurs with the comment's recommendation and is proposing to allow manufacturers the option of using the words requested. In the labeling for the principal display panel in § 352.50(b) and (c), the "Directions" in § 352.52(d), and the "Statement on product performance" in § 352.52(e)(2), the agency is providing the option of using the terms "perspiration" and "perspiring" in place of the terms "sweat" and "sweating."

50. One comment stated that "water-resistance" is the strongest claim that should be permitted for any sunscreen drug product. The comment asserted that the use of "waterproof" sunscreens can result in occlusion of sweat ducts

and hair follicles, contact dermatitis (contact and delayed hypersensitivity), and vesicular dermatitis secondary to the trapping of sweat at some point in the skin. The comment added that the closure of sweat pores can also cause miliaria crystallina and miliaria rubra (prickly heat).

Several comments maintained that consumers do not differentiate between the terms "water resistant", "waterproof," and "sweat resistant." One comment recommended reducing the number of "water-related" claims from three to one (i.e., "water resistant"). One comment stated that the Australian standard AS2604-1986 allows only the claim "water resistant" because it was felt that the claim "waterproof" is an absolute claim and would be construed by consumers that, once applied, the product need not be reapplied. This could be particularly dangerous given the possibility of removing the product while towel drying. The comment felt that the term "water resistant" indicated that some caution was still needed.

Another comment maintained that use of the terms "water resistant" and "waterproof" in sunscreen labeling is confusing and "potentially misleading" to consumers. The comment noted that an attitude and usage survey conducted in 1984 of 564 sunscreen users indicated that both of these terms seem to convey the same idea (i.e., that the product will not wash off during swimming). However, the comment stated that there was slight evidence suggesting that the term "waterproof" implies greater continued protection from the sun after being wet and that consumers preferred products that were labeled waterproof. The comment suggested that using only one term would benefit consumers. The comment asserted that because the waterproof methodology is the more stringent of the two, only products providing protection after the 80-minute water immersion tests should be allowed to make a claim and that claim should be "waterproof." The comment also suggested that the term "sweat resistant" is rarely used in labeling by any manufacturer and suggested that this term be deleted from the monograph. One comment stated that subjecting products to the more stringent standard of waterproof testing would provide a more conservative measure of the substantivity of the product and, therefore, provide the consumer with the most meaningful and accurate information on product performance.

In the Panel's recommended monograph, a "water resistant" sunscreen was described as one which

can withstand 40 minutes of water immersion (§ 352.46(a)); a "waterproof" sunscreen was described as one which can withstand 80 minutes of water immersion (§ 352.46(b)). The first comment did not submit any data or literature references demonstrating that any sunscreen products, including those described by the Panel as waterproof, occlude sweat ducts or hair follicles, or cause contact dermatitis, vesicular dermatitis, miliaria crystallina, or miliaria rubra. The Panel did not identify these conditions as occurring from the use of such products. The other comments also did not submit any data to substantiate their claims that consumers prefer the term "waterproof" or that consumers do not distinguish between "water resistant," "waterproof," or "sweat resistant." The agency therefore has no reason, based on safety concerns or consumer preference, to restrict sunscreen drug products to only "water resistant" or "waterproof" labeling claims.

The agency is concerned, nevertheless, that the term "waterproof," as used in the Panel's recommended monograph, may be confusing or misleading to consumers because of the manner in which consumers may consider this term. The term "waterproof" is defined as "impenetrable to or unaffected by water" (Ref. 1). The agency notes that the Commonwealth of Australia allows only the use of the term "water resistant" in its regulatory standards for sunscreen products (AS 2604-1986) (Ref. 2). According to the Australian Society of Cosmetic Chemists which assisted in the development of these standards, it was decided to recommend against allowing the term "waterproof" because it was an absolute claim whose meaning could be easily misconstrued by consumers (Ref. 3). The agency believes that the term "waterproof" could be interpreted by consumers to describe something that is completely resistant to water regardless of time of immersion, a meaning which is not consistent with the meaning of the term in the Panel's recommended monograph. Therefore, the agency is not proposing the labeling claim "waterproof," but is proposing instead the term "very water resistant." The term "water resistant" is defined as "resistant to wetting but not waterproof." (For a discussion of water resistant and very water resistant testing, see comment 103.)

Regarding the use of the term "sweat resistant," the agency is proposing in this tentative final monograph to permit the use of the terms "sweat resistant" or "resists removal by sweating" for a

sunscreen drug product that qualifies for the claims of "water resistant" or "very water resistant." (See comment 100.)

References

- (1) "The American Heritage Dictionary of the English Language," Houghton Mifflin Company, Boston, 1976, s.v. "water-resistant" and s.v. "waterproof."
- (2) Comment No. C82, Docket No. 78N0038, Dockets Management Branch.
- (3) Comment No. C88, Docket No. 78N0038, Dockets Management Branch.

51. In the notice of public meeting to discuss appropriate testing procedures for OTC sunscreen drug products (52 FR 33598), the agency stated that there may be situations in which use of the Panel's recommended criteria for a product to be labeled as "sweat resistant," "water resistant," or "waterproof" could lead to labeling that would be misleading to the consumer. For example, a product in the "moderate" PCD (SPF 4 to under 6) that maintained its PCD after 40 minutes of water immersion could be labeled "water resistant" whereas a product in the "ultra" PCD (SPF 15 or greater) that fell into the "maximal" PCD (SPF 8 to under 15) after the water immersion test could not. The agency was concerned that the Panel's recommended labeling would not reflect that the latter product would provide more sun protection after immersion than would the former. The agency suggested that a possible way of avoiding such a situation would be to label a product with a PCD established under the ordinary test conditions and with a PCD established under the "sweat resistant," "water resistant," or "waterproof" test conditions (52 FR 33598 at 33602).

Several comments were opposed to the idea of including two PCD's or two SPF values in the labeling of OTC sunscreen drug products. Most felt that such labeling would lead to consumer confusion. Stating that there is a history of consumer use of products with only one SPF on their label, one comment contended that providing the consumer with two numbers—one representing the SPF value before water immersion and the other after water immersion—would be confusing and would require a major re-education campaign to facilitate the public's understanding of the new labeling. Another comment stated that much effort has been made to educate the consumer to discern between waterproof and nonwaterproof products. The comment maintained that the labeling requirement for one SPF value recommended by the Panel is appropriate and represents a more conservative (and safer) approach to sunscreen products and consumer

expectations. The comment suggested that not only should one SPF number be used on the principal display panel, but also that the description "waterproof," "water resistant," or "nonwaterproof" should be used in the label to qualify the conditions under which the SPF was tested. The comment believed that such labeling would eliminate the possible confusion of the conditions to which the claims applied. Another comment suggested that the agency require a manufacturer to label a sunscreen drug product with the most conservative SPF value that reflects a product's performance. For example, if a product has waterproof properties, then the product label should display a single SPF value determined under the immersion criteria.

One comment stated that using two sets of PCD's or SPF values on a label is inherently misleading and may cause confusion because the consumer may interpret the static SPF (i.e., the initial SPF of a product before water immersion testing) as applying to the waterproof or water resistant claim on the same label. One comment argued that dual labeling is a concession to those manufacturers unable to properly formulate a product with a comparable static or waterproof SPF value. The comment added that if a dual performance standard were imposed, manufacturers would be required to double the number of exposures to each test subject or, alternatively, double the number of test subjects that must be exposed to determine the static and water immersion SPF value.

One comment stated that there is no need to provide dual labeling of static and waterproof SPF values. The comment asserted that the label of a waterproof product only needs to display the waterproof SPF value (and not the static test value). Another comment stated that current labeling of sunscreen drug products makes it clear that the SPF value on the label is the SPF that is to be expected after water immersion. Another comment stated that if a manufacturer wants to make an SPF claim higher than the postimmersion SPF value of the product, the label should not contain "water related" claims. One comment recommended that the value of the SPF be tied to claims for sweat resistance, water resistance, or waterproofing. For example, if an SPF 15 sunscreen displays the claim "water resistant," then the SPF value on the label should reflect the SPF value after 40 minutes of water immersion. Similarly, a "waterproof" sunscreen should be labeled with the SPF obtained after 80 minutes of water immersion. This

would alleviate the need for water resistance claims to be tied to PCD's. It would also eliminate the possibility of an SPF 15 sunscreen decreasing to an SPF 8 after 40 minutes of water immersion and still being labeled as "water resistant."

Conversely, two comments agreed with the agency's proposal that sunscreen drug products should be labeled with both a static and a postimmersion SPF value. One comment stated that consumers would best be served by receiving complete information regarding the degree of protection that they can expect under various conditions, and dual labeling would allow consumers to make an informed purchase decision. The comment maintained that displaying only the waterproof SPF on waterproof sunscreen drug products is potentially misleading and confusing to consumers. The comment feared that a second SPF scale for waterproof products would be created, that it would be difficult for consumers to become aware of this scale, and that consumers would not be given enough information to compare sunscreen drug products on different scales. For example, consumers trying to choose between a static SPF 25 and a waterproof SPF 15 could easily choose the higher number even though its performance in water may be worse. The comment maintained that this result would be avoided by providing the option to list both static and waterproof SPF values for products that have also been tested for waterproofing. The comment added that this option would create consumer awareness of the two scales and would provide enough information for the consumer to make a rational product selection. Another comment proposed that when both static and waterproof SPF values are available for a product, both values should be permitted on the label if there is a difference in SPF levels of more than 5.

One comment stated that it did not believe that a dual labeling of static and waterproof SPF values is necessary. However, the comment maintained that, in special situations where a manufacturer wishes to label its product with both static and waterproof SPF values that are clear, truthful, and not misleading, it should be permitted to do so. The comment added that because such situations would be relatively uncommon, the dual labeling should be optional and not required. The comment supported the concept that truthful and nonmisleading optional labeling of dual static and waterproof SPF values should be allowed but should not be required. The comment added that an SPF value

is deemed to be a static, nonwaterproof value unless the waterproof claim is affirmatively made.

The agency does not agree with the comments that dual SPF labeling of sunscreen drug products would be confusing to consumers. Although there is a history of consumer use of sunscreen products with only one SPF value in their labeling, the agency believes that displaying two SPF values on water resistant and very water resistant sunscreen drug products will help to avoid consumer confusion when trying to determine which sunscreen to purchase (e.g., whether a non-water resistant SPF 25 or a water resistant SPF 15 is a more appropriate product for use). Including both a static SPF value and a water resistant or very water resistant SPF value in the labeling of water resistant sunscreen drug products will provide consumers with more information and assist them in selecting the type of product that they desire when purchasing a sunscreen drug product. Because this information involves the SPF values of the product, the agency is proposing that it appear on the principal display panel of the labeling of the product. Furthermore, the agency does not agree with some of the comments that such labeling should be optional. If dual labeling were optional, it would be confusing to the consumer because some water resistant products might display two SPF values while other water resistant products would display only one SPF value.

One comment suggested that the description "waterproof," "water resistant," or "nonwaterproof" be used in the label to qualify the conditions under which the SPF was determined. In § 352.52(e) (2) and (3) of this tentative final monograph, the agency is proposing claims for sunscreen drug products that include "water resistant" for products that satisfy the water resistant testing procedures and "very water resistant" for products that satisfy the very water resistant testing procedures. In the absence of these claims, the agency does not believe that the consumer will expect the product to be water resistant or very water resistant. Regarding the use of the term "sweat resistant," the agency is proposing in this tentative final monograph to permit the use of the terms "sweat resistant" or "resists removal by sweating" for a sunscreen drug product that qualifies for the claims of "water resistant" or "very water resistant." (See comment 100.)

Regarding the comment that manufacturers would be required to double the number of exposures to each test subject or double the number of test

subjects if dual SPF labeling were adopted, the agency notes that water resistant and very water resistant testing requires that two SPF values be determined. As the Panel recommended in its discussion of water immersion testing (43 FR 38206 at 38263) and the agency is proposing in § 352.76 of this tentative final monograph, a sunscreen drug product must retain the same PCD after the water immersion testing as it had before water immersion testing. (See comment 101.) Therefore, for all water immersion testing, either double the number of exposures or double the number of test subjects is necessary.

In this tentative final monograph, the agency is proposing the following labeling in § 352.50, *Principal display panel of all sunscreen drug products*:

"(b) For products that satisfy the water resistant sunscreen product testing procedures in § 352.76. (1) 'Water Resistant.'

(2) 'SPF=(insert SPF value before water resistant testing) before' (select one of the following: 'sweating' or 'perspiring') 'or going into the water. SPF=(insert SPF value resulting from water resistant testing) after 40 minutes of' (select one of the following: 'sweating' or 'perspiring') 'or activity in the water.'

(c) For products that satisfy the very water resistant sunscreen product testing procedures in § 352.76. (1) 'Very Water Resistant.'

(2) 'SPF=(insert SPF value before very water resistant testing) before' (select one of the following: 'sweating' or 'perspiring') 'or going into the water. SPF=(insert SPF value resulting from very water resistant testing) after 80 minutes of' (select one of the following: 'sweating' or 'perspiring') 'or activity in the water.'

H. Comments on Labeling for Drug/Cosmetic Sunscreen Products Such as Lipsticks, Make-Up Preparations, and Lip Balms

52. Several comments suggested that certain specific types of products containing sunscreens should be exempted from some of the labeling recommended by the Panel for sunscreen drug products. One comment maintained that much of the labeling information required by the Panel's recommended monograph was developed for beach products that are used to acquire a suntan and to prevent painful sunburn. According to the comment, such labeling is "irrelevant, inappropriate, and misleading" for everyday use of nonbeach beauty products that contain a sunscreen but that are not represented for use in the prevention of sunburn.

One comment requested that everyday use, nonbeach beauty products be exempted from bearing the PCD required by the Panel in § 352.50(e) because "PCD labeling statements relate to the protection against sunburn afforded by a particular sunscreen-containing product * * * based on a Sun Protection Factor." Because nonbeach products are not represented for use in the prevention or treatment of sunburn, the comment maintained that the PCD declaration, which relates to the length of time one can intentionally be exposed to the sun without sunburning, is inappropriate. The comment stated that so long as a product containing a sunscreen ingredient is formulated to have an SPF of at least 2, the product provides an effective sunscreen and is permitted to bear claims against skin cancer and premature aging. The comment added that if declaration of the PCD is required for nonbeach products, its placement should not be required on the principal display panel.

One of the comments maintained that the general warnings recommended by the Panel in § 352.50(c)(1) are superfluous for everyday use, nonbeach products because an adult using these products would know the following: (1) That such products are for external use only and are not to be swallowed; (2) that one should avoid contact with the eyes; and (3) that one should discontinue use if signs of irritation or rash appear. One comment suggested that the specific warnings recommended by the Panel in § 352.50(c)(2)(i), "For sunscreen products providing an SPF value of 2 to under 4: Use on children under 2 years of age only with the advice of a physician," and § 352.50(c)(2)(ii), "For sunscreen products providing an SPF value of 4 or greater: Use on children under 6 months of age only with the advice of a physician," should not be required for nonbeach products. The comment asserted that the warnings appear to be designed to prompt parents to consult a pediatrician before intentionally exposing children to the sun for long periods of time. Therefore, the comment stated that these specific warnings have no relevance to everyday use, nonbeach products not labeled for the prevention of sunburn that would rarely, if ever, be used on a child under 2 years of age.

One comment stated that the directions recommended by the Panel in § 352.50(d) clearly relate exclusively to beach products. The comment suggested a simple, straightforward statement of directions, such as "Apply liberally," as sufficient for everyday use, nonbeach products.

One comment maintained that the Panel's recommended rules are designed for the labeling of sunscreen lotions, liquids, and creams that are used over large areas of the body for the prevention of sunburn. It emphasized that lip balms are formulated in a small solid stick form that is used primarily as a skin protectant on a limited, specific part of the body, and protection from the sun's rays is a significant but secondary purpose. Therefore, according to the comment, lip balms should be exempted from some of the labeling recommended by the Panel. Another comment asserted that the Panel did not take the lip balm dosage form into consideration. This comment stated that not only is it physically impossible to place all of the recommended labeling requirements on a lip balm tube, but also several of the labeling requirements are inappropriate for lip balm products.

Another comment requested that lip balms be exempted from the "Statement on Product Performance" requirements and the SPF numbering system. The comment cited the small surface area covered when lip balms are used and asserted that the SPF standards for skin protection would not apply to the lip balm's intended use on lip surfaces. The comment stated that an exemption could be based upon the designation of the product as a lip balm and/or a maximum quantity limitation such as 6 g of total ingredients or 100 milligrams (mg) of sunscreen ingredient.

Three comments suggested that the general warnings in § 352.50(c)(1) are not appropriate for lip balms. Specifically, one comment contended that the warning "For external use only, not to be swallowed" in § 352.50(c)(1)(i) is inappropriate and contradictory for lip balms. The comment asserted that people ingest minute quantities of the product under normal use conditions and that inclusion of the warning on the label would unnecessarily alarm and confuse consumers. A second comment stated that lip balms should be exempted from eye warning requirements because lip balms are not used close to the eyes. Another comment added that the warning "Avoid contact with the eyes" in § 352.50(c)(1)(ii) is unnecessary for a product that is intended for use exclusively on the lips and that is formulated in a solid dosage form that cannot be splashed into the eyes. The comment added that lip balms have been marketed for a number of years and, consequently, consumers are aware of their use and application. The comment maintained that because lip balms are applied to small areas and are

formulated with the same type base that has been used for decades without a significant number of adverse reactions, the warning "Discontinue use if signs of irritation or rash appear" in § 352.50(c)(1)(iii) should not be required for lip balms.

Another comment maintained that the warnings required by § 352.50(c)(2)(i) and (c)(2)(ii) should not apply to lip balms. Stating that although it is unlikely that the need for using a lip balm on a child 6 months of age or younger would arise, if such a need did arise, the attention of a physician would not be necessary prior to prophylactic use on the child because of the nature of the tissue and the small area involved.

One comment stated that two ingredients, padimate O and oxybenzone, present in its lip balm product have been proven nontoxic at much higher levels than those used in its formulation, and the comment cited the Panel's report to support this statement (43 FR 38239 and 38244). The comment also submitted three additional toxicity studies (Ref. 1) on its lip balm product supporting its contention that the Panel's recommended labeling is unnecessary for this product. This comment suggested placing only essential information on the label because of the limited label area, and it submitted proposed labeling for its product.

Because lip balms are not designed for use on large skin areas when swimming or sunbathing around water, one comment requested that lip balms be exempted from the directions for use recommended by the Panel. Another comment suggested the following directions for use of lip balms: "Apply liberally as needed."

The agency has tentatively determined that sunscreen-containing products (e.g., sunscreen-containing make-up preparations, skin preparations, lip balms, and lipsticks) that are not specifically indicated for the prevention of sunburn, but which only bear indications for added protection against other harmful effects of the sun such as helping to prevent lip damage, skin damage, freckling or uneven coloration, are drugs under the act. These products may contain both cosmetic and drug labeling. (See comment 27.) However, the agency agrees with the comments that such products are not adequately addressed by the Panel's recommended monograph.

When the Panel reviewed sunscreen drug products, it found that these products were used mainly for sunburn protection. The products were, for the

most part, primarily intended for use under extreme conditions, such as a day at the beach. Since then, as more information has become available regarding the adverse effects of daily exposure to the sun, more and more daily use products have been formulated to contain sunscreens. (For a further discussion of the adverse effects of sunlight, see comments 46, 53 and 56.) Such products are primarily cosmetics to which sunscreens have been added to provide protection against UV radiation. The agency now tentatively concludes that these products are drugs because they contain sunscreens and bear drug claims.

The agency believes that some of the indications recommended by the Panel in § 352.50(b)(1) (e.g., "Sunscreens to help prevent sunburn," and "Screens out the sun's harsh and often harmful rays to prevent sunburn") were intended primarily for traditional sunscreen products. Given the range of products that now contain sunscreens, these indications are not appropriate for use on all of those products. Therefore, the agency is proposing to revise the Panel's recommended § 352.50(b)(1) by adding new indications to be used on the labeling of lipsticks, make-up preparations, lip balms, and other "nonbeach" products that contain sunscreen ingredients and is moving these indications out of § 352.50. The agency is placing these indications in § 352.52 as follows: § 352.52(b)(1)(v) (Select one of the following: "Filters" or "Screens") "out the" (select one of the following: "sun's rays," "sun's harsh rays," or "sun's harmful rays") "to help prevent" (select one or more of the following: "lip damage," "skin damage," "freckling," or "uneven coloration"), and § 352.52(b)(1)(vi) (Select one of the following: "Protects from" or "Shields from") (select one of the following: "the harmful rays of the sun" or "the sun") "to help prevent" (select one or more of the following: "lip damage," "skin damage," "freckling," or "uneven coloration").

The agency agrees with the comments that the PCD labeling statements in § 352.50(e) of the Panel's recommended monograph are not appropriate or relevant to the use of "nonbeach" products such as make-up preparations, skin preparations, lipsticks, or lip balms that contain sunscreens. The agency is proposing that PCD statements for these products, as well as for other sunscreen products, be optional information that may be used in labeling if a manufacturer wishes. (See comment 44.)

The agency believes that sunscreen-containing drug products that are formulated as lip balms and lipsticks do

not require the warning "For external use only, not to be swallowed" recommended in § 352.50(c)(1)(i) of the Panel's monograph. During normal use some of the product will invariably be swallowed; therefore, the above warning might be confusing to consumers. Only minuscule amounts of a sunscreen-containing lip balm or lipstick are likely to be swallowed, and the agency believes that these amounts pose no risk to the user. Consequently, the agency tentatively concludes that the warning is not necessary for the safe use of such products. Furthermore, in the tentative final monograph for OTC skin protectant drug products published in the *Federal Register* of February 15, 1983 (48 FR 6820 at 6829), the agency also concluded that lip balm drug products do not require the warning "For external use only" to assure safe use. Therefore, in this tentative final monograph, the agency is proposing to add § 352.52(c)(3), "For products containing any ingredient identified in § 352.10 formulated as a lip balm or lipstick. The warning in paragraph (c)(1)(i) of this section is not required."

The agency believes that any sunscreen-containing drug product that may be used near the eyes should be required to display the warning in § 352.52(c)(1)(ii) of this tentative final monograph, "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water." (See comment 62.) In addition to ocular irritancy problems, a product that is not formulated specifically for the eyes could cause problems because it is not sterile. Therefore, the product should not be placed in the eyes, and consumers should be warned against "contact with the eyes" in the labeling of any product that is intended for use near the eyes. The agency is aware that, although lipsticks are not intended for use near the eyes, there are sunscreen-containing lip balms that are indicated for use on "other sunsensitive areas of the face" such as the nose (Ref. 2). Such lip balms could be used near the eyes, as could other lip balms. Consequently, the agency is proposing to require that these products display the warning.

On the other hand, the agency believes that this warning is not necessary for OTC sunscreen drug products such as lipsticks that are not normally used near the eyes. Therefore, the agency tentatively concludes that lipsticks that contain sunscreen ingredients should not be required to display the warning "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water." The agency is proposing new § 352.52(c)(4) as follows: "For products containing

any ingredient identified in § 352.10 formulated as a lipstick. The warning in paragraph (c)(1)(ii) of this section is not required."

The agency believes that the warning in § 352.50(c)(1)(iii) of the Panel's proposed monograph, "Discontinue use if signs of irritation or rash appear," is an appropriate warning for any product that contains a sunscreen ingredient. Any product intended for use on the skin may contain ingredients that cause irritation or allergic reactions in susceptible consumers. The appearance of irritation or a rash may be the result of a toxic or allergic reaction to an ingredient in a product; consumers should be adequately warned to discontinue use if such signs appear. The agency is also proposing to revise the Panel's recommended warning by adding the sentence "If irritation or rash persists; consult a doctor." (See comment 63.) Therefore, the agency is proposing the following warning in § 352.52(c)(1)(iii): "Discontinue use if signs of irritation or rash appear. If irritation or rash persists, consult a doctor." The agency is proposing to require this warning for all drug products that contain a sunscreen, irrespective of whether the product is intended for beach or nonbeach use.

The agency believes that the specific warnings proposed by the Panel in § 352.50(c)(2)(i) and (c)(2)(ii) that refer to the use of sunscreen ingredients in children are not relevant to the use of sunscreen-containing make-up products such as foundations or lipsticks that display sunscreen drug claims and that are normally used only in the adult female population. However, the agency concurs with the Panel's age limit recommendations for sunscreen-containing lip balms and skin preparations that display drug claims because such products are more likely to be used on children. The Panel found no convincing evidence that sunscreen ingredients are safe for use on children under the age of 6 months, or that sunscreen products with an SPF value of less than 4 provide reasonable protection for children between 6 months and 2 years of age. The agency has not been presented with any such evidence since the Panel completed its review. In order to be consistent with other recently published documents, the agency is deleting the Panel's recommended warnings in § 352.50(c)(2)(i) and (c)(2)(ii), as discussed below, and is including the content of the warnings in the proposed directions in § 352.52(d). (See comments 61 and 66.)

The agency agrees with the comments that the directions proposed by the

Panel are not relevant to the use of sunscreen-containing drug products, such as lip balms, make-up preparations, and skin preparations, which are not intended for beach use and do not claim to prevent sunburn. Given the similarity in products, the agency believes that the directions for skin protectants proposed in § 347.50(d) of the tentative final monograph for OTC skin protectant drug products (48 FR 6820 at 6833) are appropriate to the above dosage forms if the directions are revised to include age limitations relevant to the dosage forms. Therefore, the agency is proposing in § 352.52(d) the following directions for sunscreen-containing drug products such as lip balms, make-up preparations, skin preparations, and lipsticks:

(4) *For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52(b)(1) (v) and/or (vi) and formulated as a make-up preparation or lipstick. "Apply liberally as often as necessary."*

(5) *For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52(b)(1) (v) and/or (vi) and formulated as a lip balm or skin preparation. "Adults and children 6 months of age and over: Apply liberally as often as necessary. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."*

References

- (1) Comment No. SUP004, Docket No. 78N-0038, Dockets Management Branch.
- (2) OTC Vol. 060004

I. Comments on Indications for Sunscreen Drug Products

53. One comment stated that the primary emphasis of the Panel's report was on protection against UVB radiation but that the Panel should have addressed the question of photoprotection against UVA radiation (320 to 400 nm). The comment added that UVB radiation shorter than 310 nm contributes only 1.65 percent of the solar energy at the earth's surface. The comment maintained that although UVA radiation is less erythemogenic than UVB radiation, UVA radiation contributes to sunburn reactions when skin is exposed to the sun for prolonged periods (60 to 120 minutes). The comment stated that approximately 8 to 10 percent of the solar energy at the earth's surface is in the UVA range. The comment contended that these UVA wavelengths can stimulate the proliferation of melanocytes and the

production of new melanin, are responsible for most of the phototoxic and photoallergic skin reactions, and can contribute to wrinkling and actinic elastosis. Stating that the Panel's report contained no recommendations for the evaluation of sunscreens that absorb radiation in the UVA range, the comment offered to assist in formulating such procedures.

In response to the notice of a public meeting to discuss OTC sunscreen testing procedures (52 FR 33598) and to the January 26, 1988 meeting, the agency received several comments regarding the use of sunscreens to protect individuals against UVA radiation. One comment stated that until recently sunscreens were formulated to protect individuals against UVB radiation (290 to 320 nm) and to allow the transmission of UVA radiation (320 to 400 nm) into the skin for stimulating melanogenesis (tanning reaction). The comment stated that recent evidence appearing in recognized journals of dermatology and photobiology indicates that UVA radiation is erythemogenic and carcinogenic and that it promotes photoaging. The comment added that the growing popularity of high-intensity UVA sources for "cosmetic tanning" has raised serious concerns among dermatologists regarding the potential hazards of UVA radiation to the skin, eyes, and immune system. The comment acknowledged that "a manufacturer must obtain an IND (Investigational New Drug) application to justify its claims" for new UVA absorbing compounds. However, the comment noted that if a company manufactures a sunscreen using the "existing 21 compounds which have been approved by the FDA," the manufacturer may market a UVA sunscreen without an "IND." The comment added that the Photobiology Task Force of the AAD is interested in recommending approaches to the evaluation of UVA absorbing sunscreens and is willing to submit such recommendations to the agency if so directed.

Another comment urged the agency to reopen the administrative record to include the "labeling, evaluation, etc." of "broad-spectrum" sunscreens and to develop a detailed system for adding new active ingredients to the monograph. A third comment stated that the issues of broad spectrum sunscreens are of increasing importance to consumers, but were not directly considered in the submissions to the Panel or in the Panel's recommended rule. These issues include UVA protection and the contribution of UVA

radiation to premature aging, wrinkling, and skin cancer. The comment maintained that these issues represent a long-term, chronic health problem that should be addressed by the agency. A fourth comment requested that the agency publish a separate call for data to address sunscreens that provide UVA protection and to discuss methodologies and claims that can be made for these sunscreens.

Data and labeling regarding UVA protection were submitted to the Panel (Refs. 1 through 5), and the Panel discussed UVA radiation in its report (43 FR 38206 at 38209). Several of the 21 sunscreen active ingredients classified as Category I by the Panel have absorption spectra that extend into the UVA range. For example, dioxybenzone (260 to 380 nm) (Ref. 6), methyl anthranilate (290 to 360 nm) (Ref. 7), oxybenzone (270 to 350 nm) (43 FR 38239 and Ref. 6), sulisobenzene (270 to 360 nm) (Ref. 6), red petrolatum (260 to 380 nm) (Ref. 6), titanium dioxide (290-700 nm, UV scatter, complete block) (43 FR 38250 and Ref. 6), octyl methoxycinnamate (290 to 380 nm) (Ref. 6), and octocrylene (290 to 360 nm) (Ref. 6). Lawsone with dihydroxyacetone has been variously reported to absorb UV radiation between 290 and 400 nm (43 FR 38235) and between 290 and 340 nm (Ref. 6).

The Panel's recommended labeling claims for Category I sunscreen ingredients include claims for photoprotection against the harmful rays of the sun that cause sunburn and claims to help reduce the chance of cancer and premature aging of the skin due to the sun (43 FR 38267). However, at the time that the Panel evaluated these ingredients (1973 to 1977), UVA radiation was not commonly accepted as a significant factor in the development of these adverse effects (Refs. 8 and 9). The Panel did not differentiate between UVA and UVB radiation when discussing the adverse effects caused by the sun (43 FR 38209 through 38212). In fact, the Panel did not differentiate between UVA and UVB radiation in its labeling recommendations. For example, the Panel stated that sunscreens protect against "sunburn," the "sun's burning rays," or the "sun's harsh and often harmful rays." Since the Panel's report was published (1978), many reports have been published in the scientific literature indicating that UVA radiation, like UVB radiation, is harmful to the skin. (See comment 86.) Thus, the agency believes that consumers will benefit from labeling on OTC sunscreen drug products that clearly indicates if a

product provides protection against UVA radiation.

The agency is aware that UVA radiation contributes to both acute and chronic skin damage such as erythema, melanogenesis, carcinogenesis, drug-induced photosensitivity, photoaging, and morphological alterations of Langerhans cells (Ref. 6). Although UVB radiation is much more erythemogenic than UVA radiation, the large amount of UVA radiation present in the solar spectrum at the earth's surface results in a significant contribution to erythemogenesis. In fact, UVA radiation may contribute 15 percent of the erythema effectiveness of the solar spectrum at noon. At other times of the day, because of the greater atmospheric attenuation of shorter wavelengths with increasing zenith angle, the contribution of longer wavelengths may be relatively greater (Ref. 10). It has also been reported that UVA radiation penetrates the skin more efficiently than UVB. Approximately 40 to 50 percent of UVA radiation is transmitted through Caucasian epidermis compared to 10 to 30 percent of UVB radiation (Refs. 11 and 12). UVA radiation penetrates more deeply into the dermis than does UVB radiation (Ref. 12). In addition, the agency is concerned that sunscreens with higher SPF values allow consumers to remain in the sun for long periods of time without burning, thus increasing UVA exposure. Accordingly, protection against UVA radiation is much more important than previously realized. The agency believes that protection against UVA radiation may be as important to consumers' well-being as protection against UVB radiation.

The agency wants to ensure that a sunscreen ingredient claiming to protect consumers against UVA radiation truly offers such protection. According to a 1989 NIH consensus development statement on sunlight, UV radiation, and the skin, recent evidence suggests that the longer UVA wavelengths (i.e., UVA I, 340 to 400 nm) are less damaging than shorter UVA wavelengths (i.e., UVA II, 320 to 340 nm), but further research is needed to confirm the distinction (Ref. 13). It has been reported that long wavelength UVA radiation induces connective tissue damage that is related to human photoaging (Ref. 14) and that wavelengths longer than 340 are effective in producing tumors (Ref. 15). Sunscreen ingredients whose spectra extend only into the lower UVA range (i.e., oxybenzone and possibly lawson with dihydroxyacetone) may not absorb sufficient UVA radiation to provide an adequate level of protection against that

radiation. Thus, UVA protection claims in the labeling of products containing such ingredients would be partially false and would be misleading. To ensure that sunscreen products displaying UVA protection claims offer significant UVA protection, the agency is proposing that a Category I OTC sunscreen ingredient must have an absorption spectrum extending to 360 nm or above in order to display UVA protection claims in its labeling. A product containing such an ingredient must also demonstrate meaningful UVA protection by satisfying the UVA testing method requirements that the agency is proposing be developed and included in this rulemaking. (For a discussion of this testing method, see comment 73.) The agency requests comments on these proposals.

The agency is proposing labeling that would apply if the ingredient meets certain criteria. These criteria are: (1) the ingredient has an absorption spectrum extending to 360 nm or above in the UVA range (e.g., dioxybenzone, lawson with dihydroxyacetone, octocrylene, octyl methoxycinnamate, red petrolatum, sulisobenzene, and titanium dioxide), and (2) the product containing the ingredient demonstrates UVA protection using appropriate testing procedures that the agency is proposing be developed. The labeling for acceptable products would include the following: (Select one of the following: "Protects against," "Absorbs," "Screens out," or "Shields from") "UVA" (select one of the following: "Rays" or "radiation"). A product that contains ingredients that absorb and/or reflect both UVA and UVB radiation may also display the following labeling: "Broad spectrum sunscreen; provides protection against UVB and UVA radiation." As noted in comment 73, there is a lack of adequate information for FDA to propose a method for determining UVA protection. Accordingly, although these indications are discussed in this document for public comment, they are not currently included in the tentative final monograph. At this time, OTC sunscreen drug products may bear UVA claims provided that they (1) Contain sunscreen active ingredients that absorb UVA radiation (e.g., dioxybenzone, lawson with dihydroxyacetone, octocrylene, octyl methoxycinnamate, red petrolatum, sulisobenzene, and titanium dioxide), and (2) meet the agency's enforcement policy which allows claims that were available in labeling prior to the beginning of the OTC drug review to appear in the labeling of currently marketed products

until the rulemaking for OTC sunscreen drug products is completed, and the regulation for this class of products becomes effective (Ref. 16).

The agency does not believe that a separate call for data is necessary to address OTC sunscreens that provide UVA protection. Some data have already been submitted to this rulemaking, and this publication informs interested persons how the agency is proceeding. Any interested person may submit data and information in response to the publication of this proposed rule. If necessary, an amendment to this tentative final monograph will be published in a future issue of the Federal Register to address any comments concerning UVA claims and testing procedures received in response to this proposal.

The agency emphasizes that ingredients not included in the monograph, and new chemical entities that protect against UVA exposure, are considered to be new drugs; as new drugs they must be the subject of an approved application before they may be marketed in the United States with UVA claims. The agency's detailed comments on the data are on file in the Dockets Management Branch (Ref. 17).

References

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- (4) OTC Vol. 060135.
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UVB to Connective Tissue Damage in Hairless Mice," *The Journal of Investigative Dermatology*, 84:272-276, 1985.

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(15) Cole, C.A., P.D. Forbes, and R.E. Davies, "An Action Spectrum for UV Photocarcinogenesis," *Photochemical and Photobiology*, 43:275-284, 1986.

(16) "Food and Drug Administration Compliance Policy Guides 7132b.15 and 7132b.16," in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(17) Letters from W.E. Gilbertson, FDA, to T.P. Koestler, Westwood Pharmaceuticals, Inc., K.M. O'Brien, Schering-Plough Corporation, S. Kortschak, Mary Kay Cosmetics, Inc., N.J. Lowe, UCLA School of Medicine, M. A. Pathak, Harvard Medical School, coded LET44, LET46, LET48, LET49, and LET51, respectively, in Docket No. 78N-0038, Dockets Management Branch.

54. One comment suggested that the first sentence of the indications section (§ 352.50(b)) be revised as follows: "The labeling of the product contains a statement of the indications under the heading 'Indication(s)' and is limited to one or more of the following phrases, which may be combined to eliminate duplicative words or phrases." The comment contended that the phrase "which may be combined to eliminate duplicative words or phrases" appears in other OTC drug monographs and allows the inclusion of all pertinent information without redundancy.

The agency agrees that wherever practicable duplicative words and phrases in the indications should be eliminated. The agency has applied this principle in developing the indications proposed in this tentative final monograph. The agency has combined some of the Panel's recommended indications, revised others, and provided several optional ways for stating some indications. (See comments 56, 57, and 58.) Additionally, the agency has revised its labeling policy to allow for more alternatives in stating the indications for all OTC drug products. (See comment 39.) Therefore, it is not necessary to make the revision suggested by the comment.

55. One comment believed that sunscreen drug products with an SPF of 2 should not be allowed to make a claim for sunburn protection. The comment felt that the laboratory conditions under which an SPF is determined are

artificial and are not likely to duplicate actual usage conditions. The comment stated that sunbathers apply sunscreens while in constant physical activity, and therefore rubbing against clothing, towels, etc., is almost unavoidable. This activity plus high temperature, humidity, and sweating collectively reduce the efficacy of a sunscreen in sunlight. The comment submitted a published paper (Ref. 1) discussing studies that it contended found a poor correlation between the indoor (laboratory) SPF value and the SPF value determined in sunlight. The SPF value determined in sunlight was significantly lower, which the authors attributed to heat, perspiration, etc., during outdoor testing. Thus, according to the comment, a product with a laboratory SPF of 2 will provide virtually no protection in sunlight, and a consumer using such a product will have "a false sense of safety." The comment stated that it is widely recognized that chronic UV radiation damage is a cumulative phenomenon, with every exposure contributing to the final damage. The comment contended that individuals who are allegedly "not-sun-sensitive" and use sunscreen products with low SPF values are at risk if they use products with an SPF of 2. The comment stated that every effort should be made to "spare" individuals from unnecessary UV exposure and, therefore, the lowest allowable SPF value should be 4.

The Panel discussed various skin types and the categories of sunscreen products recommended for each skin type (43 FR 38206 at 38213 to 38215). The Panel determined that there are six skin types based on the different reactions of individuals to sunlight, i.e., whether they burn easily, moderately, or not at all. Of the six skin types, the Panel listed three types, i.e., IV, V, and VI, for individuals who burn minimally, rarely burn, or never burn. For Skin Types IV and V, the Panel recommended sunscreen products that provide a minimal amount of protection with SPF values of 2 to under 4. For individuals with Skin Type VI, the use of a sunscreen product was not recommended.

Because there is a population who could use sunscreen products providing minimal protection, the agency believes that it would be inappropriate to eliminate these products from the marketplace. Such products offer protection to those individuals who burn minimally or rarely burn. Therefore, the agency does not accept the comment's recommendation. The agency is proposing a product category designation of "minimal" for sunscreen

drug products that have an SPF value of 2 to under 4 and offer minimal protection against sunburn. As part of required labeling information, the agency is proposing a Recommended Sunscreen Product Guide that will provide consumer information on skin types and corresponding recommended SPF values of sunscreen drug products. (See comment 43.)

The agency has considered the paper submitted by the comment that shows a difference between the indoor (laboratory) SPF value and the outdoor (sunlight) SPF value (Ref. 1). The agency notes that the authors stated that the study demonstrated that the solar simulator can accurately reproduce the sunburn erythemogenic effect of natural solar radiation. However, the authors also stated that factors other than UV radiation enter into the determination of the SPF of a sunscreen product (e.g., environmental factors, such as skin temperature). The authors contended that if these environmental conditions are controlled, the SPF value obtained with a solar simulator is similar to that obtained using natural sunlight. A later study by some of the same authors (Ref. 2) showed good correlation between the indoor and outdoor SPF's of sunscreens with high substantivity. (See comment 79 for further discussion of this subject.)

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(2) Sayre, R.M., et al., "Performance of Six Sunscreen Formulations on Human Skin," *Archives of Dermatology*, 115:46-49, 1979.

56. Several comments urged the agency to adopt the Panel's recommended labeling in § 352.50(b)(1)(iv) that states, "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of these harmful effects," and in § 352.50(b)(1)(v) that states, "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of premature aging of the skin and skin cancer." One comment noted that a final rule published in the *Federal Register* of April 29, 1977 (42 FR 22018) required a warning on the labels of aerosolized products containing chlorofluorocarbons. In that rule, the agency stated that the use of aerosols containing those ingredients could contribute to degradation of the earth's ozone layer, resulting in an increase in UV radiation and a possible increase in

skin cancer. The comment stated that in recognizing the risk of skin cancer from exposure to UV radiation in that document, the agency advocated educating the public on the risk of excessive exposure to the sun. Stating that this "warning/indication" labeling is based on clear and convincing scientific evidence, the comment objected to the Commissioner's statement in the preamble to the Panel's report (43 FR 38206) that this labeling might be misleading or confusing to consumers.

A second comment contended that the Commissioner based his statement concerning the aging/cancer warning/indication labeling in part on a minority report of three of the seven Panel members, who were opposed to the use of these statements. The comment argued that the minority report did not question the conclusion of the Panel majority. According to the comment, the minority report addressed the majority's presupposition that a person will use a sunscreen product correctly and that there may be skin alterations not yet manifested that could result in skin cancer whether or not the product is used. With respect to pre-existing skin conditions that could lead to cancer, the comment stated that "no drug product will aid in the prevention of a disease condition once that condition has occurred." The comment further stated that the minority report did not fully consider the language of these statements. The comment explained that, although the statements inform the consumer that the product may help prevent the harmful effects of the sun, they do not promise that the product will absolutely prevent the harmful effects. The comment urged the Commissioner to discount the minority report and to adopt the labeling recommended by the Panel majority. The comment concluded that the proposed statements would be an effective means of educating the public to use a sunscreen product early, regularly, and liberally in order to minimize the detrimental effects of long-term overexposure to UV radiation from the sun.

The comment also suggested adding to the above statements terminology that describes premature aging of the skin due to overexposure to UV radiation, e.g., "wrinkling of the skin." Noting the Panel's statement that "Premature aging of the skin refers to the thinning, dryness, and fine wrinkling produced by the exposure of the skin to sunlight" (43 FR 38206 at 38211), the comment contended that addition of such information to the Panel's recommended statements would aid

consumers' understanding of the consequences of overexposure to the sun, and would implement the Panel's recommendations.

Two comments objected to labeling sunscreen drug products with claims concerning premature aging of the skin and skin cancer. One comment maintained that such labeling is unnecessary because everyone knows that exposure to the sun may lead to premature skin aging and skin cancer. The other comment stated that sunscreen products will not prevent skin cancer on skin that sunburns easily. This comment argued that any mention of helping to prevent cancer on the label of sunscreen products should be avoided because it may mislead people into a false sense of security. Referring to a sunscreen lotion labeled with the statement "May help prevent harmful effects * * * skin cancer," the comment recommended that the qualifying phrase "Not in high altitude" be added to the label. Referring to personal experience, the comment added that a basal cell epithelioma still developed even though a sunscreen lotion was used all summer and sun exposure was avoided between the hours of 10:00 a.m. and 4:00 p.m.

Three comments supported the indication "may reduce harmful effects of the sun" recommended by the Panel minority (43 FR 38212). One comment added that the recommended indication would be good if the word "may" is legible because consumers do not read fine print. A second comment suggested combining this indication with part of the Panel's recommended indications in § 352.50 (b)(1)(iv) and (b)(1)(v), as follows: "May reduce harmful sun rays that may lead to premature aging of the skin and skin cancer." A third comment suggested that the recommended indications in § 352.50 (b)(1)(iv) and (b)(1)(v), which refer to "liberal and regular use," should be revised to state "proper and regular use" or "when used regularly as directed."

Another comment contended that the wording of the Panel's recommended statements in § 352.50 (b)(1)(iv) and (b)(1)(v) will be exploited by advertisers and that consumers will be misled. The comment stated that it agreed to a certain extent with the report of the Panel minority (43 FR 38206 at 38212) in that "any claim of this nature should only be approved if it is supported by experimental data." According to the comment, it is not scientifically correct to state that any sunscreen will reduce the harmful effects of the sun because the protection afforded by a sunscreen product with an SPF value of 8 or more (PCD designation maximal, ultra) is

being equated with that afforded by a product having an SPF value of 2. In addition, the comment stated that the term "skin cancer" in the indication statement should be changed to "nonmelanoma skin cancer" because the claim that the regular use of sunscreens may help reduce the chance of melanoma skin cancer should be investigated before approval. Stating that the word "nonmelanoma" has no meaning to consumers, a reply comment disagreed with the recommendation that "skin cancer" be changed to "nonmelanoma skin cancer." The reply comment also contended that even an SPF of 2 will provide twice the skin's natural protection from disease states that may be caused by long-term overexposure to UVB radiation.

The agency has reviewed recently published literature (Refs. 1 through 11) that was not available to the Panel. This literature supports the Panel's view that (1) exposure to sunlight/UV radiation is related to skin cancer and premature aging (i.e., skin aging), and (2) the regular use of sunscreens will reduce individuals' risk of skin aging and skin cancer due to the sun (43 FR 38206 at 38210 to 38211). The Panel recommended that the labeling of sunscreen drug products should alert the consumer to the harmful effects of sunlight (43 FR 38211); however, the indications suggested by the Panel in § 352.50 (b)(1)(vi) and (b)(1)(vii) of its monograph are optional labeling. The agency agrees with the Panel that consumers should be alerted to the risks of premature skin aging and skin cancer due to exposure to the sun. The agency also agrees with one comment that such labeling would be an effective means of educating the public to use sunscreens to minimize the detrimental effects of long-term exposure to the sun. Because of the seriousness of these adverse effects, the agency is proposing labeling in this tentative final monograph that will require all sunscreen drug products to inform consumers that the sun may damage the skin and that using sunscreens may help to reduce the risk of damage. After carefully considering the Panel's recommendations in § 352.50 (b)(1)(iv) and (b)(1)(v), which identified the risks of skin aging and skin cancer due to the sun, the recommendations of the Panel minority which did not identify the specific risks (43 FR 38206 at 38212), the available literature (Refs. 1 through 11), and the comments regarding these labeling recommendations, the agency is proposing to revise the Panel's recommendations in § 352.50 (b)(1)(iv) and (b)(1)(v) (as described below) and

including the revised statement in § 352.52(e)(6) of this tentative final monograph.

The agency disagrees with the comment that stated that the indications that warn of harmful effects of the sun should not apply to all sunscreens, because sunscreens with low SPF values are not equivalent in protection to sunscreens with high SPF values. While the use of sunscreens with high SPF values provides greater protection from the harmful effects of the sun, any reduction in exposure to the sun, regardless of SPF value, may be of benefit in reducing the risks of harmful effects. Furthermore, consumers with nonsensitive skin who only need to use sunscreens with low SPF values should also be warned of the harmful effects of sunlight. In addition, the agency believes that a statement relating to the harmful effects of the sun should be required in the labeling of all sunscreen drug products.

The agency does not agree that the indications recommended by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v) should warn the consumer that the sunscreen product will not help protect the consumer from skin cancer at high altitudes. The amount of incident light is affected by many factors, only one of which is altitude. While the comment has merit, the agency finds it impractical to include in the labeling just one of many factors that may increase exposure. Further, this information could be misleading unless all factors that may increase exposure were included. The agency sees no reason to require such labeling. However, the agency is not opposed to such descriptive information appearing in the labeling of sunscreen drug products if manufacturers wish to include it, provided that the information does not appear in the required labeling, is truthful, and is not misleading.

The agency does not believe that "premature aging" of the skin should be defined as "wrinkling" in the indications recommended by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v). Wrinkling is only a part of the process of premature aging of the skin due to excessive exposure to UV radiation and should not be elevated to greater significance than other signs of premature skin photoaging. In addition to wrinkling, photoaged skin displays a variety of benign, premalignant and malignant neoplasms, accentuated skin furrows, sags and bags, and a leathery, nodular, yellow surface with telangiectatic (i.e., a vascular lesion formed by the dilation of a group of small blood vessels) tracteries. The most drastic of these visible aspects reflect

the profound structural changes in the dermis (Ref. 5). (For a discussion of the agency's tentative conclusion regarding the use of the term "anti-aging" or similar terms in the labeling of OTC sunscreen drug products, see part II, paragraphs B.51, 52, and 53—Summary of the Agency's Changes.)

The agency believes that changing the term "skin cancer" to "nonmelanoma skin cancer" in the indications recommended by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v), as suggested by one comment, is unnecessary. Most consumers are not likely to recognize the term or would need a specific definition to decide whether or not to use sunscreens to help reduce the chance of skin cancer. To avoid misleading those consumers who are aware of specific types of skin cancer, the agency is proposing language that refers to "some types of skin cancer" rather than "skin cancer."

The agency agrees with one of the comments that the indications proposed by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v) should be revised and is proposing to replace the Panel's recommended phrase "the liberal and regular use over the years" with the phrase "regular use * * * over the years" because regular use is more important than liberal use. The agency notes that proper use of some sunscreen formulations does not require "liberal" application. In this tentative final monograph, the agency is proposing directions for OTC sunscreen drug products that are applicable to various dosage forms. (See comment 66.)

Because this proposed statement combines the attributes of an indication and a warning and is informational in nature, the agency believes that the statement should stand on its own and be distinctive in labeling. The agency is aware that some marketed products contain labeling entitled "Red Alert" to remind consumers to avoid the sun when the skin begins to burn (turn red). The agency agrees with using the term "ALERT" to readily gain consumers' attention when reading a label. However, the agency believes that for these products the term "SUN ALERT" is more informative to consumers. Further, consumers should be advised to be careful regarding all sun exposure, not only exposure after the skin has begun to burn. Therefore, in this tentative final monograph, the agency is proposing a new heading, "SUN ALERT."

The agency is further proposing that the heading "SUN ALERT" be followed by a statement that has been developed by simplifying the "skin aging/cancer" indications recommended by the Panel

in § 352.50 (b)(v) and (b)(vi). This revision begins with a positive statement for which extensive scientific evidence exists: "The sun causes skin damage." The agency has determined that the term "overexposure," recommended by the Panel, is not necessary in this statement because any amount of sun exposure can potentially harm the skin. The amount of sun exposure that will cause harmful effects is relative to a person's skin type and predisposition to skin damage, and thus is not appropriate in labeling. The term "premature" has also not been included in the proposed statement because the agency believes that this term has different meanings to different individuals. The agency is not aware of any data showing that the term is generally understood by consumers when describing effects of the sun on the skin.

The new proposed statement includes the phrase "regular use of sunscreens over the years," which implies that any sunscreen may reduce the chance of the harmful effects due to the sun. Otherwise, the Panel's recommended statement "regular use over the years of this product" constitutes an endorsement of the specific sunscreen drug product on which the labeling statement appears. Evidence shows that any sunscreen when properly applied may help reduce the chance of the harmful effects of the sun. In addition, the term "liberal" has not been included in the statement because individual products provide adequate directions for use.

The agency invites specific comment on this proposed new "SUN ALERT" labeling statement. The agency encourages manufacturers to include this statement in the labeling of all sunscreen drug products. Until the final rule for OTC sunscreen drug products is published, manufacturers may use either the Panel's earlier recommended statement or this proposed "SUN ALERT" statement in their products' labeling. The final monograph will state the exact language that will need to be used when it becomes effective. (For further discussion of the "SUN ALERT" statement, see part II, paragraphs B.51, 52, and 53—Summary of Agency Changes.)

The agency has carefully examined the wording of the indications proposed by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v) and has revised the language to eliminate vague or unnecessary terms resulting in a single required statement. The agency believes that this statement should appear verbatim on all sunscreen drug products, regardless of any other labeling, and should be preceded by the

phrase "SUN ALERT." Any language in the product's labeling that does not relate skin aging or skin cancer as being "due to the sun" will cause the product to be misbranded under section 502 of the act (21 U.S.C. 352). (See Part II, paragraphs B.51, 52, and 53—Summary of the Agency's Changes, for labeling information that is appropriate for daily use (nonbeach products) as well as for products that are intended for occasional use (beach products).)

Therefore, in this tentative final monograph, the agency is proposing to replace the Panel's recommended § 352.50 (b)(1)(iv) and (b)(1)(v) with the following statement in § 352.52(b)(6): *For products containing any ingredient in § 352.10, the following statement may be used. "SUN ALERT: The sun causes skin damage. Regular use of sunscreens over the years may reduce the chance of skin damage, some types of skin cancer, and other harmful effects due to the sun."*

The agency is also proposing to include in § 352.52(e)(7) the following statement: *For products containing any ingredient identified in § 352.10. Any variation of the statement in § 352.52(e)(6) that does not relate skin aging or skin cancer as being "due to the sun" will cause the product to be misbranded under section 502 of the act (21 U.S.C. 352).*

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(10) "Focus on Photodamage," edited by the Skin Photodamage Foundation, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(11) Epstein, J. H., "Preventing Sun Damage," *The Skin Cancer Foundation Journal* 8:7 and 92-93, 1990.

57. One comment questioned the use of the word "before" in § 352.50(e), which states that the user may "Stay in the sun twice [4 times, etc.] as long as before without sunburning." The comment argued that "before" is very vague and could imply that a product is twice as effective as other products. The comment suggested that the statement should reflect the wording recommended by the Panel under "Additional indications" (§ 352.50(b)(2)) by stating that the user could stay in the sun two (four, six, etc.) times "longer than without sunscreen protection." Another comment suggested that the statement "Provides times your natural protection against sunburn" would be clearer than the Panel's recommended labeling.

Another comment contended that the application density used in the sunscreen testing procedures is often very different from the actual amount of sunscreen applied by a consumer during normal usage. Therefore, the claim "(this sunscreen product) provides x times your natural sunburn protection," where "x" equals the sunscreen's SPF, is usually false because the two preconditions that are necessary to support this claim are rarely met. The comment described the two preconditions as (1) the application density used by the consumer must be the same as that used in the sunscreen testing procedures, and (2) the SPF value of a sunscreen product must be the same whether tested indoors using artificial UV radiation sources or outside using the sun as the UV-radiation source.

In order to resolve this apparent dilemma, the comment suggested that the agency should disallow the claim that a sunscreen "provides x times your natural sunburn protection." The comment added that "Provides up to x times your natural sunburn protection" is a viable alternate claim. The comment maintained that if this claim were eliminated or altered as suggested, the SPF number on a product would continue to provide consumers with a means of comparing sunscreens but would be a relative, rather than an absolute, parameter for evaluating sun protection.

In § 352.50(b)(2) of its recommended monograph, the Panel included several indications that could be used in addition to the indications

recommended in § 352.50(b)(1). These additional indications are based upon a product's PCD and include two basic indications that refer indirectly to the product's SPF value. For example, in § 352.50(b)(2)(i)(f), (b)(2)(ii)(e), (b)(2)(iii)(g), and (b)(2)(iv)(e), the Panel recommended that sunscreen products could display the following indication according to their PCD: "Allows you to stay in the sun [two, four, six, or eight] times longer than without sunscreen protection." In § 352.50(b)(2)(i)(g), (b)(2)(ii)(f), (b)(2)(iii)(h), and (b)(2)(iv)(f), the Panel recommended the following: "Provides [two, four, six, or eight] times your natural protection from sunburn." In § 352.50(e)(1), *Labeling claims for Product Category Designation (PCD)*, the Panel also recommended that the following labeling statement be placed on the principal display panel of sunscreen drug products in accordance with their PCD's: " * * * (SPF [2, 4, 6, 8, or 15]). Stay in the sun [twice, 4 times, 6 times, 8 times, or 15 times] as long as before without sunburning."

The agency believes that the concept of "up to the actual SPF value of the product" suggested by the comment provides a more accurate estimate of the protection a consumer can expect from a sunscreen product than the statements recommended by the Panel. Therefore, the agency is proposing to use the wording "up to" in applicable indications. In this tentative final monograph, the agency is not proposing the Panel's recommended indications in § 352.50(b)(2)(i)(f), (b)(2)(ii)(g), (b)(2)(iii)(e), (b)(2)(iii)(f), (b)(2)(iii)(g), (b)(2)(iii)(h), (b)(2)(iv)(e), and (b)(2)(iv)(f), but is instead proposing the following indications in § 352.52 (b)(1)(iii) and (b)(1)(iv): "Allows you to stay in the sun up to (insert SPF of product up to 30) times longer than without sunscreen protection," and "Provides up to (insert SPF of product up to 30) times your natural protection from sunburn." The agency is proposing that the product's labeling display its tested SPF value, as determined by using the agency's proposed sunscreen testing procedures (see comment 45).

The agency agrees with the comment that the term "as long as before" used by the Panel in its recommended statements on product performance is vague and does not tell the consumer "before what." Moreover, the agency believes that the intent of the Panel's recommended phrase "stay in the sun [twice, 4 times, 6 times, 8 times, or 15 times] as long as before without sunburning" in the statements on product performance in § 352.50 (e)(1)(i) through (e)(1)(v) is adequately covered in the indications being proposed in

§ 352.52 (b)(1)(iii) and (b)(1)(iv) of this tentative final monograph. Therefore, the agency is not proposing the Panel's recommended phrase "stay in the sun [twice, 4 times, 6 times, 8 times, or 15 times] as long as before without sunburning" in § 352.52(e) "Statement on product performance" of this tentative final monograph. The indications that were proposed by the Panel in § 352.50 (b)(1)(iv) and (b)(1)(v) of its recommended monograph are being combined, and the combined indication is included in proposed § 352.52(b)(1)(vii). (See comment 56.)

58. Several comments contended that "tanning" and related terms with no "representation" for prevention of sunburn are not drug claims but are traditional cosmetic claims. The comments maintained that "tanning representations" may not properly be regulated in an OTC drug regulation. Accordingly, these comments suggested deleting all reference to "tanning" from the monograph and revising § 352.50(b), "Indications," to address only labeling regarding the prevention of sunburn.

One comment suggested three alternative means for regulating tanning claims. Its preferred alternative is for FDA to consider tanning claims to be cosmetic claims and to regulate them under section 602(a) of the act (21 U.S.C. 362). The comment contended that the consumer perceives "tanning" to be a cosmetic benefit in terms of a "tan equals beauty" equation. The comment recommended that manufacturers be permitted the widest latitude in placing tanning claims on the labeling of their products. The comment added that consumers will be better informed regarding the selection of suitable tanning products if information regarding skin types and the quality of tan permitted by the product is placed on the labeling. The comment stated that section 602(a) of the act gives the Commissioner authority to act if a cosmetic claim is false or misleading. The comment also contended that this approach avoids regulation where none is needed; if regulation should be needed for tanning claims, it may be implemented by proposing additional cosmetic regulations.

The second alternative suggested by the comment is that tanning claims or "representations" are descriptive of product attributes and should not be regulated as indications. Remarking that indications relate to how an active ingredient functions relative to a disease or potential disease state, the comment stated that tanning is neither a disease nor a potential disease state. The comment contended that a product's permitting of tanning and the degree,

depth, or scope of tanning are a function of the amount of sunscreen in the product and of the unique product formulation characteristics. Therefore, tanning is not an indication, but a descriptive product attribute. As a third alternative, the comment recommended that if tanning claims are included in the rulemaking as drug indications, then the monograph should be expanded to provide differential tanning information for each PCD group.

Two comments stated out that the Panel's recommended additional indications in § 352.50(b)(2)(i) and (b)(2)(ii) do not inform consumers of the degree of tanning that may be expected with minimal and moderate sunscreen products; whereas, on the other hand, the Panel allowed the following labeling for other sunscreen products: for extra sunscreen products, the phrases "limited tanning" and "extra protection;" for maximal sunscreen products, the phrases "limits tanning" and "maximal protection;" and for ultra sunscreen products, the phrases "prevents tanning" and "ultra protection." The comments added that the knowledge that individuals tan and burn to different degrees mandates that such information be provided to the consumer for all sunscreen products to permit a proper product choice. The comments argued for labeling information regarding sunscreen-containing products' tanning ability and product skin-type use information. The comments contended that without this information consumers seeking a dark, deep, or fast tan may use products that contain no sunscreens but that make claims such as "deep, dark tan."

One comment recommended that § 352.50(b)(2)(i) be expanded to include for minimal sunscreen products the statements "Permits darkest, deepest tan" and "Minimal (minimum) protection against sunburn," and that § 352.50(b)(2)(ii) be expanded to include for moderate sunscreen products the statements "Permits moderate (dark) tanning" and "Moderate protection against sunburn."

The other comment recommended that §§ 352.50(b)(2)(i) and (b)(2)(ii) be modified so that the indications will inform consumers about skin type information and the product's ability to permit increased tanning. The comment recommended that § 352.50(b)(2)(i) be expanded to include the following: "Permits fastest, darkest (maximum) tan (tanning);" "Minimal (minimum) protection against sunburn for persons who rarely burn and tan profusely;" and "Minimal (minimum) protection for persons who burn minimally and always tan well." The comment further

recommended that § 352.50(b)(2)(ii) be expanded to include the following: "Permits fast, dark (moderate) tan (tanning)," and "Moderate protection for persons who burn (sunburn) moderately and tan gradually." The comment concluded that these recommendations should only be implemented if the agency determines that tanning claims are drug claims.

Although tanning claims have traditionally been considered to be cosmetic claims, based upon numerous factors discussed below, the agency has now tentatively determined that tanning claims used in conjunction with a sunscreen ingredient are drug claims. The Panel included tanning claims in its recommended monograph for OTC sunscreen drug products because such claims are very closely related to the sunscreens ability of the products. Both the sunscreen ingredient in the product and the SPF of the product directly influence the amount of tanning that occurs (i.e., the more radiation that a sunscreen product blocks or absorbs, the less tanning that the product permits). A "tanning" product that contains a sunscreen controls a physiological process (melanogenesis), i.e., it affects the function or structure of the body and is, therefore, a drug. Even if the sunscreens activity is not mentioned in the product's labeling, its intent clearly is (1) to prevent a disease (i.e., sunburn), and (2) to affect a function of the body (i.e., prevent melanogenesis). Both of these intended uses are drug activities under section 201(g) of the act (21 U.S.C. 321(g)).

The agency agrees with one of the comments that consumers will be better informed regarding the selection of suitable sunscreen products if information related to skin types and the quality of tanning permitted by the product is in its labeling. The agency believes that tanning claims should be included in the monograph because such claims help to more fully define the skin protection qualities provided by a sunscreen drug product and help consumers to determine which product is most appropriate for them to use. Failure to provide information pertaining to the tanning potential that exists with the use of a sunscreen might encourage consumers seeking a dark, deep tan or a fast tan to use products without a sunscreen ingredient, thus exposing them unnecessarily to possible skin damage. For these consumers, a sunscreen drug product allows the acquisition of a dark tan plus, more importantly, provides protection from harmful UV radiation.

The agency disagrees with one of the comments that tanning claims are

descriptive of product attributes and, therefore, are not indications. Based upon current scientific information, the agency believes that any reference to tanning on a product that contains a sunscreen ingredient is an indication that the product will affect a function of the body, that is, prevent melanogenesis. A finding of a 1989 NIH Consensus Development Conference was that, although tanning may provide some protection against further damage by UV radiation, all evidence indicates that UV radiation-induced tanning is itself harmful to the skin (Ref. 1). Tanning is accompanied by an increase in the number of DOPA-positive melanocytes, an increase in the number and melanization of melanosomes, and an increase in dendricity of melanocytes. UV radiation also increases the transfer of melanosomes from melanocytes to keratinocytes. Following UV radiation exposure, melanosomes diffusely distributed within the keratinocytes collect above the nucleus, forming a cap over it. Hawk and Parrish (Ref. 2) state that the induction of delayed tanning (i.e., the long-lasting tan induced by repeated exposure to UV radiation) follows UVB radiation doses of about 1.5 MEDs and is probably related to UV injury to melanocytes or keratinocytes. They add that melanocytes are probably always damaged by UV radiation before melanogenesis begins because $\frac{1}{4}$ MED or less of solar-simulating radiation can lead to DNA damage in basal cells. Based on the above, the agency now considers any reference to tanning in the labeling of a sunscreen drug product to be an indication regulated by the monograph for OTC sunscreen drug products. (For further discussion of the use of "tanning" claims on sunscreen-containing products, see comment 27.)

The agency does not agree with the comments that the Panel's recommended §§ 352.50(b)(2)(i) and (b)(2)(ii) should be expanded to further inform consumers of the degree of tanning that may be expected from a sunscreen drug product. The statements recommended by the Panel are adequate to inform the consumer that sunscreen drug products that provide minimal and moderate protection also permit tanning. The agency does not believe that additional qualifying phrases or terms are necessary. The quality of tanning depends upon many things including the individual's genetic predisposition to tanning, as one comment indicated and the Panel noted (43 FR 38206 at 38210), and the length of time that the individual remains in the sun.

Therefore, the agency is proposing the tanning claims that were set out in § 352.50(b)(2)(i)(c), (b)(2)(i)(e), (b)(2)(ii)(c), (b)(2)(iii)(c), (b)(2)(iv)(b), (b)(2)(v)(b), (b)(2)(v)(e), and (b)(2)(v)(f) of the Panel's recommended monograph. These tanning claims are included in § 352.52(b)(2) "Additional indications" of this tentative final monograph and may be used in addition to the required indications in § 352.52(b)(1) if the manufacturer wishes to do so. These claims can be included in the boxed area or under "APPROVED USES" in the labeling of OTC sunscreen drug products in accordance with § 330.1(c).

The other indications recommended by one of the comments, i.e., "Minimal (minimum) protection against sunburn" and "Moderate protection against sunburn," are substantially the same as the following claims recommended by the Panel in § 352.50(b)(2)(i)(a) and (b)(2)(ii)(a): "Affords minimal protection against sunburn" and "Affords moderate protection against sunburn." The agency believes that the Panel's recommended indications can be revised to accommodate the comment's suggestion by adding the word "minimum" to the Panel's recommended indication in § 352.50(b)(2)(i)(a). In addition, the agency believes that the word "Provides" may be better understood by consumers than the Panel's recommended word "Affords" and that the words "extra" and "maximal" should be revised to "high" and "very high" to reflect the agency's proposed revision of the PCD labeling. (See comment 45.) Therefore, the agency is proposing the following indications in §§ 352.52(b)(2):

(i)(A) (Select one of the following: "Provides minimal," "Provides minimum," "Minimal," or "Minimum") "protection against sunburn."

(ii)(A) (Select one of the following: "Provides moderate" or "Moderate") "protection against sunburn."

(iii)(A) (Select one of the following: "Provides high" or "High") "protection against sunburn."

(iv)(A) (Select one of the following: "Provides very high" or "Very high") "protection against sunburn."

(v)(A) (Select one of the following: "Provides the most" or "The most") "protection against sunburn."

With regard to one comment's concern that skin type information be made available to consumers, the agency is proposing a "Recommended Sunscreen Product Guide" that includes skin type information as part of the

required labeling of OTC sunscreen drug products. (See comment 43.)

References

- (1) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference Statement, Vol. 7, Number 8, May 8-10, 1989.
- (2) Hawk, J. L. M., and J. A. Parrish, "Responses of Normal Skin to UV Radiation," in "The Science of Photomedicine," edited by J. D. Regan and J. A. Parrish, Plenum Press, New York, 1982, p. 242.

59. One comment objected to the use of indications that would state that a sunscreen drug product can completely prevent tanning. Referring to the Panel's recommended labeling for ultra sunscreen drug products (43 FR 38206 at 38214), the comment objected to the statement that the product "permits no tanning" because it is inconsistent with the scientific facts. The comment explained that the most effective products (ultra sunscreens) will significantly reduce the tanning response of an individual, but that the tanning ability of individuals varies, and this tanning ability is genetically predetermined. Explaining further, the comment added that an individual with Skin Type I or II will not tan as easily as an individual with Skin Type IV or V. The comment stated that an ultra sunscreen drug product which may not permit tanning in individuals with Skin Types I or II will certainly permit tanning, although at a reduced rate, in individuals with Skin Types IV or V. The comment requested that the statement "permits no tanning" be modified to reflect this fact. The comment suggested that this statement include the information that sunscreens with an SPF of 8 or more may not permit tanning in certain individuals (Skin Types I and II) who burn easily but tan poorly, but may permit some tanning in those individuals (Skin Types IV or V) who burn moderately or minimally. The comment also stated that tanning stimulated by UVA radiation cannot be blocked by the sunscreens that contain only the UVB absorbing active ingredients and that UVA radiation may cause tanning in individuals with a genetic predisposition and Skin Types III or IV. The Panel's recommended indications for ultra sunscreens included "Prevents tanning and sunburn" in § 352.50(b)(2)(v)(b) and "Provides the highest degree of sunburn protection and permits no tanning" in § 352.50(b)(2)(v)(e). The Panel defined ultra sunscreens as follows: "Sunscreen products that provide an SPF value of 15 or greater, offer the most protection

from sunburning and permit no suntanning," (43 FR 38206 at 38213). The Panel stated, however, that "The tanning ability of an individual is genetically predetermined and is governed by the individual's capacity to produce melanin pigment within the pigment cells (melanocytes) when stimulated by UVB and UVA," (43 FR 38210).

The agency is proposing the term "ultra high" to describe sunscreen drug products that provide the most protection from UV radiation and is defining such products in § 352.3(b)(5) as follows: "Sunscreen products that provide an SPF value of 20 to 30, offer the most protection from sunburning, and permit no suntanning." The agency agrees that sunscreen drug products with the same SPF value may completely inhibit tanning in some individuals while perhaps permitting other individuals to tan. However, the labeling of a product cannot describe all possibilities without becoming cumbersome. The agency believes that the Panel's recommended labeling that refers to the different degrees of tanning permitted by various products is appropriate to inform the consumer regarding the protective qualities of that product. Therefore, the agency is including the labeling recommended by the Panel in § 352.50(b)(2)(v)(b) of its monograph in proposed § 352.52(b)(2)(v)(B).

The agency is combining the labeling recommended by the Panel in § 352.50(b)(2)(e) and (b)(2)(f) of its monograph and is including the revised additional indication in proposed § 352.52(b)(2)(v)(E) as follows: "Provides the highest degree of" (select one of the following: "sunburn" or "sunscreen") "protection and permits no tanning."

60. One comment objected to the Panel's definition of a "sunscreen opaque sunblock" in § 352.3(c) as "An opaque sunscreen active ingredient that reflects or scatters all light in the UV and visible range * * * and thereby prevents or minimizes sunburn and sunburn." The comment argued that the definition of the term "sunblock" need not be limited to opaque substances and that this definition does not reflect what the comment felt to be consumer comprehension of a sunblock as a physical or chemical substance that prevents or minimizes sunburn. The comment stated that the Panel's recommended additional indication for ultra sunscreen products in § 352.50(b)(2)(v)(b), "Prevents tanning and sunburn," and suggested that if a sunblock prevents sunburn, and an ultra sunscreen prevents sunburn, then an

ultra sunscreen must be a sunblock. The comment recommended that "sunblock" be included as an additional indication for ultra sunscreens in § 352.50(b)(2)(v) because this term is meaningful to consumers seeking a product that will prevent sunburn.

In its discussion of sunscreen agents, the Panel classified therapeutic sunscreens into categories based upon their UV radiation screening capacity (43 FR 38206 at 38213). One of the categories adopted by the Panel in its effort to find meaningful terms to describe the use of sunscreen agents was "sunscreen opaque sunblock agent," which it defined as "an opaque agent that reflects or scatters all light in the UV and visible range at wavelengths from 290 to 777 nm and thereby prevents or minimizes sunburn and sunburn." Sunscreen active ingredients that are not opaque sunblocks act by absorbing UV radiation. These active ingredients do not necessarily absorb all UV radiation. Opaque sunblocks, however, reflect or scatter all light. Titanium dioxide is the only Category I sunscreen active ingredient recommended by the Panel that fits the definition of an "opaque agent" (43 FR 38206 at 38250). Zinc oxide, for which the agency is proposing a Category III classification, may also fit the definition of a sunblock. (See comment 36.) The Panel also noted that transparent sunblock agents are not yet available in the OTC drug marketplace. The comment did not submit any evidence supporting its contention that consumers think of a sunblock as a physical or chemical substance that prevents or minimizes sunburn. The agency believes that the term "sunblock" should refer to sunscreen drug products containing opaque sunscreen active ingredients.

The agency does not agree with the comment that if a sunblock prevents sunburn, and if an ultra high sunscreen prevents sunburn, then an ultra high sunscreen must be a sunblock. (See comment 45 for a discussion of new terminology for PCD's.) An ultra high sunscreen drug product may contain an opaque sunblock ingredient, or it may contain a sunscreen ingredient that is not an opaque sunblock ingredient so long as the final product provides an SPF of 20 to 30. A product with a high SPF may also contain an opaque sunblock ingredient or a sunscreen ingredient that is not an opaque sunblock ingredient so long as the final product provides an SPF of 12 to under 20. (For a discussion of SPF values as they relate to PCD's, see comment 45.) High and ultra high sunscreen products that contain a sunscreen opaque

sunblock ingredient may display the indication in § 352.52(b)(3) *For products containing the active ingredient identified in § 352.10(s) that provide an SPF of 12 to 30, the following labeling statement may be used: "Reflects the burning rays of the sun."*

The agency does not agree with the comment's recommendation that "sunblock" be included as an additional indication for ultra high sunscreen drug products because the term "sunblock" is not an indication for use. Rather, it is a term that is descriptive of product performance or the name of a type of ingredient that may be used in a sunscreen drug product. The agency agrees with the comment that the descriptive term "sunblock" would be informative to users of OTC sunscreen drug products. The agency believes that the term "sunblock" may be used as an additional statement of product performance on sunscreen drug products that contain the ingredient titanium dioxide and provide an SPF of 12 or higher. Therefore, the agency is proposing the following additional statement in § 352.52(e)(5) *For products containing the active ingredient identified in § 352.10(s) that provide an SPF of 12 to 30, the following labeling statement may be used: "Sunblock."*

J. Comments on Warnings for Sunscreen Drug Products

61. Two comments urged that the Panel's recommended warnings in § 352.50(c)(2) (i) and (ii) be deleted. The warning in § 352.50(c)(2)(i) states that sunscreen products providing an SPF value of 2 to under 4 should be used on children under 2 years of age only with the advice of a physician. The warning in § 352.50(c)(2)(ii) states that sunscreen products providing an SPF value of 4 or greater should be used on children under 6 months of age only with the advice of a physician. Both comments stated that these warnings would dissuade the use of sunscreens on children, with one comment adding that children are in need of greater protection from the sun than adults.

One comment contended that these warnings could communicate to the parent that it is better to expose the child to the sun with no protection than to protect the child with a sunscreen product. This comment also stated that the Panel may have recommended these warnings because of its concern about the permeability of children's skin. The comment added that in 1976 Maibach had presented data to the Panel showing that within days after birth a child's skin behaves much the same as adult skin regarding permeability (Ref. 1). According to the comment, the greater

permeability of a child's skin as compared to an adult's skin has not been established. Consequently, the comment contended that "the risks attendant to inclusion of the warning far outweigh the benefits achieved by the deletion of the warnings."

A third comment disagreed with the Panel's conclusion at 43 FR 38217 that sunscreen products should not be used on children under 6 months of age. The comment strongly recommended that sunscreen products with high SPF values be used on babies if they are exposed to direct or indirect sunlight but added that direct exposure should be avoided.

The literature and data concerning sunscreens that the Panel reviewed included information on the percutaneous penetration of drugs and chemicals in infants and young children. The Panel did not find any convincing evidence that sunscreen active ingredients are safe for use on children under the age of 6 months and recommended that sunscreen products should not be used on children under 6 months of age. The Panel also recommended that sunscreen products with an SPF value of 2 to under 4 should not be used on children under 2 years of age (43 FR 38217). In other words, only sunscreen products providing a minimum SPF of 4 should be used on children between the ages of 6 months and 2 years. All sunscreen products, regardless of their SPF value, may be used on children 2 years of age and older.

The agency believes that sunscreen products may help to protect a child under the age of 6 months from the damaging effects of sunlight. However, the possible adverse effects of sunscreen active ingredients on a child of that age also must be considered. The agency, like the Panel (43 FR 38217), is concerned that biological systems that metabolize and excrete drugs absorbed through the skin may not be fully developed in children under the age of 6 months.

The agency agrees that children between 6 months and 2 years of age need sunscreen protection. Based on this need, the agency is proposing that only sunscreens that have a minimum SPF value of 4 or more be used on children in this age group. The agency does not believe that a sunscreen with an SPF value less than 4 provides enough protection for children in this age range. The agency also believes that children under 6 months of age should not be in the sun for prolonged periods of time. Therefore, they have little or no need for sunscreens. If, by chance, an infant under 6 months of age should

need a sunscreen, the parent should ask a doctor which sunscreen to use. Therefore, the agency concurs with the Panel's age limitation recommendations for sunscreen drug products. The agency notes, however, that in the Panel's recommended monograph, the age limitations in the recommended warnings in § 352.50(c)(2)(i) and (c)(2)(ii) were also included in the directions in § 352.50(d)(1)(i) and (d)(1)(ii) (43 FR 38268). In other recently published tentative final monographs, the agency has been including age limitation information in the directions for use. Therefore, the agency is deleting the Panel's recommended warnings in § 352.50(c)(2)(i) and (c)(2)(ii), but the content of the warnings, with some minor format changes, is being proposed in the directions included in § 352.52(d). (See comment 66.)

Reference

(1) Transcript of the 27th Meeting of the Topical Analgesic Panel, November 18, 1976, pp. 4 to 44, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

62. One comment objected to the Panel's recommended warning in § 352.50(c)(1)(ii), "Avoid contact with the eyes." The comment contended that this warning might discourage consumers from using sunscreen products on the face. The comment asserted that such use of sunscreen products should be encouraged because the face is the part of the human body most often exposed to UV rays and skin cancer occurs more frequently on the face than on other parts of the body. The comment suggested the following warning instead, which, it stated, would not be so general as to discourage use of sunscreens in the eye area and would tell the consumer what to do if the product did enter the eye: "If contact with eyes occurs, flush eyes with tepid water." The comment stated that according to the Panel (43 FR 38206 at 38244), padimate O is not a primary irritant to the cornea or iris at concentrations of 2 and 5 percent; therefore, an eye-contact warning should not be required for products containing this ingredient. Adding that certain products such as lip balms with sunscreens are not indicated for use near the eyes, the comment requested that lip balms be exempt from any eye warning requirement.

The agency believes that the warning "Avoid contact with the eyes" should appear in the labeling of all sunscreen-containing products except for those products that are not intended for use around or near the eyes, such as lip balms and lipsticks. (See comment 52.) The agency considers this warning to be

necessary because most sunscreen products are used on the face and can accidentally get into the eyes. Moreover, the agency believes that a warning statement similar to that suggested by the comment would be additional useful information to a consumer because any sunscreen used on a consumer's face could get into the eyes. Similar warnings (e.g., "Avoid contact with eyes. In case of contact, flush eyes with water" and "Avoid contact with eyes, eyelids and mouth. If contact occurs, rinse thoroughly with water.") currently appear on some OTC sunscreen drug products (Ref. 1). The agency notes that the comment has included the word "tepid" in the warning to describe the type of water that should be used to rinse the eyes. However, the comment did not provide any reason for this change. The agency is not aware of any reason to specify that "tepid" water must be used. Accordingly, the agency is proposing to amend the Panel's recommended warning in § 352.50(c)(1)(ii) as follows: "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water." and to include the revised warning in proposed § 352.52(c)(1)(ii).

The agency disagrees with the comment that products containing padimate O should not be required to bear the eye-contact warning. The Panel stated that 2 and 5 percent padimate O in mineral oil was not a primary irritant to the cornea and iris of test animals. The Panel noted that, in one study, 2 percent padimate O was at the upper limit of the mild primary irritant range in regard to its effect on this conjunctiva, as hyperemia was observed. In other eye irritation studies, 5 percent padimate O caused slight redness of the conjunctiva of each test animal on the first and second days following treatment (43 FR 38244). The Panel did not review all possible sunscreen drug product formulations. The agency believes that vehicles used to formulate the various sunscreen products may have different effects on the eye(s) and might also cause irritation. Therefore, if padimate O is included in the final monograph (see preamble discussion of padimate O above), products containing this active ingredient would not be exempted from the eye-contact warning.

Reference

(1) Labeling contained in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

63. Several comments described adverse reactions resulting from the use of sunscreen drug products containing aminobenzoic acid. One comment

reported experiencing swelling of the face, swelling of the eyes causing them to close, and an allergic skin reaction after using a sunscreen drug product containing aminobenzoic acid in a cream formulation. The comment recommended that the labels of sunscreen drug products containing this ingredient display a prominent warning for the benefit of consumers with allergies. A second comment reported that several trials had shown aminobenzoic acid to sting and burn. (No supporting data or literature references were submitted.) The comment stated that only 3 percent aminobenzoic acid is allowed in Europe and that no European company uses aminobenzoic acid. The comment submitted an abstract of a presentation by Hodges, et al. (Ref. 1) regarding the sensitizing effect of aminobenzoic acid in a test on *Escherichia coli* (*E. coli*). A third comment expressed concern that the warning on a sunscreen drug product containing aminobenzoic acid was not strong enough. The comment, from a consumer who once had skin cancer, reported experiencing a rash after using the product on a substantial area of the body. The comment added that many people who will use these sunscreens have had skin cancer or very sensitive skin. A fourth comment recommended that FDA publicize safety guidelines for sunscreen ingredients and, if hazards are present, weigh these hazards against the hazards of overexposure to sun-sensitive people.

One comment requested that the agency consider labeling sunscreen drug products in clear, bold letters as either "PABA SUNSCREEN" or "NON-PABA SUNSCREEN." The comment stated that products appropriately labeled will enable consumers to choose the proper sunscreen. Two other comments disagreed with this comment. One comment stated that because PABA (i.e., aminobenzoic acid) and its derivatives are active sunscreen ingredients, they must already be listed in the labeling of OTC sunscreen drug products. The comment maintained that consumers who are concerned about the presence of these ingredients need only check the active ingredient list to ascertain their presence in the sunscreen drug product. The comment added that requiring a statement in "bold letters" is unnecessary and urged the agency not to adopt this recommendation. The other comment stated that there is no reason to treat aminobenzoic acid differently from other sunscreen active ingredients.

The agency is aware that some individuals can have moderate or acute adverse reactions to active ingredients which cause no reactions in most

people. The Panel, in reviewing the submitted literature on the safety of aminobenzoic acid, determined that the incidence of adverse reactions to aminobenzoic acid was low and individual intolerance was rare (43 FR 38206 at 38220). In the submitted abstract (Ref. 1), Hodges, et al. report on the survival levels of a repair deficient strain of *E. coli* following exposure to 313 nm UV radiation and to varying concentrations of aminobenzoic acid up to a maximum of 0.1 percent. The abstract states that the survival level of the bacteria decreases with increasing concentrations of aminobenzoic acid. The abstract does not explain how the effect of aminobenzoic acid on the survival level of a repair resistant strain of *E. coli* can be extrapolated to humans.

The agency has reviewed its adverse reaction files for the years 1979 to 1989; 14 cases of adverse reactions associated with the use of sunscreen products containing aminobenzoic acid were reported to FDA (Ref. 2). The reports show that allergic reaction, rash, pruritus, dermal exfoliation, and a few other problems occurred. However, only one report showed a serious reaction that might be attributed to aminobenzoic acid. Because the reported adverse reactions were mostly dermal problems, the agency agrees with the Panel that the appropriate warning for sunscreen products containing aminobenzoic acid would be "Discontinue use if signs of irritation or rash appear." However, the agency is proposing to add to the Panel's recommended warning additional guidance to the consumer, i.e., "If irritation or rash persists, consult a doctor." This addition to the warning is proposed in § 352.52(c)(1)(iii). The agency believes that these proposed warning statements are sufficient to alert consumers to the possibility of an allergic reaction to aminobenzoic acid or any other sunscreen active ingredient. Therefore, it is unnecessary for a product to be labeled as either a "PABA SUNSCREEN" or a "NON-PABA SUNSCREEN." In addition, the agency notes that the official name for PABA is aminobenzoic acid and that is the name that should be used in labeling (see comment 30).

References

- (1) Hodges, N.D.M., S.H. Moss, and D.S.G. Davies, "The Sensitizing Effect of a Sunscreen Agent, Para-aminobenzoic Acid, on Near Ultraviolet Induced Damage in a Repair Deficient Strain of *Escherichia coli*," abstract of a paper presented at the 7th International Congress on Photobiology, September 1976, Rome.
- (2) Department of Health and Human Services, Food and Drug Administration,

Adverse Reaction Summary Listings for the years 1979 to 1989, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

64. In response to the January 26, 1988 public meeting at which sunscreens with SPF values above 15 and sunscreen testing methods were discussed, one comment suggested that sunscreens with SPF values of 15 or above should include ingredients that offer UVA protection or prominently state that the product does not provide UVA protection. The comment indicated that the consumer is entitled to know if a high SPF product does or does not provide substantial protection against UVA because the scientific literature suggests that UVA is just as likely as UVB to contribute to photoaging and skin cancer and, in cases of prolonged exposure, erythema.

Another comment also indicated that the consumer is entitled to know if a high SPF product does or does not offer substantial broad spectrum protection. The comment contended that consumers purchasing high SPF products are as much interested in the antiaging and anticancer benefits of the products as they are in the erythema protection benefits. Moreover, the comment added, the proposed monograph encourages consumers to focus on photoaging and skin cancer concerns in that it permits manufacturers to claim that sunscreen drug products offer such protection. Because both UVA and UVB spectra contribute to photoaging and skin cancer, as well as erythema, the comment recommended that the agency consider requiring manufacturers to disclose the absence of UVA protection in high SPF products.

One comment was concerned that subjects taking part in the testing of high SPF sunscreen drug products will receive very high doses of intermediate and long-wave UVA radiation unless the product under test contains an agent that blocks out these wavelengths, or the solar simulator is appropriately filtered. The comment added that similar concerns apply, to some extent, to the use by consumers of products that do not include an appropriate UVA blocking agent. Another comment stated that for sunscreens with SPF values higher than 10, the amount of unfiltered UVA is such that aggression of tegument tissues is important. The comment added that this type of aggression is not detected by erythema, which is the recommended and available end point for the sunscreen testing procedures.

As stated in comment 53, the agency is aware that UVA radiation contributes to both acute and chronic skin damage

such as erythema, melanogenesis, carcinogenesis, drug-induced photosensitivity, and photoaging. Sunscreens with higher SPF values allow consumers to remain in the sun for long periods of time without burning, thus increasing UVA exposure. The agency believes that protection against UVA radiation may be as important to a consumer's well-being as protection against UVB radiation. Therefore, the agency is proposing in this tentative final monograph conditions under which an OTC sunscreen drug product may identify itself as a "broad spectrum" sunscreen. Such a product would be able to include UVA protection claims in its labeling as discussed in comment 53.

Regarding the comments' recommendation that manufacturers be required to disclose in labeling the absence of UVA protection in some high SPF products, the agency believes there is some merit to this recommendation. Persons using such products have a tendency to remain in the sun for long periods of time, with increased exposure to UVA radiation. The agency is proposing in this tentative final monograph that sunscreen drug products that provide both UVA and UVB protection be allowed to state that they are a "broad spectrum" sunscreen and that they provide protection against UVA radiation. FDA believes that the message that the comments have recommended (i.e., does not provide UVA protection) would be useful to consumers, and the agency wants to develop language that would be meaningful to consumers. (Normally, the labeling of OTC drug products does not contain "negative" statements—i.e., that the product does not do a certain thing. Some manufacturers have done so for ingredients voluntarily, e.g., "Contains no caffeine.") Possible language that could be used in this situation includes "does not provide UVA protection" or "does not provide broad spectrum protection." The agency invites further comment as to whether such information should be required in the labeling of OTC sunscreen drug products and how it could best be presented to users of these products. The agency also requests available data that show consumers' understanding and knowledge of terms such as "UVA," "UVB," and "broad spectrum" as related to sunscreen drug products. At this time, the agency is not proposing any specific language requiring a manufacturer to disclose the absence of UVA protection for a sunscreen product with an SPF value of 15 or above. The agency also invites comments as to

whether such information should appear only in the labeling of sunscreen drug products with an SPF value of 15 or above or should appear in the labeling of any sunscreen drug product not providing such protection regardless of its SPF value. The agency will address this issue further in a future issue of the *Federal Register* after evaluating the comments received.

65. One comment stated that care must be taken in recommending sunscreens for chronic use because they suppress cutaneous vitamin D₃ synthesis. To support its contention, the comment cited a recent paper by Matsuoka, et al. (Ref. 1) in which a single application of an aminobenzoic acid-containing sunscreen (SPF 8) interfered with the cutaneous synthesis of vitamin D₃.

Although exposure of the skin to UVB radiation produces a variety of pathological effects such as sunburn, immunological changes, and skin cancer, UVB radiation is essential for the endogenous production of vitamin D₃. The relationship of sunshine to vitamin D₃ and the normal growth and development of the skeleton is well known (Ref. 2). The agency is aware that there is evidence that vitamin D₃ synthesis is inhibited by the use of sunscreen drug products. However, Matsuoka, et al. (Ref. 1) stated that the effect of sunscreen drug products to limit or prevent the cutaneous production of vitamin D₃ is probably of little consequence for children and young adults who obtain adequate vitamin D nutrition from their diet and frequent exposure to sunlight. They added that the elderly, who are more prone to developing vitamin D deficiency, could increase their risk of vitamin D deficiency if they consistently apply a sunscreen before going outdoors. The authors suggested that elderly chronic users of sunscreens should be routinely investigated for vitamin D deficiency. A 1989 NIH consensus development conference basically agreed that, in the United States, sunscreen inhibition of vitamin D₃ synthesis does not present a health hazard for the pediatric population, although deficiencies may exist in elderly populations (Ref. 2). Matsuoka, et al. (Ref. 1) recommended that elderly persons who might be at risk from constant use of a sunscreen may be advised to take supplemental vitamin D₃ or to omit sunscreen use and expose their skin only to suberythral doses of sunlight. In the case of prolonged outdoor activities, a topical sunscreen may be applied immediately after the initial exposure.

The comment did not distinguish between the use of sunscreens by any age group. The agency does not believe that there should be a warning on sunscreen drug products regarding vitamin D₃ suppression, because such a warning might discourage the use of sunscreens, especially in children. Both Matsuoka, et al. (Ref. 1), and the NIH consensus development conference (Ref. 2) stated that the inhibition of vitamin D₃ synthesis by sunscreens does not present a health hazard for the pediatric population. Further, the agency considers the use of sunscreens in children to be especially important because much of the skin damage that appears in adulthood is a cumulative result of sun exposure in childhood (Ref. 3). The NIH consensus development conference stated that it is important for the public health that sunscreen drug products be used frequently and properly (Ref. 2). The agency concurs and is proposing labeling that it hopes will meet these objectives. The agency invites public comment on whether any of the above information related to the use of sunscreens by elderly persons should appear in the labeling of sunscreen drug products.

References

- (1) Matsuoka, L.Y., et al., "Sunscreens Suppress Cutaneous Vitamin D₃ Synthesis," *Journal of Clinical Endocrinology and Metabolism*, 64:1165-1168, 1987.
- (2) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference Statement, Vol. 7, Number 8, May 8-10, 1989.
- (3) Stern, R.S., M.C. Weinstein, and S.G. Baker, "Risk Reduction for Nonmelanoma Skin Cancer with Childhood Sunscreen Use," *Archives of Dermatology*, 122:537-545, 1986.
- (4) "Cancer of the Skin," edited by the Task Force on Pamphlets, American Academy of Dermatology, Evanston, IL, 1986.

K. Comments on Directions for Sunscreen Drug Products

66. Referring to the "Directions for use" in § 352.50(d), in which the Panel recommended that all sunscreen products be applied liberally, one comment contended that liberal or heavy application is not required for some formulations to be effective and, in some cases, may decrease efficacy. The comment stated that because certain vehicles "crack, peel or pill" when applied too heavily, these products require an even application to dry skin. The comment argued that, because sunscreen products are available in a variety of forms (oils, lotions, creams, sprays, etc.), the monograph should allow manufacturers to develop specific application

instructions based on clinical experience with the formulation.

The agency has reviewed the suggested changes and agrees with the comment that the proper use of some formulations does not require liberal or heavy application for the reasons stated by the comment. Therefore, to allow for variations in the application of different product formulations, the agency believes that the Panel's recommended directions in § 352.50(d) (1) and (2) may not be adequate for all types of sunscreen drug products.

To accommodate the various dosage forms of sunscreen drug products that are available, the agency is including in proposed § 352.52(d) only brief, required directions for sunscreen drug products. The monograph will also provide that manufacturers can voluntarily expand and supplement these required directions with more detailed instructions applicable to a particular product formulation and dosage form. In addition, as discussed in comment 105, the agency is proposing that manufacturers determine the waiting period (the time between applying a sunscreen drug product and exposing the test site to water, if applicable) for water resistant and very water resistant sunscreen drug products and include this information in the labeling. Accordingly, the agency is proposing the following directions in § 352.52(d):

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions". More detailed directions applicable to a particular product formulation (e.g., cream, gel, lotion, oil, spray, etc.) may also be included.

(1) *For products containing any ingredient in § 352.10 that do not satisfy the water resistant or very water resistant testing procedures in § 352.76.* "Adults and children 6 months of age and over: Apply" (select one or more of the following, as applicable: "liberally," "generously," "smoothly," or "evenly") "before sun exposure. Reapply after swimming, excessive" (select one of the following: "sweating," or "perspiring,") "or anytime after towel drying. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

(2) *For sunscreen products containing any ingredient in § 352.10 that satisfy the water resistant or very water resistant testing procedures in § 352.76.* "Adults and children 6 months of age and over: Apply" (select one or more of the following, as applicable: "liberally," "generously," "smoothly," or "evenly") "(insert appropriate time interval, if a

waiting period is needed) before sun or water exposure. Reapply after" [select one of the following: "40 minutes" (if water resistant) or "80 minutes" (if very water resistant)] "of swimming or excessive" (select one of the following: "sweating," or "perspiring,") "or anytime after towel drying. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

67. Referring to the directions for water resistant sunscreen drug products recommended by the Panel in § 352.50(d)(2)(i), one comment objected to the requirement for reapplication after 40 minutes in the water. Because a product must retain its original PCD after 40 minutes of swimming in order to qualify as water resistant, the comment found the requirement to reapply the product after this time period to be contradictory. The comment requested that the monograph be revised to allow manufacturers the option of testing to determine the minimum immersion period that would cause a reduction in the product's PCD value and then labeling the product with the reapplication instructions based on these test results.

Alternatively, the comment stated that those manufacturers not wanting to conduct further tests would be required to use the 40-minute reapplication time. The comment added that these options should also apply to the directions for waterproof and sweat resistant products. (The agency is substituting the term "very water resistant" in place of the term "waterproof" in this tentative final monograph. See comment 50.)

Another comment stated that the Australian standard, AS2604-1986, allows only the claim "water resistant," but gives reasonable scope in that the label claim can include how long consumers can stay in the water before reapplication is necessary. For example, the comment noted that several products are now claiming "water resistant for up to two hours."

The agency disagrees with the comment's suggestion that the monograph be revised to allow manufacturers to test for the minimum immersion period that would cause a reduction in the product's PCD and to include this time for reapplication of the product in the directions for use. The directions to reapply a water resistant sunscreen drug product after 40 minutes in water are based on the testing guidelines for establishing that the product is water resistant. In order to be labeled as a water resistant sunscreen drug product, the SPF value of the product after water immersion testing

must remain within the PCD range into which the product was originally categorized. This time is included in the monograph directions applicable to such a product because it ensures a safe lower limit of the effectiveness of the product.

The agency believes that permitting a proliferation of reapplication times, based upon the actual time period a product can retain its PCD while undergoing water immersion testing, would lead to consumer confusion and may be unsafe. In general, sunscreen drug products should be reapplied frequently in order to be most effective. The agency believes that consumers should be encouraged to reapply water resistant or very water resistant sunscreen drug products at minimal time intervals. A water resistant or very water resistant sunscreen drug product should enable an individual to maintain a certain level of protection from the harmful rays of the sun. This is especially important for individuals with a high risk of wash-off such as children who may be constantly in and out of the water and who may remain in a beach/pool environment for long periods of time. The agency considers two designations (i.e., water resistant for 40 minutes and very water resistant for 80 minutes) to be adequate as to the number of categories and times appropriate for the safe and effective use of such products. The agency believes that requiring the labeling to state that the product should be reapplied after 40 minutes for water resistant or after 80 minutes for very water resistant sunscreen drug products helps to ensure that consumers receive maximum protection from sunlight both when in and out of water.

Regarding the comment's statement that the options it suggested for water resistant products should also apply to very water resistant and sweat resistant sunscreen drug products, the agency agrees with the reapplication times included in the Panel's recommended directions in § 352.50(d)(2)(ii) for very water resistant sunscreen drug products. If the product maintains its PCD after 80 minutes of water immersion, it can be labeled "very water resistant" and contain directions for reapplication after 80 minutes. The agency is not including the Panel's recommended "sweat resistant" test or directions for use of products that satisfy the sweat resistance test in this tentative final monograph. A product that passes the water resistant or very water resistant tests is also permitted to make "sweat resistant" claims. (See comment 100.)

The agency believes that consumers should be directed to reapply water

resistant and very water resistant sunscreen drug products after 40 or 80 minutes, as appropriate. Therefore, the agency is including the Panel's recommended times for reapplication of water resistant and very water resistant sunscreen drug products in the directions for use of these products in proposed § 352.52(d)(2).

68. One comment recommended that labeling directions include the following statement in block letters: "FOR INFORMATION, ASK A PHARMACIST." The comment contended that consumers, especially the young, do not read directions and that a grading system for sunscreens would be confusing. The comment added that pharmacists could put up informative posters or displays and distribute leaflets prepared in English and Spanish at no cost to the government.

As discussed in comment 44, the grading system is clearly explained in the labeling recommended by the Panel and proposed in § 352.52(e). Therefore, the agency sees no need to require the labeling statement requested by the comment. The agency has stated many times that the pharmacist is a valuable source of health care information. Pharmacists are available to provide information about the grading system for sunscreens to consumers who require assistance.

L. Comments on Professional Labeling for Sunscreen Drug Products

69. Several comments requested labeling that includes indications for the use of sunscreens for pathological conditions. Some of these comments requested professional labeling, while others requested consumer labeling.

One comment stated that the Panel should have included a discussion of special types of sunscreens useful for patients with polymorphic photodermatitis, drug photosensitivity, and other types of photodermatitis. A reply comment agreed with the comment and suggested that a section for professional labeling be incorporated into the tentative final monograph to include an indication for patients with solar urticaria, polymorphic light eruptions, drug photosensitivity, and other types of photodermatitis where sunscreen therapy is indicated. The reply comment felt that the Panel recognized that some suncreening agents, such as the benzophenones, provide protection through extended wavelength regions, and that opaque sunscreens containing a physical suncreening agent, such as titanium dioxide, also provide broad-spectrum protection. This comment stated that it

"would support indications for products with an appropriate absorption spectrum for the prevention of, or decrease exacerbation of, diseased states effected by the specific spectra screened by the screening products."

One comment from a person who has systemic lupus erythematosus (SLE) stated that this condition is exacerbated by exposure to sun, fluorescent lights, X-rays, etc. The comment added that people with this problem need accurate information on sunscreen preparations, such as how often to reapply the product, ability to protect, etc. The comment expressed support for appropriate labeling of a sunscreen product that might help persons with SLE to avoid flareups of fever and pain caused by the sun's rays.

One comment stated that there was a need in the proposed labeling system for "one more category" that would be for persons with reactions such as a rash on exposure to sunlight. The comment requested labeling information that would allow persons who develop a rash on exposure to sunlight to choose an effective sunscreen product without consulting a doctor.

Although many photodermatoses have been described, the exact etiology of most of these light-related skin diseases is not known (Ref. 1). The agency does not believe that the labeling for OTC sunscreen drug products should include indications for the use of sunscreens to protect against photodermatoses. In order to prescribe the appropriate sunscreen drug product for a particular photodermatitis, it is necessary to know the action spectrum (i.e., limits of the wavelength region) that causes a particular photodermatitis (Ref. 2) because that portion of the spectrum must be blocked in order to protect against the photodermatitis. Pathak, et al. (Ref. 2) have identified various action spectra for responses of human skin to solar radiation. The condition of variegate porphyria can be caused by a range of wavelengths between 390 and 600 nm with a maximum effect between 390 and 420 nm. Drug photosensitivity reactions can be caused by wavelengths between 300 and 400 nm with a maximum reaction between 320 and 380 nm. The range of effective wavelengths implicated in certain solar urticaria is 290 to 380 nm with a maximum reaction between 290 and 320 nm (Ref. 2). In order to successfully protect against a photodermatitis with a sunscreen drug product, the agency believes that a clinical diagnosis is necessary. Sun protection measures in persons with photodermatoses must be individualized to reflect the nature of

the disorder, the causative wavelengths of sunlight, the individual's exposure habits, and the severity of the disease. The recommended measures for individuals with photodermatoses vary from disease to disease and may be very different from the recommendations for individuals without such conditions (Ref. 3). Because such determinations cannot be made by the consumer, the agency concludes that indications for the use of sunscreen drug products for protection against photodermatoses should only be made in a professional context.

Regarding professional labeling specific to photodermatoses, the comments suggested indications for special types of sunscreen products that may be useful for persons with photodermatitis. However, the comments did not provide any data to establish appropriate indications for such use. Therefore, the agency has no basis at this time for including professional or consumer labeling in the tentative final monograph. Nevertheless, the agency invites the submission of data that would establish appropriate professional labeling for sunscreen drug products for persons with photodermatitis and the other conditions described by the comments. (See comment 33.) Any data submitted on specific claims for specific sunscreen ingredients will be reviewed by the agency and addressed in the final monograph.

The agency notes that many of the conditions described by the comments may be caused by or exacerbated by exposure to UVA radiation (Ref. 2). If a Category I sunscreen ingredient is shown to have an absorption spectrum that extends to 360 nm or above in the UVA range, and a product containing that ingredient can demonstrate UVA protection using appropriate testing procedures that the agency is proposing be developed, that product may include UVA protection claims in its labeling. (See comment 53.) Such a claim would imply nonspecific protection against UVA induced photodermatoses.

References

- (1) Ippen, H., "Photodermatoses," in "The Science of Photomedicine," edited by J.D. Regan and J.A. Parrish, Plenum Press, New York, pp. 349-350, 1982.
- (2) Pathak, M., et al., "Protection of Skin Against Solar Radiation," in "The Science of Photomedicine," edited by J.D. Regan and J.A. Parrish, Plenum Press, New York, pp. 447-450, 1982.
- (3) American Academy of Dermatology Consensus Statement, "Photoaging/Photodamage as a Public Health Concern," Consensus Conference on Photoaging/

Photodamage, Boston, p. 7, March 3 and 4, 1988.

M. Comments on Combination Sunscreen Drug Products

70. One comment requested that allantoin combined with aminobenzoic acid be reclassified from Category III to Category I as a sunscreen drug product. The comment noted that the Panel accepted the safety of allantoin combined with aminobenzoic acid, but requested further chemical data affirming that this formulation is a discrete chemical entity (a complex) and not a mixture, as well as additional data confirming its effectiveness as a sunscreen complex. The comment stated this formulation is a true chemical entity as shown by (1) the IR and UV absorption curves of allantoin combined with aminobenzoic acid, and (2) the fact that the solubility of the complex is 1 to 2 percent or more, whereas the solubility of a mixture is only 0.5 to 0.75 percent. The comment added that the complex acts synergistically and contributes to the formulation's moisturizing properties. In the case of a mixture of allantoin and aminobenzoic acid, the comment contended each component acts independently and not synergistically. The comment argued that testing in over 500 subjects demonstrates that allantoin combined with aminobenzoic acid is effective, safe, soothing, moisturizing, and is an anti-irritant. The comment concluded that the submitted data confirm the safety and effectiveness of allantoin combined with aminobenzoic acid in concentrations from 2 to 6 percent with an SPF value from 6 to 15 (Ref. 1).

As mentioned by the comment, the Panel determined that allantoin combined with aminobenzoic acid is safe, but concluded that the data are insufficient to demonstrate effectiveness. The Panel recognized that allantoin-aminobenzoic acid in combination has shown sunscreens activity equivalent to aminobenzoic acid alone. However, the submitted studies did not show that the combination of allantoin and aminobenzoic acid possesses any greater sunscreen potential than aminobenzoic acid alone (43 FR 38256). In addition, data submitted to the Panel referred to allantoin combined with aminobenzoic acid as a complex; however, the studies did not show that there was complexation involved between allantoin and aminobenzoic acid or that any modification had resulted which would alter in any way the individual characteristics of the parent compounds (43 FR 38206 at 38256 to 38257).

The agency has reviewed the data submitted by the comment, which include UV and IR spectroscopy curves that were originally submitted to the Panel, and other chemical, clinical, and safety data (Ref. 1). The agency concludes that the chemical data are insufficient to demonstrate clearly that allantoin and aminobenzoic acid form a discrete chemical entity whose properties are different from those exhibited by the mixture described by the comment. From the data, it is not possible to conclude that a complex is formed that exhibits chemical and physical properties not shown by a mixture of the components. In addition, the data do not address the effectiveness of allantoin combined with aminobenzoic acid as a sunscreen agent. Therefore, the agency is proposing that allantoin combined with aminobenzoic acid remain in Category III in this tentative final monograph when labeled only as a sunscreen. The agency's detailed comments and evaluation of the data are on file in the Dockets Management Branch (Refs. 2 and 3).

The agency notes, however, that 0.5 to 2 percent allantoin is proposed as a Category I skin protectant active ingredient (see the tentative final monograph for OTC skin protectant drug products published in the *Federal Register* of February 15, 1983; 48 FR 6832) and that Category I sunscreen active ingredients may be combined with Category I skin protectants. (See comment 71.) Therefore, aminobenzoic acid, a Category I sunscreen, may be combined with allantoin, a Category I skin protectant, provided the combination is labeled as both a sunscreen and a skin protectant.

References

- (1) Comment No. C00040, Docket No. 78N-0038, Dockets Management Branch.
- (2) Letter from W.E. Gilbertson, FDA, to S.B. Mecca, Schuylkill Chemical Co., coded ANS 81/01/09 to C00040, Docket No. 78N-0038, Dockets Management Branch.
- (3) Letter from W.E. Gilbertson, FDA, to S.B. Mecca, Schuylkill Chemical Co., coded C00073/ANS, Docket No. 78N-0038, Dockets Management Branch.

71. One comment stated that the Panel discussed its desire to permit combinations of sunscreen and nonsunscreen active ingredients, but failed to provide for these combinations in its recommended monograph. To remedy this oversight, the comment recommended that the following section be established in the monograph: "*§ 352.30 Combination of sunscreen and nonsunscreen active ingredients.* Two or more sunscreen active ingredients may be combined with other active ingredients provided that the

ingredients are generally recognized as safe and effective."

Although the Panel concluded that "sunscreen active ingredients may be combined with other active ingredients, e.g., skin protectants, provided that the ingredients are generally recognized as safe and effective, i.e., Category I active ingredients" (43 FR 38206 at 38217), it did not include any such combinations in its recommended monograph nor did the comment provide any information on specific combinations. The agency's combination policy for OTC drugs in § 330.10(a)(4)(iv) provides for the combination of two or more safe and effective active ingredients when each ingredient makes a contribution to the claimed effect(s); when combining of the active ingredients does not decrease the safety or effectiveness of any of the individual active ingredients; and when the combination, when used under adequate directions for use and warnings against unsafe use, provides rational concurrent therapy for a significant proportion of the target population. In addition to the above requirements, the agency's "General Guidelines for OTC Drug Combination Products" (Ref. 1) provide that Category I active ingredients from different therapeutic categories may be combined to treat different symptoms concurrently only if each ingredient is present within its established safe and effective dosage range and the combination meets the OTC combination policy in all other respects.

In some cases, the agency believes that combination drug products containing Category I sunscreens and active ingredients from other therapeutic categories may be rational. In situations where the skin is subjected to the combined effects of the sun and wind that could result in irritating and potentially harmful effects such as chafing, cracking, and windburn as well as sunburn, the agency believes that a combination drug product containing a sunscreen and a skin protectant is a rational combination. Certain skin protectant ingredients (i.e., allantoin, cocoa butter, dimethicone, glycerin, petrolatum, shark liver oil, and white petrolatum) are used to help prevent and temporarily protect chafed, chapped, cracked, or windburned skin and lips. (See § 347.50(b)(2) of the tentative final monograph for OTC skin protectant drug products (February 15, 1983; 48 FR 6820 at 6832).) The agency notes that several products submitted to the Topical Analgesic Panel contained ingredients such as lanolin, cocoa butter, allantoin, glycerin, or petrolatum in combination with sunscreen ingredients. In addition to sunscreens

claims, these products displayed skin protectant labeling claims such as "Protects from drying by sun, wind, water," and "Moisturizes skin to help protect against dryness and chapping due to exposure to sun and wind," (Refs. 2, 3, and 4). The agency believes that the data submitted to the Topical Analgesic Panel (Refs. 2 and 3) support the safety and effectiveness of such products. Moreover, because the pharmacological action of Category I sunscreens is similar (i.e., the ingredients screen or scatter the UV radiation from the sun) and because the pharmacological action of certain skin protectants is similar (i.e., the ingredients are chemically inert compounds that form a barrier on the skin and protect it against drying and other irritations), the agency concludes that any Category I sunscreen active ingredient can be safely and effectively combined with the following Category I skin protectant active ingredients: allantoin, cocoa butter, dimethicone, glycerin, petrolatum, shark liver oil, and white petrolatum. Accordingly, the agency is proposing to include new paragraphs (b) (1) and (2) in § 352.20, to read as follows: "(b)(1) Any single sunscreen active ingredient when used in the concentration established in § 352.10 may be combined with one or more skin protectant active ingredients identified in § 347.10 (a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in subpart D of this part and provided the product is labeled according to § 352.60" and "(b)(2). Two or more sunscreen active ingredients when used in the concentrations established in § 352.20(a)(2) may be combined with one or more skin protectant active ingredients identified in § 347.10 (a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in subpart D of this part and provided the product is labeled according to § 352.60." (See comment 37 for a discussion of minimum dosage limits for combination sunscreen drug products.)

The agency does not consider all skin protectant active ingredients to be appropriate for combining with a sunscreen. Certain skin protectant ingredients (i.e., aluminum hydroxide, calamine, kaolin, zinc acetate, zinc carbonate, and zinc oxide) are indicated only for drying the oozing and weeping of poison ivy, poison oak, and poison sumac. There does not appear to be any

need to combine these ingredients with sunscreen ingredients, nor is the agency aware of any such products currently being marketed. Accordingly, such combinations are not being proposed in this tentative final monograph. However, the agency invites comment on this proposal.

The agency has determined that appropriate labeling for combination products containing sunscreen and skin protectant active ingredients would be any applicable sunscreen indication proposed in § 352.52(b) along with the skin protectant indication proposed in § 347.50(b)(2). Because consumers use a sunscreen-skin protectant drug product primarily as a sunscreen and because proper application is important to the safe and effective use of a sunscreen drug product, the combination product should be labeled with the sunscreen directions for use in § 352.52(d) of this tentative final monograph that are appropriate to the indication used on the product, the dosage form, and the substantivity of the product (e.g., a lipstick that contains a sunscreen and displays the indication "Filters out the sun's rays," should bear the following directions: "Apply liberally as often as necessary."). (See comments 52 and 66 for further discussion of these directions.) The agency does not believe that any special labeling is necessary for the warnings required on sunscreen-skin protectant drug products. The warnings for each ingredient as established in the warning sections of the respective OTC drug monographs are appropriate, except the agency does not find the general warning proposed in § 347.50(c)(3) for OTC skin protectant drug products to be necessary for sunscreen-skin protectant drug products. This warning states: "If condition worsens or does not improve within 7 days, consult a doctor." Based on the above, the agency is proposing to include the following labeling requirements for the indications and directions of sunscreen-skin protectant combination drug products in § 352.60 *Labeling of combination sunscreen drug products*, (b), (c), and (d), respectively.

"For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). In addition to any or all of the indications for sunscreens in § 352.52(b), the indication for skin protectants in § 347.50(b)(2) of this chapter should be used."

"For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The warning for skin protectants in § 347.50(c)(3) is not required."

"For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The directions for sunscreens in § 352.52(d) should be used."

The agency believes that labeling specific to combination drug products need appear only in one monograph, which should be the one most pertinent to the intended target population of the combination product. The agency believes that a drug product intended and labeled for use as a sunscreen and as a skin protectant is primarily a sunscreen and that labeling for such a product should appear in the monograph for OTC sunscreen drug products. However, the agency will include a cross-reference to this combination in the final monograph for OTC skin protectant drug products so that interested parties will know where to find the pertinent information about these products.

Similarly, a combination of a sunscreen and hydroquinone, a skin bleaching active ingredient, may be included in the final monograph for OTC skin bleaching drug products to be published in a future issue of the **Federal Register**. That combination product is primarily for skin bleaching, and its labeling is included in § 358.50 of the skin bleaching tentative final monograph. For informational purposes, the agency is proposing to include a cross-reference to that combination in § 352.20(c) of this tentative final monograph to read as follows: *"For sunscreen and skin bleaching combinations. See § 358.50 of this chapter."*

The agency does not find any other combination products containing sunscreen and nonsunscreen active ingredients appropriate at this time. The agency invites further comments and supporting data on such combination drug products.

References

- (1) Food and Drug Administration, "General Guidelines for OTC Drug Combination Products," September 1978, Docket No. 78D-0322, Dockets Management Branch.
- (2) OTC Vol. 060002.
- (3) OTC Vol. 060065.
- (4) OTC Vol. 060076.

N. General Comments on Testing Procedures for Sunscreen Drug Products

72. Several comments agreed that testing is necessary to ensure that OTC sunscreen drug products meet the standards set forth in the monograph. However, these comments argued that testing procedures should be in the form of guidelines that outline a currently acceptable method of evaluating OTC

sunscreens drug products and should not be included in the monograph. Two comments stated that the agency had proposed this approach in other OTC drug monographs such as the monograph for OTC antiperspirant drug products. Another comment stated that such an approach would be highly desirable for SPF measurement in view of the international character of the sunscreen drug products market, where many identical formulations are sold in various countries around the world.

One comment added that maintaining the testing procedures for OTC sunscreen drug products in the form of guidelines would allow a company to use either the method specified in the guidelines or any other properly validated method that can be shown to assess performance at least as accurately as the guideline method. One comment stated that once alternative methods were validated, they would enjoy the same status as the proposed guidelines without the need to be submitted and approved through a rulemaking procedure. Another comment stated that the agency should explicitly state that other validated methods, or validated modifications of the methods proposed, are acceptable provided they are shown to evaluate performance consistently with and at least as accurately as the guideline method.

Some comments argued that establishing the testing procedures for sunscreen drug products as guidelines would build flexibility into the system and allow for easier handling of advances and improvements to the testing methodology. One comment maintained that mandating specific test protocols that must be followed to substantiate efficacy tends to stifle scientific and technological investigation in these areas. The comment contended that parties affected by the rules are often unwilling to support additional research because any changes proposed would have to go through a lengthy rulemaking procedure before being accepted. The comment added that other advances would be likely to cause the whole procedure to be repeated again and again. One comment stated that it is essential to have the best data available on which to base regulatory decisions and that the best way to have current data available is to provide for new and improved testing methods to be used.

The agency does not agree with the comments that testing procedures should be guidelines rather than be included in the monograph. The agency notes that the seriousness of the consequences that may result if a consumer relies upon an inaccurately

labeled sunscreen (e.g., one that promises more protection than it actually affords) mandates that the final formulation of OTC sunscreen drug products be tested using standardized and validated testing procedures. Labeled SPF values should be based on testing conducted under the most carefully controlled conditions so that results are as accurate as possible. The outcome of an accurate and reproducible testing procedure ensures that competitive products on the market with the same SPF value provide essentially the same degree of protection. The agency believes that this can be accomplished best by requiring all manufacturers to use fully evaluated and validated testing procedures for testing the final formulation of OTC sunscreen drug products. The data from this testing need not be submitted to FDA by the manufacturer. The agency intends to use the testing procedures set forth in the final monograph for any necessary compliance testing of these products. The agency concludes that these testing procedures should be codified in the Code of Federal Regulations (CFR).

The agency agrees that it is essential to have the best data available on which to base regulatory decisions and encourages the development of new methods for testing sunscreen drug products. (See comment 53.) Properly validated, alternate methods for determining the SPF value of OTC sunscreen drug products would be acceptable so long as they have been evaluated and accepted by the agency. Such methods must be submitted to the agency as a petition under the rules established in § 10.30 of this chapter. The petition should contain data to support the modification or data demonstrating that an alternative testing procedure provides results of equivalent accuracy. All information submitted will be subject to the disclosure rules in Part 20 of this chapter. If acceptable, these alternative methods could be included in the monograph. The petition process is included in § 352.77 of this tentative final monograph.

Regarding one comment's statement that the agency had agreed to permit testing guidelines in the case of antiperspirant drug products, the agency notes that the consequences of a consumer using an ineffective antiperspirant drug product are not as serious as those that might be expected should a consumer use an ineffective sunscreen drug product. (For further discussion of the adverse effects of sunlight and the serious consequences that may occur if a consumer uses an

ineffective sunscreen, see comments 27, 53, and 56.)

Final formulation testing procedures are included in the monographs for OTC antacid drug products in 21 CFR part 331 and for OTC first aid antibiotic drug products in 21 CFR part 333. Such testing procedures are also included in the tentative final monograph for first aid antiseptic drug products published in the *Federal Register* of July 22, 1991 (56 FR33644). The agency points out that several revisions to the antibiotic testing procedures have been accomplished in a timely fashion by using the normal OTC drug review rulemaking procedures. Accordingly, the agency finds no valid reasons not to include the testing procedures for OTC sunscreen drug products in this tentative final monograph.

O. Comments on Testing Procedures for UVA Sunscreen Drug Products

73. In response to the January 26, 1988 public meeting at which sunscreen testing methods were discussed, several comments addressed testing methodologies for sunscreens that absorb UVA radiation. One comment stated that increasing concern over the long-term effects of UVA radiation has generated a new interest in the development of UVA sunscreens. Despite this concern, the comment noted that the agency had not proposed any methodology for assessing the photoprotective properties of such sunscreens. Another comment noted that there have been significant discussion and some publications regarding the appropriate way of claiming a protection factor against UVA radiation. The comment recognized that protection against UVA radiation is important for reducing the harmful effects of UVA radiation on the skin as well as for reducing the risks of photosensitization in susceptible individuals. The comment mentioned the difficulty in evaluating the direct effects of UVA radiation in nonphotosensitized individuals (a large dose of UVA radiation is needed to produce a measurable endpoint). The comment suggested the use of topical 8-methoxypsoralen (8-MOP) plus UVA irradiance as one way of determining a phototoxic protection factor (PPF) for UVA protective sunscreens. (8-MOP is one of several photosensitizing chemicals which when applied topically or taken orally causes the skin to become abnormally sensitive to certain wavelengths, usually in the UVA range.)

One comment stated that the determination of a UVA radiation-induced MED value ratio with and

without topical application of sunscreen is appropriate for assessing UVA absorbing sunscreens. However, the comment maintained that methods involving the determination of a minimum phototoxic dose ratio in the presence of a topically applied 0.1-percent solution of 8-MOP and subsequent UVA irradiation in the presence and absence of UVA absorbing sunscreens have limited value. Although the comment did not submit an alternative approach, it did assure the agency that the Photobiology Task Force of the AAD would cooperate in developing a test for evaluating UVA sunscreens.

Another comment stated that many currently marketed sunscreen products contain a UVA absorbing active ingredient. However, a universally acceptable quantitative measure of the UVA protection afforded by such products has not been established. Therefore, the comment considered it necessary for the agency to provide manufacturers with guidelines for a testing methodology for UVA absorbing sunscreens. The comment stated that published results for benzophenone-3 and Parsol 1789 demonstrate UVA protection factors ranging from slightly more than 1 to almost 5. Maintaining that the techniques used for obtaining those results involve human evaluations that include (1) measurements of 8-MOP or anthracene phototoxicity, (2) delayed erythema, (3) immediate tanning, and (4) delayed tanning, the comment added that all but the latter produce a clearly defined end-point in Type I and Type II individuals. The comment stated that although phototoxicity studies give higher protection factors than the other techniques, the erythema effectiveness spectrum for sensitized skin is different from that for normal skin, and the results obtained from phototoxicity studies cannot be extrapolated to a "normal" situation. The comment stated that, for the above reasons, delayed erythema in unsensitized subjects is the most meaningful parameter for evaluating UVA protection. The comment maintained that a UVA protection factor expressed in terms of protection against delayed erythema would be analogous to the SPF and would have similar advantages and disadvantages. The advantage is that sunburn or delayed erythema is a measurable end-point, and sunburn protection is needed. A disadvantage is that the relevance of sunburn protection to protection from skin cancer and photoaging are not known, particularly in the case of UVA radiation. The

comment acknowledged that the dose requirements for UVA erythema are high and require prohibitively long exposures. However, it maintained that this problem could be solved by using a modified solar simulator with a quartz lens that concentrates the UVA energy within a small area.

One comment claimed that the additional UVA protection afforded by higher SPF's has been advanced as the main reason to allow unlimited SPF label claims. The comment stated that if the primary benefit of SPF's over 30 is protection from UVA radiation, then a methodology should be devised to measure and quantify the amount of this protection. The comment maintained that merely raising the SPF number, which is an indication of UVB protection, is a misdirected effort toward accomplishing this goal. Another comment also recommended that the agency develop appropriate terminology for the protection factor of UVA absorbing sunscreens. Stating that the term "sun protection factor" or "SPF" is well accepted for UVB absorbing sunscreens, the comment maintained that the term "SPF" should not be applied to UVA protection.

The agency believes that including UVA protection information in the labeling of those OTC sunscreens that provide such protection is important in order to fully inform the consumer. However, currently there is no generally acceptable method for determining a meaningful UVA protection factor that is analogous to the SPF. Several methods have been used with varying degrees of success. In one study (Ref. 1), photoprotection against UVA radiation by three sunscreens was evaluated in humans, with delayed erythema, immediate pigmentation, or delayed melanogenesis used as endpoints in normal skin, in skin sensitized with 8-MOP, and in skin sensitized with anthracene. The individual protection factor for each of these endpoints was calculated as the ratio of the threshold dose in the protected skin to that in unprotected skin. UVA protection factors were found to be significantly higher in sensitized skin compared with normal skin. However, the investigators concluded that UVA protection factors obtained in sensitized skin are probably not relevant to normal skin and that pigmentation, either immediate or delayed, is a reproducible and useful endpoint for the routine assessment of photoprotection of normal skin against UVA.

In another study (Ref. 2), the UVA erythema-protective effectiveness of a sunscreen containing an investigational new drug, butyl

methoxydibenzoylmethane, in combination with a Category I OTC sunscreen, padimate O, was evaluated using subjects sensitized with 8-MOP. One portion of the study was done outdoors using natural sunlight, and the other portion was done indoors using a solar simulator. A PPF was derived from the ratio of the minimal phototoxic dose of UVA that produced delayed erythema (72 hours) on sunscreen-protected and unprotected skin. The study demonstrated that the combination of 3 percent butyl methoxydibenzoylmethane and 7 percent padimate O provided significantly greater protection than the other sunscreen formulations and that the PPF values determined indoors and outdoors were comparable. The investigator noted that this method has a number of advantages. First, it avoids the long exposure times and larger doses of UVA radiation required to produce erythema in nonsensitized skin. Second, it minimizes a potential source of error by reducing the thermal component of UVA erythema that is a consequence of long exposures with high intensity UVA sources. Third, the use of topical 8-MOP rather than oral 8-MOP to sensitize small areas of skin reduces the time of UVA exposure, the need for ocular protection, and the risk of other adverse reactions associated with systemic 8-MOP. Fourth, shorter UVA exposure times make the study more practical for both the investigator and the subject and reduce the erythemogenic effects of any contaminating UVB radiation to insignificant levels. However, the investigator also pointed out that the PPF values achieved by this method are applicable to subjects sensitized with 8-MOP and are not necessarily applicable to normal individuals.

In 1985, at the agency's request, the Dermatologic Drugs Advisory Committee evaluated a study (Ref. 3) similar to the one described above (Ref. 2) except that some of the subjects were sensitized with orally-ingested 8-MOP and others were sensitized with topically-applied 8-MOP. PPF values were derived from erythema reactions at 48 and 72 hours. Melanogenic protection factors (MPF) were derived from pigmentation responses at 12 to 14 days. The Committee agreed that the use of 8-MOP to accelerate the subject's response to UVA radiation is an acceptable method to qualitatively determine UVA protection. It also concluded that PPF values derived from 48- and 72-hour erythema reactions and MPF values derived at 12 to 14 days are appropriate endpoints.

The agency believes that a testing method similar to the one described by Lowe, et al. (Ref. 2) could be used to demonstrate that an ingredient provides protection against UVA radiation. However, at this time, the agency does not have enough information or data to propose a method for determining UVA protection in this tentative final monograph. A method should be developed and validated in the same manner as was the sunscreen testing procedure for protection against UVB radiation that is being proposed in this tentative final monograph. Any such method should clearly demonstrate that a particular product provides significant protection against UVA radiation. It should include the use of a control sunscreen preparation that absorbs UVA radiation and that can be used to assure the reliability of the testing procedure and equipment. Even though it may not result in a meaningful PPF or UVA protection factor, a standardized UVA testing method should demonstrate that a sunscreen ingredient either does or does not protect against UVA radiation. Therefore, the agency is requesting comments and data regarding an appropriate testing methodology for OTC sunscreen drug products that afford UVA protection.

At this time, the agency does not believe that it is appropriate for an OTC sunscreen drug product to display a PPF value in its labeling because a PPF value is obtained with methods that use chemically photosensitized skin and is not necessarily relevant to the protection of normal skin. Other UVA testing methods that use normal skin are not sufficiently developed or standardized to produce valid UVA protection factors. If a testing method is developed that results in a meaningful PPF or UVA protection factor, the agency will consider allowing that factor to be included in OTC sunscreen labeling. The agency's comments on the data are on file in the Dockets Management Branch (Ref. 4).

References

- (1) Kaidbey, K., and R. W. Gange, "Comparison of Methods for Assessing Photoprotection Against Ultraviolet A In Vivo," *Journal of the American Academy of Dermatology*, 16:346-353, 1987.
- (2) Lowe, N. J., et al., "Indoor and Outdoor Efficacy Testing of a Broad Spectrum Sunscreen Against Ultraviolet A Radiation in Psoralen-sensitized Subjects," *Journal of the American Academy of Dermatology*, 17:224-230, 1987.
- (3) Summary Minutes of the 26th Meeting of the Dermatologic Drugs Advisory Committee, Food and Drug Administration, November 18, 1985, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(4) Letters from W. E. Gilbertson, FDA, to T. P. Koestler, Westwood Pharmaceuticals, Inc., K. M. O'Brien, Schering-Plough Corporation, N. J. Lowe, UCLA School of Medicine, and M. A. Pathak, Harvard Medical School, coded LET45, LET47, LET50, and LET52, respectively, in Docket No. 78N-0038, Dockets Management Branch.

P. Comments on the Standard Preparation for the Testing Procedures for Sunscreen Drug Products

74. Referring to the Panel's discussion of a standard homosalate-containing sunscreen used in the method for determining SPF values (43 FR 38206 at 38259), one comment stated that the formula for this standard was prepared and evaluated by a collaborative industry group consisting of several independent industrial photobiology laboratories and investigators. The validity of the testing methodology and confirmation of an SPF value of 4 for the standard homosalate sunscreen were submitted to the Panel (Ref. 1). After the submission of these data, however, it was observed during routine shelf-life evaluations of the standard that the stability of this formulation was not adequate for use as a standard. Thus, a revised formulation with improved stability characteristics was prepared and again evaluated by five independent laboratories and investigators. Subsequently, the comment submitted the results of this testing to the agency and concluded that the "revised" formulation is more appropriate for validating the test methodology at the SPF 4 level (Ref. 2). The comment recommended that § 352.40 of the Panel's report be amended to include the revised formulation and its manufacturing directions.

The agency has determined that the improved stability characteristics of the revised 8-percent homosalate standard formulation make it more appropriate for use as a sunscreen standard than the standard preparation originally submitted to the Panel. The agency notes that the SPF of the revised preparation is 4.47 with a standard deviation of 1.279, while the SPF of the standard reviewed by the Panel was 4.24 with a standard deviation of 1.14. However, the results of the collaborative study performed on the revised formulation (Ref. 2) indicate that general agreement between laboratories performing SPF testing can be achieved using this revised standard formulation. In addition, the results from SPF testing recently submitted to the agency (Refs. 3 and 4) demonstrate the reliability of the revised 8-percent homosalate preparation. (See comment 75.) The agency is aware that the revised 8-percent homosalate formulation is

currently being used by most manufacturers of OTC sunscreen drug products as a reference control for their sunscreen testing procedures (Ref. 5). Therefore, the agency is including the revised formulation and its manufacturing directions in proposed § 352.70(a) and (b) as follows:

"(a) *Laboratory validation.* A standard sunscreen shall be used concomitantly in the testing procedures for determining the SPF value of a sunscreen product to ensure the uniform evaluation of sunscreen products. The standard sunscreen shall be an 8-percent homosalate preparation with a mean SPF value of 4.47 (standard deviation = 1.279). In order for the SPF determination of a test product to be considered valid, the SPF of the standard sunscreen must fall within the standard deviation range of the expected SPF (i.e., 4.47 ± 1.279), and the 95-percent confidence interval for the mean SPF must contain the value 4.

(b) *Preparation of the standard homosalate sunscreen.* The standard homosalate sunscreen is prepared from two different preparations (preparation A and preparation B) with the following compositions:

COMPOSITION OF PREPARATION A AND PREPARATION B OF THE STANDARD SUNSCREEN

Ingredients	Percent by weight
Preparation A:	
Lanolin	5.00
Homosalate	8.00
White petrolatum	2.50
Stearic acid	4.00
Propylparaben	0.05
Preparation B:	
Methylparaben	0.10
Edetate disodium	0.05
Propylene glycol	5.00
Triethanolamine	1.00
Purified water U.S.P.	74.30

Preparation A and preparation B are heated separately to 77 to 82 °C, with constant stirring, until the contents of each part are solubilized. Add preparation A slowly to preparation B while stirring. Continue stirring until the emulsion formed is cooled to room temperature (15 to 30 °C). Add sufficient purified water to obtain 100 grams of standard sunscreen preparation.

The agency's comments on the data are on file in the Dockets Management Branch (Ref. 6).

References

- (1) OTC Vol. 060169.
- (2) "Comparative Study on a New Standard Sunscreen Formula," Comment No. C00046,

Docket No. 78N-0038, Dockets Management Branch.

(3) Comment No. 00080, Docket No. 78N-0038, Dockets Management Branch.

(4) Comment No. 00083, Docket No. 78N-0038, Dockets Management Branch.

(5) Letter from G.N. McEwen, Jr., The Cosmetic, Toiletry and Fragrance Association, Inc., and W.W. Bradley, The Proprietary Association, to W.E. Gilbertson, FDA, coded LET75, Docket No. 78N-0038, Dockets Management Branch.

(6) Letter from W.E. Gilbertson, FDA, to J.D. Cope, Nonprescription Drug Manufacturers Association, coded LET40, Docket No. 78N-0038, Dockets Management Branch.

75. The agency's initial evaluation of the Panel's report and of the comments received raised some questions regarding the use of the 8-percent homosalate formulation as the standard for the validation of sunscreen drug product testing. Results from two collaborative studies submitted to the agency (Refs. 1 and 2) were inconsistent and produced SPF values that placed the 8-percent homosalate standard formulation into different PCD's. From this information, the agency concluded that the SPF and PCD of the 8-percent homosalate formulation had not been precisely established. Therefore, in the notice announcing a public meeting to discuss sunscreen testing procedures (52 FR 33598 at 33600), the agency reopened the administrative record. The agency asked whether new data had become available since the 8-percent homosalate standard formulation was originally tested that would provide additional information regarding the reliability of that formulation.

In response, the agency received several comments favoring retention of a revised 8-percent homosalate preparation as the standard for validation of sunscreen testing procedures (Ref. 2). (For a discussion of the revised homosalate formulation that was submitted to the agency in response to the Panel's report, see comment 74.) Two comments stated that the homosalate preparation is not a standard in the normal meaning of the word. The comments asserted that the preparation actually is a reference control to ensure that the testing facility and the equipment being used to conduct the SPF evaluations provide results within an acceptable range of variation. One comment added that use of the reference control ensures that the SPF calculated for a test product is valid and reproducible. Another comment referred to the results of interlaboratory testing of the 8-percent homosalate formulation that placed it in two different PCD's. The comment maintained that such results are not

unexpected because the nominal SPF value of the preparation is on the PCD boundary. Thus, according to the comment, these results are not in themselves an indication of excessive variation.

The comment further suggested that the sunscreen monograph contain guidelines as to how testing laboratories should use the results obtained from the testing of the "control" formulation. For example, the comment asked if all the test results should be invalidated if the "control" SPF is outside the 90-percent confidence interval expected for the control. The comment also stated that the control should be as well characterized as possible, including its physical and chemical stability.

Another comment stated that currently there is no mandatory rejection of data based upon the results of the control. Testing facilities are not required to test the 8-percent homosalate control along with each product test. The comment suggested that, for each test panel, an appropriate control sunscreen should also be tested, and the validity of the test should depend upon the results of the testing of the control sunscreen. If the results of the control sunscreen are found to be significantly different from the "nominal" value, then the sample sunscreen test should be invalid. The comment believed that such a requirement would ensure compliance by various testing laboratories to a common reference system. Another comment stated that the collaborative studies submitted previously to the Panel and the agency (Refs. 1 and 2) established consistent results among laboratories for the 8-percent homosalate standard and established its PCD as "Moderate Sun Protection" and its SPF value as 4. The comment maintained that after 12 years of consistent use of the 8-percent homosalate preparation, it was satisfied that the preparation has adequately fulfilled its purpose as a reference control. The comment added that the current 8-percent homosalate standard is the revised formulation that was previously submitted to the agency (Ref. 2). The comment was not aware of any new comparative testing done on this formulation, and stated that there was no particular need to change the current standard. The comment noted, however, that any changes regarding testing methodology, especially those affecting statistics or application density, will also affect the SPF and PCD of the 8-percent homosalate standard or any other standard that might be chosen.

Stating that it had used the 8-percent homosalate standard for the past 9 years

or more, one comment stated that it had evaluated the SPF value of this formulation in nearly 500 volunteers. The testing occurred both under indoor conditions using UV radiation from a solar simulator equipped with a xenon-arc lamp and under outdoor conditions using natural sunlight. The comment maintained that if the formulation is correctly manufactured and used within 3 to 6 months of preparation, it provides an SPF of 4.0 ± 0.5 when a solar simulator is used as the source of UV radiation. However, under outdoor conditions, the comment added that the 8-percent homosalate preparation provides an SPF of 2.5 to 3.0. Maintaining that the homosalate formulation is useful, adequate, and acceptable for use as an internal standard for testing sunscreen formulations having SPF values in the range of 4 to 8, the comment recommended that the agency retain this internal standard.

The CTFA stated in 1987 that over the past 10 years, the industry has developed a massive block of test data that substantiates the validity of the 8-percent homosalate preparation. CTFA submitted new data from sunscreen testing conducted by four laboratories during 1985 through 1987 (Ref. 3) and contended that the results show a consistent response for the homosalate control both within and between laboratories. The comment asserted that these data substantiate the reliability of the 8-percent homosalate control for sunscreen testing of products over the entire range of SPF's currently marketed. Another comment also submitted recent data and stated that these data confirm that the formula is predictable and reliable as used in its testing facilities (Ref. 4).

The agency believes that the new data (Refs. 3 and 4) that have been submitted support the reliability of the revised 8-percent homosalate standard preparation for testing sunscreens with SPF values of 15 or below. The data submitted by CTFA (Ref. 3) include information accumulated on over 1,700 subjects over 2 to 3 years by four different laboratories. These data indicate a mean SPF value equal to approximately 4, with a standard deviation around 0.7 for the 8-percent homosalate standard. The other data submission (Ref. 4) contains results from 100 subjects, with a mean SPF value of 4.35 and a standard deviation of 0.61. These data are consistent with the results of the CTFA submission (Ref. 3). The agency notes that these new data (Refs. 3 and 4) are consistent with the initial test results of the revised formulation of the 8-percent homosalate

preparation, which indicate a mean SPF of 4.47 with a standard deviation of 1.279 (Ref. 2). (See comment 74.)

The agency notes that one comment suggested that the homosalate standard is appropriate for testing sunscreens with SPF values of 4 to 8. Another comment believed that it was appropriate for sunscreen testing of products over the entire range of SPF's currently marketed. The agency agrees with the Panel that an 8-percent homosalate preparation may be used to validate the testing procedures for products with SPF's up to and including 15. However, there is currently not enough information available for the agency to determine that the use of this standard is valid for testing sunscreens with SPF values above 15. (See comments 77 and 78.)

The agency considers the 8-percent homosalate formulation not to be a standard within the normal meaning of that word. Rather, it is a control that should be used to validate the testing procedure, equipment, and facilities. As such, it plays no part in the calculation of the SPF value for the test product. However, the agency believes that the homosalate control should be tested at the same time as the test product for every SPF determination. If the SPF of the homosalate preparation is within acceptable limits of variability of the validated mean, then the SPF determined for the test product can be considered valid, if it meets all other requirements for acceptable limits of variability. The 95-percent confidence interval for the mean SPF of the data from the control product should contain the value 4. If it does not, the study should be considered invalid. These provisions are included in the sunscreen testing procedures being proposed in this tentative final monograph.

Regarding one comment's statement that the 8-percent homosalate preparation provides an SPF of 2.5 to 3.0 under outdoor conditions, the agency is not including outdoor testing procedures in this monograph. (See comment 79.) The agency's comments on the data are on file in the Dockets Management Branch (Ref. 5).

References

- (1) OTC Vol. 060169.
- (2) "Comparative Study on a New Standard Sunscreen Formula," Comment No. C00046, Docket No. 78N-0038, Dockets Management Branch.
- (3) Comment No. 00080, Docket No. 78N-0038, Dockets Management Branch.
- (4) Comment No. 00083, Docket No. 78N-0038, Dockets Management Branch.
- (5) Letters from W.E. Gilbertson, FDA, to M.B. McTernan, Johnson and Johnson, and

E.E. Kavanaugh, Cosmetic, Toiletory and Fragrance Association, coded LET39 and LET57, respectively, Docket No. 78N-0038, Dockets Management Branch.

76. Referring to the Panel's discussion of a standard sunscreen (43 FR 38206 at 38259), one comment contended that the international sunscreen testing experience with a homosalate formulation as a sunscreen standard is rather poor. The comment recommended that 5 percent PABA (aminobenzoic acid) should be used as the standard sunscreen because the international literature mentions it as a widely-known formulation. The comment asserted that in sunscreen testing it is important that the sunscreen standard have an SPF value of at least 4 or, preferably, an SPF value of 6.

The comment did not provide any literature references to support its contention that 5 percent aminobenzoic acid is frequently referred to in the international literature. Also, no data were submitted to demonstrate that 5 percent aminobenzoic acid should be preferred over the Panel's proposed 8 percent homosalate formulation as a sunscreen standard. The agency is aware that the Panel reviewed data from a collaborative study involving comparative testing of standard sunscreen products. In this study, two different sunscreen preparations containing either 8 percent homosalate or 4 percent aminobenzoic acid were tested by six laboratories (Ref. 1). The results showed that individual subjects using the 4-percent aminobenzoic acid sunscreen in an alcoholic vehicle had mean SPF values ranging from a low of 6.4 to a high of 9.7. The mean SPF value for the entire group of 60 volunteers was approximately 7, with a standard deviation of 1.61. The SPF values for the 8-percent homosalate formulation were not as scattered or as variable as the SPF values for the 4-percent aminobenzoic acid formulation. The results for the 8-percent homosalate gave an individual mean SPF that ranged from a low value of 3.8 to a maximum value of 6.0. When all the data were compiled for the homosalate formulation, the mean SPF value was 4.24 with a standard deviation of 1.14. The investigators reporting on the comparative testing of aminobenzoic acid and homosalate as sunscreen standards suggested that the 4-percent aminobenzoic acid in alcohol appears to be more difficult to spread uniformly on the test site. This difficulty might have contributed to the wide variation in the test results.

The agency is unaware of any data demonstrating that a 5-percent aminobenzoic acid formulation referred to in the comment is superior as a

sunscreen standard to the 8-percent homosalate formulation proposed by the Panel and revised by the agency.* Furthermore, additional data supporting the reliability and wide acceptance of the revised 8-percent homosalate standard were submitted to the agency in 1987 (Refs. 2 and 3). (These data are discussed in comments 74 and 75.) The agency tentatively concludes that the revised 8-percent homosalate formulation is suitable to use in the testing procedures to ensure the uniform evaluation of OTC sunscreen drug products. The agency is including the revised formulation for the 8-percent homosalate standard and directions for its manufacture in proposed § 352.70(b). (See comment 74.)

References

- (1) OTC Vol. 060169.
- (2) Comment No. C00080, Docket No. 78N-0038, Dockets Management Branch.
- (3) Comment No. C00083, Docket No. 78N-0038, Dockets Management Branch.

77. In the notice of public meeting to discuss appropriate testing methods for OTC sunscreen drug products (52 FR 33598 at 33602), the agency asked for comment and supporting data on the following question: "Can these higher SPF values be accurately determined using currently available sunscreen testing procedures?" The agency also asked for the submission of appropriate testing methods if the currently recognized sunscreen testing procedures are not considered adequate.

Six comments responded to the agency's question regarding the adequacy of using currently available testing procedures for sunscreen drug products claiming to have SPF values in excess of 15. The comments agreed that the current testing methods are adequate for evaluating such formulations. However, only two comments provided data from actual studies.

One comment (Ref. 1) submitted data on a sunscreen formulation that was tested at two different laboratories which utilized the methods found in the Panel's testing procedures in subpart C of its recommended monograph (43 FR 38206 at 38265). In one laboratory, test results from 21 subjects produced a mean SPF value of 36.88. Results from the 25 subjects tested at the second testing facility produced a mean SPF value of 34.1. The comment also submitted data on another sunscreen formulation. The test results from 20 subjects resulted in a mean SPF value of 29.16. Furthermore, the comment claimed that *in vitro* testing, consisting of optical measurement, yielded SPF values of 32 and 26.5, respectively, for these two formulations. The comment

noted that because no recognized alternate validating methodology is available, it is impossible to answer whether these results are "accurate." However, the comment maintained that the results are reproducible and consistent with optical transmission properties measured in vitro on the skin. The comment added that the principles of testing are the same for both high SPF and low SPF products and that there are no physiological differences in the responses that would necessitate a different testing procedure.

Another comment (Ref. 2) submitted the results of five studies, each involving about 20 subjects. Three of the studies were performed in one laboratory, while the other two were performed in another testing facility. The studies were basically designed according to the Panel's recommended testing procedure. All five studies used test products which produced mean SPF values that exceeded 15. These values ranged from 24.4 to 36. The standard deviation of the results ranged from 1.6 to 5.05, and the standard error percentage of the mean ranged from 0.91 to 2.95.

Regarding the data submitted by the first comment (Ref. 1), the agency believes that the results of tests on the same formulation on humans at two testing laboratories give some indication of reproducibility. Moreover, the results support the use of the Panel's method for evaluating sunscreens with SPF values higher than 15. The in vitro results may also be supportive, but the comment did not submit those data.

It is unclear from the data submitted by the second comment (Ref. 2) whether the test products were the same formulation and should have produced the same mean SPF value, or whether they were different products. In addition, it could not be determined whether the 8-percent homosalate control was used in two of the studies (Refs. 3 and 4), and the light source was not well defined in another two studies (Refs. 5 and 6). The agency acknowledges that it is possible to obtain consistent SPF values above 15 in the context of one study. The unresolved problems are whether high SPF values are reproducible among testing laboratories, and whether such values are valid.

The agency notes that the 8-percent homosalate control used in some of these submitted studies has an SPF value of approximately 4. The agency is proposing that one or more standard preparations with SPF values higher than 4 be developed for testing sunscreens with higher SPF values (see comment 78). Also, such standard

preparations, when developed and validated, would be used to develop new testing procedures or to validate existing testing procedures for sunscreen drug products with SPF values higher than 15. At this time, such standards are not available.

The agency has determined that the submitted data are not sufficient to demonstrate that the testing methods currently used to evaluate sunscreen drug products with SPF values up to 15 are equally applicable to evaluating sunscreen drug products with SPF values above 15. The agency believes that collaborative studies using an appropriate control preparation are necessary. The agency invites further comment on this matter. If necessary, the agency will publish an amendment to this tentative final monograph to address any new data submitted regarding testing procedures for sunscreens with high SPF values (above 15), so that the public may comment before a final rule is published. The agency's comments on the data are on file in the Dockets Management Branch (Ref. 7).

References

- (1) Comment No. C00083, Dockets No. 78N-0038, Dockets Management Branch.
- (2) Comment No. C00080, Dockets No. 78N-0038, Dockets Management Branch.
- (3) Kaidbey, K., "The Evaluation of a Suncare Product for its Ability to Resist Wash-Off, Protocol 1308," unpublished report in Appendix 16, Comment No. C00080, Docket No. 78N-0038, Dockets Management Branch.
- (4) Kaidbey, K., "Evaluation of a Suncare Product for its Ability to Resist Wash-Off, Protocol 1588," unpublished report in Appendix 17, Comment No. C00080, Docket No. 78N-0038, Dockets Management Branch.
- (5) Epinette, W.W., and A. McCarthy, "Final Report: Sunscreen Evaluation, Project No. CN-0028," unpublished report in Appendix 15, Comment No. C00080, Docket No. 78N-0038, Dockets Management Branch.
- (6) Epinette, W.W., and C.L. Hughes, "Final Report: Sunscreen Evaluation, Project No. CN-0043," unpublished report in Appendix 18, Comment No. C00080, Docket No. 78N-0038, Dockets Management Branch.
- (7) Letters from W.E. Gilbertson, FDA, to M.B. McTernan, Johnson and Johnson, and E.E. Kavanaugh, Cosmetic, Toiletry and Fragrance Association, coded LET38 and LET41, respectively, in Docket No. 78N-0038, Dockets Management Branch.

78. In the notice of a public meeting to discuss appropriate testing procedures for OTC sunscreen drug products, the agency stated that it was concerned about using a standard preparation that may have a relatively low SPF value of 4 to validate a sunscreen testing procedure that is supposed to determine a wide range of SPF values (currently SPF 2 to SPF 30

and higher) (52 FR 33598 at 33600). The agency asked whether standard formulations with SPF values higher than 4 would make the determination of SPF values higher than 8 and 15 more accurate. The agency stated that it believed that two or three standard preparations should be available having SPF values representing the entire range of possible SPF values (e.g., SPF 8 and SPF 20 or SPF 4, SPF 15, and SPF 25). The agency also asked if sunscreen preparations were available that would be appropriate for use as standard preparations when testing sunscreen drug products with estimated SPF values greater than 15. If so, the agency requested that data on such preparations be submitted.

Several comments agreed with the agency that additional standard or control preparations with SPF values higher than 4 should be available for sunscreen drug product testing. One comment agreed with the agency on the usefulness of a low and a high SPF control and recommended that the homosalate control be retained for low SPF products. The comment stated that it is aware of prototype control formulations that would fulfill the requirements for a high SPF control. Another comment recommended that two standard preparations with SPF values of 4 and 9 should be available and added that it is essential that a choice be left to the investigator to use either of the standards depending upon the expected SPF testing range. Another comment suggested that standard formulations should have SPF values of 4 and 12.

Some comments recommended that, in addition to the SPF 4 standard control, a standard preparation with an SPF of 15 should be available. One comment stated that one or two additional standards should be available and that one of these standards should have an SPF value of greater than or equal to 15. The comment added that both the level of absorbers and the vehicle (sunscreen base) of the standard preparation must be clearly defined. Another comment stated that for testing sunscreens with SPF values under 15, the 8-percent homosalate standard, as defined and recommended by FDA, or the 2.7 percent cinnamate, as defined and recommended by DIN, should be used. However, for evaluating sunscreen preparations with SPF values higher than 15, the comment recommended that a standard which has an SPF of at least 15 and which does not contain substances known as reflectors should be used. The comment stated that this standard may contain either UVB filters with extended absorption in the UVA

range or a pure UVA absorber plus a UVB absorber.

One comment suggested that the sunscreen testing methodology should spell out which control formulation should be used with which range of expected SPF values. For example, the SPF 4 control should be used where the expected SPF of the test product is 2 to less than 8, and the SPF 15 control should be used where the expected SPF is 8 to 30. Another comment stated that the control standards should be run at least once a year in the laboratory test, but another comment proposed that the standard should be run twice a year.

One comment stated that the use of a high SPF control would improve the accuracy of the testing procedure and provide a benchmark of compliance for testing laboratories. The comment stated that it is willing to provide formulations for use as high SPF (and waterproof) reference standards, but because these formulations are proprietary, they could not be disclosed publicly. The comment stated that it could provide finished products with SPF values of "8+" and "20+" (both waterproof) to the industry for a fee in line with the costs of producing, validating, and distributing the materials and submitted data on the SPF testing of these products (Ref. 1). Another comment noted that it was planning to submit data in support of a control for high SPF testing, but realized that such data could not be submitted before the administrative record closed in April, 1988. The comment stated that it would submit the data as part of a petition to reopen the administrative record to consider these data and requested that the agency give favorable consideration to such a petition. [No such petition has been submitted to date.] The comment stated its willingness to work with the agency to develop and validate an additional control.

The agency believes that the 8-percent homosalate standard preparation proposed in this tentative final monograph is suitable for testing sunscreens with lower estimated SPF values (which may include values up to and including 15). (See comment 75.) However, the agency believes that one or more additional standard preparations with SPF values higher than 4 (e.g., SPF 15, 20, or 25) may be desirable for testing sunscreens with higher SPF values (i.e., SPF values higher than 15). Depending on the SPF values of the additional standard preparations, one of those preparations may be deemed more appropriate to use to test products with an estimated SPF value of 15. At this time, the agency does not have enough data or

information to reach a conclusion regarding the use of other suitable standards or their formulations. Only one comment submitted data on higher SPF standard preparations, one with an SPF of "8+" and one with an SPF of "20+" (Ref. 1). These data are not sufficient to verify the reliability of these preparations. For the preparation with an SPF of "8+," the comment submitted data on 120 subjects, but for the preparation with an SPF of 20, it submitted data on only 20 subjects. In both cases, mean SPF values higher than the expected SPF value were obtained. The agency would need more within-laboratory data as well as data from different laboratories before it could determine if these standard preparations were appropriate. In addition, the agency notes that the formula of any standard preparation required by an OTC drug monograph must be in the public domain so that the preparation can be prepared in any laboratory.

The agency appreciates the interest shown by two comments in developing standard preparations for the testing of higher SPF sunscreens. However, no data or information regarding additional standard preparations has been submitted at this time. The administrative record will be open for 1 year following publication of this document to accept new data relating to these proposals. If additional data are submitted, the agency will, if necessary, publish an amendment to the tentative final monograph in a future issue of the *Federal Register* to state its proposals regarding appropriate standard preparations for testing of higher SPF sunscreens.

Regarding the suggestion that the standard preparation should be run once or twice a year, the Panel recommended in § 352.40(a) of its monograph that the standard preparation should be run every time (i.e., concomitantly) a sunscreen drug product is tested. The agency agrees and is including this requirement in proposed § 352.70(a).

Reference

(1) Comment No. C00083, Docket No. 78N-0038, Dockets Management Branch.

Q. Comments on Indoor vs. Outdoor Testing Procedures for Sunscreen Drug Products

79. One comment disagreed with what it believed was the Panel's opinion that determination of the SPF value under laboratory conditions (with artificial light sources) will produce more reliable and reproducible SPF values than those achieved using natural light. Referring to personal

experience in testing sunscreen products, the comment stated that artificial light sources have given a higher SPF value than natural sunlight and offered to submit such data if requested. The comment pointed out that the physical properties of sunscreen products always tend to be altered when tested under natural light, and that the combined effects of UVB, UVA, visible, and IR radiation are more pronounced under outdoor conditions. In view of the availability of reliable meters to measure light fluences (amounts of light) and of good facilities to conduct outdoor testing, the comment concluded that the Panel should have insisted that at least one study be conducted under outdoor conditions in order to obtain a true SPF value, adding that the cost of such testing is not an excuse when the principal issue concerns the health of people and when the major objectives are to minimize or prevent skin cancer and wrinkling of the skin. For these reasons, the comment argued that indoor as well as outdoor testing should be mandated by FDA.

A second comment agreed with the Panel's recommendation that both artificial and natural light can be used in the testing of sunscreens (43 FR 38206 at 38259). However, the comment suggested that final sunscreen formulations should be required to undergo at least one outdoor simulated-use test with natural sunlight. The comment maintained that artificial light sources should be used only in research and development programs to identify formulations that appear to have merit under laboratory conditions and to partially evaluate formulations with very high protective factors, explaining that the SPF of such formulations "might range from 8X to 18X in the laboratory environment, but that range narrows considerably (from 4X to 6X with some formulations) when the products are tested under natural sunlight-simulated-use conditions." The comment concluded that it would be reasonable to require all sunscreens (even those with protection in the range of 8X or greater) to demonstrate performance under natural sunlight-simulated-use conditions. The comment requested that the tentative final monograph explain the role of artificial and natural light testing in the development of sunscreen drug products, and provide guidelines for natural sunlight testing and recommendations for preferred simulated-use conditions.

One reply comment questioned the validity of the above comments and supported the Panel's recommendations regarding both solar simulator testing

and natural sunlight testing. The reply comment stated that it believed laboratory conditions using artificial light can be constructed to parallel outdoor conditions without the variables associated with outdoor testing. It believed that "solar simulator testing provides a means of standardization, a means of assuring reproducible results and ultimately, and most importantly, a means of insuring uniform product labeling." The reply comment contended that the same amount of erythemal energy is required to produce a sunburn using either a xenon arc solar simulator or natural sunlight, and that, as long as other environmental factors are reproduced, the SPF of a sunscreen drug product is reproducible under laboratory conditions using a xenon arc solar simulator. The reply comment submitted a published paper (Ref. 1) and the results of studies, previously submitted to the Panel for review, which it said demonstrated reproducible results in various laboratories, using the xenon arc solar simulator (Ref. 2).

Another comment, responding to the January 26, 1988 public meeting to discuss sunscreen testing procedures, stated that it did not support an outdoor test. The comment maintained that although sunscreens are applied for use in natural sunlight, this source of UV radiation is too variable and too unpredictable for routine use in the assessment of a large number of commercial sunscreen products.

The Panel did not recommend the use of an artificial light source over natural sunlight for determining SPF values. In discussing testing procedures for determining the SPF value of a sunscreen product, the Panel considered the use of artificial light (i.e., a solar simulator) and the use of natural sunlight as light sources (43 FR 38206 at 38259 and 38260). The Panel discussed the advantages and disadvantages of using these light sources for determining SPF values. The Panel described an artificial light source in § 352.41(a) and discussed the use of a natural light source in § 352.41(b) of its recommended monograph. It outlined procedures for determining SPF values using an artificial light source in § 352.43 and for the determination of SPF values using sunlight in § 352.44. However, the Panel did not favor one method over the other.

The use of SPF values evolved from research and development efforts involving both natural and artificial light sources. The agency believes that labeled SPF values should be based on testing conducted under the most

carefully controlled conditions so that the results are as accurate and reproducible as possible. Accurate and reproducible testing procedures ensure that competitive products with the same SPF values have essentially the same effectiveness.

The agency agrees with the reply comment that indoor testing using a properly filtered and calibrated solar simulator provides an appropriate means of standardizing SPF measurements by providing controls over most of the variables that cannot be controlled in outdoor testing. (For a discussion of solar simulators, see comment 86.) The agency believes that indoor testing ensures reproducible results because it is easier to control significant variables such as temperature and humidity. Outdoor testing of sunscreen products is not reproducible from day to day because of uncontrollable variables such as changing cloud cover, changing radiation intensity with time, changing sun angle to the body surface with time, and variable heat-induced sweating. A solar simulator produces a constant spectrum at a constant angle with a high output in the UV range of 290 to 400 nm (43 FR 38260). It is a more reliable source of UV radiation than the sun whose spectrum changes continuously depending upon angle, altitude, pollution, and the amount of ozone in the atmosphere (Ref. 3). Additionally, although there is not enough sunlight in a day to conduct outdoor testing of sunscreens with high SPF values, testing of these products may be done quickly and efficiently using a high intensity solar simulator.

The agency has reviewed the published paper and the results of a study submitted by the reply comment (Refs. 1 and 2) as well as a later publication not available to the Panel (Ref. 4). The agency tentatively concludes that SPF values determined by indoor testing compare favorably with SPF values determined by outdoor testing. The study by Sayre, et al. (Ref. 1) showed that the MED for unprotected skin induced by a solar simulator was similar to the MED values obtained in outdoor testing using natural sunlight. SPF values obtained for products tested indoors using solar simulators were consistently higher than the SPF values obtained outdoors using natural sunlight. However, the study demonstrated that if certain critical environmental conditions, such as temperature, are controlled, the SPF value of a sunscreen product determined with an artificial light source is similar to that obtained using natural sunlight. A subsequent study by

Sayre, et al. (Ref. 4) suggests that when testing sunscreens for substantivity (resistance to water wash-off), varying environmental conditions are not considerations because the substantiveness of the sunscreen formulation negates the effects of heat and humidity on the SPF determination. The data in this study demonstrate good correlation between the indoor and outdoor testing results of substantive sunscreen formulations.

The agency believes solar simulator testing is a more accurate method of determining SPF values for product labeling than outdoor testing. Carefully controlled solar simulator testing provides a convenient means of standardization among laboratories and is not affected by variable outdoor environmental conditions. Therefore, the agency is proposing only general testing procedures in § 352.72 that use an artificial light source, as specified in § 352.71, for determining SPF values. Accordingly, the agency is not including the Panel's recommended § 352.41(b) "Natural light source (sunlight)" and § 352.44 "Determination of SPF value using natural light source (sunlight)" in this tentative final monograph. In addition, the Panel's reference to natural sunlight testing in § 352.42(h) "Response criteria" is not being proposed.

References

- (1) Sayre, R. M., et al., "The Correlation of Indoor Solar Simulator and Natural Sunlight," *Archives of Dermatology*, 114:1649-1651, 1978.
- (2) Comment No. SUP002, Docket No. 78N-0038, Dockets Management Branch.
- (3) Urbach, F., "The Biological Effects of Ultraviolet Radiation," Pergamon Press, New York, pp. 359-373, 1969.
- (4) Sayre, R. M., et al., "Performance of Six Sunscreen Formulations on Human Skin," *Archives of Dermatology*, 115:46-49, 1979.

80. One comment suggested that a conversion factor of 0.7 be used to correct for the observation that the calculated SPF of sunscreen drug products is higher when tested indoors using an artificial UV light source than when tested outdoors using natural sunlight. The comment maintained that this approach would also provide for retaining the 2 milligram/centimeter squared (mg/cm²) application density in the sunscreen testing procedures. At the same time, it would result in an SPF value that would better reflect the actual sunscreen protection the consumer would experience in natural sunlight.

The agency does not believe that the testing procedures should include a conversion factor of 0.7 to adjust a calculated SPF that has been determined using an artificial light

source. The proposed sunscreen testing method using an artificial light source is reasonable, but not absolutely, comparable to sun exposure conditions. As discussed in comment 79, there are inherent variables in sunscreen testing done under outdoor conditions. The agency believes that indoor testing with an artificial light source is a more accurate method of determining SPF values than is outdoor testing. Furthermore, the comment did not submit data to demonstrate a constant relationship between SPF values determined using an artificial light source and SPF values determined under natural sunlight conditions. Nor were data provided to support the suggested conversion factor. Therefore, the agency is not including a conversion factor in the proposed sunscreen testing methods.

81. Referring to the Panel's discussion of environmental conditions for testing sunscreen products in sunlight (43 FR 38206 at 38260 and 38266), one comment provided possible specifications for the testing of the standard sunscreen formulations in natural sunlight. To circumvent environmental variables, the comment suggested the following possible specifications for weather (and environmental) conditions: no intermittent clouds (less than 2 percent), ambient temperature of 84 °F to 88 °F, haze (minimal), and humidity of 50 to 70 percent. Among other environmental variables affecting the testing of standard formulations, the comment listed wind, air quality index, and other exposure conditions, such as latitude and the time of the year. The comment did not suggest any specifications for these conditions. The comment predicted that test failures would result if cloudiness became excessive. Therefore, the comment urged the agency to place very strict limits on weather variations during the testing of standard formulations.

The Panel discussed the effect of atmospheric conditions and geographic latitude on the development of the MED in fair-skinned people (43 FR 38206 at 38210). Atmospheric conditions alter the solar erythemal intensity and, depending upon the latitude, also affect the exposure time required to induce one MED. Although testing of sunscreen products in natural sunlight provides useful information, such testing is associated with many variables, such as those mentioned by the comment. Accordingly, the agency is not proposing natural sunlight testing as a regulatory standard. For a discussion on the determination of SPF values using

an artificial light source, see comment 79.

82. Noting the subject selection procedures in § 352.42(a), one comment stated that the selection of subjects with Skin Types I, II, and III seems appropriate for evaluations using artificial light. For natural sunlight testing, however, the comment contended that subject selection should be restricted to test subjects with moderate skin pigmentation. The comment argued that restricting the skin type for natural sunlight tests should decrease subject variation in evaluating the test and control formulations. The comment added that the conditions of simulated use during natural sunlight testing of sunscreens should be specified. It cited "no swimming" and "schedule of exercise" as examples of conditions that should be specified.

As described in comment 79, natural sunlight testing of sunscreen drug products provides SPF values that vary too greatly to be useful in assigning PCD claims. Therefore, the agency is proposing only artificial light testing procedures. Thus, it is not necessary to specify conditions for natural sunlight testing of sunscreens.

R. Comments on Artificial Light Sources

83. One comment disagreed with the Panel's statement that solar simulators of 150 Watts (W) usually produce 10 or 12 solar constants (43 FR 38206 at 38260). The comment explained that solar simulators "based on the principle reported by Berger, where the radiation is reflected from visible light and an IR reflecting dichroic mirror, produce the equivalent of ten to twelve times the amount of UV radiation contained in mid-latitude noon sunlight." The comment added that if most of the visible light and IR radiation were not removed from the beam, severe burns would result. Therefore, the comment felt that the Panel's statement is too broad and incorrect. For similar reasons, the comment also objected to the Panel's statement concerning solar simulators producing 40 solar constants (43 FR 38260) and contended that because not all solar simulators are built on the Berger principle, they will emit a variety of intensities of UV radiation depending on their design and construction.

The Panel defined a solar constant as "the total amount of energy at all wavelengths per square meter, available from the sun, at the earth's surface" (43 FR 38260); however, as the comment stated, solar simulators recommended for sunscreen testing emit only UV wavelengths of radiation. A true solar constant also includes energy from visible light and IR radiation. The

agency believes that the Panel's report would have been more precise had it read "solar constants of UV radiation." Concerning the comment's objection that solar simulators will emit a variety of intensities of UV radiation depending on their design, the Panel stated that the "more powerful instruments can produce up to 40 solar constants." The Panel recognized that solar simulators may emit a variety of intensities of UV radiation when it qualified its statement by saying "up to" 40 solar constants.

84. One comment questioned the Panel's statement, in its discussion of light sources and monitoring (43 FR 38206 at 38260), that the UV intensity of a solar simulator will be reported in J/m². The comment stated that if the J/m² refers to "the total output of a solar simulator without specifying spectrum, the results in terms of numbers will be most misleading." Further, the comment claimed that the statement is technically incorrect because Joules represent the dose of radiation and not the intensity, which is measured in Watts per meter squared (W/m²). The comment maintained that a solar simulator's effectiveness for sunscreen testing should be measured by multiplying its output spectrum by an agreed upon action spectrum for erythema. The comment added that the dose of radiation should be expressed as "erythema effective Joules/m²," and the intensity of radiation should be expressed as "erythema effective Watts/m²." The comment stated that a number of action spectra for skin erythema have been published and that it is of particular importance for the sunscreen rulemaking that "the FDA specify one action spectrum which will then be used for appropriate integrations." The comment added that because the majority of the sun's energy output is in the visible and IR range, and the UV radiation component rarely exceeds a few percent of the total and changes rapidly with time, measurement of the sun's intensity without making the corrections suggested above will produce useless results. Therefore, the comment felt that radiometers for measuring the sun's intensity should also be calibrated in "erythema effective Joules/m²," if a dose is being measured, or in "erythema effective Watts/m²," if intensity is being measured.

A second comment felt that, although the monograph appropriately does not specify the scale to be used in measuring the output of solar simulators, the Panel's report is confusing regarding the units in which radiometers should be calibrated. The comment cited the following statements from the Panel's report (43 FR 38260):

"The output of a solar simulator is measured in units of Joules * * * The UVL [UV light] intensity of a solar simulator will be reported in J/m²." The comment stated that this requirement would restrict the use of monitoring devices (such as the widely used Robertson-Berger (R-B) meter) that meet all other Panel-recommended requirements for radiometers but that provide output in terms of sunburn units/hour. The comment suggested that the Commissioner clarify that the radiation of solar simulators need not be measured in terms of Joules.

The first comment is correct regarding the Panel's use of "intensity" instead of "dose" in its discussion of solar simulators. The agency believes that the proper nomenclature should be the currently accepted CIE definitions of units applicable to all radiation (Refs. 1, 2, and 3). The acceptable quantities are "radiant power," which has units of Watts, and "radiant energy," which has

units of Joules. "Irradiance" is the radiant power incident upon a surface per unit area of the surface and is expressed in W/m². "Radiant exposure" is the energy equivalent of irradiance and is expressed in J/m². Additionally, the term "spectral irradiance" refers to the irradiance of the source restricted to a narrow wavelength band of the spectrum, and is expressed in terms of Watts per square meter per nanometer (W/m²-nm).

In § 352.43, "Determination of SPF value using artificial light source," the Panel defined UV radiation exposure in units of time. The agency believes that it is more accurate to express dose as the "erythema effective exposure," in units that define the total amount of erythema effective energy applied to the testing subsite, i.e., as J/m². Thus, in order to determine the erythema effective exposure, the measured output from the solar simulator (spectral irradiance, W/m²-nm) must be weighted using an

agreed-upon erythema action spectrum. And this spectrum must have weighting factors that have a different effectiveness for producing erythema with different wavelengths of UV radiation.

The agency is aware that although various erythema action spectra have been published, none have been universally adopted (Ref. 4). The agency agrees with the first comment that an action spectrum for erythema should be agreed upon. The CIE has proposed a reference action spectrum based upon a statistical analysis of the results of several published studies carried out since 1964 (Ref. 4). The agency believes that the CIE's proposed reference action spectrum is appropriate for use in the testing procedures for OTC sunscreen drug products. The following equations describe the proposed reference spectrum:

$$V_i(\lambda) = 1.0(250 < \lambda < 298 \text{ nm})$$

$$V_i(\lambda) = 10^{0.094(298-\lambda)}(298 < \lambda < 328 \text{ nm})$$

$$V_i(\lambda) = 10^{0.015(328-\lambda)}(328 < \lambda < 400 \text{ nm})$$

The data contained in the action spectrum are to be used as spectral weighting factors to calculate the erythema effective exposure of a solar simulator as follows:

$$E = \sum_{250}^{400} V_i(\lambda) * I(\lambda)$$

where:

E=Erythema Effective Exposure (dose)
V_i=Weighting Factor (Erythema Action Spectrum)
I=Spectral Irradiance (W/m²-nm)

The agency believes that adoption of this erythema action spectrum would represent a significant step forward in the development of standardized equipment for the testing of sunscreen drug products. Therefore, the agency is proposing to modify § 352.43 of the Panel's recommended monograph to include this action spectrum and the proposed calculation to determine the erythema effective exposure. This information appears in proposed § 352.73(a), (b), and (c).

The agency is using the term "erythema effective exposure" in place of the term "exposure time interval" in the SPF calculation as follows:

SPF value=the ratio of erythema effective exposure (J/m²) (MED (PS)) to

the erythema effective exposure (J/m²) (MED (US)). The agency invites comments on this proposal.

The agency agrees with the second comment that the Panel's report is confusing regarding the units in which radiometers should be calibrated. The agency does not agree, however, that the radiation of solar simulators need not be measured in terms of Joules. The agency believes that the CIE units mentioned above should be used in all sunscreen testing, including the calibration of equipment. The agency acknowledges that requiring the output of a solar simulator to be measured in Joules does mean that the "widely used" R-B meter cannot be used to measure the output of solar simulators. However, radiometers, including the R-B meter, have limited value for measuring the output of simulators. Considering present technology, the agency recommends the use of spectroradiometers or similar spectrally sensitive devices for measuring the radiant energy output from solar simulators (Refs. 5 and 6). (See comment 88.)

Because natural sunlight is not being proposed as a testing light source in this tentative final monograph, the agency is not addressing the requirements for radiometers to measure natural sunlight.

However, any specifications for instruments to be used for measuring solar simulators may also be used for measuring natural sunlight.

References

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- (2) Sliney, D., and M. Wolbarsht, "Safety with Lasers and Other Optical Sources," Plenum Press, New York, pp. 54-60, 1980.
- (3) Kaufman, J.E., editor, "Measurement of Light and Other Radiant Energy," in "IES Lighting Handbook," Illuminating Engineering Society of North America, New York, 1984.
- (4) McKinlay, A.F., and B.L. Diffey, "A Reference Action Spectrum for Ultraviolet Induced Erythema in Human Skin," *CIE Journal*, 6:17-22, 1987.
- (5) Diffey, B.L., "A Comparison of Dosimeters Used for Solar Ultraviolet Radiometry," *Photochemistry and Photobiology*, 46:55-60, 1987.
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85. Referring to the Panel's statement that approximately 6x10⁶ J/m², as measured by a recording radiometer, will evoke 1 MED in Skin Types I and II (43 FR 38206 at 38262), one comment stated that the number is meaningless and that such a dose can be obtained from the sun without any UVB being

present in the beam. The comment felt that all such doses should be reported as "erythema effective J/m²." The comment also objected to the Panel's statement at 43 FR 38262 that "duration of sun exposure will be documented in Joules/m² or in R-B counts." It is not duration of sun exposure, the comment claimed, but UVB dose that should be documented, particularly since J/m² or R-B counts refer to dose. Likewise, the comment felt that the number 4.5×10^6 J/m², presented as an example of an MED for a type I subject in the Panel's discussion of a test protocol design (43 FR 38262), is another meaningless number. The comment stated that dose should always be expressed in erythema effective J/m². The comment added that the doses presented in the Panel's discussion of the calculation of the SPF value using a recording radiometer (43 FR 38263) should also be expressed in "erythema effective J/m²."

The agency agrees with the comment that the quantities 6×10^6 J/m² and 4.5×10^6 J/m², alone, without reference to a band of the solar spectrum are not useful. The Panel used these figures as examples of appropriate amounts of solar exposure needed to evoke 1 MED in subjects with Skin Types I and II. Likewise, in the Panel's report (43 FR 38206 at 38263), 6×10^6 J/m² is used in an example given for the determination of the SPF value from an MED obtained using a recording radiometer. Although it is possible to receive a dose of 6×10^6 J/m² of radiant energy from the sun without any UVB being present, it is unlikely that exposure to natural sunlight would be completely devoid of any UVB radiation. Further, the Panel only used these numbers as examples in its discussion of the methods involved in determining the SPF value of a sunscreen product using natural sunlight as a light source.

The agency is not proposing the Panel's recommended testing procedures for the determination of SPF values using natural sunlight testing (see comment 79). Therefore, it is not necessary to address the comment's concerns about the dose of natural solar radiation measured in sunscreen drug product testing. However, with respect to indoor testing using a solar simulator, the agency now prefers to express dose as the "erythema effective exposure," in units that define the total amount of erythema effective energy applied to the testing subsite (J/m²). (See comment 84.) In order to ensure that only erythema effective radiation emitted by a solar simulator is measured for sunscreen drug product testing, an action spectrum for erythema and the units of radiant energy must first be established. The

agency has proposed an action spectrum for erythema and discussed the appropriate units for measuring radiant energy elsewhere in this document. (See comment 84.)

86. One comment stated that the artificial light source used in testing to determine SPF values should not be restricted to xenon lamps. The comment referred to the Panel's statement that the xenon arc solar simulator is the preferred artificial light source (43 FR 38206 at 38259 and 38260). The comment suggested that, in the tentative final monograph, the agency should de-emphasize the use of the xenon arc lamp over other artificial light sources unless it can be demonstrated to be superior through corroborative testing. The comment contended that Westinghouse FS 40 sunlamps provide a useful laboratory source for UVB radiation and have two advantages over the xenon arc lamp: (1) the absence of discomfort to the subject during the challenge to UV radiation, and (2) an area of coverage of over 20 times greater than that of a 150 W xenon arc lamp. The comment argued that the FS 40 sunlamp results in greater effectiveness in laboratory studies because the exposure of 16 to 24 treatment sites in testing of a product with SPF values of 8 or 10 can be completed within 16 to 20 minutes. The same experiment with one subject and a 150 W xenon arc lamp would take about 1½ hours.

A second comment stated that experience with xenon arc solar simulators is insufficient to determine whether a correlation exists between SPF values determined using them as the light source and SPF values determined using natural sunlight. The comment suggested that the Panel's testing procedures also allow for the use of other light sources, such as the Weinsberger Solarium or Osram Vitalux.

A reply comment contended that the light sources suggested by the above comments, e.g., the FS series of fluorescent sunlamps and the filtered intermediate pressure mercury vapor sunlamp (such as the Osram Vitalux) do not adhere to the Panel's recommendations for an appropriate light source and could cause misvaluation of the sunscreen product. The comment stated that these two types of light sources emit radiation shorter than 290 nm and, as a result, may produce erythema responses with nonsolar radiation. The comment added that the Osram lamp also emits a line spectrum that is not continuous. Therefore, the lamp deviates from natural sunlight and from the Panel's recommendations for an appropriate light source. The comment supported

the Panel's recommendation to use solar simulator light sources that emit a continuous UVB spectrum of 290 to 320 nm with not more than 1 percent of the emitted radiation shorter than 290 nm.

In the notice of public meeting to discuss sunscreen testing procedures (52 FR 33598 at 33599), the agency questioned the variability of the data submitted to the Panel in support of the recommended testing methods and proposed several possible modifications to these testing methods in an effort to improve them. In response to the publication and the subsequent meeting held on January 26, 1988, the agency received several comments that addressed the solar simulator as a possible source of error in the sunscreen testing procedures.

Four of these comments suggested that light sources other than the xenon arc solar simulator were appropriate for use in sunscreen testing. Stating that the light source is one of the remaining variables in the existing methods for SPF determination, one comment submitted testing results obtained in France (Ref. 1). This comment maintained that these data suggest that the use of different light sources now specified by existing methods is unlikely to affect results significantly. Another comment stated that a frequent problem of the xenon arc solar simulators is that their spectral characteristics can change following alteration or damage to the filtration system used with these machines. Noting that there are alternative UV sources that are utilized for sunscreen testing, the comment stated that four Osram lamps are used in the DIN methods. The comment added that high pressure mercury halide sources have also been used. The comment maintained that even though these sources are not as solar simulating as a perfectly filtered xenon arc source, their spectral characteristics remain constant. The comment subsequently presented data purporting to show that similar SPF values are derived when using either an appropriately filtered xenon arc solar simulator or a high pressure mercury halide source even though the high pressure mercury halide lamp emits a discontinuous spectrum (Ref. 2). Stating that both instruments have advantages, the comment noted that the advantages of the mercury halide source include ease of use and stable spectral output reliability. The comment suggested that alternative UV sources be permitted providing that they possess appropriate quantities of UVA and UVB as terrestrial sunlight. The comment also suggested that nonxenon arc sources be tested with SPF assays and

compared to xenon arc simulators prior to acceptance of an allowed UV radiation source.

Two comments cited a recent publication (Ref. 3) to support a contention that, for testing sunscreen products with an SPF under 15, either a xenon arc or a mercury halide lamp can be used with similar results. However, both comments claimed that for sunscreens with an SPF over 15, a xenon arc solar simulator should be used. Another comment maintained that the testing of sunscreen drug products with an SPF of 15 or higher is best achieved by using high-intensity xenon arc lamps of 1 kilowatt (kw) or greater and that the Panel-recommended 150 W xenon arc lamp is inadequate for this purpose. One comment noted that an Ultravitalux lamp, which is a "line source mercury arc," has very little emission in the UVA range. This comment stated that when UVA absorbers are added to sunscreen formulations, the Ultravitalux lamp will overestimate the efficacy of protection against a solar source.

Five comments maintained that the solar simulator should be the light source of choice for sunscreen drug product testing. Three comments suggested that the sunscreen monograph should include specifications for acceptable light sources for testing sunscreens. One comment initially suggested that the solar simulator should be filtered to match the spectrum of the sun at a 60° angle; however, the comment subsequently recommended that the light source should be filtered to match the spectrum of the sun at 75° above the horizon. Another comment recommended that because the sun angle rarely exceeds 80° elevation, except in the tropics, a spectrum similar to an 80° elevation should be used and should give adequate safety factors. One of the comments stated that the xenon arc light source should be filtered with "WG 320, 1 mm thickness."

One comment explained that because the biological effectiveness of UV radiation wavelengths from 295 to 400 nm drops rapidly by a factor of over 1,000, the emission spectrum (i.e., spectral power distribution) of the UV radiation source will greatly influence SPF values. The comment stated that: (1) The sun emits a polychromatic continuum of different wave lengths; (2) low pressure fluorescent sun lamps emit a continuum mainly in the UVB, or mainly in the UVA range; (3) high pressure mercury arcs provide discontinuous line spectra; and (4) high intensity solar simulators, based on xenon, xenon-mercury, or doped tungsten may mimic solar UV radiation,

but they require special filtration to shape the UVB spectrum and to remove intense visible and IR radiation. The comment added that the age of the lamp, temperature of the bulb or arc, and the age of the filters will influence both spectral power distribution and irradiance.

The comment recommended that for purposes of SPF testing, light sources with a spectral power distribution closely representing that of sunlight should be used and that the light source should not emit radiation below 290 nm. Stating that the power consumption (i.e., 150 W, 2500 W, etc.) is immaterial, the comment maintained that only the spectral power distribution counts. Adding that accurate spectroradiometry methods are now available, the comment stressed that it is important that the spectral power distribution of the light source be known exactly and that equipment be monitored regularly. According to the comment, spectral power distribution and irradiance of filtered light sources vary in the first minutes of operation. For that reason, testing should not begin until 30 minutes after the equipment has been turned on to allow all systems to come to operating temperature and spectrum. This practice is particularly important when new lamps or filters are installed, in which case the solar output of the light source should be monitored frequently during the early times of operation.

The agency points out that the Panel (43 FR 38206 at 38265) did not restrict the artificial light source for sunscreen drug product testing to xenon arc solar simulators; they were recommended as the preferred artificial light source (43 FR 38260). The agency believes that the Panel recommended xenon arc solar simulators as the preferred light source because it had more information and more experience with these light sources than with other light sources.

The agency does not consider the data submitted by two of the comments (Refs. 1 and 2) sufficient to demonstrate that light sources with emission spectra different from that of sunlight can produce results equivalent to those obtained using a xenon arc lamp. In one study (Ref. 1), the investigators determined the SPF of the standard preparation used in the DIN sunscreen testing procedure using a modified DIN testing procedure in which a xenon arc solar simulator replaced the solar simulator normally used. Using 22 subjects and the modified DIN method, they determined that the geometric mean of the SPF was 3.53 and concluded that this result compared favorably with the SPF of 3.7 obtained

when the DIN standard preparation is evaluated using the normal DIN testing procedures. However, for a true comparison, the same batch of sunscreen standard should have been evaluated by both methods on the same 22 subjects. The agency also notes that these data merely indicate that the light source may have no effect on the determination of a low SPF. There are no data showing that the light source will not affect the determination of a high SPF such as 15.

The second set of data (Ref. 2) consists of two SPF values for each of five sunscreens. One SPF was determined using a metal halide light source, and the other was obtained using a xenon arc source. No other information or data were included. These data are not adequate to demonstrate the comparability of light sources for sunscreen testing procedures.

At this time, the agency agrees with the Panel that xenon arc solar simulators are the preferred light source for sunscreen testing because they emit a continuous spectrum that can be filtered to match sunlight. However, the agency acknowledges that other light sources may be used providing that they meet the specifications being proposed in § 352.71. (See comment 87.)

The agency believes that the light source is a significant factor that can affect the outcome of sunscreen testing. It is important, therefore, that the monograph testing procedures include adequate specifications describing an appropriate light source. The Panel defined an appropriate solar simulator for sunscreen testing as a light source having "(1) A continuous emission spectrum in the UVB (290 to 320 nm); (2) Less than 1 percent of its total energy contributed by nonsolar wavelengths (wavelengths shorter than 290nm); and (3) No more than 5 percent of its erythemically effective energy contributed by nonsolar wavelengths," (45 FR 38259 and 28260). The Panel provided these specifications for a solar simulator in § 352.41(a) of its recommended monograph, but did not identify any specific light source which would meet these criteria.

The knowledge regarding solar simulators, the erythema action spectrum, and the role of UVA in the production of skin damage has increased greatly since the Panel's report was published in 1978. The agency believes that the specifications for a solar simulator recommended by the Panel for sunscreen testing should be revised based on this new information. Although the Panel recommended that the solar simulator

used for sunscreen testing should emit a continuous UV spectrum from 290 to 320 nm (UVB radiation), the agency now believes that the solar simulator used to determine the SPF value of a sunscreen product should mimic the harmful spectrum of the sun as closely as possible and should include both the UVB and UVA spectra. The agency notes that the Panel's recommended labeling claims for Category I sunscreens include photoprotection against harmful rays of the sun that cause sunburn, cancer, and premature aging of the skin (i.e., skin aging). Although UVA radiation has been traditionally thought to contribute little to the deleterious effects of the sun, recent studies have shown that UVA is erythemogenic (Refs. 4 and 5). One study strongly suggests that UVA wavelengths of 315 to 340 nm, which are abundant in solar UVA, are most responsible for UVA induced photoaging (Ref. 6). UVA radiation can also augment the acute and chronic effects of UVB radiation (Refs. 7 through 11). In addition, the agency notes that some of the Category I sunscreens protect against UVA radiation as well as UVB radiation. The agency, therefore, concludes that the solar simulator used for sunscreen testing should emit a continuous UV spectrum from 290 to 400 nm (UVB and UVA radiation), similar to that of the sun at sea level. (For a discussion of sunscreens that protect against UVA radiation and UVA labeling claims, see comment 53.)

Regarding which sunlight spectrum should be used as the model that a solar simulator should mimic, the agency notes that one comment recommended matching sunlight at an 80° solar elevation. Another comment initially recommended matching sunlight at a 60° solar elevation but later recommended a 75° solar elevation. There are two ways of describing the position of the sun in the sky. The comments' method uses the angle of the solar elevation above the horizon to describe the position of the sun. The other method uses the angle of the sun measured from the sun's zenith. A solar elevation of 80° equals a zenith angle of 10°. In this rulemaking, the agency is using the zenith angle to describe the position of the sun in the sky.

The agency is aware that the spectral quality of the sun is not constant and is dependent upon the effective thickness of the atmosphere through which the radiation must pass. The effective thickness of the atmosphere is dependent upon various factors including the latitude and altitude of the observer and the zenith angle of the sun (Ref. 12). The agency realizes the

importance of specifying which sunlight spectrum should be used for testing sunscreen drug products and believes that a zenith angle of 10° represents a reasonable angle to specify in the testing procedures. Therefore, the agency is proposing that the solar simulator used for sunscreen testing should have a spectrum similar to sunlight at sea level from the sun at a zenith angle of 10°. The agency invites comment on this proposal.

Regarding one comment's recommendation that the xenon arc light source should be filtered with "WG 320, 1 mm thickness," the agency is not including specific filters in its specifications for solar simulators. The agency is not restricting the light source for sunscreen testing to xenon arc lamps, but is including specifications that the light source used for sunscreen testing must meet. In order to fulfill these specifications, light sources must be appropriately filtered. However, the filters necessary to obtain the proper spectrum depend upon the unfiltered output of the light source. Therefore, it would be inappropriate for the monograph to specify specific filters. However, the agency is proposing that a solar simulator be properly filtered so that its output simulates sunlight at sea level from the sun at a 10° zenith angle between 290 and 400 nm.

The agency is aware that, due to fluctuations in electrical supply and ambient temperature, the spectral output of solar simulators can change significantly during the period of time immediately after being switched on (Ref. 13). This is more pronounced when optical filters are used. Thus, the agency is proposing in § 352.71 that a solar simulator should not have significant time-related fluctuations in radiation emissions after an appropriate warm-up period. The investigator should carefully evaluate the solar simulator being used in order to determine the time period required for warm-up. Because a uniform exposure is important to the outcome of sunscreen testing, the agency is also proposing that the solar simulator have good beam uniformity (within 10 percent) in the exposure plane. The agency is also proposing that a solar simulator be measured periodically with an accurately calibrated recording instrument. (See comment 87.)

The Panel recommended that a solar simulator should have less than 1 percent of its total energy output contributed by nonsolar wavelengths shorter than 290 nm and not more than 5 percent of its total energy output contributed by wavelengths longer than 400 nm (43 FR 38206 at 38259).

However, the Panel's reasons for choosing these limits are not clear. Ideally, a solar simulator used for testing sunscreen drug products should emit only solar UV radiation. Extraneous radiation only adds to the error of the testing method. Although the Panel's recommended limits are adequate and are being proposed in this document, the agency believes that these limits could be more narrowly defined because the design of solar simulators is better today than when the Panel report was published. For example, it is possible that a solar simulator could have less than 0.1 percent of its total energy output contributed by nonsolar wavelengths shorter than 290 nm and not more than 1 percent of its total energy output contributed by wavelengths longer than 400 nm. Therefore, the agency is requesting comments on the amount of extraneous radiation that should be allowed in the output of a solar simulator.

The agency is revising the specifications proposed by the Panel in § 352.41(a) of its monograph to reflect these changes and is including new specifications in proposed § 352.71 to read as follows:

A solar simulator used for determining the SPF of a sunscreen drug product should be filtered so that it provides a continuous emission spectrum from 290 to 400 nanometers similar to sunlight at sea level from the sun at a zenith angle of 10°; it has less than 1 percent of its total energy output contributed by nonsolar wavelengths shorter than 290 nanometers; and it has not more than 5 percent of its total energy output contributed by wavelengths longer than 400 nanometers. In addition, a solar simulator should have no significant time-related fluctuations in radiation emissions after an appropriate warm-up time, and it should have good beam uniformity (within 10 percent) in the exposure plane. To ensure that a solar simulator delivers the appropriate spectrum of UV radiation, it must be measured periodically with an accurately-calibrated spectroradiometer system or equivalent instrument.

The agency invites further comment on these proposed specifications.

References

- (1) Comment No. C00076, Docket No. 78N-0038, Dockets Management Branch.
- (2) Comment No. C00089, Docket No. 78N-0038, Dockets Management Branch.
- (3) Gabriel, K. L., et al., "Sun Protection Factor Testing: Comparison of FDA and DIN Methods," *Journal of Toxicology-Cutaneous and Ocular Toxicology* 6:357-370, 1987.

(4) Kaidbey, K. H., and A. M. Kligman, "The Acute Effects of Longwave Ultraviolet Radiation in Human Skin," *Journal of Investigative Dermatology*, 72:253-256, 1978.

(5) Parrish, J. A., K. F. Jaenicke, and R. R. Anderson, "Erythema and Melanogenesis Action Spectra of Normal Human Skin," *Photochemistry and Photobiology*, 36:187-191, 1982.

(6) Kligman, L. H., "Photoaging: Manifestations, Prevention and Treatment," *Dermatologic Clinics*, 4:517-529, 1986.

(7) Paul, B. S., and J. A. Parrish, "The Interaction of UVA and UVB in the Production of Threshold Erythema," *Journal of Investigative Dermatology*, 78:371-374, 1982.

(8) Willis, L. A. M. Kligman, and J. Epstein, "Effects of Long Ultraviolet Rays on Human Skin: Photoprotective or Photoaugmentative," *Journal of Investigative Dermatology*, 59:416-420, 1973.

(9) Willis, L. A. M. Menter, and H. J. Whyte, "The Rapid Induction of Cancers in the Hairless Mouse Utilizing the Principle of Photoaugmentation," *Journal of Investigative Dermatology*, 76:404-408, 1981.

(10) Forbes, P. D., et al., "Simulated Stratospheric Ozone Depletion and Increased Radiation Effects on Photocarcinogenesis in Hairless Mice," *Cancer Research*, 42:2796-2803, 1982.

(11) Staberg, B., et al., "The Carcinogenic Effect of UVA Radiation," *Journal of Investigative Dermatology*, 81:517-519, 1983.

(12) Forbes, P. D., "Workshop on Production and Measurement of Ultraviolet Light: Light Sources for Solar Simulation in Photocarcinogenesis Studies," International Conference on Ultraviolet Carcinogenesis, National Cancer Institute Monograph No. 50, 1977.

(13) Diffey, B. L., "The Stability of Light Sources: Implications for Photobiological Studies," *Photochemistry and Photobiology*, 47:317-320, 1988.

87. One comment questioned the Panel's exemption of the xenon lamp from validation by "corroborating natural sunlight testing." The comment stated that validation was required for all other artificial light sources, even though these might have a UV spectrum comparable to "xenon light" (43 FR 38206 at 38260). The comment believed that industry has interpreted the Panel's report to mean that the xenon lamp replaces and is more desirable than natural sunlight testing. The comment felt that the Panel's position is faulty because it does not recognize the limitations of solar simulators, i.e., that simulated sunlight is not natural sunlight, and that "simulators are often used in a laboratory environment under conditions that don't even approximate (let alone simulate) use conditions." A second comment noted that the activity of all xenon arc solar simulators is not based on the same principle, i.e., radiation reflected from visible light and an IR reflecting dichroic mirror. Therefore, the comment stated xenon

lamps will emit a variety of intensities of UV radiation, depending on their design and construction. A reply comment questioned the validity of the objections by the first comment and stated that at least two highly reputable and respected manufacturers currently produce xenon arc lamps under sufficiently controlled procedures to effectively eliminate concerns about the standardization of these light sources between manufacturers.

The agency agrees with the Panel that a properly filtered xenon arc solar simulator is the preferred artificial radiation source. The xenon arc solar simulator was first described in 1969 by Berger (Ref. 1), and solar simulators have been widely used in photobiological research since then. According to Sayre (Ref. 2), the design of these instruments has changed little. According to Diffey (Ref. 3), the technology of optical radiation sources is well established, and the factors that can affect the stability and the life of these lamps is well documented. Currently, a number of xenon arc solar simulators systems are commercially available to provide solar simulated radiation (Ref. 2). The agency notes that in the Panel's recommended monograph and in proposed § 352.71, a specific type of light source is not mandated; only the specifications of the light source are described. These specifications ensure that the solar simulator emits a spectral distribution of UV radiation that is most similar to that produced by the sun. (See comments 85 and 86 for further discussion of artificial light sources.)

Regarding one comment's belief that industry has interpreted the Panel's report to mean that indoor testing is preferable to natural sunlight testing, the agency has determined that indoor testing is as accurate and more reproducible than outdoor testing. (See comment 79.)

As the second comment noted, all xenon arc solar simulators do not produce identical intensities of UV radiation. While one type of xenon arc solar simulator may produce a spectral distribution very similar to that produced by natural sunlight, another xenon simulator may produce a slightly different spectrum. Solar simulators may also emit different spectra as the lamp and its filters age. Therefore, the agency emphasizes that all artificial light sources, including xenon arc solar simulators, must be measured periodically with an accurately calibrated spectroradiometer system or equivalent instrument. Testers must ensure that the lamps used deliver the appropriate spectrum of UV radiation

and comply with the specifications in proposed § 352.71. (See comment 88 below for a detailed discussion on the monitoring for artificial light sources.) Therefore, the agency is revising the last sentence of the Panel's recommended § 352.41(a) to read as follows: "To ensure that the solar simulator delivers the appropriate spectrum of UV radiation, it must be measured periodically with an accurately-calibrated spectroradiometer system or equivalent instrument." Also, as noted in comment 86, this revised sentence is included in proposed § 352.71. The agency invites comment as to whether a specific time period (e.g., "measured every 3, 6, or 12 months") should be substituted for "measured periodically" in the above statement.

References

(1) Berger, D. S., "Specification and Design of Solar Ultraviolet Simulators," *Journal of Investigative Dermatology*, 53:192-199, 1969.

(2) Sayre, R. M., "UV Solar Simulation," *Photochemistry and Photobiology*, 47:52S, 1988.

(3) Diffey, B. L., "The Stability of Light Sources: Implications for Photobiological Studies," *Photochemistry and Photobiology*, 47:317-320, 1988.

88. Referring to the Panel's discussion regarding monitoring of the xenon arc solar simulator (43 FR 38206 at 38260), one comment stated that thermopiles are useful in measuring UV, visible, and IR radiation. The comment stated that the Panel, however, did not mention using appropriate filters to screen out visible and IR radiation for obtaining the UV flux incident on the skin surface. The comment added that using filters is important not only for monitoring the correct dosimetry of UV radiation, but also for eliminating IR radiation that is significantly present in the xenon arc emission.

The agency agrees with the intent of the comment. However, considering present technology, the agency believes that spectroradiometry (measurement of wavelengths in the form of spectra), or similar spectrally sensitive techniques, should be used to characterize the output from a solar simulator (Ref. 1). Although the Panel recommended the use of calibrated thermopiles to measure the output of solar simulators (43 FR 38260), the agency believes that the thermopile is not an appropriate instrument for performing measurements of solar simulators. For measuring the output from a solar simulator, a radiometer must have accurate sensitivity in the UV spectral region and be equipped with an appropriate mechanism to filter out any visible light or IR radiation that may be emitted by the solar simulator. Even a

properly calibrated radiometer, if unfiltered, will measure the total energy output of the light source regardless of the wavelengths present or the intensities of those wavelengths. As a solar simulator ages, it frequently emits progressively less UV radiation although its emissions in the visible and the IR spectrum continue to remain relatively constant. An unfiltered radiometer may not detect these changes.

There are several ways to determine radiometric values which, when correctly used, yield the same physical values. The agency is not requiring a specific method. The following suggestions are offered to establish the important parameters; physically equivalent alternatives are also acceptable.

Measurements should be performed using generally accepted radiometric principles and techniques. The quantity to be measured should be reported in spectral irradiance values which have units of $W/cm^2 \cdot nm$. For solar simulators, all measurements should be made on the complete device consisting of the light source and any related housing, filtration, or attachments manufactured or assembled for use with the device. Although filtered radiometers may be used to measure the output of solar simulators, the agency believes that such meters have limited value because they do not measure the spectral distribution of the light source. Accordingly, the agency recommends that spectroradiometers, or similar spectrally-sensitive instruments, be used. Spectroradiometry is the most fundamental method for measuring the radiant energy output (Refs. 2 and 3). Sophisticated instruments for the measurement of spectral irradiance should be used to adjust for spectral output distribution changes caused by such factors as filtration, distance from the source, warm-up time, and lamp age. Additionally, in order to use biological weighting functions, the spectral distribution of the source must be determined.

The spectroradiometric measurements on the solar simulator should be made at the same distance from the lamp that will be used for the sunscreen testing exposures. The measurements on the continuum part of the spectrum should be made at intervals of no more than 10 nm in the UV wavelength region below 400 nm. In addition, the spectral lines in the emission should be measured with a sufficiently narrow spectral bandpass ($\leq 2nm$) so as to adequately measure the level of radiation being emitted in those lines.

The measurements should be made with instruments calibrated against

standards of spectral irradiance. These standards should have been calibrated either by the U.S. National Institute for Standards and Technology (NIST) (formerly the National Bureau of Standards (NBS)) or by another laboratory against standards calibrated by NIST using NIST-recommended or generally accepted techniques. The instruments should be calibrated on a regular basis, sufficient to document the integrity of the data.

The use of other types of radiometers may be of limited value if properly calibrated and used. There have been attempts to develop radiometers with spectral responses incorporating biological weighting functions. Because biological weighting functions change dramatically with wavelength in the UV spectral region, it is imperative that radiometers be carefully designed for useful results. There are radiometers that measure the photopic (spectral response similar to what the human eye sees) functions well, but this is not the case for other weighting functions (Ref. 3). The principal problem is measuring UV radiation while rejecting all visible light and IR radiation. In addition, because the agency's proposed erythema action spectrum (see comment 84) covers the entire solar UV spectral region from 290 to 405 nm, a radiometer that measures the entire UV spectrum is needed.

As stated above, a spectroradiometer system or equivalent instrument is preferred for measuring the output of a solar simulator. The agency is specifying in § 352.71 that an "accurately calibrated spectroradiometer system or equivalent instrument" be used. (See comment 87.)

References

- (1) Ben-Hur, E., and I. Rosenthal, editors, "Photomedicine Vol. III," CRC Press, Inc., Boca Raton, FL, pp. 110-117, 1987.
- (2) Diffey, B. L., "A Comparison of Dosimeters Used for Solar Ultraviolet Radiometry," *Photochemistry and Photobiology*, 46:55-60, 1987.
- (3) Sliney, D., and M. Wolbarsht, "Safety with Lasers and Other Optical Sources," Plenum Press, New York, pp. 439-466, 1980.
- (4) Berger, D. S., "The Sunburning Ultraviolet Meter: Design and Performance," *Photochemistry and Photobiology*, 24:587-591, 1976.

89. One comment suggested that, in addition to the R-B meter, the Panel should have recommended other UV measuring instruments that are reliable, well calibrated, give radiant energy in Watt-seconds per square centimeter, and have continuous measurement capability. Arguing that the R-B meter is an expensive research instrument that is not readily available, the comment

described another, less expensive instrument that it had found to be very reliable for both the indoor and outdoor measurement of UV radiation. Another comment stated that specific references to the R-B meter should be deleted from § 352.44. The comment stated that, if proper control formulations are used to validate test results and calculate the SPF value, the monitoring device becomes secondary to the control formulation. The comment mentioned that the R-B meter is available from only one commercial source, and this limitation could place unnecessary restraints on natural sunlight-simulated use testing. The comment recommended that § 352.44 either be expanded to be more representative of the available instrumentation or be generalized with no reference to specific instrumentation. Another comment stated that the wording of § 352.44 is adequate because it provides that radiometers other than the R-B meter may be used. Another comment stated that the R-B meter is widely used and widely available.

The Panel discussed the use of the R-B meter for monitoring the amount of exposure to natural sunlight during the testing of a sunscreen drug product (43 FR 38206 at 38260). Citing a compilation of data from various radiation studies (Ref. 1), the Panel stated that the R-B meter has proved to be successful in monitoring and reproducing solar erythemal exposures. The Panel also stated that other recording radiometers are in use that perform a similar function. The Panel did not limit its recommendation for radiometric instruments to the R-B meter only. Concerning the comment's recommendation that the agency delete references to the R-B meter in § 352.44 and expand this section to include other types of radiometric instrumentation, the agency is not including the Panel's recommended § 352.44 in this tentative final monograph. (See comment 79.)

The agency earlier discussed the R-B meter as a monitor of the output of solar simulators used in sunscreen drug product testing. (See comment 84.) The R-B meter is only one of the recording radiometers that can be useful, and the agency is not mandating any specific instrument for monitoring solar simulators.

Reference

- (1) Measurement of Ultraviolet Radiation in the United States and Comparisons with Skin Cancer Data, OTC Volume 06A185, Docket No. 78N-0038, Dockets Management Branch.

90. One comment stated that a major factor that affects the erythema response of individuals and the resulting SPF and

PCD determinations is the xenon arc lamp solar simulator and its four major components: the quartz bulb, dichroic mirror, W. G. cut-off filters used at the UV radiation exit site, and the line voltage. The comment stated that the first three of these components become coated with dust particles, smoke, and laboratory-derived gaseous films from acids, ammonia, etc. To minimize variations in UV intensity, the comment recommended that the light box be kept covered with a black cloth cover when not in use, and that variations in line voltage be minimized by a voltage stabilizer.

The comment's recommendations appear reasonable in the absence of any contrary evidence. Parties who conduct tests on OTC sunscreen drug products should consider these recommendations as part of their test procedures.

S. Comments on the Design of the Testing Procedures for Sunscreen Drug Products

91. Referring to the agency's public meeting on sunscreen testing procedures and statistical methods held on January 26, 1988, one comment recommended that the testing procedures specify product "blinding." The comment stated that many laboratories already include "blinding" as part of their testing procedures but felt that this procedure should be mandatory to eliminate any product bias during subjective evaluation of the MED.

In a supplementary submission (Ref. 1), the comment maintained that potential investigator bias in clinical studies involving SPF determinations can be eliminated or reduced in several ways. Stating that sunscreen formulations (e.g., lotions, creams, gels, and solutions) can be packaged in identical appearing containers prior to testing, the comment maintained that such a blinding procedure is essential when the person applying the products is also evaluating the erythema on the test sites 16 to 24 hours later. However, the comment added that this blinding procedure can only be completely successful if all the formulations are identical in consistency and color. Moreover, the comment pointed out that the major disadvantage with this procedure is the need to retest repackaged units to ensure that the concentration of the active ingredients has not changed during repackaging. The comment added that this procedure does not contribute much to the study blinding if a mixture of sunscreen formulations (e.g., gel and cream) are evaluated in the same study or if

sunscreens of different SPF estimates are used.

According to the comment, a second way to eliminate investigator bias is to randomize the application of sunscreen formulations to the test sites. Such randomization (generated from computer or random number tables) eliminates investigator bias with respect to evaluation of erythema scores on a specific test site or sites. An untreated test site may be included in the randomization if necessary. Because the erythema score on the untreated irradiated area is used in the SPF calculation of all sunscreens evaluated, the comment stated that any investigator bias in reading the erythema scores on the untreated, irradiated area will be constant for all formulations.

In order to eliminate bias, the comment stated that it is imperative to blind the erythema evaluator with respect to the application of the products to the treatment sites and, if possible, to the times of UV irradiation. The comment maintained that prior knowledge of these variables may easily influence the reading of the MED by the evaluator, which would ultimately affect the calculated SPF.

The Panel did not require "blinding" in its recommended testing procedures for sunscreen drug products. However, the agency agrees with the comment that blinding would be a desirable part of the sunscreen testing procedures. The agency believes that the person who applies the sunscreen to the test site and administers the doses of UV radiation should not evaluate the erythema end points after the waiting period. In addition, if two or more sunscreens are being tested at the same time, they should be applied to the testing subsites in a randomized manner. If only one sunscreen is being tested, the agency believes that the doses of UV radiation should be applied in a random manner. In addition to being run the day prior to the test, a MED(US) (i.e., an untreated control site) should be run concurrently with the test sunscreen(s). The agency is proposing such a requirement in § 352.73(b). (See section II.B.—*Summary of Agency's Changes*, paragraph 40, of this document.)

The agency is aware that including an untreated control site in the randomization scheme could expose the test subject to an excessive dose of UV radiation on unprotected skin. To prevent this from occurring, the agency is proposing that the untreated control site be exposed to a series of UV radiation doses that are appropriate to determining the test subject's inherent MED as proposed in § 352.73. The agency is also proposing that the

appropriate standard preparation be included in the randomization pattern. Therefore, the agency is proposing that a standard preparation, as specified in § 352.70, be run every time a sunscreen drug product is tested. If the SPF of the sunscreen standard falls outside its specified range, the entire test should be considered invalid. (See comment 78.)

The comment suggested that one way to eliminate potential bias in clinical studies involving SPF determinations is to package the test sunscreen formulations in identical packages. If the above procedures are followed, the agency does not believe that test sunscreen formulations need to be packaged in identical containers.

The agency believes that blinding procedures should be included in the sunscreen testing procedures and, thus, is proposing to revise the Panel's recommended § 352.42(e), *Application of test materials*. The following sentences are being added to the end of paragraph (e): "If two or more sunscreen drug products are being evaluated at the same time, the test products and the standard sunscreen, as specified in § 352.70, should be applied in a blinded, randomized manner. If only one sunscreen drug product is being tested, the testing subsites should be exposed to the varying doses of UV radiation in a randomized manner." The agency is also proposing revisions in the Panel's recommended § 352.42(h), *Response criteria*, by adding the following sentence at the beginning of the paragraph: "In order that the person who evaluates the MED responses does not know which sunscreen formulation was applied to which site or what doses of UV radiation were administered, he/she must not be the same person who applied the sunscreen drug product to the test site or administered the doses of UV radiation." The agency is including these revisions in proposed § 352.72(e) and § 352.72(h), respectively.

Reference

(1) Comment No. C101, Docket No. 78N-0038, Dockets Management Branch.

92. One comment, submitted in response to the Panel's report, suggested that the testing of sunscreen agents with the solar simulator should also be performed on skin areas below the belt line, where no sun has typically changed skin color. The comment asserted that most people have tanned skin areas on the back from the neck to the belt line. Another comment referring to the subject selection procedures for testing sunscreen drug products was submitted in response to the public meeting held on January 26, 1988. At that meeting and in the notice

announcing the meeting (52 FR 33598 at 33599), the agency expressed concern regarding the apparent variability of data generated by the testing procedures recommended by the Panel. The comment stated that guidelines for the selection of subjects are not rigidly defined in the Panel's recommended monograph. The comment suggested that deviations in SPF determinations may result from the enrollment of subjects that do not meet the necessary criteria. Stating that volunteers of Skin Types I, II, and III are essential for evaluating the SPF value of the test product, the comment added that these subjects must not have undergone sunbathing or been exposed at a tanning salon for at least 30 days prior to enrollment as a test volunteer. The comment stated that the site for product application must be clearly defined, and products should not be tested on the habitually sun-exposed areas of the upper back (suprascapular region) or on the anterior forearms. The comment considered any fair-skinned subject who claims to be Skin Type I, II, or III, but who has a tanned back or who exhibits an intense immediate pigment darkening (IPD) reaction, as contributing to significant deviations in the determination of SPF values. The comment recommended that such subjects be dropped from the study after MED tests have been performed on day one of the test. The comment emphasized that fair-skinned individuals with untanned backs of Skin Types I, II, and III should be selected for the evaluation of sunscreen test products; individuals with tanned backs or those who have recently been exposed to the sun should be excluded. The comment added that the MED values of different regions of any test subject vary [e.g., the MED of the upper back (suprascapular) is always higher than the MED of the lower or central back (infrascapular)]. The comment maintained that the MED near the anterior cubital region of the upper arm is less than the MED of the volar antibrachial region of the lower arm due to the variations in the thickness of the stratum corneum and pigment content of the epidermis. The comment stated that such variations significantly influence the SPF determination. The comment concluded that to achieve uniformity in test results, the site for evaluation of sunscreen formulations should be specified, and it should preferably be the back area involving the infrascapular region.

The agency agrees with the second comment. Procedures for the selection of test subjects should be clearly

defined, and the site for product application should be the carefully inspected back between the beltline and the shoulder blades (scapulae) lateral to the midline. The Panel's recommended sunscreen testing procedures clearly define the criteria for the selection of test subjects and test sites. In § 352.42 of the Panel's recommended monograph, only fair-skinned volunteers with Skin Types I, II, and III are to be selected for enrollment in testing a sunscreen product. If a test subject has areas on the back that are unsuitable for testing a sunscreen product, then that subject should not be included in the study. In discussing the procedure for inspecting the test site of a potential test subject, the Panel recommended that a physical examination should determine the presence of sunburn, suntan, scars, active dermal lesions, and uneven skin tones on the areas of the back to be tested (43 FR 38206 at 38265).

The Panel also considered the areas of the body that are suitable for sunscreen testing and recommended the area of the back between the belt line and the shoulder blade, and lateral to the midline (43 FR 38265). The Panel stated that the back offers a large surface area which is best suited for testing and comparing a number of sunscreen samples. Also, the back has been traditionally used by manufacturers for testing new sunscreen agents. It is important to use the same skin site on the body for testing because comparisons must be made between treated and untreated areas, and areas treated with different ingredients. Using the same skin site helps to minimize testing result differences that are due to variations in skin sites rather than to actual differences between ingredients.

The first comment did not specify particular areas below the belt line that would be suitable for sunscreen testing, nor did it submit data that would demonstrate that the use of such areas will provide consistent test results that allow accurate comparisons between treated and untreated areas. Therefore, the agency accepts the Panel's recommendation that the area to be tested shall be the back between the beltline and the shoulder blade (scapulae) and lateral to the midline and is proposing this requirement in § 352.72(d).

The second comment did not provide any data to demonstrate that test subjects who exhibit an intense IPD reaction contribute to erroneous test results. In § 352.42(h), the Panel recommended that all immediate responses, including "immediate darkening or tanning" be recorded. The Panel did not, however, recommend

that subjects who displayed immediate reactions be excluded from testing. The agency is not now proposing to revise the Panel's recommendation. However, if adequate data are submitted demonstrating that an intense IPD reaction contributes to the variability of sunscreen test results, the agency will consider excluding such subjects by modifying § 352.72(h) concerning response criteria and/or § 352.72(i) concerning rejection of test data.

93. In its notice of a public meeting to discuss appropriate testing procedures for OTC sunscreen drug products (52 FR 33598 at 33601), the agency questioned the amount of test sunscreen and standard sunscreen that should be applied to the test subject. The agency noted that the Panel had recommended application of 2 mg/cm² (the application density). An independent sunscreen testing expert had suggested to the agency that 1 mg/cm² may be a more appropriate amount of sunscreen to use in the testing procedure because 1 mg/cm² more accurately reflects the amount of product normally used by a consumer. The agency commented that use of 1 mg/cm² would undoubtedly produce lower SPF values and suggested that this may be a way to accommodate the new higher SPF values because using this amount of the product may produce SPF values that more closely approximate the time a product will provide protection.

The agency received 24 comments in response to its question. The majority of the comments, including two manufacturer's associations in the United States, advocated continuing the use of an application density of 2 mg/cm². Nine comments, including one from a European manufacturer's association, suggested or recommended that the standard density of sunscreen product per application should be in the range of 1 to 1.5 mg/cm².

Comments advocating an application density of 1.5 mg/cm² stated that this particular issue is one which goes far beyond the simple question of how much sunscreen a consumer may typically apply. These comments stated that the published data on the application rates of sunscreens seem to be confusing because they vary over a wide range. One comment stated that, based on published studies and unpublished communications (Ref. 1), there is not a "universal" application amount which will be appropriate in all cases. The product type, its viscosity, the product container, consumer use habits, and the areas of the body to which the sunscreen is being applied are among the factors which determine

how much product a consumer may typically apply. Therefore, the comment noted, it should not be surprising that the application density amounts found in the literature vary from about 0.6 mg/cm² to 20 mg/cm². The comment stated that, although at first glance it may appear not to make any difference which amount one chooses to use for the test conditions, it is important that the testing procedure result in SPF values which reflect actual consumer protection.

The comment stated that several studies and comments have demonstrated that most products tested according to the current United States procedure (using 2 mg/cm²) have sun protection values which promise a higher protection than is usually experienced by a typical consumer under actual use conditions in natural sunlight (Ref. 1). The comment added that the test procedure should result in SPF values which are, in the majority of cases, reflective of actual consumer protection in natural sunlight. Otherwise, according to the comment, currently allowable label claims such as "Stay in the sun X-times as long as before without sunburning" are misleading and incorrect for the majority of consumers. The comment stated that using a smaller application amount, such as 1.5 mg/cm², will result in SPF values which more accurately reflect the actual protection a typical consumer will enjoy in natural sunlight. The comment contended that the DIN method for evaluating sunscreens, which uses an application amount of 1.5 mg/cm²±10 percent, results in SPF values more clearly reflecting actual consumer protection in natural sunlight. The comment felt that reducing the application amount to 1 mg/cm² may result in SPF numbers that are too low. The comment concluded that an application density of 1.5 mg/cm² would be the most appropriate to use for determining SPF values. According to the comment, use of this density would be a significant step towards a uniform, worldwide testing procedure that would ensure a certain level of protection from a product regardless of where in the world it was purchased.

A majority of comments, however, strongly advocated retention of 2 mg/cm² as the specified application density. Acknowledging that an international reference system of SPF values is a desirable goal, one comment stated that until all other details of the testing protocol are also identical (e.g., the light source used for testing), a change in the application density to a common level will not accomplish that end. The comment added that a review of the

literature supports the use of 2 mg/cm² as a meaningful test density that has been in use for 10 years.

Another comment noted that no other countries' standards use an amount as low as 1 mg/cm². The Australian standard is 2 mg/cm², and Japan and Britain generally follow the proposed FDA guidelines. Germany uses an application density of 1.5 mg/cm² ± 10 percent. Another comment stated that insofar as international uniformity is sought, 2 mg/cm² is a more appropriate figure than 1.5 mg/cm². The comment maintained that climate, geography, latitude, population diversity and size, and the multitudes of lifestyles that include year-round sunbathing make the United States a more reliable international model upon which to base sun exposure standards than Germany.

One comment noted that there are many published studies which discuss the average use level of lotions or sunscreen drug products. It cited a study by Schlagel and Sanborn (Ref. 2) which demonstrated that ointments or creams were applied to skin at a use rate of 2.4 mg/cm² when used to cover the whole body. The comment also mentioned a study by Hoppe (Ref. 3) in which the average use rate for sunscreen drug products was determined to be 4.0 mg/cm² for creams, 2.1 mg/cm² for lotions, and 0.75 mg/cm² for oils. The comment concluded that, for two of the three categories of sunscreen drug products, the use rate was greater than 2 mg/cm². The comment added that the results of a study by Lynfield and Schechter (Ref. 4), in which they investigated how vehicles were applied, demonstrated that application rates varied among individuals up to 100 percent, confirming that sunscreen application is a highly subjective exercise. The comment stated that this study found usage of a sunscreen lotion to be 1.3 mg/cm² 1.3 mg/cm². The comment maintained that it is especially interesting that 1.3 mg/cm² was the average application density when the subject was instructed to apply "thinly," whereas in the United States, the labeling of sunscreen products generally encourages "liberal" application.

The comment also discussed a study by Stenberg and Larko (Ref. 5) which indicated that the actual application of sunscreen preparations by individuals results in a layer thickness closer to 1 mg/cm² than 2 mg/cm². It stated that a publication of the Skin Cancer Foundation (Ref. 6) interpreted the study (Ref. 5) to mean that some individuals may be using "inadequate" amounts of sunscreen for achieving proper sun protection and emphasized

the need to use enough sunscreen to protect against sunburn and long-term skin damage. The comment noted that the Skin Cancer Foundation reiterated its support of the 2 mg/cm² level "recommended by dermatologists" (Ref. 6). The comment concluded that it is more in the public interest to encourage liberal use of sunscreens than it is to change the application density of SPF testing.

The comment further stated that, in over 10 years of testing sunscreens by the proposed FDA guidelines, it has become apparent that 2 mg/cm² is an amount which can be uniformly applied to the test site. The comment stated that use of a smaller amount makes uniform application much more difficult, and that some dosage forms cannot be uniformly applied at lower levels. The comment mentioned the wealth of preclinical information in the scientific literature regarding the effects of sunscreens in preventing skin cancer and premature aging. The comment stated that such tests have generally been conducted using the 2 mg/cm² sunscreen application rate. The comment expressed concern that a change in the application density will make past scientific studies difficult to interpret for comparative purposes. As a result, the comment contended that the scientific community would lose 10 years of valuable historical data that are the basis of much of the educational position of the AAD and the Skin Cancer Foundation. The comment emphasized that there is no scientific support indicating that any other application amount, including 1 mg/cm² or 1.5 mg/cm², is better, more accurate, or more reflective of consumer use. Another comment stated that a change in the application density ought to be considered by the agency only when the results are necessary for adequate protection of the public health.

Several comments noted that consumers have learned by experience what level of labeled SPF they need individually to help prevent sunburn. These comments asserted that radically altering the system for determining SPF values would lead to confusion and inappropriate choices of sunscreen products. One comment stated that consumers in the United States now have over 10 years of experience with products tested at 2 mg/cm², they have become familiar with the benefits provided by these SPF's based on that testing, and they purchase products on the basis of that familiarity. The comment maintained that lowering the application density in the SPF determination would, in many cases, alter the SPF value, leading to industry-

wide relabeling and/or reformulation of most sunscreen drug products. The comment felt that, from the consumer's point of view, such a change would require a complete revision in his or her sunscreen buying habits. Noting that an individual who burns moderately and tans gradually typically wants and uses an SPF 4, the comment contended that a product with an SPF of 4 based on a 1 mg/cm² application density would provide more protection than he or she expects or wants. The comment felt that it is not sound public policy for FDA to disturb an established labeling scheme when the change will confuse consumers and the agency has no information that the change will provide any real benefits.

Another comment agreed with the comment above and strongly recommended retention of the 2 mg/cm² application density. Noting that its sunscreen products are labeled with a toll free number to allow consumers to readily report their concerns or complaints, the comment stated that during the past 2 years, data from this consumer contact line, along with all other correspondence, indicate that only 10 reports of sunburning are received per one million units of sunscreen product distributed. The comment contended that these data suggest that consumers are not being misled by SPF claims and are choosing the products appropriate to their skin type and sun exposure habits. The comment added that its sunscreen products include the instructions to apply "liberally" or "generously." The comment asserted that from the low incidence of reported sunburn it can be inferred that these instructions are being followed. The comment concluded that consumers are adequately choosing and applying sunscreen products with the proper SPF and that the current testing methodology is using the appropriate amount of sunscreen for determining SPF values.

The agency agrees with the majority of the comments. Changing the amount of sunscreen used in the sunscreen testing procedures from 2 mg/cm² to 1.5 or 1 mg/cm² would negatively affect consumers and the scientific community.

The agency agrees with one comment that using 2 mg/cm² of sunscreen product in the testing procedure ensures a more uniform application over the test area and thus contributes to a more accurate method of determining SPF values for product labeling. According to published literature (Refs. 2 through 5), actual application density of sunscreen drug products by consumers varies greatly, ranging from a high

amount of 4.0 mg/cm² to a low amount of 0.75 mg/cm² (Ref. 3). Because of the thickness and viscosity of some sunscreen formulations, amounts smaller than 2 mg/cm² may be difficult to apply uniformly. If the application density is not uniform across all the testing sites, the resultant MED's are not indicative of the true protection provided by the test product. The SPF calculated from those MED's would be meaningless. Labeled SPF values should be based on testing conducted under the most carefully controlled conditions, so that the results are as accurate and reproducible as possible. The outcome of an accurate and reproducible testing procedure ensures that competitive products with the same SPF values provide essentially the same degree of protection.

Most consumers accept and understand the currently used SPF system. This system effectively communicates to consumers the amount of protection that can be expected from the product. The agency believes that changing this aspect of the SPF system would result in unnecessary consumer confusion and would not be in the public interest.

The agency points out that the SPF value is not an absolute predictor of sunscreen protection. There are many variables involved in sunscreen use (e.g., skin type, latitude, altitude, whether the consumer is at the beach or in a city, and spreading characteristics of the product). The value of the SPF is that it is derived by strictly standardized testing procedures and, therefore, provides a convenient means of product-to-product comparison. The SPF provides consumers a means to evaluate and compare sunscreen drug products based upon the consumer's previous experience in the sun and previous use of products with an identified SPF value. The agency believes that currently there is no scientific need to change the sunscreen testing procedures to include an application density lower than 2 mg/cm².

Based on the above discussion, the agency is proposing that 2 mg/cm² be the amount of sunscreen used in the testing procedures in § 352.72(e).

References

- (1) Comment No. APE003, Docket No. 78N-0038, Dockets Management Branch.
- (2) Schlager, C. A., and A. B. Sanborn, "The Weights of Topical Preparations Required for Total and Partial Body Irritation," *Journal of Investigative Dermatology*, 42:253-256, 1964.
- (3) Hoppe, U., "Photostabilität und Hautaffinität," *Journal of the Society of Cosmetic Chemists*, 25:667-680, 1974.

(4) Lynfield, Y. L., and S. Schechter, "Choosing and Using a Vehicle," *Journal of the American Academy of Dermatology*, 10:56-59, 1984.

(5) Stenberg, C., and O. Larko, "Sunscreen Application and its Importance for the Sun Protection Factor," *Archives of Dermatology*, 121:1400-1402, 1985.

(6) Skin Cancer Foundation, "Sunscreen Skimping," *Sun and Skin News*, 3:2, 1986.

94. In § 352.42 of its recommended monograph, the Panel stated that groups of 20 subjects should be used for each test panel for determining SPF values. The Panel added that "the standard error shall not exceed ± 5 percent of the mean. An appropriate number of additional subjects shall be used to determine the PCD, if a PCD does not fall within the limits of the standard error."

One comment mentioned an apparent contradiction between the Panel's definition of standard error for a 20-subject test group (i.e., 25 percent divided by $\sqrt{20}$, which equals 5.59 percent) and the Panel's later statement that the "standard error" should not exceed ± 5 percent of the mean (43 FR 38206 at 38261). The comment assumed that the Panel intended that the standard deviation of the sample should be used to calculate the standard error because the stated standard error for 20 subjects exceeds 5 percent by the definition given. The comment suggested that an additional definition of standard error is required. The comment recommended that the required number of subjects be based on the confidence interval of the mean at a 90-percent level and that the minimum number of subjects should be eight. The comment added that to categorize a product as being within a PCD, the 90-percent confidence interval should fall entirely within a PCD.

Another comment stated that when the Panel initially considered test subject populations, it had considered subject populations ranging from 8 to 12 subjects. However, based upon the collaborative study on standard sunscreen product testing submitted to the Panel by CTFA and NDMA (Ref. 1), the Panel concluded that 20 test subjects would provide a better estimate of a product's SPF value and PCD. The comment stated that this study demonstrates that the inherent standard deviation of the tests performed should not exceed 25 percent of the average SPF for the test formula, regardless of the laboratory in which the test was performed. The comment maintained, therefore, that the Panel felt no advantage accrued from using confidence limits that are dependent upon the standard error or standard

deviation of the test results. The comment asserted that the standard error could be specified thereby controlling the precision of the categorization. The comment suggested that the statistical method proposed by the previous comment (i.e., number of subjects based on the confidence interval of the mean at a 90-percent level with the minimum number of subjects set at eight) should be rejected and the method included in the Panel's recommended § 352.42(g) should be used.

Another comment suggested revising the last sentence of the Panel's recommended § 352.42(g) as follows: "An appropriate number of additional subjects should be used to determine the PCD, if the mean of the SPF test when combined with the allowable minus standard error result in a value below the minimum limit of the PCD." One comment requested that the last sentence of § 352.42(g) be replaced by the following statement: "If the standard error exceeds 5 percent, an appropriate number of additional subjects shall be used to determine the PCD so that the standard error is within this limit."

In the notice announcing a public meeting on sunscreen testing procedures (52 FR 33598 at 33600), the agency stated that it was considering revising the Panel's recommended § 352.42(g) as follows: "Number of subjects. Groups of at least 20 subjects shall be used for each test panel. The panel size shall be fixed in advance and additional subjects shall not be added." The agency asked that, if this change is not acceptable, what is the best method for evaluating sunscreen test data to determine if additional subjects are needed to obtain a valid SPF value, and what is the minimum number of subjects required? The agency invited public comment on the possible change.

Most of the comments agreed that (1) test panels should consist of at least 20 subjects, (2) the size of the test panel should be fixed in advance, (3) the limitations that the standard error should be less than ± 5 percent should not apply, and (4) the testing procedures should make it clear that the addition of subjects to the test panel to achieve the desired minimum is acceptable under specific conditions. One comment maintained that any SPF value derived from a minimum of 8 subjects per test product would not provide convincing data of SPF values acceptable at 99 percent confidence limits.

Another comment, agreeing that at least 20 subjects are needed to complete a test with acceptable data, recommended that the agency recognize the following specific conditions

requiring the rejection of data and the subsequent addition of subjects to the test panel: (1) When the exposure series of a given subject fails to elicit an MED response on either the treated or unprotected skin sites, and (2) when responses on the treated sites are randomly absent. The comment also suggested that if a subject withdraws from the test due to illness, schedule or work conflicts, etc., it should be permissible to replace such subjects on an "as-needed" basis because over-recruitment for a study in anticipation of such withdrawals is expensive, inefficient, and unnecessary.

One comment agreed that the agency should allow a limited number of subjects (e.g., 3 to 5) to be added to a test panel if the criteria for PCD are not met due to deviations resulting from inconclusive SPF data. Another comment recommended that the total number of "replaceable" test panel members be limited to 5; if this number is exceeded, the entire test should be repeated. The comment added that the requirement that "the standard error shall not exceed ± 5 percent of the mean" is an arbitrary and unsubstantiated limitation and should not be applied.

One comment stated that it has been a common practice to use data from a smaller panel for a preliminary SPF determination and to supplement this panel with enough test subjects to bring the total panel size to a minimum of 20 for the final SPF determination. The comment recommended that this concept should be recognized in the final monograph. The comment proposed that § 352.42(g) be revised to read as follows: "Number of subjects. Group of at least 20 subjects shall be used for each test panel. The panel size shall be fixed in advance and additional subjects shall not be added unless individuals need to be dropped from the study for noncompliance or other legitimate, not test-related reasons or if their response to the test conditions is such that it will not allow a statistical evaluation. The total number of replaceable individuals shall not exceed 5 individuals. It is not required that the entire panel be subjected to the test at the same time."

Conversely, one comment suggested that 20 subjects appears to be the maximum needed for each test panel. It added that a lower number may be possible provided that criteria are built into the method that lay down maximum tolerances on the deviations between readings on each subject. Another comment suggested that panels could be restricted to 10 or 12 persons if the MED of each person is determined

in advance and the product's SPF is approximated. One comment stated that it could neither concur with nor refute the adequacy of 20 subjects based upon the documentation provided for review.

One comment stated that experience in Australia demonstrates that a panel size of 10 subjects yields results similar to those obtained on the same formulation in the United States when 20 subjects are used. The comment suggested that the upper limit on panel size should be fixed, for example at 25, and that the test data should be rejected if, for example, 20 valid results are not obtained. The comment added that it is appropriate to retain the Panel's proposed limit on the standard error of the mean.

One comment agreed with the agency's position stated in the notice of public meeting (52 FR 33598 at 33600) that substitutions or additions to a panel should not be allowed. The comment maintained that where all sites on the sunscreen protected area show erythema, these data should be incorporated into the estimate of the mean instead of merely rejecting them as indeterminate results. The comment suggested that if any panelist showed all irradiated spots on the sunscreen protected site, statistical analysis should automatically be handled by a nonparametric test, such as the modified median test or the Wilcoxon signed ranks test. The comment stated that the purpose of using such methods is to ensure that detrimental (yet valid) test results be included in the determination of the SPF estimate and not excluded because they were nondetermined. The comment maintained that this method would more conservatively estimate the protection provided by the test sunscreen.

One comment stated that the final monograph should be very specific in outlining criteria that would disqualify a test subject; the monograph should allow for subsequently replacing that individual on the test panel. For example, the comment stated that if a test subject were erythematous on all subsites, one could not calculate an SPF value and using another test subject should be permissible. Likewise, it should be acceptable to replace a test subject because of noncompliance or other reasons unrelated to the test. Another comment stated that criteria for adding additional subjects are outlined in the Panel's report (43 FR 38206 at 38266) and recommended retaining this procedure. The comment stated that the statistical procedures should provide for the addition of test subjects in the event that the SPF variability precludes

placing the product in the desired PCD. Additional subjects should be limited to the smallest number necessary to classify the mean SPF value ± 5 percent standard error of the mean or to classify the mean SPF with a power coefficient of 0.8.

The agency recognizes the possibility that during the testing of sunscreen drug products some subjects may not produce data suitable for analysis. Additionally, there may be instances where a subject must withdraw from a study and a question may arise about replacing this subject. Nevertheless, once a subject enters a study, the subject should be considered as part of the study. If the subject withdraws before any data are obtained, the subject may be replaced because the person has not really become part of the study. However, once data are obtained on a subject, the person should not be replaced but should be considered as producing nonvalid data for analysis. The reason for this approach is that preliminary data obtained may influence a subject's decision to leave the study and thus may introduce biases. In general, the guiding principle should be that new subjects are not allowed. Therefore, the agency has determined that the appropriate approach is for test panels to start at a fixed number (the agency is proposing that that number not exceed 25), from which at least 20 subjects must produce valid data for analysis. Nonvalid test data should be rejected, but the subjects should not be replaced. If there are more than five nonvalid subjects, the study should be considered a failure.

The agency agrees that the standard error criterion recommended by the Panel in § 352.42(g) is confusing. Accordingly, that criterion is not being proposed. Instead, the agency is proposing a one-sided t-test to analyze the data obtained from the sunscreen testing procedures. The analysis of sunscreen testing data is discussed further in comment 97.

Therefore, the agency is proposing the following in § 352.72(g): "*Number of subjects.* A test panel shall consist of not more than 25 subjects with the number fixed in advance by the investigator. From this panel, at least 20 subjects must produce valid data for analysis."

All subjects producing valid data must be used in the analysis. Likewise, any subject producing nonvalid data must be omitted from the analysis. Nonparametric tests, such as the modified mean test or the Wilcoxon signed ranks test, should not be used to analyze indeterminate test results. In § 352.42(i) "Rejection of test data," the Panel recommended the following as

valid reasons to reject subject data: (1) The exposure series fails to elicit an MED response on unprotected skin sites; or (2) responses on treated sites are randomly absent, which indicates the product was not spread evenly. The agency agrees with the Panel, but believes that subject noncompliance is an additional reason for rejecting data. Therefore, the agency is proposing to revise the Panel's recommendation by adding the phrase "or if the subject was noncompliant (e.g., subject withdraws from the test due to illness or work conflicts, subject does not shield the exposed testing site from further UV radiation until the MED is read, etc.)." The information on "Rejection of test data" appears in proposed § 352.72(i).

The agency agrees with one comment's suggestion that it is not necessary or practical to test the entire panel of test subjects at the same time. Testing a limited number of subjects per day over a period of several days should not compromise the testing so long as the testing is properly controlled (e.g., the light source is calibrated, concomitant testing of the standard preparation is done, the SPF of the standard preparation falls within the range specified in § 352.70, etc.). However, the agency does not believe that it is necessary to include such a stipulation in the monograph.

Reference

(1) Comment No. SUP002, Docket No. 78N-0038, Dockets Management Branch.

95. Several comments presented suggestions and recommendations to clarify the definition and precision of measurement of the "minimal erythema dose (MED)" recommended by the Panel in §§ 352.42(h) and 352.43 of its testing procedures. Three comments stated that the MED should be defined as the minimal erythema producing uniform redness and sharp borders (or erythema reaching all borders). One comment stated that using "any perceptible change" or "just perceptible change" as the endpoint of erythema response will result in doubtful determinations. The comment stated that one of the great problems in deciding upon a definition of "MED" occurs when high SPF sunscreens are tested with solar simulators, because these sunscreens are very effective in absorbing UVB radiation and very long irradiation times are needed. Therefore, significant amounts of UVA radiation are delivered to the skin, so that erythema at the sunscreen-protected sites is mainly due to UVA radiation. In patients with Skin Type II and III, immediate pigmentation is produced, some of which lasts for 24 hours. Consequently, sites will appear

faintly tanned with doses well below those producing erythema and the question of "just perceptible change" becomes difficult to answer. The comment also maintained that it has been shown that it takes significantly less UVA energy to produce erythema with a high irradiance UVA emitting radiation source than with a less intense one (Ref. 1). Because modern solar simulators are designed to give high irradiance (up to 100 milliwatts/cm² UVA) so as to shorten irradiance times, the comment stated that MED values (determined using "just perceptible erythema" criteria) may vary greatly between investigators depending upon the radiation source used.

The comments suggested various postexposure (after irradiation) time limits for the evaluation of an erythema reaction to UV radiation: 22 to 24 hours, 22 to 24 hours (± 10 percent), and 22 hours (± 10 percent). Maintaining that erythema due to UVA radiation has an earlier onset than that of UVB, but has a prolonged peak, one comment concluded that 22 to 24 hours should be satisfactory for both.

Three of the comments suggested environmental conditions under which MED values should be determined. Two maintained that the MED should be read under a tungsten light source. Another comment suggested that the erythema response of the skin of all test subjects should be evaluated under the same conditions of illumination. If natural light is not available, the comment suggested all test subjects be examined under a 100-W tungsten light bulb. The comment added that fluorescent light should not be used to assess the MED because major deviations in MED values can result if some subjects are examined under natural light and some are examined under cool, white fluorescent light. All three comments stated that the posture or body position should be the same for all test subjects. One comment maintained that the visually recognizable erythema response often varies with the posture (e.g., the exposed back when examined in a prone position versus a vertical or standing position). Another comment contended that the MED should be read with the subject in the same position as during irradiation. Two of the comments suggested that the MED readings be done in rooms where the external temperature is between 20 and 25 °C.

In §§ 352.42(h) and 352.43 of its recommended monograph, the Panel defined the MED as "the time of exposure that produces the minimally perceptible erythema at 16 to 24 hours postexposure." The agency believes that

this definition should be clarified and narrowed. The Panel stated that immediate pigmentation fades in 30 to 60 minutes (43 FR 38206 at 38266). However, more recent information indicates that immediate pigmentation or immediate tanning may persist with higher doses of UV radiation for 1/2 to 1 hour, up to 24 hours, or (rarely) for 36 to 48 hours after prolonged exposure (Ref. 2). Therefore, the agency agrees with the comments that immediate pigmentation may interfere with an investigator's perception of minimally perceptible erythema. This is especially true when testing a high SPF sunscreen product, where a large dose of UV radiation is required, or if the MED evaluation is done at 16 hours postexposure. Sunscreen testing results will be more accurate and comparable if the MED is defined as the smallest dose of UV radiation that produces redness reaching the borders of the exposure site, and if the MED is determined at 22 to 24 hours postirradiation rather than 16 to 24 hours postirradiation. This time is consistent with those requested by the comments.

The agency has considered the comments' suggested environmental conditions under which the MED should be determined (i.e., light source, position of the body, and temperature of the room). The Panel did not include such conditions in § 352.42(h) of its recommended monograph. Nonetheless, the agency agrees with the comments that some environmental conditions should be included in the sunscreen testing procedures.

In discussing testing procedures, the Panel stated that when reading the MED, the investigator should use a constant light source such as an incandescent or warm white fluorescent lamp at a fixed distance (43 FR 38206 at 38260). The agency believes that there is little difference between the light emitted from an incandescent (i.e., tungsten) light and a warm white fluorescent light. The illumination level at the site of inspection is more important than the source of illumination. The agency notes that various illumination levels are recommended for other types of critical observations (i.e., 300 lux for medication preparation areas, 500 lux for emergency room treatment areas, and 22,000 lux for the emergency table in an operating room) (Ref. 3). The agency believes that 500 lux is an appropriate illumination level for evaluating the MED. Therefore, the agency is proposing in § 352.72(h) that the source of illumination should be either a tungsten light bulb or a warm white fluorescent light bulb that

provides a level of illumination at the test site within the range of 450 to 550 lux.

The agency agrees with the comments that the MED should be assessed with the subject in the same position used when the test site was irradiated. Hawk and Parrish (Ref. 2) state that MED assessments should always be made with the subject in the same position to prevent MED variations. The agency is proposing this requirement in § 352.72(h). However, the agency does not believe it is necessary to specify a particular position.

There is insufficient information to determine whether the temperature of the room in which the MED is assessed has an effect on the MED. Therefore, the agency is not proposing a specific temperature, but is requesting further comment.

Based on the above, the agency is proposing to include in § 352.72(h) the following: " * * * the MED is determined 22 to 24 hours after exposure. The erythema responses of the test subject should be evaluated under the following conditions: the source of illumination should be either a tungsten light bulb or a warm white fluorescent light bulb that provides a level of illumination at the test site within the range of 450 to 550 lux, and the test subject should be in the same position used when the test site was irradiated. Testing depends upon determining the smallest dose of energy that produces redness reaching the borders of the exposure site at 22 to 24 hours postexposure for each series of exposures * * *." The agency is also proposing in § 352.73 that the MED is the lowest dose of radiation that produces uniform redness reaching the borders of the exposure site at 22 to 24 hours postexposure.

The agency is also proposing to provide a definition of MED in § 352.3 by adding new paragraph (a) as follows: "Minimal erythema dose (MED). The smallest dose of ultraviolet (UV) radiation (expressed as Joules per meter squared) that produces redness reaching the borders of the exposure site." Other definitions in § 352.3 are being renumbered to adjust for the addition of new paragraph (a).

References

- (1) Kagetsu, N., R. W. Gange, and J. A. Parrish, "UVA-Induced Erythema, Pigmentation, and Skin Surface Temperature Changes Are Irradiance Dependent," *The Journal of Investigative Dermatology*, 84:445-447, 1985.
- (2) Hawk, J. L. M., and J. A. Parrish, "Responses of Normal Skin to Ultraviolet Radiation," in "The Science of Photomedicine," edited by J. D. Regan and J.

A. Parrish, Plenum Press, New York, pp. 227, 240, and 241, 1982.

(3) "Institutions and Public Buildings; Health Care Facilities," in "IES Lighting Handbook," 1981 Application Volume, edited by J. E. Kaufman and H. Haynes, Illuminating Engineering Society of North America, New York, pp. 7-4 to 7-17, 1981.

96. Two comments argued that in the Panel's sunscreen testing procedures smaller increments in exposure time would provide more accuracy in determining SPF values that exceed 15. In § 352.43 of its recommended monograph, the Panel included a geometric series of time intervals represented by $(1.25)^n$, such that each exposure time interval is 25 percent greater than the previous time (43 FR 38206 at 38265 to 38266). One comment requested that § 352.43 be revised to read "The time intervals selected shall be a geometric series represented by $(1.X)^n$, where X is greater than zero but less than or equal to 25." Several comments suggested that this section be revised to read, "The time intervals selected shall be a geometric series represented by $(1.X)^n$ wherein each exposure time interval is X percent greater (X must not exceed 25 percent) than the previous time * * *."

In its notice of a public meeting to discuss appropriate sunscreen testing procedures, the agency stated that exposure times are crucial to the accurate determination of SPF values and PCD's (52 FR 33598 at 33601). However, the agency expressed concern over the Panel's recommended time intervals. The agency stated that there may be little justification for geometrically increased exposure time intervals because use of such intervals offers less precision in the upper SPF ranges. The agency added that precision in the upper SPF ranges has become increasingly important because of the appearance on the OTC market of sunscreen drug products with SPF values much higher than 15 (i.e., up to 30). Because the MED can be measured with equal precision across the full range of an arithmetically arranged series of exposure times, the agency stated it was considering using an arithmetical progression of at least 11 exposure times increasing in 4-second increments, beginning with a 10-second exposure and ending with a 50-second exposure time (i.e., 10, 14, 18, 22, 26, 30, 34, 38, 42, 46, and 50 seconds).

A number of comments objected to the proposed arithmetic progression. Most of the comments preferred a geometric progression method similar to the one recommended by the Panel in § 352.43. Several comments added that this method has been successfully used

by industry for many years. Some comments contended that the fundamental relationship between SPF values and sunscreen spectral absorbency is logarithmic and, therefore, the correct approach is the use of geometric progressions. Another comment stated that the SPF is a ratio of two independently determined values; statistically, ratio values are treated with geometric techniques in order to compensate for the higher expected variance simply because the value is a ratio of two independently-variable measurements. The comment maintained that the precision of the SPF ratio depends on both variables, i.e., the protected skin MED (numerator) and the unprotected skin MED (denominator), but more critically on the denominator which is the smaller quantity. The comment argued that the agency's proposed arithmetic progression would, in many instances, use larger exposure intervals for the unprotected irradiated sites than the Panel's recommended 25-percent exposure intervals, and would compromise rather than improve precision.

One comment contended that a valid scientific rationale for using geometrically increasing time intervals is to relate the SPF values to the time exposures. The comment stated that available data provided only limited ability to examine the need for geometric time increments. The comment added that careful consideration should be given to the spacing of the geometric progression to ensure that there are not large intervals at the upper end of the range of exposure times, thereby eliminating overestimations of the SPF values. One comment maintained that there is little in the photobiologic literature to support arithmetic progressions. Other comments stated that the references cited in the meeting notice (52 FR 33598 at 33602) in support of the agency's proposal do not contain any data supporting use of arithmetic progressions for sunscreen testing.

Two comments stated that an arithmetically arranged series of exposures would result in differences in redness between exposure sites that are too small for the trained human eye to distinguish, i.e., the agency's geometric dosing schedule is based on MED determination sensitivity of which the human eye is incapable. Thus, such a procedure would make the results more subjective rather than more precise as the agency intended.

Many comments expressed concerns for the well-being of the test subjects. They maintained that the agency's proposed arithmetic progression would

subject the test subjects to at least 11 UV radiation exposures, resulting in great risk, discomfort, injury, and unnecessary UV radiation exposure. One comment stated that for a single SPF determination the agency's proposed arithmetic progression would require a minimum of 33 irradiated sites (including the standard), more than half of which could develop a sunburn reaction. The comment added that the agency's proposal would increase the time that a test subject would be exposed to the solar simulator. In order to test a sunscreen with a theoretical SPF of 22, the comment asserted that the exposure time would be increased from about 60 minutes to 135 minutes. The comment concluded that this proposed procedure would make it impractical to test samples with an SPF higher than 22. Another comment agreed that the risk of exposure to UV radiation to test subjects, the time required for testing, and the number of testing sites would increase with the agency's proposed methodology. The comment stated that the increase in the number of testing sites becomes critical when testing water resistant sunscreen drug products, which require additional test sites.

Two comments suggested that a preliminary range-finding pilot study involving 3 subjects should be performed prior to testing an experimental product on a 20-person test panel. A pilot study would prevent the needless overexposure and "UV burn" of a large number of test subjects that results from the occasional overestimation of a product's SPF or from the underestimated substantivity of a "wash-off" sunscreen drug product. One comment recommended that the maximum erythema on the protected skin not be induced by more than twice the MED on the protected skin. Several comments stated that the radiation exposure times specified by the agency in the public meeting notice (52 FR 33598 at 33601) are not applicable to all xenon arc radiation sources, because some xenon arc sources may require longer or shorter time exposures due to higher wattage or radiation intensity.

Another comment considered the use of a geometric or arithmetic progression in determining the relevant exposure times. If a geometric progression series is used, the comment asserted that the important issue is that the "multiplier factor has to be determined very carefully."

Several comments suggested various methods of determining the exposure intervals to accommodate OTC sunscreen drug products with SPF values in excess of 15. One comment

contended that a better approach would be to use a geometric series of 5 exposure times rather than the agency's proposal for an arithmetic progression of 11 exposure times. The comment suggested that the exposure intervals of the geometric series should be calculated as follows: (1) $(1.25)^X$ for products with an estimated SPF less than 8, (2) $(1.20)^X$ for products with an estimated SPF from 8 to 15, and (3) $(1.15)^X$ for products with an estimated SPF greater than 15. Two comments from a manufacturers' association added that industry should have the option of choosing smaller increments than 25 percent, if desired, in order to achieve greater precision when testing for SPF values. For example, the time intervals selected should be a geometric series represented by $(1.X)^N$ such that each exposure time interval is X percent times greater (X must not exceed 25 percent) than the previous time interval. Another comment recommended a two-tier approach with a cut-off point between SPF 6 and 8. Below SPF 6 or 8, a geometric series based on $(1.25)^n$ would be used. Above SPF 6 or 8, "smaller increments of $(1.25)^n$ " corresponding to $(1.12)^n$ would be used.

One comment strongly recommended that the agency adopt the delivery of UV radiation in terms of mJ/cm^2 , and not in seconds or minutes. Several comments added that the term "light exposures" discussed in the "Exposure times section" of the public meeting notice (52 FR 33598 at 33601) should be expressed in the context of "dose" rather than "time." According to the comments, the term "dose" would allow for the use of both radiance and time as variables.

The agency agrees with several comments that the expression of radiation exposures be in terms of dose rather than time. The term "dose" is more appropriate because it allows for the use of both radiance and time as variables. Although the Panel defined UV radiation exposure in units of time, the agency believes that it is more accurate to express dose as the "erythema effective exposure," in units that define the total amount of erythema effective energy applied to the testing subsite (J/m^2). (The agency is using the term "exposure dose" rather than "exposure time" in this tentative final monograph. See comments 84 and 85.)

The agency agrees with the suggestion that a preliminary range-finding study be performed prior to testing a new sunscreen product on a test panel. The study would prevent unnecessary risks of discomfort, injury, and overexposure to UV radiation to the test subjects.

However, there is insufficient information to establish specific requirements for a preliminary range-finding study at this time. Therefore, the agency is not now proposing such a study in the monograph, but is inviting additional comments and data as to appropriate requirements for such a study.

The agency also agrees that an arithmetic progression of determining exposure doses in the SPF testing for OTC sunscreen drug products is not the method of choice, for the following reasons: the arithmetic progression of exposure doses would: (1) Expose the test subjects to higher doses of UV radiation than necessary, particularly at the higher end of the exposure series; (2) provide differences in redness between exposure sites that are too small for the trained eye to distinguish; (3) prolong the time required to deliver exposure doses to the test subjects; and (4) reduce flexibility in exposure doses needed to accommodate different solar simulators. A geometric progression that is modified to take into account the higher SPF values is more appropriate for determining exposure doses, for the following reasons: (1) It reduces the risk of exposure to UV radiation to the test subjects by decreasing testing time and the number of exposure sites, and (2) a geometric series covers a larger range of exposure doses with fewer exposures.

The agency believes that a geometric series with only five exposure doses may produce overestimations of the true SPF values, thereby producing biased estimates. The possible production of biased estimates is illustrated in the following example: if the MED(US) is 30 J/m² and the product being tested has an expected SPF of 8, the exposure doses would be 0.69X, 0.83X, 1.0X, 1.2X, and 1.44X, using 1.20 as the base in a geometric series. Here, X is set to yield the estimated SPF, e.g., $X = 30 \text{ J/m}^2 \times 8 = 240 \text{ J/m}^2$ of exposure doses. The exposures would be 165.6, 199.2, 240, 288, and 345.6 J/m², respectively.

For the above example, a substantial number of MED(PS) would be observed at 240 J/m², as well as 199.2 and 288 J/m². If the same number of subjects are observed at the 199.2- and 288-J/m² exposure doses, the mean SPF would be greater than the expected SPF of 8. For example, if out of 20 subjects, 10 MED(PS) were observed at 240 J/m², 5 at 199.2 J/m², and 5 at 288 J/m², the corresponding SPF values for these MED(PS) values are 8.00, 6.64, and 9.6, respectively. In this example, an MED(PS) of 288 produces an SPF of 9.6, which is 1.6 units above the expected SPF value of 8, while an MED(PS) of 199.2 produces an SPF of 6.64, which is

only 1.36 units different from the expected value of 8. Because the exposure dose of 288 J/m² is a greater distance from 240 than 199.2 is from 240, each time a MED(PS) greater than 240 is produced, it is assigned an undue extra large value. Ultimately, the effect produces an overestimation of the average SPF value.

The major reason for the overestimation is that the geometric series is implemented in such a way that it has a nonsymmetric assignment of SPF values. When an MED(PS) exceeds the expected MED(PS), it produces a corresponding SPF farther away from the expected SPF value than when the observed MED(PS) is below the expected SPF value.

The agency believes that exposure doses are crucial to the accurate determination of SPF values and PCD's. A geometric series similar to that proposed by the Panel, but modified to include 2 additional exposure doses equally spaced around the expected SPF, would eliminate the overestimation of the true SPF value of a product with a high SPF value. This procedure would also restrict the testing range for products with low SPF values. The doses selected would consist of a geometric series of 5 exposures where the middle exposure is placed to yield the expected SPF plus 2 other exposures, placed symmetrically around the middle exposure.

The agency agrees with one comment that different exposure doses are appropriate for determining different SPF values for greater accuracy. The exposure doses for the geometric series should be calculated as follows: (1) (1.25)X for products with an estimated SPF less than 8, (2) (1.20)X for products with an estimated SPF from 8 to 15, and (3) (1.15)X for products with an estimated SPF greater than 15. The use of dosage intervals smaller than 25 percent is necessary to eliminate bias in the testing and to ensure accurate SPF determinations of sunscreen drug products with high estimated SPF values. The agency is proposing that the exposure intervals selected be a geometric series represented by (1.X)ⁿ such that each exposure dose is X percent greater than the previous dose (X must not exceed 25 percent).

For products with expected SPF values less than 8, the exposure doses could be 0.64X, 0.80X, 0.90X, 1.00X, 1.10X, 1.25X, and 1.56X, where X represents the expected SPF of the product. For products with expected SPF values between 8 and 15, the exposure doses could be 0.69X, 0.83X, 0.91X, 1.00X, 1.09X, 1.20X, and 1.44X, where X represents the expected SPF of

the product. For products with expected SPF values greater than 15, the exposure doses could be 0.76X, 0.87X, 0.93X, 1.00X, 1.07X, 1.15X, and 1.32X, where X represents the expected SPF of the product. Accordingly, the agency is proposing to revise the Panel's recommended determination of SPF values (§ 352.43) by including a new paragraph in proposed § 352.73(c) as follows:

Determination of individual SPF values. A series of UV radiation exposures expressed as Joules per meter squared (adjusted to the erythema action spectrum calculated according to § 352.73(a)) is administered to the subsite areas on each subject with an accurately calibrated solar simulator. A series of seven exposures shall be administered to the protected test sites to determine the MED of the protected skin (MED(PS)). The doses selected shall consist of a geometric series of five exposures, where the middle exposure is placed to yield the expected SPF plus two other exposures placed symmetrically around the middle exposure. The exact series of exposures to be given to the protected skin shall be determined by the previously established MED(US) plus the expected SPF of the test sunscreen. For products with an expected SPF less than 8, the exposures shall be the MED(US) times 0.64X, 0.80X, 0.90X, 1.00X, 1.10X, 1.25X, and 1.56X, where X equals the expected SPF of the test product. For products with an expected SPF between 8 and 15, the exposures shall be the MED(US) times 0.69X, 0.83X, 0.91X, 1.00X, 1.09X, 1.20X, and 1.44X, where X equals the expected SPF of the test product. For products with an expected SPF greater than 15, the exposures shall be the MED(US) times 0.76X, 0.87X, 0.93X, 1.00X, 1.07X, 1.15X, and 1.32X, where X equals the expected SPF of the test product. The MED is the lowest dose of radiation that produces uniform redness reaching the borders of the exposure site at 22 to 24 hours postexposure. The SPF value of the test sunscreen is then calculated from the dose of UV radiation required to produce the MED of the protected skin and from the dose of UV radiation required to produce the MED of the unprotected skin as follows: $\text{SPF value} = \frac{\text{ratio of erythema effective exposure (Joules per meter squared)}}{\text{MED(PS) to the erythema effective exposure (Joules per meter squared)}} \text{MED(US)}$.

Reference

(1) Magnus, I., "Reductions of Normal Skin to UVR and to Visible Light," in "Dermatological Photobiology," Blackwell

Scientific Publications, Oxford, pp. 117-163, 1976.

T. Comments on the Statistical Analysis of Results from the Testing Procedures for Sunscreen Drug Products

97. Many comments questioned aspects of the Panel's recommended testing procedures and statistical methods for determining the SPF and the PCD of sunscreen drug products. The agency discussed these comments in the notice of public meeting to discuss sunscreen testing procedures (52 FR 33598 at 33599 and 33600), and proposed two approaches to analyzing the data generated by sunscreen drug product testing. The first method utilizes the testing procedures proposed by the Panel but adds one step to the determination of the PCD. The added step is equivalent to performing a one-sided t-test at the 0.05 level of significance, where the null hypothesis is that the mean SPF is less than the minimal SPF of the assigned PCD. The second method concentrates on the boundaries between the PCD's rather than on the actual SPF values of the sunscreen drug product. Following the establishment of a MED for unprotected skin, protected skin is tested at exposure times chosen so that the corresponding SPF's are slightly less than the lower bounds of the intervals defining the various PCD's. This procedure does not distinguish between SPF's in the same PCD but does distinguish between SPF's in different PCD's. The agency requested comments on the Panel's proposed procedure for sunscreen testing as well as the two methods outlined in the notice of public meeting.

The agency received many comments opposing the binomial method. The comments supported the Panel's recommended testing procedure as modified by adding a one-sided t-test to determine SPF values and PCD categories. Several comments stated that the current procedure is a fair and conservative method for categorizing observed SPF measurements into PCD determinations. The comments stated that no rationale was presented by the agency as to why the simple descriptive method currently in use is not adequate and acceptable. One comment maintained that the fact that the current method has been in use for nearly 12 years provides tangible evidence that it is reasonable and appropriate.

Another comment emphasized that an SPF value is not an absolute, but is instead an indication of relative performance. The comment stated that statistical procedures must be adequate for analyzing and classifying sunscreen drug products in a manner that is

understandable and meaningful to the consumer. The comment concluded that the system that has been in place for over 10 years accomplishes this purpose. The comment acknowledged that refinements can be accomplished by adopting the one-sided t-test or the Wilcoxon signed ranks test as an acceptable method.

Several comments stated that the modified Panel method allows for the determination of SPF values as well as PCD categories. One comment stated that the PCD is an arbitrarily assigned limit, while the SPF is an experimentally derived value. This comment asserted that it is not necessary to be too stringent in compliance with PCD's so long as the SPF is accurately determined. The comments maintained that a distinct advantage of the t-test is that it encompasses the current procedure for conducting SPF testing; plus, it provides a simple computational procedure for a statistical test that projects the results to the entire population.

One comment suggested that if more precision is needed in assessing the PCD by the "t" test method, the significance level may be set at 0.01 rather than at 0.05 when SPF values are evaluated. Another comment recommended the following modification to make the t-test even more useful. It stated that if the significance level were set at 0.10 rather than 0.05, this would allow for slightly more variability in the SPF range and still enable the product to be placed in the PCD that is appropriate for its mean SPF, without adverse impact on consumers.

Three comments stated that, although preferable to the binomial method, the t-test method has one difficulty: Variability, even from high outlying values, can cause the product being tested to fall below the intended PCD. One comment stated that variability is inherent in the results from this type of testing, particularly with higher SPF products. Two comments stated that such variability can be minimized by allowing for dosing increments smaller than 25 percent, especially when testing products with higher SPF values. One comment added that a minimum of exposures can reduce the chance for variability.

Many comments maintained that the binomial procedure proposed by the agency is not appropriate for classifying observed SPF data into PCD categories. Some comments opposed adoption of the binomial method of analysis because it does not provide for the determination of SPF values. One comment cited data from a consumer survey (Ref. 1) that purports to

demonstrate that SPF numbers are a major factor that consumers use in selecting an appropriate sunscreen drug product. Another comment added that the binomial method does not distinguish between SPF's in the same PCD category and that products with very similar SPF's may be classified into different PCD's. Two comments stated that the binomial method lacks the sensitivity of the t-test, and it is more difficult to reject the null hypothesis using the binomial analysis than using the t-test.

Some comments pointed out that the binomial method may result in unnecessary UV exposure. Three comments stated that using the set exposure times in this method would expose a panelist to much more UV radiation than necessary and might even cause severe sunburn. One comment stated that the exposure of a panelist to 14.9 X MED(US), when the proposed protection factor for the product is SPF 2 to 4, would result in severe over exposure. The comment added that the fixed exposure schedule would not allow the current flexibility in modifying the exposure schedule to more closely fit the expected SPF of the product. Another comment stated that because the exposure levels proposed in the binomial procedure are not currently used, there is a lack of historical data on this method. The comment contended that predictions on the effects of using this test are difficult to surmise without a historical perspective.

One comment stated that neither of the proposed methods was adequate and that simpler calculations would be preferable. The comment suggested that the variability inherent in the use of sunscreen drug products by consumers is so high that the statistical refinement suggested is unnecessary in calculating SPF values. The comment added that, if the proposed method is adopted, manufacturers may be forced to aim for higher mean SPF values to allow inclusion of products in current PCD categories. The comment asserted that this will be an unnecessary cost with no real benefit to the consumer. The comment maintained that consumers have had several years to work out which products are suitable for their use and that a change in labeling now would necessitate a further period of adjustment. The comment added that there are very few complaints that sunscreen drug products fail to provide the expected level of protection. Two other comments stated that the agency should reject each of the methods proposed and accept the Panel's recommendation.

Some comments recommended that any scientifically valid statistical analysis method should be permitted to calculate the results of sunscreen product testing. Some comments suggested the Wilcoxon rank sum test as an equally valid method. According to the comments, this method could be used with the current exposure techniques and still have the benefits of the binomial procedure (i.e., no assumption of a normal distribution and less sensitivity to outlying values). One comment added that the Wilcoxon test takes advantage of the interval nature of the data and, therefore, is more sensitive than the binomial procedure and close in sensitivity to the t-test procedure. As stated above, another comment mentioned that the Wilcoxon signed ranks test could provide refinements in the existing procedures.

The agency agrees with the majority of the comments that the Panel's recommended method, as modified by the addition of a one-sided t-test, is the preferred method for calculating SPF values and for categorizing sunscreen drug products into PCDs. The statistical procedure used to calculate the relative protection provided by sunscreen drug products should be based upon the determination of SPF values. Consumers understand and depend upon SPF values when choosing a sunscreen. The Panel's recommended method as modified by the one-sided t-test being added in this tentative final monograph provides an SPF value that can be used to place the product into a PCD for labeling purposes.

The one-sided t-test employs the mean of its observations (i.e., SPF values) as a point estimator, and it incorporates the variability of the data (i.e., the standard deviation). This method classifies a sunscreen drug product into a PCD only where there is statistically significant assurance that the product belongs in the PCD. The agency also points out that this statistical procedure has good power. Further, the modified method is safer than the binomial method because the test subject is exposed to less UV radiation.

The agency is proposing that a sunscreen drug product may display its tested SPF value in its labeling rather than the lowest SPF value in the PCD as the Panel recommended. (See comment 44.) However, a product should only be labeled with a particular SPF if there is sufficient statistical evidence to conclude that the true SPF is at least as high as the label SPF. In order to provide statistical significance to the SPF value that consumers use when choosing products, the agency is

proposing that the SPF value permitted in labeling be the largest whole number that is excluded by a 95-percent one-sided confidence interval for the mean SPF.

Regarding the suggestions for making the t-test more useful by setting the significance level at 0.10 or 0.01 rather than 0.05, there is no basis for allowing for more variability in the SPF range with a 0.10 level of significance, or for being more rigid by using a 0.01 level of significance. The agency considers a 0.05 level of statistical significance to be a standard; it should not be changed without compelling reasons.

The agency recognizes that the Panel's method modified by the addition of the t-test is not the only valid method available. However, it is the best method currently available and is being proposed in § 352.73. By knowing in advance the statistical analysis to be used, there will not be an incentive for an investigator to select a method that will produce the desired SPF or PCD for a particular data set. Further, the agency believes it is desirable to have all data for different manufacturer's products analyzed by the same method. Therefore, the agency is proposing § 352.73 to include a one-sided t-test as follows:

(d) *Determination of the test product's SPF value and PCD.* Use data from at least 20 test subjects with n representing the number of subjects used. First, for each subject, compute the SPF value as stated in § 352.73(b) and (c). Second, compute the mean SPF value, $\bar{x}$, and the standard deviation, s , for these subjects. Third, obtain the upper 5-percent point from the t distribution table with $n-1$ degrees of freedom. Denote this value by t . Fourth, compute $ts/\sqrt{n}$. Let this quantity be denoted by A (i.e., $A = ts/\sqrt{n}$). Fifth, calculate the SPF value to be used in labeling as follows: The label SPF equals the largest whole number less than $\bar{x} - A$. Sixth and last, the drug product is classified into a PCD as follows: if $20 + A < \bar{x}$, the PCD is Ultra High; if $12 + A < \bar{x} < 20 + A$, the PCD is Very High; if $8 + A < \bar{x} < 12 + A$, the PCD is High; if $4 + A < \bar{x} < 8 + A$, the PCD is Moderate; if $2 + A < \bar{x} < 4 + A$, the PCD is Minimal; if $\bar{x} < 2 + A$, the product shall not be labeled as a sunscreen drug product and may not display an SPF value.

Reference

(1) Comment No. C00083, Appendix 3, Docket No. 78N-0038, Dockets Management Branch.

98. Several comments recommended the use of a geometric mean rather than an arithmetic mean when calculating the SPF value. One comment

maintained that the geometric mean will dampen the variability of the widely ranging data often present in SPF test data. Another comment stated that the DIN testing procedures use the geometric mean rather than the arithmetic mean.

The agency believes that it is invalid to use the geometric mean in the t-test that is being proposed for use in calculating the SPF. The standard deviation is based on the arithmetic mean, and a "t" ratio of the geometric mean to the standard deviation based on the arithmetic mean is meaningless. Also, an attempt to use the geometric mean in the computation of the standard deviation would produce a meaningless measure of dispersion. Therefore, the agency is proposing to calculate the arithmetic mean of the data to determine the SPF value of the product.

However, it might be useful to modify the statistical analysis procedure further by performing the t-test on logs of the SPF data. Analysis of the logs of the SPF is equivalent to using the geometric mean as a measure of the average for the original data. This procedure might be useful if the data have a few very large SPF values which have a detrimental effect on the standard deviation computed on the original data. The agency invites comment on this modification.

99. In response to the agency's two proposed statistical methods for analyzing data (i.e., the one-sided t-test and the binomial method), one comment submitted an alternative method based upon statistical tolerance intervals. This comment suggested that sunscreen drug products should be labeled with interval PCD's. The comment stated that the determination of the interval range for an SPF would be based on the value of the lower 95-percent confidence interval for the mean or a procedure based on the binomial distribution. The comment stated that SPF determinations become more variable as the SPF value gets higher. In these cases, the average SPF value is not representative of the data because of the wide range of the SPF values. Therefore, the comment recommended that product SPF labeling should not be based solely on a product's average SPF. The comment maintained that its recommendation would not change if PCD intervals were used as a labeling device rather than individual SPF values. In either case, according to the comment, the variability of the individual SPF values using the testing procedures currently in place do not permit sufficient precision in the

estimation of the mean SPF value for a sunscreen product.

The comment contended that a product should be labeled on the basis of a 95-percent lower confidence interval for the mean SPF value. The comment stated that a disturbing feature of the lower confidence limits is that most of them exclude a high percentage of the individual SPF values. The comment maintained that confidence intervals provide a lower boundary on the mean SPF value for a product but do not provide limits for individual SPF values. The comment asserted that for a given product the lower confidence interval will exclude a higher percentage of the individual SPF values as the sample size is increased. According to the comment, the SPF values excluded will approach a limit of approximately 50 percent, because the lower limit will approach the true mean SPF value.

The comment maintained that if the intent of SPF labeling is to ensure that individual users of sunscreen products are provided with the protection indicated on the label of a product, SPF labeling should not be based solely on a lower confidence interval for a product's mean SPF value. The comment added that this recommendation, like the previous one, is equally applicable to the labeling of products by SPF values and by PCD intervals.

The comment stated that if each of the above recommendations were followed, the current methods for product labeling would be discarded. The comment asserted that a statistical tolerance intervals test would ensure that products are adequately labeled to protect consumers. Also, the statistical tolerance intervals test would establish an acceptable measure of the variability of test results in the determination of SPF designations. The comment maintained that a tolerance interval provides a lower bound on the SPF values for individuals, rather than for the mean of a population of individuals as does a confidence interval. The comment added that a tolerance interval is as easy to implement as a confidence interval. The comment stated that the form for a lower tolerance interval for an individual SPF value is $y - ks < \text{SPF}$, where y and s are the average and sample standard deviation of a sample of n SPF values, and k is a factor obtained from statistical tables for tolerance intervals.

The comment maintained that tolerance limits are much lower than the confidence limits and that they generally cover the entire sample of individual SPF values. The comment

also stated that the lower tolerance interval is closer to actual data values when the SPF values exhibit small variability. Thus, the comment concluded that the tolerance intervals satisfy the two criteria stated above and lead to a third recommendation that product SPF labeling should be based on a lower tolerance interval for an individual consumer's SPF value.

Stating that this third recommendation has a solid statistical foundation, the comment maintained that it addresses one of the key underlying problems with the implementation of clinical testing of sunscreen products: the incorporation of the variability of test results in the setting of SPF values. The comment stated that, unlike the confidence interval approach, the tolerance intervals approach incorporates the variability of individual SPF values, not just the variability of the estimate of the mean SPF value. The comment added that the tolerance intervals approach has the seemingly undesirable effect of resulting in lower assigned SPF values for a product. However, the comment stated that, in reality, it is simply an acknowledgement of the variability inherent in the current testing procedures. The comment stated that the tolerance intervals approach, however, does not alleviate the problem of variability, because it would utilize the lower confidence limit for the mean to determine in which interval a product would be placed. Thus, the difficulties with the use of a lower confidence limit discussed above still apply to PCD designations using this proposal.

The comment stated that a product that has an SPF mean around the limit of a PCD could, through the variability associated with the test results, be assigned to one PCD or a bordering PCD almost at random and that this could imply to a consumer that the product has more protection than it actually has. Further, the labeling of SPF values using statistical tolerance intervals eliminates the need for PCD designations. Under this method, tolerance intervals directly address the key problem, protection of the individual consumer, rather than attempting to address a related but clearly not equivalent problem, the variability of average SPF values. The comment stated that the consumer would be protected with tolerance intervals through lower SPF designations when variability is excessive.

The agency agrees with the comment that the use of a 95-percent lower confidence interval for SPF labeling is preferable to the use of only the

calculated average SPF in the labeling of sunscreen drug products and is proposing such as the fifth step in § 352.73(d). (See comment 97.) However, the agency does not agree that a statistical tolerance intervals test is an acceptable alternative to the one-sided t-test. The one-sided t-test makes a statement about the mean or average SPF. It does not make inferences about particular individuals. Some individuals will receive less protection than the stated SPF, but others will receive more protection. The tolerance intervals procedure makes a statement about the range of SPF values that most of the population of users would achieve. This inference is not usually made in drug testing, and the agency believes that there is no justification for using this procedure for sunscreen drug products. In addition, the validity of the suggested tolerance intervals procedure depends upon the assumption of normality of the underlying distribution. No justification has been presented for this assumption. Unlike the t-test, which tends to be valid if the underlying distribution is not normal, the tolerance intervals procedure depends heavily upon the normality of the underlying distribution for its validity. Therefore, the agency is not including a tolerance intervals statistical analysis method, but instead is proposing that the statistical analysis of sunscreen testing data be done using a one-sided t-test. (See comment 97.)

U. Comments on Water Resistant and Very Water Resistant Testing Procedures for Sunscreen Drug Products

100. Referring to the Panel's statement that a water immersion test is a more severe test of a sunscreen product than a sweat resistance test (43 FR 38206 at 38263), one comment stated that a product that passes the water resistance test should also be permitted to use the term "sweat resistant" and any other claims permitted for products passing the sweat resistance test.

A reply comment disagreed with the above comment and argued that the physical mechanism of removal of the sunscreen product is clearly different in the two tests. The water immersion test recommended by the Panel in § 352.46 requires that the sunscreen product resist removal by water applied "over" the product; the "sweat resistance" test recommended in § 352.45 requires that the sunscreen product resist removal by sweat emerging from "underneath" the product. Contending that there is no assurance that a product that resists removal by one physical action will also resist removal by the opposite physical action, the reply comment pointed out

that the difference between the chemistry of water and the chemistry of sweat requires different test standards. The reply comment further stated that if §§ 352.45 and 352.46 remain in the monograph, separate tests should be maintained for product performance claims of "water resistance" and "sweat resistance." Another comment recommended that the determination of the SPF value of a product be conducted under the combined stress of sweating and swimming.

The agency agrees with the Panel that the "water resistant" test is a more severe test of a sunscreen product than the "sweat resistant" test (43 FR 38206 at 38261). The water resistant tests have a longer time of exposure to water and include a 40- to 80-minute period of moderate activity. The agency disagrees with the reply comment that the difference in the chemistry of water and sweat requires different test standards. The composition of sweat and water differ, but the composition of each is variable. The composition of sweat varies from subject to subject and the composition of tap water varies depending on the source. Sweat is composed predominantly of water (Refs. 1 and 2) and has only traces of lactate, urea, ammonia, sodium chloride, potassium, and other substances (Ref. 3). The Encyclopedia of Biochemistry (Ref. 1) states that "the composition of sweat is about 99 percent water * * *." White et al. (Ref. 2) states that the sweat glands release virtually pure water. Sweat, which is about 99 percent water with a pH from 5 to 7.5 (Ref. 1), can be considered similar to various types of water. The degree of variability in the content of treated water, untreated water, or different sources of water can be high. (See comment 104.) In addition, swimming pool and sea water contain different quantities of other minerals and chemicals, and the pH varies depending on the water source. Therefore, the agency believes that, for the purposes of sunscreen drug product testing, sweat and water are sufficiently similar so as not to require different test standards.

The agency agrees with the reply comment that the physical mechanisms by which a sunscreen product resists removal by sweat and water immersion are different. However, the "wash-off" effects of sweat emerging from underneath the product can be expected to be less than the "wash-off" effects from water over the product. The requirement for a "water resistant" claim is for the product to retain the same PCD after 40 minutes of swimming as it had before being exposed to water. If any sunscreen product can withstand

40 minutes of water immersion and retain its original PCD or can withstand 80 minutes of water immersion required for a "very water resistant" claim (see comment 50) and retain its original PCD, the agency and Panel agree that the product can also withstand 30 minutes of sweating and retain its PCD (see the Panel's recommended § 352.50(e)(2)(i)(a)(3) and (b)(3)). Therefore, the agency believes that it is appropriate for a product that passes the water resistance and very water resistant tests to also be permitted to make claims that satisfy the sweat resistance test.

The agency agrees that a sunscreen product that passes the "water resistant" test should be permitted to use the claim "sweat resistant." The agency has reviewed the available information and concludes that for sunscreen drug products that have passed the tests in § 352.76 of this tentative final monograph for water resistant and very water resistant claims, an additional test to support a sweat resistance claim is unnecessary and possibly hazardous.

The agency is concerned that those who serve as subjects for "sweat resistant" testing could be unduly harmed by heat stress. The Panel's recommended procedure in § 352.45 for determining sweat resistance includes inducing copious sweating for 30 minutes by exposing the subjects to a temperature of 35 to 38 °C (95 to 100 °F) and 70 to 80 percent humidity, with little air movement. The Panel cautioned that, for safety purposes, older people should not be used and subjects should have their pulse and temperature taken every 15 minutes. Even with these safeguards, however, the agency believes that this test presents an unnecessary risk when the less-hazardous water resistance testing can be used in support of a sweat resistant claim. Further, the agency is unaware of any sunscreen products that make "sweat resistant" claims but do not also make "water resistant" claims. Accordingly, the agency concludes that the potential benefits of the sweat resistance test do not outweigh the possible risks to the test subject.

The agency disagrees with the recommendation that the SPF value of a product should be done under the combined stress of sweating and swimming. The determination of an SPF value is a test independent of stress. The requirement that the product be labeled with the appropriate PCD provides sufficient information for consumers to choose the proper sunscreen product for their individual needs.

In summary, the agency is proposing to permit the use of the terms "sweat

resistant," "perspiration resistant," "resists removal by sweating," or "resists removal by perspiring" for a sunscreen drug product that qualifies for the claim of "water resistant" or "very water resistant." The agency is proposing the phrase "sweat resistant" or "perspiration resistant" in § 352.52 (e)(2) and (e)(3) and is not proposing § 352.50(e)(2)(i)(c) as recommended by the Panel (see comment 103). The agency is not including the Panel's recommended "sweat resistant" test in the testing procedures and is proposing only the procedures for "water resistant" and "very water resistant."

References

- (1) Williams, R. J., and E. W. Lansford, Jr., editors, "The Encyclopedia of Biochemistry," Reinhold Publishing Corporation, New York, pp. 774-775, 1967.
- (2) White, A., et al., "Principles of Biochemistry," 7th Ed., McGraw-Hill Book Company, New York, p. 152, 1983.
- (3) Sato, K., "Eccrine Sweat Glands," in "Dermatology in General Medicine," edited by T. B. Fitzpatrick, et al., McGraw-Hill Book Company, New York, pp. 195-209, 1987.

101. Referring to the Panel's recommended procedures for testing water resistance and waterproof claims in § 352.46 (a) and (b), one comment stated that the criteria for these tests are not defined. The comment mentioned that both procedures simply state that "A sunscreen product that can withstand 40 (80) minutes of water immersion may claim to be water resistant (waterproof)." However, the Panel's discussion of these tests (43 FR 38206 at 38263) and the sweat resistance test (§ 352.45) require that the product demonstrate the same PCD before and after water immersion. The comment requested that this standard also be included in the water resistance and waterproof testing procedures.

The agency agrees with the comment that the criteria for passing the Panel's recommended tests in § 352.46 (a) and (b) should be defined and included in the testing procedures. Therefore, the agency is proposing in § 352.76(a) to replace the Panel's recommended sentence "A sunscreen product that can withstand 40 minutes of water immersion may claim to be water resistant" with the following sentence: "If the sunscreen product retains the same PCD after 40 minutes of water immersion as it had before water immersion, the claim of 'water resistant' may be made." In § 352.76(b), the agency is proposing to replace the Panel's recommended sentence "A sunscreen product that can withstand 80 minutes of water immersion may claim to be waterproof" with the following sentence: "If the sunscreen

product retains the same PCD after 80 minutes of water immersion as it had before water immersion, the claim of 'very water resistant' may be made." (See comment 50 regarding use of the term "very water resistant" instead of "waterproof.")

102. One comment believed that the Panel's recommendations to use an artificial light source for substantiating the claim of sweat resistance (43 FR 38206 at 38262) are ideal but far from being realistic or achievable. If the Panel feels that a sunscreen product should retain the same PCD after the sweat test as before the sweat test, the comment explained, "there will be a tendency on the part of the regulatory agency to disapprove such claims for failure in compliance; because, every sunscreen product, no matter how good it is, will not give the same protection factor value before and after the stress of swimming. The product after the stress of sweating will always be giving a lower protection factor value (hence, a lower PCD designation)."

The comment offered the following example: Products with an SPF value of 12 or more (PCD maximal or ultra) tend to show a decreased SPF value after the stress of swimming or sweating, e.g., an SPF of 12 may decrease to an SPF of only 8 (a decrease of nearly 33 percent). The same SPF value cannot be achieved for various reasons (e.g., elution changes due to the partition coefficient, thinning of the applied film, alteration in physical properties, etc.). Another comment also contended that the same SPF value will never be obtained after swimming because 15 to 20 percent of the sunscreen effectiveness will be lost depending on the base (vehicle) used in the product. The first comment concluded that, if the criteria recommended by the Panel are retained, the tendency on the part of the manufacturer will be to claim a low SPF value. Thus, in order to have a claim of "sweat resistance" or "water resistance," the comment argued, a manufacturer could only claim an SPF value of 8.

The comment felt that less effective products (i.e., products with a low SPF value but which retained the original SPF value after the stress of sweating) had a marketing advantage because these products could not be denied a claim of sweat resistance. The comment gave the following example: a product with an SPF value of 4 (before and after sweating) could have a claim of sweat resistance, whereas a superior product with an SPF value of 8 or more could not qualify for such a claim because its SPF value decreases to 6 after the stress of sweating. The comment felt this

problem could be resolved by allowing the sweat resistance claim if the SPF value differences before and after the stress of sweating are less than 20 percent, provided the initial SPF value is at least 8 or 10.

The agency is not proposing the Panel's recommended testing procedure for a sweat resistance claim in this tentative final monograph (see comment 100). Accordingly only the comments' concerns about the test for water resistance are being addressed. The agency is aware of two studies, conducted since publication of the Panel's report, that determined the water resistance effectiveness of single-ingredient and combination sunscreen products (Refs. 1 and 2). One study (Ref. 1) used the protocol recommended by the Panel, and the second study (Ref. 2) used a similar protocol involving a 10-minute whirlpool treatment. In both studies, the SPF values for several different sunscreen ingredients alone and for combinations of sunscreen ingredients were determined before and after the water treatment. A decrease in the SPF values occurred for all of the products tested, including sunscreen drug products previously determined to be water resistant. With some products, e.g., 5 percent aminobenzoic acid, the decrease in the SPF values after the water treatment was significant. In other cases, e.g., 8 percent octyldimethyl aminobenzoic acid plus 3 percent oxybenzone, the decrease in the SPF value after the water treatment was minimal. Because every product was affected, the agency believes that some allowance for a decrease in SPF values after the water test should be made.

The Panel recommended that a sunscreen drug product must retain the same PCD, not the same SPF value, after the test as it had before the test (43 FR 38263). A product can experience a reduction in SPF value and still remain in the same PCD. For example, a product with a PCD of very high has an SPF value of 12 to under 20. If the product has an SPF value of 20 before the water test, it must have an SPF value of 12 or above after the test in order to retain the same PCD and make the claim for water resistance. The SPF value of the product could decrease by as much as 40 percent and the product would still be classified under the same PCD. Even sunscreen drug products that offer less protection, e.g., products with a moderate PCD, can undergo a reduction in SPF value after exposure to water and still remain in the same PCD. Therefore, the agency believes that the range of SPF values listed for each PCD recommended by the Panel is sufficiently broad to provide for a

reduction in the SPF value after the water test. This criterion in the test for water resistant and very water resistant claims is proposed in § 352.76. (See comment 101.)

References

- (1) Kaidbey, K. H., and A. M. Kligman, "An Appraisal of the Efficacy and Substantivity of the New High-Potency Sunscreens," *Journal of the American Academy of Dermatology*, 4:566-570, 1981.
- (2) Sayre, R. M., et al., "Performance of Six Sunscreen Formulations on Human Skin," *Archives of Dermatology*, 115:46-49, 1979.

103. One comment referred to the Panel's recommended testing procedure in § 352.46 for determining whether a sunscreen product is water resistant or waterproof. The comment stated that: (1) The terms "water resistant" and "waterproof" should be defined; (2) the criteria are unrealistic, arbitrary, and scientifically not established; (3) 2 water immersion periods of 20 minutes with moderate activity in water (a total of 40 minutes) are not essential for ascertaining the water resistance of a sunscreen product because the average person rarely remains in water for 40 minutes; and (4) 3 water immersion periods of 20 minutes with moderate activity in water (a total of 60 minutes) are totally unrealistic. A similar comment stated that it is inconsistent that FDA would demand proof that the 8-percent homosalate standard is validated before accepting and promulgating the in vivo sunscreen testing procedures, and at the same time, promulgate in vivo water resistant testing procedures which have not been validated. The comment maintained that the same exacting standards should be required for all in vivo testing procedures that substantiate labeling claims upon which consumers rely. Another comment added that it would not differentiate between water resistant and waterproof because several studies have shown that the average swimming time is not more than 10 minutes.

The agency believes that the term "waterproof" has a different meaning from that intended by the Panel for a sunscreen product; therefore, the agency is proposing the term "very water resistant" instead of the term "waterproof." (See comment 50.) Although the Panel recommended testing procedures for determining whether sunscreen drug products are "water resistant" or "waterproof" (§ 352.46(a) and (b)), the agency does not agree with the comment that these terms are not defined. A "water resistant" sunscreen resists removal for at least 40 minutes in the water, and a "very water resistant" (waterproof)

sunscreen resists removal for at least 80 minutes in the water. (For a further discussion of these terms, see comment 50.)

The comments did not elaborate on the statement that the testing criteria necessary to establish a claim of water resistant or very water resistant are unrealistic, arbitrary, and scientifically not established. At the time of the Panel's deliberations there were no adequate standards on which to base water resistant and very water resistant claims. Thus, to establish criteria for testing water resistant and very water resistant sunscreen products (Ref. 2), the Panel proposed a testing method that it considered to be a reasonable and fair representation of swimming habits. Since the Panel completed its deliberations, the procedures it recommended have been tested and found to provide a good measure of the water resistance of sunscreen products. Studies have shown that the substantivity of such products has improved over the years (Refs. 3 and 4). Kaidbey and Kligman (Ref. 3) evaluated sunscreen products using the Panel's recommended procedures and found that certain sunscreen products, especially some of the newer products, were more resistant to wash-off than others. Further, such products, after undergoing water treatment, maintained an SPF number closer to the original SPF number. In addition, in a communication with the agency, the Nonprescription Drug Manufacturers Association, a trade association of OTC drug manufacturers, stated that the Panel's recommended testing methods are frequently used in determining water resistant and waterproof claims (Ref. 5). Thus, the agency disagrees with the comments' assertions that these procedures are unrealistic, arbitrary, and scientifically not established.

The agency also does not accept one comment's claim that a total of 40 minutes of moderate activity in water is not essential for ascertaining the water resistance of a sunscreen product because the average person rarely remains in the water for 40 minutes. The comments did not provide any evidence to support their statements that the average person rarely remains in the water for 40 minutes or that the average swimming time is not more than 10 minutes. Likewise, the agency disagrees with one comment's claim that 60 minutes of moderate activity in water is an unrealistic time period to determine that a sunscreen product is waterproof. The Panel concluded that two 20-minute periods of moderate activity in water (for a total of 40 minutes) is an appropriate test for

determining the water resistance of a sunscreen product. Likewise, four 20-minute periods of moderate activity in water (for a total of 80 minutes) was recommended to establish that a product is very water resistant. The Panel chose the 20-minute water immersion periods because unpublished marketing data revealed that a typical population of adults and children under 12 years of age goes into the water 3.6 times for an average duration of 21 minutes per immersion at the beach or pool, and has an average total immersion time of approximately 80 minutes (Ref. 1). Further, the data indicated that 38 percent of users do not reapply a sunscreen product after swimming. By selecting a water immersion period of 40 minutes for a water resistance claim and 80 minutes for a very water resistant claim, the Panel chose reasonable average times that a product should withstand removal by water in order to show effectiveness as a water resistant or very water resistant sunscreen product. The agency considers a sunscreen drug product that can be removed by water in less than 40 minutes as not appropriate as a water resistant or very water resistant sunscreen. A water resistant or very water resistant sunscreen product should enable an individual to maintain a certain level of protection from the harmful rays of the sun after an average period of swimming without the need to reapply the product. For example, children are constantly in and out of the water, and may stay for hours at a time in the beach/pool environment. These individuals are at the greatest risk for "wash-off." They are also at the greatest risk of subsequent adverse effects if the SPF value of a sunscreen is overstated based on test methods that underestimate the exposure time to water immersion of very active individuals. Therefore, the agency believes that test times must approach the longer times that some consumers will be immersed in water, rather than "average" times which would significantly underestimate immersion times of a high-risk group. The agency concurs with the Panel's recommendations concerning testing procedures for water resistant claims in sunscreen drug product labeling; however, as noted above, the agency is proposing to replace the Panel's recommended term "waterproof" with the term "very water resistant."

References

- (1) OTC Vol. 060168.
- (2) Summary Minutes of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn

Treatment and Prevention Drug Products, March 4 and 5, 1976, OTC Vol. 06ATPM, Docket No. 78N-0038, Dockets Management Branch.

(3) Kaidbey, K. H., and A. M. Kligman, "An Appraisal of the Efficacy and Substantivity of the New High-Potency Sunscreens," *Journal of the American Academy of Dermatology*, 4:566-570, 1981.

(4) Sayre, R. M., et al., "Performance of Six Sunscreen Formulations on Human Skin," *Archives of Dermatology*, 115:46-49, 1979.

(5) Comment No. C00075, Docket No. 78N-0038, Dockets Management Branch.

104. One comment contended that the Panel's recommended testing procedure, in § 352.46, for determining if a sunscreen is water resistant or waterproof cannot be controlled because of the high degree of variability in the content of fresh water. (The test is to be performed in an indoor fresh water pool.) The comment stated that fresh water has, depending on its source, different pH values and different amounts of minerals and chemicals (such as chlorine and fluoride), which may influence the solubility of the sunscreen ingredient in the product. Because the Panel did not define the term "fresh water," the comment stated that FDA must provide, in the regulation, specifications for the fresh water in order to standardize the procedures for testing the effectiveness of water resistant and waterproof sunscreen products.

FDA proposes to define "fresh water" for the purpose of this tentative final monograph as clean drinking water that meets the standards established by the United States Environmental Protection Agency (EPA). Tap (piped) water for drinking and domestic use is generally supplied by rivers, lakes, wells, and springs. Water from a public water system is filtered and treated with chemicals in water treatment plants to kill bacteria, soften the water, and improve its taste (if it is to be consumed). The treated water might even go to another reservoir such as a swimming pool or a whirlpool and undergo further treatment if it is used by the public for swimming, in a factory, or a sunscreen testing laboratory, etc.

The EPA is responsible for establishing the minimum standards for all water systems that provide water suitable for human consumption to the public. Service to the public includes factories and private housing developments, communities, camping sites, etc. EPA regulations provide the maximum contaminant levels for organic and inorganic chemicals other than fluoride, for disease-causing microorganisms, etc., in drinking water. (See the National Interim Primary Drinking Water Regulations in 40 CFR

Part 141.) FDA does not believe that additional specifications for the water used for sunscreen testing are necessary. Accordingly, FDA is defining "fresh water" in § 352.76 as clean drinking water that meets the standards in 40 CFR Part 141.

105. One comment stated that the Panel's recommended instructions concerning the waiting period between applying a sunscreen drug product and exposing the test site are inconsistent with the testing procedures for water resistant and waterproof claims in the Panel's report. The general testing procedure in § 352.42(f) specifies a waiting period of at least 15 minutes after application of the sunscreen before exposing the test site; whereas, the procedures in § 352.46(a)(1) and (b)(1) for testing water resistant and waterproof claims require that application of the sunscreen be followed by the waiting period indicated on the sunscreen drug product's labeling. The comment further noted that a waiting period is not included under the product labeling requirements of the Panel's recommended monograph. The comment suggested that, for uniformity, the individual testing procedures should all reference § 352.42 "General Testing Procedures."

The Panel intended for the "General Testing Procedures" in § 352.42 to apply to the individual testing procedures for water resistant and very water resistant claims (see comment 50 on the substitution of the term "very water resistant" for the term "waterproof"). However, the Panel did not find it necessary to restate in § 352.46 the detailed general testing procedures for the determination of the SPF value. The agency believes that a cross-reference would be useful for clarity. Therefore, the agency is proposing to add a statement to the introductory text of § 352.76 that states: "The general testing procedures in § 352.72 should be used as part of the following tests, except where modified in this section."

The agency disagrees with the comment's claim that the Panel's recommended waiting periods are inconsistent. One waiting period (in § 352.42(f)) refers to the time between applying a sunscreen drug product and exposing the test site to the UV radiation source. The other waiting period (in § 352.46(a)(1) and (b)(1)) refers to the time between applying a sunscreen drug product and exposing the test site to water. In the *General Testing Procedures* in § 352.42, the Panel recommended a waiting period of at least 15 minutes. This waiting period occurs prior to exposing the test site to the UV radiation source for the

determination of the product's SPF value. Every sunscreen drug product must have its SPF value measured according to these procedures. For products claiming to be water resistant or very water resistant, the static (i.e., initial) SPF is measured after a 15 minute waiting period, according to § 352.42. When determining the water resistant SPF, another waiting period, as determined by the manufacturer, elapses before the test site is exposed to water in accordance with § 352.46. After exposure to water, the SPF of the product is again determined. If the product maintains the same PCD after the amount of water exposure specified in either § 352.46 (a) or (b), it can be labeled with either a water resistant or a very water resistant claim. (See comment 102.)

For products that make water resistant and very water resistant claims, the Panel recommended that the waiting period should be that indicated on the product labeling (43 FR 38206 at 38266 and 38267). The agency agrees with the Panel that the waiting period for each water resistant and very water resistant product should be individually determined by the product's manufacturer. Water resistant and very water resistant sunscreen drug products are specifically formulated to withstand wash-off by water. The degree of water resistance of such products varies and is greatly influenced by the vehicle in which the sunscreen ingredient is incorporated. As stated by the Panel at 43 FR 38218, "the persistence, penetration, and resistance of the active ingredients to abrasion, sweating, and washing often depends upon the vehicle." A waiting period may be necessary for some water resistant products (e.g., to allow the product to dry) in order to provide better resistance to water, and the waiting periods for different sunscreen products may vary. For these reasons, the agency is proposing the Panel's recommendations regarding waiting periods in §§ 352.72(f) and 352.76(a)(1) and (b)(1).

With regard to the comment's statement that waiting periods are not included in the Panel's recommended monograph labeling, the agency believes that consumers should be informed if a waiting period is necessary for the most effective use of water resistant and very water resistant sunscreen drug products. Therefore, the agency is proposing that the manufacturers determine the waiting periods for the most effective use of their products and include this information in the directions for their product (see comment 66).

106. Four comments addressed the Panel's recommended testing procedure

in § 352.46 for determining if a sunscreen product is water resistant or waterproof. (The agency is using the term "very water resistant" rather than waterproof. See comment 50.) One comment requested that: (1) A whirlpool testing method be included as an alternative testing procedure for water resistant and very water resistant claims; (2) the 20-minute drying periods between immersion periods be deleted; and (3) in analyzing data, the projected slope technique not be excluded from acceptability to product labeling. The comment maintained that such techniques as linear regression and least square techniques require data obtained for different amounts of water exposure, and could not be used under the present proposed procedure. The comment contended that the complexity of the Panel's proposed procedure (e.g., the time an investigator must spend with each subject, the number of subjects required, and the requirement for the testing facilities to be close to a swimming pool) makes conducting these tests very expensive in terms of manpower, equipment, and resources. In addition, without access to a close indoor pool, water resistant and very water resistant testing would require the use of an outside swimming pool, which would limit periods of testing to good weather only. Further, if that were to occur, the testing would be subject to many uncontrolled environmental variables such as the weather. The comment added that if the swimming pool is not located in the same facility as the testing area and solar simulator, transportation of the subjects between the pool and the testing facility would be required, thereby adding further variability in test results between laboratories. The comment concluded that the proposed requirements could eliminate most comparative testing of sunscreen products and stop laboratories from performing such tests.

The comment contended that a testing method using a whirlpool would be more economical and accessible than a method using an indoor swimming pool, provide better standardization of the test environment, and provide better control of environmental variables such as sun exposure, water temperature, and chlorination. In addition, the whirlpool could be located close to the solar simulator testing area.

The comment submitted a summary of the results of tests conducted to determine if a sunscreen is water resistant or very water resistant using the procedure proposed in § 352.46 and using a whirlpool. The tests compared results obtained in large or small whirlpools to those obtained in a

swimming pool for a number of sunscreen products with various SPF values. All SPF determinations for water resistant and very water resistant were performed with solar simulators in accordance with the Panel's recommended procedures, except that not all studies included 20 test subjects. Based on the results obtained, the comment concluded that under indoor laboratory testing conditions using a whirlpool bath: (1) The environment and the well-being of the volunteers can be more carefully monitored, and indoor heating can be carefully controlled to maintain the volunteer's temperature; (2) the solar simulators can be more rigorously maintained; (3) an acceptable laboratory test using an indoor whirlpool can lead to "a better discussion and treatment of other environmental factors not directly applicable in a swimming pool environment," e.g., the influence of temperature, humidity, and wind; and (4) testing can be performed year-round.

The comment added that its data indicate there is no difference in product effectiveness introduced by inclusion of the Panel's recommended 20-minute drying period between water exposure periods. The comment concluded that this condition appeared to needlessly complicate the testing procedure, and requested that it be deleted. However, the comment did not submit data comparing test results with and without the 20-minute drying period.

A second comment proposed a water resistance test using either a jacuzzi or a swimming pool for sunscreen drug products with an SPF value of 15 or more. The proposed water resistance testing involved the application of the sunscreen product followed by a 15-minute waiting period at room temperature before entering the water. The subject would then bathe in a pool or jacuzzi (temperature between 25 and 30 °C) for 20 minutes. This would be followed by a 20-minute drying period, then by a 10-minute mild shower (temperature between 33 and 37 °C, minimum 2 liters/minute), and then by a 10-minute drying period. The MED of the protected skin would be determined before the procedure for bathing and immediately after the last drying period. The comment stated that the ratio of "bathings/no bathing" of protected sites should be better than 0.8 (i.e., the decrease in SPF should not be more than 20 percent after the test). The comment stated that a product that does not fulfill this water resistance test could not claim to belong to "class I" or to "ultra-sun protection."

A third comment recommended that specific guidelines be provided for water immersion testing. The comment did not provide any guidelines for such testing but did indicate that guidelines for factors such as temperature, method of agitation, and movement should be specified for manufacturers to employ in determining substantivity.

A fourth comment opposed adding a requirement for a very water resistant standard control to the water resistant testing procedures. The comment stated that the current static standard is adequate to fulfill the purpose of the control and can be used in conjunction with the very water resistant testing without a problem. The comment concluded that nothing would be gained by adding a requirement for a very water resistant standard control.

The agency agrees that a whirlpool or jacuzzi is an acceptable alternate to an indoor swimming pool in the testing procedure recommended by the Panel in § 352.46. These facilities provide an appropriate means of standardizing water resistant testing among laboratories by providing control over most of the variables. Whirlpools and jacuzzi are similar to an indoor swimming pool in that they provide: (1) Adequate control of environmental factors, e.g., temperature and humidity; (2) proximity to the testing sites; and (3) year-round testing capabilities because testing would not be weather dependent. Additionally, whirlpools and jacuzzi are economical and provide a more rigorous water challenge to test the water resistant properties of the sunscreen drug product. The agency believes that indoor testing helps ensure reproducible results because it is easier to control indoor environmental variables such as temperature and humidity. An accurate and reproducible testing procedure can ensure that competitive products with the same water resistant labeling have essentially the same effectiveness (see comment 79). Therefore, the agency is proposing that the testing procedure (§ 352.46) be revised to state that an indoor fresh water pool, whirlpool, and/or jacuzzi maintained at 23 to 32 °C shall be used in the testing procedures to determine if a sunscreen drug product is water resistant or very water resistant. This revised testing procedure is in proposed § 352.76.

The agency does not agree with one comment's suggestion that a total of only 30 minutes of water immersion is adequate for ascertaining the water resistance of a sunscreen drug product. The Panel concluded that two 20-minute periods of moderate activity for a total of 40 minutes in the water is an

appropriate test for determining water resistance (43 FR 38206 at 38263). Likewise, the Panel recommended four 20-minute periods of moderate activity in water (for a total of 80 minutes) to establish that a product is very water resistant. (See discussion in comment 103.) The comment did not provide any test data or other evidence to support its suggestion for moderate activity in water for 30 minutes.

The agency also disagrees with another comment's request to delete the Panel's recommended 20-minute drying period between immersion periods. The Panel reviewed an unpublished consumer marketing survey (Ref. 1) that studied typical water immersion behavior patterns among sun care product users and used these data to establish the 20-minute water immersion periods. Although the survey did not specifically address the amount of time spent out of the water between the immersion periods, the agency considers the Panel's 20-minute drying periods reasonable and a fair representation of the swimming habits of individuals at the beach or swimming pool. The survey indicates that the typical population does spend time out of the water and then reenters the water several times. The agency believes that a water resistant or very water resistant sunscreen drug product should enable an individual to maintain a certain level of protection from the harmful rays of the sun after an average period of swimming, including time spent out of the water between immersions, without the need to reapply the product. If data are submitted that support deleting the 20-minute drying periods between immersion periods, the agency will consider revising the testing procedure to delete the drying periods.

Regarding specific guidelines for water immersion testing, the agency notes that the Panel required that the water temperature be 23 to 32 °C. Further, the Panel stated that the pool and air temperature and the relative humidity should be recorded. The agency agrees with these Panel recommendations and, in addition, agrees with the comments that more specific guidelines (e.g., water and air temperature, humidity, and minimum size of the whirlpool or jacuzzi) should be included in the testing procedures for sunscreen drug products. However, the comments provided no specific guidelines that might be used for water resistant testing procedures or data concerning the use of such guidelines. Therefore, the agency is proposing in § 352.76 that the water temperature of the indoor pool, whirlpool, or jacuzzi be maintained at 23 to 32 °C and is

requesting comment and data on including other specific environmental guidelines, such as those noted above, that would improve the water resistant testing procedures.

The agency agrees with one comment that an additional control standard for water resistant testing serves no added benefit because the current 8-percent homosalate standard adequately fulfills the purpose of serving as a control for the SPF testing procedure. The Panel stated in its recommended water resistant testing procedures in § 352.46 that "The standard sunscreen is not used in these tests." The agency is concerned that this statement could imply that the 8-percent homosalate standard is not required for the SPF testing procedure. Therefore, the agency is not proposing this sentence in § 352.76.

Regarding the acceptability of a projected slope technique for the analysis of data for product labeling, the statistical analysis of data from sunscreen drug product testing is addressed in comment 97.

Reference

(1) OTC Vol. 060168, Docket No. 78N-0038, Dockets Management Branch.

V. Comments on In Vitro Testing for Sunscreen Drug Products

107. Referring to the Panel's recommended testing procedure in § 352.46 for determining if a sunscreen is water resistant or waterproof, one comment recommended that an in vitro substantivity test with isolated specimens of epidermis be used. The comment described the procedures for the in vitro test as follows: (a) Obtain small specimens of skin (5 inches by 2 inches) from postmortem cases; (b) isolate the epidermis by treating the skin specimen at 60 °C for 30 to 60 seconds; (c) measure the transmission spectra of the isolated and untreated epidermis between a spectral range of 200 to 400 nm; (d) apply the sunscreen lotion (2 mg or 2 microliters/cm²), select the minimum and the maximum time for diffusion of the applied sunscreen agent, determine the chemical conjugation of the sunscreen, and measure the transmission spectra after 30- and 60-minute intervals; (e) immerse the specimen in water with constant mechanical stirring for varying periods of time ranging from 10 to 90 minutes; (f) measure the transmission spectra of the specimen after immersion in water for these varying intervals of time; (g) determine the amount of sunscreen agent left on the specimen before and after immersion in water; (h) determine the percent transmission changes in the

spectral range of 200 to 400 nm; and (i) calculate the substantivity or water resistance. The comment added that the variables in this test can be controlled.

Another comment submitted in response to the January 1988 public meeting to discuss sunscreen testing methods acknowledged that human testing is the accepted method for determining SPF values. The comment added that in vitro methods are nevertheless being developed and should be encouraged.

The agency agrees that in vitro testing of sunscreen drug products may be useful and encourages the development of such testing methods. The agency has reviewed the in vitro substantivity test suggested by the comment and believes it may be suitable for obtaining an approximate measure of a sunscreen product's water resistance. However, the agency needs further details about the procedure to properly evaluate it. The protocol offered by the comment is very brief and does not contain enough information for adequate performance of the test and interpretation of the results. While the protocol appears to have merit, it needs to be expanded, developed, and compared to in vivo methods for determining water resistance. Sayre, et al. (Ref. 1) have tested a similar in vitro procedure for determining the water resistance of several sunscreen products using the epidermis of hairless mice in a spectrophotometric assay. The results showed clear differences in substantivity among several sunscreen ingredients using this in vitro method. The results from the in vitro method were reported to be similar to those determined by the in vivo method.

The agency points out that while data from in vitro tests using isolated skin samples may offer some supportive evidence of water resistance, in vivo tests for determining the effectiveness and substantivity of a sunscreen product are still required. Isolated skin specimens do not behave like natural living skin, e.g., they do not sweat, vary in temperature, or develop erythema. Therefore, such in vitro tests alone are not suitable for determining the effectiveness or substantivity of a sunscreen drug product. In addition, comparative evaluations between in vitro and in vivo methods must be performed in order to establish a direct correlation between these methods. Therefore, the agency believes that additional studies with in vitro procedures using isolated skin samples need to be performed and evaluated

before these methods can be considered for inclusion in a monograph.

Reference

(1) Sayre, R. M., et al., "Sunscreen Testing Methods: In Vitro Predictions of Effectiveness," *Journal of the Society of Cosmetic Chemists*, 31:133-143, 1980.

W. Comment on Safety Testing for Sunscreen Drug Products

108. Stating that the 3 methods of patch testing recommended by the Panel for final products or Category III ingredients are acceptable methods (43 FR 38206 at 38218), one comment requested that a routine patch test method proposed by the International Contact Dermatitis Research Group (ICDRG) also be included as an acceptable method. The comment cited two references in which the ICDRG method is described (Refs. 1 and 2) and added that many sunscreen products have been previously evaluated by this patch test method, which is an accepted method in Europe.

The 3 methods of patch testing recommended by the Panel are part of a general discussion of test methods applicable to human safety testing of Category III ingredients or final-formulated products (43 FR 38218). Because these tests have proven valuable in predicting skin irritancy and potential sensitization, the Panel recommended that these methods be considered for providing adequate data to establish the safety of OTC sunscreen ingredients. The Panel did not recommend that any specific patch test be included in the monograph.

The agency has not addressed specific testing methods for determining the safety of OTC sunscreen drug products in this tentative final monograph; the agency is not, therefore, recommending the use of a particular patch test. Each manufacturer or sponsor should determine which scientifically valid patch test to use to evaluate the safety of its sunscreen drug product. Before utilizing a new patch testing method for sunscreen drug products, the sponsor may want to discuss the use of the method with the agency.

References

- (1) International Contact Dermatitis Research Group, "Routine Patch Test Series: 1974," *British Journal of Dermatology*, 89:437-438, 1973.
- (2) Magnusson, B., "Patch Testing," in "Sunlight and Man," edited by M. A. Pathak, et al., Tokyo University Press, Tokyo, pp. 799-812, 1974.

III. The Agency's Tentative Conclusions and 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 padimate A from Category I to Category II for concentrations of 5 percent and higher and to Category III for concentrations less than 5 percent. As a convenience to the reader, the following list is included as a summary of the categorization of sunscreen active ingredients recommended by the Panel and the proposed categorization by the agency. In this list, sunscreen active ingredients are identified by their current established name. If the current established name is different from that used by the Panel, the Panel's designation is indicated by footnote.

Sunscreen active ingredients	Panel	Agency
Allantoin/aminobenzoic acid complex.	II	III
Aminobenzoic acid	I	I
Bomelone	III	III
Cinoxate	I	I
Diethanolamine methoxycinnamate ¹ .	I	I
Digalloyl trioleate	I	I
Dioxybenzone	I	I
Dipropylene glycol salicylate.	III	III
Ethyl 4-[bis(hydroxypropyl)aminobenzoate.	I	I
2-Ethylhexyl 4-phenylbenzophenone-2-carboxylic acid.	II	II
Glyceryl aminobenzoate	I	I
Homosalate	I	I
Lawson with dihydroxyacetone.	I	I
Menthyl anthranilate	I	I
3-(4-methylbenzylidene)-camphor.	II	II
Octocrylene ²	I	I
Octyl methoxycinnamate ³ ...	I	I
Octyl salicylate ⁴	I	I
Oxybenzone	I	I
Padimate A (up to 5 percent).	I	III
Padimate A (5 percent or higher) ⁵ .	I	II
Padimate O	I	I
Phenylbenzimidazole sulfonic acid ⁶ .	I	I
Red petrolatum	I	I
Sodium 3,4-dimethylphenylglyoxylate.	II	II
Sulisobenzene	I	I
Titanium dioxide	I	I
Trolamine salicylate ⁷	I	I

Sunscreen active ingredients	Panel	Agency
Zinc oxide ⁸		III

¹Identified by the Topical Analgesic Panel as diethanolamine p-methoxycinnamate.

²Identified by the Topical Analgesic Panel as 2-ethylhexyl-2-cyano-3,3-diphenylacrylate.

³Identified by the Topical Analgesic Panel as ethylhexyl p-methoxycinnamate.

⁴Identified by the Topical Analgesic Panel as 2-ethylhexylsalicylate.

⁵Not evaluated by the Topical Analgesic Panel.

⁶Identified by the Topical Analgesic Panel as 2-phenylbenzimidazole-5-sulfonic acid.

⁷Identified by the Topical Analgesic Panel as triethanolamine salicylate.

2. Testing of Category II and Category III conditions.

The Panel recommended testing guidelines for sunscreen drug products (43 FR 38206 at 38258 and 38259). Interested persons may communicate with the agency about the submission of data and information to demonstrate the safety or effectiveness of any sunscreen 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 placing the labeling sections of this tentative final monograph in Subpart C. In addition, the agency is renumbering the testing sections, §§ 352.40 through 352.46, of the Panel's recommended monograph as §§ 352.70 through 352.76 and is placing these sections in Subpart D.

2. Because the term "ultraviolet radiation" is preferred when speaking of the wavelengths between 100 and 400 nm, the agency is using the term "ultraviolet radiation" instead of "ultraviolet light" throughout the tentative final monograph. (See comment 2.)

3. To clarify that the scope of this monograph extends only to drug products and to be consistent with the

format of other OTC drug monographs, the word "drug" is being added to § 352.1 to read as follows: "An over-the-counter sunscreen drug product in a form suitable for topical administration * * *." (See comment 25.)

4. The agency is proposing to provide a definition of MED in § 352.3 by adding new paragraph (a) as follows: "Minimal erythema dose (MED). The smallest dose of ultraviolet (UV) radiation (expressed as Joules per meter squared) that produces redness reaching the borders of the exposure site." The other definitions in § 352.3 are being renumbered to adjust for the addition of new paragraph (a). (See comment 95.)

5. The agency is proposing to revise the Panel's recommended definitions in § 352.3(a)(3), (4), and (5) to reflect new terminology and SPF ranges for PCD's and is including the revised definitions in § 352.3(b)(3), (4), and (5). (See comments 44 and 45.)

6. The agency is revising the Panel's recommended definition for a sunscreen active ingredient in § 352.3(b) and is including the revised definition in proposed § 352.3(c) as follows: "Sunscreen active ingredient. An active ingredient that absorbs at least 85 percent of the radiation in the UV range at wavelengths from 290 to 320 nanometers, but may or may not transmit radiation at wavelengths longer than 320 nanometers." (See comment 17.)

7. Based upon data showing that padimate A is a weak phototoxic agent, the agency is classifying padimate A at 5 percent and higher concentrations in Category II and in concentrations less than 5 percent in Category III. (See comment 35.)

8. Although the Panel did not include zinc oxide in its report on OTC sunscreen drug products, the agency is proposing in this tentative final monograph to classify zinc oxide in Category III. (See comment 36.)

9. Because a sunscreen active ingredient's performance is not totally dependent upon the concentration of the active ingredient in the drug product, the agency is proposing only maximum concentrations in § 352.10. However, because the agency is concerned that each ingredient of a combination drug product contributes to the effect of the product, the agency is proposing minimum concentrations for sunscreens used in combination with one another in § 352.20. (See comment 37.)

10. The agency is proposing that any Category I sunscreen active ingredient can be safely and effectively combined with certain Category I skin protectant active ingredients (allantoin, cocoa

butter, dimethicone, glycerin, petrolatum, shark liver oil, and white petrolatum) in § 352.20(b)(1) and (2) as follows: "(1) Any single sunscreen active ingredient when used in the concentration established in § 352.10 may be combined with one or more skin protectant active ingredients identified in § 347.10(a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in Subpart D of this part and provided the product is labeled according to § 352.60" and "(2) Two or more sunscreen active ingredients when used in the concentrations established in § 352.20(a)(2) may be combined with one or more skin protectant active ingredients identified in § 347.10(a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in Subpart D of this part and provided the product is labeled according to § 352.60." (See comment 71.)

11. The agency concludes that OTC sunscreen drug products with SPF values higher than 15 are beneficial to consumers and is proposing in §§ 352.50 and 352.52 that the upper limit for SPF values be 30. The agency is also proposing that a sunscreen drug product should display its tested SPF value up to 30. The agency believes that SPF values should be displayed on the principal display panel of OTC sunscreen drug products and is, therefore, proposing a new § 352.50 that requires SPF values to appear on the principal display panel.

The agency is proposing to renumber the Panel's recommended § 352.50 "Labeling of sunscreen products" as § 352.52. (See comments 45, 46, and 47.)

12. The agency believes that including both a static and a water resistant SPF value in the labeling of water resistant and very water resistant sunscreen drug products will be beneficial to the consumer. Therefore, the agency is proposing such labeling in § 352.50(b). (See comment 51.)

13. The agency has determined that some of the Panel's recommended indications can be combined and simplified. In this tentative final monograph, the agency is combining the indications recommended by the Panel in § 352.50(b)(1)(ii) and (b)(1)(iii) and is proposing the combined indication in § 352.52(b)(1)(i) as follows: (Select one of the following: "Filters" or "Screens") "out the sun's" (select one of the following: "burning" or "harsh and often harmful") "rays to prevent

sunburn." The agency is also combining the additional indications recommended by the Panel in § 352.50(b)(2)(v)(e) and (b)(2)(v)(f) and is proposing the combined indication in § 352.52(b)(2)(vi)(E) as follows:

"Provides the highest degree of" (select one of the following: "sunburn" or "sunscreens") "protection and permits no tanning."

14. The agency has determined that sunscreen-containing products that are not indicated for the prevention of sunburn, but only for added protection against the sun are drug products. Because such products are not adequately addressed by the Panel's recommended monograph, the agency is proposing to include the following new indications in § 352.52(b)(1) as follows: § 352.52(b)(1)(v) (Select one of the following: "Filters" or "Screens") "out the sun's" (select one of the following: "sun's rays," "sun's harsh rays," or "sun's harmful rays") "to help prevent" (select one or more of the following: "lip damage," "skin damage," "freckling," or "uneven coloration"), and § 352.52(b)(1)(vi) (Select one of the following: "Protects from" or "Shields from") (select one of the following: "the harmful rays of the sun" or "the sun"). (See comment 52.)

15. The agency is proposing to replace the Panel's recommended labeling in § 352.50(b)(1)(iv) and (b)(1)(v) with the following statement in § 352.52(e)(6): "SUN ALERT: The sun causes skin damage. Regular use of sunscreens over the years may reduce the chance of skin damage, some types of skin cancer, and other harmful effects due to the sun." This statement will be required on all sunscreen drug products. The agency is also proposing the following in § 352.52(e)(7): "Any variation of the statement in § 352.52(e)(6) that does not relate skin aging or skin cancer as being 'due to the sun' will cause the product to be misbranded under section 502 of the act (21 U.S.C. 352)." (See comment 56.)

16. The agency believes that the information in the Panel's indications in § 352.50(b)(2)(i)(f), (b)(2)(i)(g), (b)(2)(ii)(e), (b)(2)(ii)(f), (b)(2)(iii)(g), (b)(2)(iii)(h), (b)(2)(iv)(e), and (b)(2)(iv)(f) and in the phrase "Stay in the sun (twice, 4 times, 6 times, 8 times, or 15 times) as long as before without sunburning" in the statements on product performance in § 352.50(e)(1)(i) through (e)(1)(v) can be better presented to consumers if those indications and phrases are revised. Therefore, the agency is not including those recommendations from the Panel, but is instead proposing the following in § 352.52(b)(1)(iii) and (b)(1)(iv),

respectively: "Allows you to stay in the sun up to (insert SPF of product up to 30) times longer than without sunscreen protection," and "Provides up to (insert SPF of product up to 30) times your natural protection from sunburn." (See comment 57.)

17. The agency is proposing to revise the Panel's recommended indications in § 352.50(b)(2)(i)(a), (b)(2)(ii)(a), (b)(2)(iii)(a), (b)(2)(iv)(a), and (b)(2)(v)(a) and to include the revised indications in § 352.52(b)(2)(i)(A), (b)(2)(ii)(A), (b)(2)(iii)(A), (b)(2)(iv)(A), and (b)(2)(v)(A). (See comment 58.)

18. In order to be consistent with other recently published tentative final monographs, the agency is proposing to delete the Panel's recommended warnings in § 352.50(c)(2)(i) and (c)(2)(ii). The content of the warnings with some minor format changes is proposed in the directions included in § 352.52(d). (See comment 61.)

19. The agency is proposing to revise the Panel's recommended warning in § 352.50(c)(1)(ii) as follows: "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water." The revised warning is proposed in § 352.52(c)(1)(ii). (See comment 62.)

20. The agency is proposing to revise the Panel's recommended warning in § 352.50(c)(1)(iii) by adding the sentence "If irritation or rash persists, consult a doctor." The revised warning is proposed in § 352.52(c)(1)(iii). (See comment 63.)

21. The agency believes that sunscreen-containing lip balms and lipsticks do not require the warning recommended by the Panel in § 352.50(c)(1)(i). Therefore, the agency is proposing new § 352.52(c)(3), "For products containing any ingredient identified in § 352.10 formulated as a lip balm or lipstick. The warning in paragraph (c)(1)(i) of this section is not required." (See comment 52.)

22. The agency does not believe that sunscreen-containing lipsticks should be required to display the warning "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water." Therefore, the agency is proposing to add new § 352.52(c)(4) "For products containing any ingredient identified in § 352.10 formulated as a lipstick. The warning in paragraph (c)(1)(ii) of this section is not required." (See comment 52.)

23. To accommodate the various dosage forms of sunscreen drug products that are available, the agency is including only brief, required directions that can be expanded with more detailed instructions applicable to a particular product formulation and dosage form. In addition, the agency is

proposing that manufacturers determine the necessary waiting period between applying a sunscreen drug product and exposing the test site to water, if applicable, for water resistant and very water resistant sunscreen drug products and include this information in the directions for use. Accordingly, the agency is proposing these requirements in the directions in § 352.52(d). (See comment 67.)

24. The agency is combining the directions recommended by the Panel in § 352.50(d)(1)(i) and (d)(1)(ii) and is proposing the combined directions in § 352.52(d)(1). The agency is also combining the directions recommended by the Panel in § 352.50(d)(3)(i) and (d)(3)(ii) and is proposing the combined directions in § 352.52(d)(3) of this tentative final monograph.

25. The agency is also proposing specific directions for sunscreen-containing drug products such as lip balms, make-up preparations, skin preparations, and lipsticks in § 352.52(d) as follows:

"(4) For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52(b)(1)(v) and/or (b)(1)(vi) and formulated as a make-up preparation or lipstick. 'Apply liberally as often as necessary.'

(5) For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52(b)(1)(v) and/or (b)(1)(vi) and formulated as a lip balm or skin preparation. 'Adults and children 6 months of age and over: Apply liberally as often as necessary. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor.' (See comment 52.)

26. The agency is proposing to allow manufacturers the option of using the word "perspiration" for "sweat" and the word "perspiring" for "sweating" in §§ 352.50(b) and (c) and 352.52(d) and (e). (See comment 49.)

27. The agency is not proposing the Panel's recommended term "waterproof" in this tentative final monograph, but is proposing instead the term "very water resistant" in §§ 352.50(c) and 352.52(d) and (e). (See comment 50.)

28. The agency is proposing to revise the Panel's recommended PCD labeling in § 350.50(e) to more accurately reflect the actual protective values of sunscreen drug products and that PCD labeling claims be optional. The agency is also proposing the terms "minimal," "moderate," "high," "very high," and "ultra high" to identify PCD's. The agency is proposing this revised PCD

labeling in § 352.52(e). (See comments 44 and 45.)

29. The agency believes that it is appropriate for a sunscreen drug product that passes the water resistance and very water resistance tests to be permitted to make claims regarding sweat resistance in addition to making claims regarding water resistance. Therefore, the agency is proposing to permit the use of the terms "sweat resistant," "perspiration resistant," "resists removal by sweating," or "resists removal by perspiring" for a sunscreen drug product that qualifies for the claim of water resistant or very water resistant. The agency is proposing the phrase "sweat resistant" or "perspiration resistant" in § 352.52(e)(2) and (e)(3) and is not proposing § 352.50(e)(2)(i)(c) as recommended by the Panel. In addition, the agency is not including the Panel's recommended sweat resistant test in § 352.46 in the sunscreen testing procedures. (See comment 100.)

30. The agency is proposing the following additional statement in § 352.52(e)(5): "For products containing the active ingredient identified in § 352.10(s) that provide an SPF of 12 to 30, the following labeling statement may be used. 'Sunblock.'" (See comment 60.)

31. The agency is proposing to include the following labeling requirements for the indications, warnings, and directions of sunscreen-skin protectant combination products in § 352.60(b), (c), and (d), respectively, concerning labeling of combination sunscreen drug products: "For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). In addition to any or all of the indications for sunscreens in § 352.52(b), the indication for skin protectants in § 347.50(b)(2) of this chapter should be used."

"For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The warning for skin protectants in § 347.50(c)(3) is not required."

"For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The directions for sunscreens in § 352.52(d) should be used."

The agency is also proposing a new § 352.20(c) to include a cross reference to the combination of a sunscreen active ingredient and a skin bleaching active ingredient. Labeling for this combination will be included in the final monograph for OTC skin bleaching drug products. (See comment 71.)

32. Because the improved stability characteristics of a revised 8-percent

homosalate standard make it more appropriate for use in the testing procedures for sunscreen drug products than the standard originally submitted to the Panel, the agency is proposing the revised formulation and its manufacturing directions in § 352.70(a) and (b). In addition, the agency is including in § 352.70(a) the following statement: "In order for the SPF determination of a test product to be considered valid, the SPF of the standard sunscreen must fall within the standard deviation range of the expected SPF (i.e., 4.47 ± 1.279), and the 95-percent confidence interval for the mean SPF must contain the value 4." (See comments 74 and 75.)

33. The agency is not including the Panel's recommended § 352.41(b) "Natural light source (sunlight)" and § 352.44 "Determination of SPF value using natural light source (sunlight)," in this tentative final monograph. In addition, the Panel's reference to natural sunlight testing in § 352.42(h) "Response criteria" is not being included. (See comment 79.)

34. The agency is revising the light source specifications proposed by the Panel in § 352.41 of its monograph and is proposing new specifications in § 352.71. Also in § 352.71, the agency is specifying that an "accurately-calibrated spectroradiometer system or equivalent instrument" be used to measure the output of a solar simulator. (See comments 86 and 88.)

35. The agency believes that blinding procedures should be included in the sunscreen testing procedures. Therefore, the agency is proposing blinding procedures in § 352.72(e) "Application of test materials" and § 352.72(h) "Response criteria." (See comment 91.)

36. In this tentative final monograph, the agency is not including the Panel's recommended § 352.42(g) but is proposing the following in § 352.72(g): "Number of subjects. A test panel shall consist of not more than 25 subjects with the number fixed in advance by the investigator. From this panel, at least 20 subjects must produce valid data for analysis." In addition, the agency is proposing to revise the Panel's recommended § 352.41(i) "Rejection of data" by adding the phrase "or if the subject was noncompliant (e.g., subject withdraws from the test due to illness or work conflicts, subject does not shield the exposed testing site from further UV radiation until the MED is read, etc.)" and is including the revised section in § 352.72(i). (See comment 94.)

37. The agency is proposing that § 352.72(h) include the following: " * * * The MED is determined 22 to 24 hours after exposure. The erythema

responses of the test subject should be evaluated under the following conditions: the source of illumination should be either a tungsten light bulb or a warm white fluorescent light bulb that provides a level of illumination at the test site within the range of 450 to 550 lux, and the test subject should be in the same position used when the test site was irradiated. Testing depends upon determining the smallest dose of energy that produces redness reaching the borders of the exposure site at 22 to 24 hours postexposure for each series of exposures * * * . The agency is also proposing in § 352.73 that the MED is the lowest dose of radiation that produces uniform redness reaching the borders of the exposure site at 22 to 24 hours postexposure. (See comment 95.)

38. In § 352.73(c) the agency is proposing to revise the Panel's recommended determination of SPF values in § 352.43 to include a geometric series of 5 exposures plus 2 other exposures placed symmetrically around the middle exposure. In addition, the agency is proposing that the exposure doses for the geometric series shall be calculated as follows: (1) (1.25)X for products with an estimated SPF less than 8, (2) 1.20X for products with an estimated SPF from 8 to 15, and (3) (1.15)X for products with an estimated SPF greater than 15. (See comment 96.)

39. The agency is proposing an erythema action spectrum and a proposed calculation to determine the erythema effective exposure in § 352.73. The agency is also proposing to replace the term "exposure time interval" in the SPF calculation in § 352.73 with the term "erythema effective exposure." (See comments 84 and 85.)

40. The Panel recommended in § 352.43 of its monograph that the MED(US) be determined on the day before evaluating the MED(PS) of the test sunscreens and the standard sunscreen. The agency agrees that it is necessary to establish the inherent MED of the test subject prior to evaluating a test sunscreen drug product so that the investigator can select appropriate doses of UV radiation to administer to the test subsites based upon the individual's predetermined MED(US) and the expected SPF of the test product. The agency is proposing that an MED(US) be determined on a day prior to the testing of the sunscreen drug product and that this previously established MED(US) be used to determine the testing doses of UV radiation. However, the agency also believes that the MED(US) and the MED(PS) that are used in the calculation of the SPF value of a sunscreen drug product should be determined on the

same day. Such concomitant testing will eliminate any discrepancies resulting from day to day variations that may exist in the testing environment. Therefore, the agency is proposing in § 352.73 that, in addition to establishing an MED(US) on a day prior to the testing of the sunscreen drug products, a second MED(US) must be established on the same day as the MED(PS). The MED(US) that is established concomitantly with the MED(PS) is to be used in the calculation of the test product's SPF value.

41. The agency is including a statistical analysis based upon the t-test to be used in analyzing the results of the testing procedures for sunscreen drug products. Therefore, in § 352.73, the agency is proposing to include a one-sided t-test. The agency is also proposing the use of a 95-percent lower confidence interval to establish a statistically significant SPF value for use in OTC sunscreen drug product labeling. (See comment 97.)

42. In § 352.76(a) the agency is proposing the following sentence at the end of the section: "If the sunscreen product retains the same PCD after 40 minutes of water immersion as it had before water immersion, the claim of 'water resistant' may be made." In § 352.76(b), the agency is proposing the following sentence at the end of the section: "If the sunscreen product retains the same PCD after 80 minutes of water immersion as it had before water immersion, the claim of 'very water resistant' may be made." (See comment 101.)

43. The agency is proposing in § 352.76 of this tentative final monograph a definition of "fresh water" as clean drinking water that meets the standards in 40 CFR Part 141. (See comment 104.)

44. To clarify that the procedures in "General Testing Procedures" in § 352.72 apply to the individual testing procedures for water resistant and very water resistant claims, the agency is proposing a cross reference in § 352.76 as follows: "The general testing procedures in § 352.72 should be used as part of the following tests, except where modified in this section." The agency is also deleting the Panel's recommended statement in § 352.46 that states that "The standard sunscreen is not used in this test," and requiring that the 8-percent homosalate standard be used in the general testing procedures in § 352.72. (See comments 105 and 106.)

45. The agency is proposing testing procedures in § 352.76 to state that an indoor fresh water pool, whirlpool, and/or jacuzzi maintained at 23 to 32 °C shall be used in the water resistant or

very water resistant testing procedures. (See comment 106.)

46. The agency is proposing to amend the cosmetic regulations in 21 CFR Part 700 by adding § 740.19 as follows: "Suntanning preparations. The labeling of suntanning preparations that do not contain a sunscreen ingredient must display the following warning: 'Warning—This product does not contain a sunscreen and does not protect against sunburn.'" (See comment 29.)

47. The agency is also proposing to revise the cosmetic regulations in 21 CFR Part 700 by adding § 700.35 to state that if a cosmetic product uses the word "sunscreen" anywhere in its labeling, the term "sunscreen" must be qualified by describing the cosmetic benefit provided by the sunscreen. (See comment 27.)

48. Because the trade correspondence TC-61 will be superseded by the requirements of the final monograph for OTC sunscreen drug products, the agency intends to revoke TC-61 and will publish a notice of revocation and the final monograph for OTC sunscreen drug products concurrently. (See comment 27.)

49. 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 other 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.

50. For an active ingredient to be included in an OTC drug final monograph, it is necessary to have publicly available sufficient chemical information that can be used by all manufacturers to determine that the ingredient is appropriate for use in their products. The recent discovery of a nitrosamine contaminant in sunscreens containing padimate O (see discussion above) illustrates the importance of requiring that sunscreen ingredients are adequately characterized and that these standards are published in an official compendium. Only a few of the sunscreen active ingredients that the Panel classified as Category I are standardized and characterized for quality and purity and are included in official compendia. Aminobenzoic acid, cinoxate, dioxybenzone, oxybenzone and titanium dioxide are currently

included as articles in the U.S.P. (Ref. 1). The remaining sunscreen active ingredients, including the homosalate control preparation used in the sunscreen testing procedures, are currently not adequately characterized.

The agency believes that it would be appropriate for interested parties to develop with the United States Pharmacopoeial Convention appropriate standards for the quality and purity of the sunscreen ingredients that are not already included in official compendia. In this tentative final monograph diethanolamine methoxycinnamate, digalloyl trioleate, ethyl 4-[bis(hydroxypropyl)] aminobenzoate, glyceryl aminobenzoate, homosalate, lawsone with dihydroxyacetone, menthyl anthranilate, octocrylene, octyl methoxycinnamate, octyl salicylate, phenylbenzimidazole sulfonic acid, red petrolatum, sulisobenzene, and trolamine salicylate are proposed in Category I. However, should interested parties fail to provide necessary information so that appropriate standards may be established, these ingredients will not be included in the final monograph. The same standards should also be developed for any Category II or III ingredients for which data are submitted for inclusion in the final monograph.

Reference

(1) "United States Pharmacopeia XXII—National Formulary XVII," United States Pharmacopoeial Convention, Inc., Rockville, MD, pp. 63, 312, 455, 986, and 1380, 1989.

51. The agency has determined that the medical literature supports the Panel's conclusion that overexposure to sunlight/UV radiation is related to skin cancer and premature aging of the skin. (See comments 46 and 56.) The Panel recognized the epidemiological evidence that skin cancer and degenerative skin changes (elastotic degeneration), referred to as premature aging of the skin, are related to chronic exposure to the UV radiation from the sun (43 FR 38206 at 38211 and 38212). This damage is cumulative, and many years may pass before skin changes appear.

The agency notes that premature aging of the skin caused by excessive exposure to the sun is a distinct process very different from normal chronologic or intrinsic aging of the skin. Some of the differences observed between photoaged skin and chronologically aged skin were discussed in a 1986 review article (Ref. 1). For example, photoaged skin displays massive quantities of elastic fibers that degenerate into an amorphous mass while normally aged skin displays a

slightly increased, but almost normal, amount of elastic tissue. Although, the dermis of photoaged skin becomes thicker than normal, the dermis of normally aged skin becomes thinner. Photoaged skin contains an increased number of hyperactive fibroblasts, an increased number of mast cells, and a mixed inflammatory infiltrate. In normally aged skin, the fibroblasts are decreased in number and inactive, the mast cells are decreased in number, and there is no inflammation. The agency emphasizes that the use of sunscreens has no effect on the normal process of aging, either aging of the skin or of the entire body.

The Panel noted that dermatologists routinely instruct their patients who have skin cancer on sun-exposed areas to wear long sleeves and a wide-brim hat, to avoid sun exposure between 10 a.m. and 2 p.m. solar time, and to use a sunscreen liberally every day (43 FR 38206 at 38212). The reason that most physicians recommend sunscreens for skin cancer patients is to reduce the risk of skin cancer that may not appear for 10 to 20 years, resulting from current exposure to the sun. It is not intended that the use of sunscreens will heal damage resulting from sun exposure that occurred years earlier.

The agency recognizes that many consumers could benefit from protection against everyday chronic exposure to UV radiation in addition to obtaining protection against periodic, acute exposure such as is encountered at the beach. For example, daily protection from exposure to UV radiation could be useful for many outdoor workers (e.g., construction workers, traffic policemen) and other persons involved in long-term outdoor activities. These individuals would require the most frequent sunscreen application. In addition, individuals who jog, play tennis, walk, drive, or garden may also need protection from UV radiation exposure. The AAD notes that 90 percent of all skin cancers occur on parts of the body that are unprotected by clothing. Farmers, outdoor workers, sports enthusiasts, and others who by choice or necessity spend numerous hours in the sun are likely candidates for leathery complexions and solar keratoses (Ref. 2). The AAD recommends that for optimal protection against developing skin cancer, people should avoid constant overexposure to the sun from infancy through adulthood. By selecting appropriate clothing and applying the proper sunscreens, persons can enjoy outdoor activities in the sunshine while still maintaining healthy and attractive skin throughout life.

The agency is unaware of specific data demonstrating a need for protection from UV light generated indoors, such as in an office building. Most scientific sources, including an NIH Consensus Development Conference (Ref. 3), have concluded that daily sun protection is needed for routine outdoor exposure but have not made recommendations regarding the need for protection indoors. A statement issued by the NIH Consensus Development Conference (Ref. 3) recognizes that unshielded fluorescent bulbs used for illumination are a potential source of artificial UV radiation. An unresolved issue is the amount of UVA emitted by such sources and the long-term effects of this exposure. More research on indoor sources of radiation is needed to identify possible problems. In the absence of definitive data, the AAD provides no recommendations on the use of sunscreens indoors. The agency invites comments, data, and information on the usefulness of sunscreens indoors.

Because of the documented importance and value of sunscreen drug products for many consumers, the agency concludes that the marketing of sunscreen drug products for daily use is beneficial, provided the products are appropriately labeled. Therefore, in this tentative final monograph, the agency is proposing labeling that is appropriate for daily use (nonbeach products) as well as for products that are intended for occasional use where intense sun exposure is likely to occur (beach products). (See comment 52.)

The Panel's recommended monograph included the following two indications for all sunscreen drug products: (1) "Over-exposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of these harmful effects," and (2) "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of premature aging of the skin and skin cancer."

The Panel recommended these indications because it (1) believed that overexposure to sunlight/UV radiation is related to skin cancer and premature aging of the skin and (2) the regular use of sunscreens will reduce consumers' risk of these adverse effects (43 FR 38206 at 38210 and 38211).

The agency agrees that it is important that consumers be alerted to the risks of premature aging and skin cancer that may result from overexposure to the sun. The agency believes that including such information on all sunscreen drug

products would be an effective means of educating the public to use sunscreens to minimize the detrimental effects of long-term exposure to the sun. Therefore, because of the seriousness of these adverse effects, the agency is proposing not to include the statement as an optional indication but rather as a required statement in the labeling of all sunscreen drug products. The agency is proposing a different statement than that recommended by the Panel, however, because it believes that this statement will better alert and inform consumers that the sun may damage the skin and that using sunscreens may help to reduce the risk of damage. This statement is proposed in § 352.52(e)(6) of this tentative final monograph under the heading "SUN ALERT" as follows: "The sun causes skin damage. Regular use of sunscreens over the years may reduce the chance of skin aging, some types of skin cancer, and other harmful effects due to the sun." (See comment 56.)

It is very important that the labeling of sunscreen drug products convey accurate information to consumers and that consumers are not misled. The agency believes that any labeling on sunscreen drug products that refers to skin aging or skin cancer should not be taken out of context, and that the labeling should directly relate the skin aging or skin cancer as being due to sun exposure. Labeling that does not directly relate these adverse effects as being due to sun exposure is misleading. Therefore, in § 352.52(e)(7) of this tentative final monograph, the agency is proposing the following: "Any variation of the statement in § 352.52(e)(6) that does not relate skin aging or skin cancer as being 'due to the sun' will cause the product to be misbranded under section 502 of the act (21 U.S.C. 352)." The agency will evaluate claims made on OTC sunscreen drug product labels on a product-by-product basis, under section 502 of the act (21 U.S.C. 352), to determine whether those claims are false or misleading.

For examples of acceptable and unacceptable labeling, (see section II.B.52 and 53—*Summary of Agency Changes* of this document.

References

- (1) Kligman, L. H., and A. M. Kligman, "The Nature of Photoaging: Its Prevention and Repair," *Photodermatology* 3:215-227, 1986.
- (2) "Cancer of the Skin," edited by the Task Force on Pamphlets, American Academy of Dermatology, Evanston, IL, 1986.
- (3) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference

Statement, Vol. 7, Number 8, May 8-10, 1989.

52. The agency is aware that most manufacturers of sunscreen skin care products have recognized that the specific term "anti-aging" or similar absolute terms are not appropriate for use in labeling of either an OTC drug or cosmetic product. At the agency's urging, the majority of manufacturers are not currently using such terms on products containing Category I sunscreen ingredients.

The agency issued a number of regulatory letters (Ref. 1) to companies marketing skin creams and lotions with therapeutic labeling claims. None of the products were marketed or promoted as beach products. Most of the products did not contain sunscreens and were marketed as facial creams with claims such as the following: "anti-aging total skin supplement," "anti-age daytime skin treatment," "reverses signs of facial aging," "prevent, postpone, and minimize the effects of the aging process," "recreate the structure of a youthful skin," "helps to rebuild the intercellular structure of your skin," and "cause cells to divide and reproduce faster." However, some of the products contained sunscreen ingredients and, in addition to anti-aging claims similar to those described above, displayed claims such as "enhanced with two sunscreens: Filters for UVA and UVB," "helps prevent lines and wrinkles by guarding against UV damage," "special UVA and UVB screening agents help prevent permanent tissue damage caused by sun exposure * * * designed to shield the skin against the specific factors that accelerate the signs of aging," and "filters out damaging UV light rays."

In its regulatory letters, the agency pointed out that such claims represent and suggest (1) that the product is intended to affect the structure and function of the human body and (2) that the product is adequate and effective for such uses as recreating the structure of young skin, rebuilding the intercellular network of skin, and other claims. The agency stated that such claims cause the product to be regarded as a drug as defined in section 201(g) of the act (21 U.S.C. 321(g)). The agency also stated that because it was unaware of any substantial scientific evidence that demonstrated that the products were generally recognized as safe and effective for their intended uses, these products were "new drugs" within the meaning of section 201(p) of the act (21 U.S.C. 321(p)). In addition, many of the products that contained sunscreen ingredients were not labeled with adequate directions for use. Moreover,

some products contained a purported sunscreen ingredient that was not generally recognized as safe and effective for its intended use and were, therefore, unapproved new drugs.

One regulatory letter was sent to a company that marketed a product, "ANTI-AGING COMPLEX," that contained a sunscreen among other ingredients. According to the letter (Ref. 2), the labeling of the product stated or suggested that the product minimizes the aging effects that can result from ultraviolet rays, aids maturing skin while new cells rise to the surface through a special balance of skin cell protectors, and helps the skin hold vital moisture deep within the epidermis. The agency stated that these claims cause the product to be a drug, and that, because the drug is not generally recognized as safe and effective for its intended use, the product is a new drug. In a written response to the agency (Ref. 3), the company insisted that it had consistently labeled the product as an OTC drug/cosmetic in compliance with the act and the proposed rule for OTC sunscreen drug products. The company stated that the use of the name "Anti-Aging" for its product is not false or misleading because, when taken in the context of the claims, indications, and declaration of active ingredients, the terms clearly demonstrate that the product is intended to minimize the visible signs of aging associated with incidental sun exposure. According to the company, the product's labeling included the following claims, among others: (1) "With proper care and protection, it is possible to moderate the influence of environmental factors, helping to minimize the visible signs of aging," (2) "Minimizes the aging effects which can result from incidental sun exposure during everyday activities," and (3) "A unique formula that contains ingredients designed to shield your skin against specific factors that accelerate the signs of aging." As support for such claims, the manufacturer pointed to the indications proposed by the Topical Analgesic Panel in § 350.50 (b)(iv) and (b)(v) of its recommended monograph for OTC sunscreen drug products (e.g., "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of these harmful effects." See 43 FR 38206 at 38267.) The company added that although its claims do not follow the language of the monograph verbatim, they are consistent with the language in the monograph and that consistency is all

that is required under the agency's OTC labeling "flexibility policy."

Another regulatory letter (Ref. 4) was issued regarding "AGE-LESS ANTI-AGING DAILY FACE CAPSULES." The letter cited labeling statements such as the following: "AGE-LESS ANTI-AGING DAILY FACE CAPSULES * * * HELPS PREVENT THE VISIBLE SIGNS OF AGING. Your skin starts aging from the very first day it's exposed to the environment. But this skin aging can be controlled. AGE-LESS is a highly effective protective complex. It filters out damaging UV light rays * * *." The agency stated that these claims suggest that the product is adequate and effective for such uses as preventing the visible signs of aging and controlling skin aging. The agency added that it was not aware of any substantial scientific evidence that demonstrates the safety and effectiveness of this product for its intended use, nor was it aware that this drug was generally recognized as safe and effective for its intended uses. In a reply letter (Ref. 5), the company stated that its products were labeled in accordance with the proposed monograph for OTC sunscreen drug products. The letter included a lengthy discussion regarding the value of incorporating a sunscreen into daily-use products. The company also submitted proposed new labeling as follows: "AGE-LESS Anti-Aging Daily Face Capsules with Sunscreen. Sunscreen may help prevent the premature aging of the skin caused by overexposure to the sun. SPF 4."

As mentioned above, much of the industry is not currently using such labeling information and has recognized that the specific term "anti-aging" is not appropriate. It should be further noted that the term "anti-aging" does not relate the aging in question to either skin or the sun. The agency objects to the use of that term in the labeling of OTC sunscreen drug products or any other topically applied OTC drug product. The agency is not aware of any scientific studies that establish the safety and effectiveness of a topically-applied OTC drug for the intended use of reversing or delaying the intrinsic aging process, as implied in the "anti-aging" labeling claim. There is no support for such a claim in the Panel's recommended monograph, which does not include the specific term "anti-aging" among its indications (43 FR 38206 at 38267 and 38268). The agency is not proposing the term "anti-aging" as an allowable labeling claim in this tentative final monograph. Therefore, any claim that includes the term "anti-aging" or any similar term is Category II.

The agency does not believe that "premature aging" of the skin should be defined as "wrinkling." Wrinkling is only a part of the process of premature aging of the skin from excessive exposure to UV radiation (Ref. 6). Wrinkling should not, therefore, be elevated to greater significance than other signs of premature skin photoaging. In addition to wrinkling, photoaged skin displays a variety of benign, premalignant and malignant neoplasms, accentuated skin furrows, sags and bags, and a leathery, nodular, yellow surface with telangiectatic (i.e., a vascular lesion formed by the dilation of a group of small blood vessels) tracteries. The most drastic of these visible aspects reflect profound structural changes in the dermis.

The agency also objects to the use of the term "anti-aging" or similar terms (e.g., AGELESS) in the product names of OTC sunscreen drug products. As stated in 21 CFR 201.128, the intended use of a product may be evidenced by labeling claims, other oral or written statements, or other circumstances in the labeling or marketing indicating that the product is offered for a purpose for which it is neither labeled nor advertised. The agency considers a product's name to be an integral part of the labeling of the drug. A drug product's intended use can be inferred from the product's name. The agency believes that use of the term "anti-aging," or equivalent language, in a sunscreen drug product's name could lead consumers to assume that the product will protect against chronological aging, a use for which the product is not labeled and is not generally recognized as safe and effective. The agency considers such terms in a sunscreen product's name to be inappropriate and misleading.

The agency is aware that the phrase "photoaging of the skin" has been used in the labeling of sunscreen drug products as an alternative to the phrase "premature aging of the skin due to overexposure to the sun." Although the scientific community may equate the term "photoaging of the skin" with "premature aging of the skin," the agency is not aware of specific information demonstrating that the average consumer recognizes that the phrase "photoaging of the skin" refers to premature aging of the skin caused by sunlight. Therefore, in this tentative final monograph, the agency is requesting comment on whether "photoaging of the skin" is an appropriate alternative phrase for the phrase "skin aging due to the sun."

In order to provide guidance regarding alternative language for claims pertinent to skin aging due to the sun,

the agency is providing in this document some examples of acceptable and unacceptable language that may appear on sunscreen drug products. Acceptable language clearly links the effect (i.e., skin aging) with the cause (i.e., the sun or ultraviolet radiation). Examples of some acceptable language regarding premature aging of the skin include the following:

(1) "Sunscreen may reduce the chance of skin aging caused by exposure to the sun."

(2) "While biological aging is inevitable, sunscreen may help protect skin from aging caused by exposure to ultraviolet radiation from the sun."

(3) "Skin can age prematurely from exposure to the sun. Sunscreen may help reduce the chance of this type of aging."

(4) "May help inhibit the signs of skin aging caused by exposure to ultraviolet rays from the sun."

Sunscreen labeling relating to skin aging caused by the sun that does not clearly link the cause to the effect is unacceptable. The agency considers the following examples pertaining to premature aging of the skin unacceptable:

(1) Statements that include only the term "anti-aging." As discussed above, the agency does not believe that the term "anti-aging" by itself is adequate language to describe the action of a sunscreen drug product and is in fact misleading.

(2) "Helps prevent lines and wrinkles by guarding against UV damage." As discussed above, "premature aging of the skin" cannot be defined as "wrinkling" or "lines" because wrinkling is only a part of the process of premature aging of the skin and should not be elevated to greater significance than other signs of premature skin photoaging.

(3) Statements including terms such as stops, reverses, or reduces the signs of aging. These statements make no reference to premature aging of the skin or that such aging is due to the sun. The agency is not aware of any data showing that the use of a sunscreen stops, reverses, or reduces the signs of aging.

(4) "Helps to minimize the visible signs of aging," when used in conjunction with a sunscreen ingredient. This statement makes no reference to aging of the skin or that the skin aging is due to the sun. As noted above in (3), the agency is not aware of any data showing that the use of a sunscreen has any effect on aging.

(5) "Prevent (or reduce) skin aging caused by exposure to ultraviolet rays." The agency objects to the absolute term "Prevent (or reduce)" used in this claim.

The statement proposed in § 352.52(e)(6) of this tentative final monograph is a qualified statement that use of a sunscreen drug product "may reduce the chance of * * * adverse effects of the sun. The agency concludes that a qualified statement is appropriate, and that the use of absolute terms such as "prevent" is not justified in the labeling of sunscreen drug products.

(6) "Reverses aging of the skin caused by exposure to the sun." The agency is aware of some investigations showing that sunscreens can promote the repair of UV radiation-induced dermal damage (Refs. 6 and 7). However, these results are not conclusive. Therefore, at the present time the use of such claims on sunscreen drug products would be premature.

The agency invites comments on these and any other related statements that might be used in the labeling of OTC sunscreen drug products.

References

- (1) Letters from D. L. Michels, FDA, to L. Lauder, Estee Lauder; I. Alfin, Alfin Fragrances, Inc.; H. B. Waldron, Avon Products, Inc.; J. Correz, Cosmair, Inc.; W. Slater, Christian Dior Perfumes, Inc.; A. Philip, Shiseido Co., Ltd.; P. Rogers, Clarins, USA Inc.; F. Borghese, Orlane/Caron Group; A. Arpel, Adrian Arpel; M. Huber, Max Huber Research Labs, Inc.; R. Perelman, Germaine Monteil Cosmétiques Corp.; J. F. Ronchetti, Elizabeth Arden, Inc.; R. Stephens, Princess Marcella Borghese, Inc.; C. D'Alessio, Chanel, Inc.; I. Forsythe, Jacqueline Cochran la prairie; J. Correz, Biotherm (Division of Cosmair, Inc.); T. Munchak, Frances Denney, Inc.; M. Lowenthal, Almay, Inc.; P. Berge, Charles of the Ritz; R. Ballatico, Prince Matchabelli Inc.; J. Light, Jason Natural Cosmetics; R. Perry, Rachel Perry, Inc.; and J. Harmon, Coty Division of Pfizer, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (2) Letter from G. E. Vince, FDA, to R. R. Rogers, Mary Kay Cosmetics, Inc., dated February 12, 1990, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (3) Letter from T. R. Tunnell, Mary Kay Cosmetics, to D. L. Graham, FDA, dated March 7, 1990, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (4) Letter from J. J. Faline, FDA, to R. Perelman, Revlon, Inc., dated September 28, 1988, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (5) Letter from A. J. Lorman, for Revlon, Inc., to I. Flaum, FDA, dated October 27, 1988, in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (6) Kligman, L. H., and A. M. Kligman, "The Nature of Photoaging: Its Prevention and Repair," *Photodermatology*, 3:215-227, 1986.
- (7) Kligman, L. H., et al., "Sunscreens Promote Repair of Ultraviolet Radiation-Induced Dermal Damage," *The Journal of Investigative Dermatology*, 81:98-102, 1983.

53. Skin cancer is a serious concern to all consumers. According to the American Cancer Society, more than 600,000 people were diagnosed with basal-cell and squamous cell carcinomas in 1990, up from 400,000 in 1980. In addition, 35,000 more people were diagnosed with melanoma in 1990 (Ref. 1). Because of the seriousness of skin cancer, the agency believes that sunscreen drug product labeling related to skin cancer should be especially limited and carefully stated. It is very important that the labeling of sunscreen drug products not include any phrases or terms that may induce a false sense of security in sunscreen users.

Although there is extensive epidemiological evidence supporting the direct role that UV radiation plays in basal cell and squamous cell carcinomas, the relationship between UV radiation exposure and melanoma is not as clear (Ref. 2). As noted in comment 56, the labeling statement proposed by the agency in § 352.52(e)(6) of this tentative final monograph takes into account the likelihood that all skin cancers may not be correlated to UV radiation exposure. This labeling information states that "Regular use of sunscreens * * * may reduce the chance of * * * some types of skin cancer * * * due to the sun."

In addition, skin cancer is a long-term consequence of exposure to UV radiation. It normally manifests itself several years after the causative UV radiation exposure. Using a sunscreen now does not protect consumers against the development of a skin cancer that was initiated by UV exposure that occurred 20 or 30 years ago.

The agency is aware of at least one product, SKIN CANCER GARDE, that displays labeling that emphasizes the product's purported effectiveness in preventing skin cancer (Ref. 3). The product displays labeling statements such as: (1) Skin Cancer Garde" in which the word "skin" is substantially smaller and less distinct than the words "Cancer Garde," and (2) "Many skin cancers may be avoided by taking adequate precaution against excessive sun exposure."

The agency considers the use of the term "Cancer Garde" in the labeling of the product "SKIN CANCER GARDE" misleading. It is an overly positive statement that may lead consumers to assume that use of the product will absolutely prevent skin cancer, when such is not necessarily the case. The proposed statement related to premature aging of the skin and skin cancer proposed by the agency in this tentative final monograph is qualified, i.e., "may reduce the chance of * * * skin

cancer," and any skin cancer prevention language that is displayed in the labeling of sunscreen drug products should reflect the tentativeness of the FDA approved labeling. Such language should also clearly relate the skin cancer to exposure to the sun or ultraviolet rays.

The agency believes that the following claims are examples of acceptable labeling pertaining to skin cancer for sunscreen drug products:

- (1) "May reduce the chance of some kinds of skin cancers caused by exposure to the sun that would otherwise appear 20 years from now."
- (2) "Regular, everyday use of this product from childhood on, may reduce the chance of some types of skin cancers caused by exposure to the sun".

These statements accurately reflect the intent of the "premature aging/cancer" statement proposed by the agency in this tentative final monograph. The agency believes that this is important information that should be provided to consumers; however, the information must be stated in such a manner so that consumers are not misled to believe that the product will provide more protection than it actually does.

The agency considers the following claims as examples of unacceptable labeling pertaining to skin cancer:

- (1) "Cancer Garde" or "Cancer Guard" as the name of a product.
- (2) "Prevents skin cancer that may result from exposure to the sun".

As discussed above, the agency considers such labeling to be misleading because consumers may be led to believe that use of the product will absolutely prevent cancer, when such is not the case.

The agency invites comments on these and any other related statements that might be used in the labeling of OTC sunscreen drug products.

References

- (1) Greeley, A., "No Safe Tan," in FDA Consumer, May, 1991, pp. 16-21.
- (2) "Sunlight, Ultraviolet Radiation, and the Skin," National Institutes of Health Consensus Development Conference Statement, Vol. 7, Number 8, May 8-10, 1989.
- (3) OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

IV. Recent Developments

A. Padimate O Safety Concerns

In the advance notice of proposed rulemaking for OTC sunscreen drug products, the Topical Analgesic Panel recommended that 21 ingredients, including padimate O, be generally recognized as safe and effective for use

in OTC sunscreen drug products. Padimate O is octyl dimethyl aminobenzoic acid ester. In evaluating the safety of padimate O, the Panel reviewed animal and human toxicological data that included oral LD₅₀ results, primary irritation and sensitization studies, and eye irritation studies (43 FR 38206 at 38244). However, the Panel did not review any mutagenicity or carcinogenicity data for padimate O or for any other sunscreen ingredient.

Recently, FDA identified a new nitrosamine contaminant isolated from sunscreen drug products that contain the ingredient padimate O. Chou, Yates, and Wenninger (Ref. 1) developed a method for the identification and determination of this new nitrosamine, N-methyl-N-nitrosoaminobenzoate octyl ester (NMPABAO), chemically known as 2-ethylhexyl 4-(N-methyl-N-nitrosamino) benzoate. They used this method to analyze 17 commercially available sunscreen drug products containing padimate O and demonstrated that 14 of the products contained NMPABAO at levels ranging from 60 to 1,960 parts per billion (ppb). The presence of NMPABAO in all samples with more than 1,000 ppb was confirmed by mass spectroscopy.

Three discreet problems arose as a result of discovering the NMPABAO contamination of padimate O-containing sunscreen drug products: (1) Because NMPABAO was a new nitrosamine, its mutagenic and carcinogenic potential was unknown, (2) many questions were raised regarding the validity of the analytical methods used by the agency to isolate the nitrosamine, and (3) the photostability of NMPABAO was not known.

1. Toxicological Data

An unpublished report describing the results from an Ames test of NMPABAO was submitted to the agency (Ref. 2). The results of this test were purported to indicate that NMPABAO might be mutagenic. The agency is also aware of unpublished studies examining NMPABAO for mutagenicity in tests using *Salmonella typhimurium* (Ref. 3) and mouse lymphoma cells (Ref. 4). The results of another study were submitted to the agency in which the carcinogenic potential of NMPABAO was tested by measuring unscheduled deoxyribonucleic acid (DNA) synthesis (UDS) in the Rat Hepatocyte Primary Culture/DNA Repair Assay (Ref. 5). The agency has also tested NMPABAO and padimate O using the same assay (Ref. 6).

In the unpublished report describing positive results from an Ames test (Ref.

2), an ingredient purported to be NMPABAO was tested with two *Salmonella* strains (*Salmonella typhimurium* TA 100 and TA 1535) with and without in vitro metabolic activation by Aroclor-induced rat liver S-9 preparation. Doses ranged from 0.5 to 50 micromoles (μ moles) per plate in the presence of the metabolic activation system. The data for the experiments without metabolic activation are from strain TA 1535 only, and doses ranged from 1 to 50 μ moles per plate. Concurrent solvent and positive controls were performed with each experiment.

No increase in mutant counts was seen in strain TA 1535 in the absence of metabolic activation. In the presence of metabolic activation, increases in mutant counts occurred at doses of 10 μ moles per plate and higher, and these increases were dose related up to the 50 μ mole maximum dose. In strain TA 100, in the presence of metabolic activation, increases exceeded a doubling of the spontaneous count at doses of 1 μ mole per plate and higher. These increases were dose related up to the 50 μ mole maximum dose. This indicates that the test sample used is mutagenic, but that its mutagenic activity is not very strong in the assay as performed. Impurities in the sample could account for the mutagenic activity at this dose and at higher doses.

The methodology used for these experiments is not explained in any detail, and the report contained no information on the purity of the compound. For example, the amount of S-9 used per plate is not given. The report does not state whether a plate incubation protocol or a preincubation protocol was used. The report states that the positive responses seen exceed those seen with the well-known carcinogen dimethylnitrosamine (DMN). The agency notes that DMN is generally considered to be a very weak mutagen and gives a positive response only under proper conditions in the *S. typhimurium* mutagenicity assay.

The report on this *Salmonella* assay (Ref. 2) states that interpretation of these results should include the following considerations: (1) Metabolic activation in this assay was provided by liver enzymes, and, therefore, the results cannot be extrapolated to assume that skin enzymes would also activate this compound to a mutagenic form, (2) the results obtained with rat enzymes cannot be extrapolated to human enzymes; and (3) the report noted that mutagenic activity does not imply carcinogenic activity.

The agency points out that there are a number of nitrosamines that give very

weak responses in the standard plate incorporation *Salmonella* assay. The mutagenicity of such compounds can often be better detected by using a preincubation protocol or by using Syrian golden hamster S-9 rather than rat S-9 for the metabolic activation system.

In another study (Ref. 3), other investigators were unable to duplicate the positive results described in the above assay (Ref. 2). NMPABAO and a structurally related positive control, N-nitrosopiperidine, were tested for mutagenicity in the *S. typhimurium* assay (Ref. 3). The two compounds were initially tested in the *Salmonella* plate incorporation assay using dimethyl sulfoxide (DMSO) as the solvent. NMPABAO was negative with all five *Salmonella* tester strains without metabolic activation and with liver S-9 preparations from Fischer 344 rats and Syrian golden hamsters. In contrast, N-nitrosopiperidine induced positive responses in tester strains TA 98 and TA 100 but only in the presence of hamster S-9.

Because it has been reported that neither the plate incorporation assay nor the use of DMSO may be the optimal conditions for expression of a mutagenic response for some nitrosamines, the compounds were retested with *Salmonella* using a preincubation procedure and acetone as the solvent. Under these conditions, the results were the same with NMPABAO as those obtained in the plate incorporation assay. There were no increases in the number of revertants in any of the five tester strains. With N-nitrosopiperidine, dose-related responses were obtained with TA 98, TA 100, and TA 1535, in the presence of hamster S-9. The investigators concluded that NMPABAO is not mutagenic in *S. typhimurium*.

NMPABAO and two positive control chemicals, 3-methylcholanthrene (MCA) and ethyl methanesulfonate (EMS), were tested in the mouse lymphoma (L5178Y) mutagenesis assay (Ref. 4). NMPABAO was negative with and without Aroclor-induced rat liver S-9 metabolic activation using either DMSO or acetone as the solvent. In contrast, the direct-acting mutagens, EMS and MCA, in the presence of rat liver S-9, induced mutations.

In another test for genotoxicity (Ref. 5), NMPABAO was tested for its ability to induce DNA repair in primary rat hepatocytes. The positive control in this test was 4-(methylnitrosoamino)-1-(pyridyl)-1-butanone (NNK). NMPABAO and the positive control, NNK, were examined at three concentrations: 10^{-2} , 10^{-3} , and 5×10^{-3} moles (M). NMPABAO showed no apparent

induction of UDS at all test concentrations. In contrast, the positive control, NNK, showed significant and dose-dependent induction of UDS at 10^{-2} and 5×10^{-3} M.

Although the results of this assay were negative, indicating that NMPABAO is not genotoxic, the agency notes that there were several problems in the performance of this test. Because all the slides in this experiment were not scored, the agency questions the suitability of the hepatocyte preparation. If cell attachment and survival are poor, a very potent inducer of UDS may score positive with only a few cells. However, a weak inducer of UDS may be missed. Because this report does not include data on cell survival (cell attachment or cytotoxicity), it is difficult to evaluate the cell status on UDS data alone.

A recently published consensus report on the Primary Rat Hepatocyte Assay for UDS (Ref. 7) states the need for three experiments per data point and an initial screening experiment for an assessment of cytotoxicity. Another report, by Swierenga, et al. (Ref. 8), also stresses the need for information on cytotoxicity.

In 1991, the agency tested both NMPABAO and padimate O for UDS in primary rat hepatocytes (Ref. 6). Two UDS experiments were performed. One experiment tested NMPABAO at dose levels ranging from 0.713 to 2.92 micrograms/milliliter ($\mu\text{g/mL}$), and the second tested padimate O at dose levels ranging from 0.010 to 10 microliters/milliliter ($\mu\text{L/mL}$). The controls were (1) a solvent control (1 percent DMSO), (2) a negative medium control, and (3) a positive control of 2-acetylaminofluorene (2-AAF) at 1.0 and 2.5 $\mu\text{g/mL}$.

Both NMPABAO and padimate O were soluble in DMSO. However, doses of 0.73, 1.46, and 2.92 mg/mL of NMPABAO and 1, 5, and 10 $\mu\text{L/mL}$ of padimate O were insoluble when added to the aqueous cell culture medium. Heavy, oil-like droplets that dispersed evenly in the aqueous medium when vortexed were noted at the above doses of NMPABAO and padimate O. Although faint turbidity was observed at lower dose levels, no heavy oil droplets were apparent as were with the higher doses.

The data show that neither NMPABAO nor padimate O induced UDS in rat hepatocyte cultures. Values for both net nuclear grain count and percent cells in repair were similar to the negative control and solvent control values. In contrast, the positive control, 2-AAF, induced a dose dependent increase in net nuclear grain counts.

Cytotoxicity was qualitatively evaluated as cell number and morphology. Intermediate doses of NMPABAO (11.4 to 365 $\mu\text{g/mL}$) and padimate O (0.1 to 0.5 $\mu\text{L/mL}$) showed evidence of cytotoxicity compared to control values. Cytotoxicity was not observed at the lower doses of NMPABAO (0.71 to 5.7 $\mu\text{g/mL}$) or padimate O (0.01 to 0.05 $\mu\text{L/mL}$) nor at the higher doses of NMPABAO (730 to 2920 $\mu\text{g/mL}$) or padimate O (1 to 10 $\mu\text{L/mL}$). However, the heavy oil appearance of the test agents in media at these higher dose levels suggests that the compounds may not have reached the cells attached to the bottom of the culture dish. The agency, however, concludes that, in these experiments, neither NMPABAO nor padimate O appears to induce UDS at cytotoxic or non-cytotoxic dose levels.

The agency believes that the results of this study confirm the lack of solubility of NMPABAO at concentrations of 0.73 to 2.92 mg/mL and the moderate solubility of NMPABAO at concentrations of 182.5 and 365 $\mu\text{g/mL}$, thus explaining some of the questions raised by the results of the first DNA repair assay (Ref. 5) discussed above. Furthermore, cytotoxicity was evident in hepatocyte cultures between 11.4 and 365 $\mu\text{g/mL}$ NMPABAO, which suggests that NMPABAO reached the cells at the bottom of the culture dish at these dose levels. NMPABAO and padimate O do not appear to damage DNA, as evaluated by the DNA repair assay, at non-toxic doses when the chemical is soluble in the medium, at cytotoxic doses when the chemical is both soluble and partially soluble in the medium, and at non-cytotoxic doses when the chemical is insoluble in the medium.

The structure-activity relationships in carcinogenesis by N-nitroso compounds have been reviewed (Ref. 9). Some 250 N-nitroso compounds have been studied in rats, and many have been studied in mice and hamsters, to provide reliable carcinogenesis data. The similar carcinogenic actions of certain groups of N-nitroso compounds can be related to their generation of similar simple moieties having certain organs as their target.

Although NMPABAO has not been tested in an animal bioassay for carcinogenesis, certain predictions can be made based on its chemical structure. Most nitrosamines that are carboxylic acids or esters are not carcinogenic, probably due primarily to their being ionized (esters are likely to be hydrolyzed), which prevents their entry into cells; and also possibly because of electronic effects (Ref. 9). For example, N-nitrosopiperidine (which is

structurally related to NMPABAO) produces tumors of the nasal mucosa, esophagus, and liver of the rat. An esterified derivative, α -phenyl-2-piperidinacetic acid methyl ester, tested negative for carcinogenesis in the rat. Based on this correlation, esterification of a carcinogenic nitrosamine greatly reduces or eliminates the carcinogenic potential of the compound. Chemically, NMPABAO is an ester of a carboxylic acid and, based on its chemical structure, would not be predicted to be carcinogenic in an animal bioassay.

2. Analytical Methods

The agency informed industry trade associations of this potential problem and a need for immediate examination in letters dated July 25, 1989, to the CTFA (Ref. 10) and the NDMA (Ref. 11). In those letters, the agency stated that it intended to reopen the administrative record for OTC sunscreen drug products for the submission of information and data regarding (1) the presence of nitrosamine contaminants in padimate O and other sunscreen ingredients with a related chemical structure and (2) the effect such contaminants may have on the safety of these ingredients. After those letters were issued, it became apparent that this problem was more complex than originally thought and that it could not be resolved immediately. Because industry and the agency began addressing this problem quickly, the agency determined that it was not necessary to reopen the administrative record for the rulemaking for OTC sunscreen drug products prior to the publication of this tentative final monograph.

After these letters were sent to CTFA and NDMA, a comment was submitted to the agency (Ref. 12) asserting that the FDA assay method for nitrosamines is inappropriate for sunscreen-containing drug products. The comment stated that this method actually creates conditions for artifact nitrosation to occur during the sample preparation phase. The comment submitted a proposed alternative assay method for determining trace levels of NMPABAO in commercial sunscreens. The comment asserted that the design of its method overcomes potential artifact nitrosation. The assay method proposed by the comment utilizes a HPLC/Thermal Energy Analyzer. The comment maintained that its method avoids the technical pitfalls of the FDA method (1) by using hexane in place of dichloromethane as the extracting solvent and (2) by not using extraneous quenching agents, such as ammonium sulfamate. Stating that its method is simple, direct, and does not involve

"foreign" reagents, the comment added that the method demonstrates excellent recovery of NMPABAO from spiked samples. The comment added that, in limited trials, recovery of NMPABAO from spiked samples has been demonstrated to be up to 90 percent depending upon the complexity of the sample being assayed. The comment maintained that, conversely, one sample assayed by the FDA method showed approximately 1,500 ppb of NMPABAO. However, the same sample showed less than 20 ppb (lowest detectable limit) of NMPABAO when assayed by the comment's proposed HPLC/Thermal Energy Analyzer method. The comment maintained that this discrepancy is further evidence that the FDA method generates artifact nitrosamines.

The agency recently received new data (Ref. 13) purporting to verify the validity of the alternative assay method proposed by the comment (Ref. 12). A series of experiments were undertaken by two independent laboratories. These experiments included studies to establish the linearity of the HPLC-Thermal Energy Analyzer detector response, to measure the original background levels of NMPABAO in the lotion, to determine the recovery and reproducibility of NMPABAO from spiked lotion, and to ascertain if the method itself promotes artifactual formation of NMPABAO. Both laboratories used the same SPF 15 sunscreen lotion containing 8 percent padimate O and the same batch of purified NMPABAO. The results obtained by both laboratories agree well and demonstrate that the proposed alternative method can be performed by analysts in different laboratories to yield reproducible and accurate determinations of NMPABAO in commercial sunscreen drug products. The data demonstrate that the method is applicable to all vehicle systems evaluated thus far, including lotions, creams, gels, and oils. The results show a minimum detectable limit of approximately 30 ppb by this procedure, NMPABAO recovery of greater than 80 percent, and high reproducibility. The results demonstrate that the procedure does not generate NMPABAO artificially during the sample preparation.

The proposed alternative assay method was used by one of the laboratories to evaluate 22 randomly selected commercial sunscreen drug products for NMPABAO levels. Four of these sunscreen drug products contained NMPABAO at levels higher than 100 ppb. The highest level of NMPABAO detected was 216 ppb.

The submission concluded that these studies, as well as the biological studies submitted to the agency (Ref. 5), indicate that the presence of NMPABAO in sunscreen drug products containing padimate O is not a public health concern. The submission contended that, when analyzed using a scientifically validated method, commercial sunscreen drug products appear to have insignificant levels of NMPABAO. The submission concluded that the results of these tests support the long history of padimate O as a safe and effective sunscreen ingredient.

The agency recently reevaluated its method for the identification and determination of NMPABAO (Ref. 14). Its reevaluation included recovery studies for NMPABAO from representative sunscreen drug products, as well as studies of possible chromatographic interference with NMPABAO and of the nitrosation potential of the test reagents. The tests also investigated, by use of inhibitors and a secondary amine marker, the occurrence of artifact nitrosation. The basic method used for detecting nitrosation potential of the sample preparation system involved the addition of a readily-nitrosatable secondary amine (marker) to the product prior to analysis. Detection of the nitrosated marker would suggest that one or more components of the system had the potential for causing artifact nitrosation during sample preparation.

The agency found that the solvents and reagents used in its procedure for assaying NMPABAO contained no compounds that would interfere with the HPLC/Thermal Energy Analyzer determination of NMPABAO. The studies also demonstrated that the presence of nitromusk fragrances in sunscreen drug products would not interfere with the HPLC/Thermal Energy Analyzer determination of NMPABAO. The evaluation of Celite for nitrosation potential demonstrated that some batches contained a nitrosating agent. Therefore, to avoid artifact nitrosation resulting from Celite used in this method, each batch of Celite must be tested for nitrosating potential before use. Results of these studies also showed that ammonium sulfamate, mixed tocopherols, ascorbyl palmitate, squalene, Volpo 5, and ammonium sulfamate mixed with Volpo 5 are not effective as nitrosation inhibitors in sunscreen matrices.

The agency method was corroborated by recovery studies in which a known quantity of NMPABAO and a known quantity of padimate O were added to a nitrosating agent-free sunscreen drug

product that did not contain padimate O. The results of the recovery studies indicate that this analytical method adequately recovers NMPABAO from sunscreen matrices.

In June 1990, the agency agreed to participate in a joint laboratory study to compare the recovery efficiency of its analytical method for NMPABAO and the proposed alternative method developed by a manufacturer of sunscreen drug products (Ref. 15). The agency recommended that the manufacturer prepare the samples for the study and submit them to FDA as "blind" samples. The manufacturer submitted to FDA four 50 gram (g) samples, in duplicate, fortified with NMPABAO at different levels. The manufacturer also provided duplicate 100 g blank lotions containing padimate O with no added NMPABAO for blank and artifact determinations, and a reference NMPABAO standard in isooctane. The manufacturer disclosed to FDA the NMPABAO fortification levels after the analyses were completed. The FDA method utilized a column chromatographic extraction of a sample-Celite mixture with organic solvents, concentration of the resulting eluate, and determination of NMPABAO by HPLC coupled to a Thermal Energy Analyzer (Ref. 16). The proposed alternative method involved partition of a sample with organic solvent, concentration of the extract, reconstitution in an organic solvent, centrifugation, and analysis by HPLC coupled to a Thermal Energy Analyzer (Ref. 13). Both methods utilized a nitrosation inhibitor to prevent artifactual formation of NMPABAO during sample analysis. The agency analyzed the test samples using both its and the proposed alternative methods. The manufacturer analyzed the samples by the proposed alternative method. The agency made two modifications to the proposed alternative method before analyzing samples: (1) A valve between the HPLC and the Thermal Energy Analyzer, specified in the proposed alternative method to divert the HPLC mobile phase from the Thermal Energy Analyzer, was omitted because it was not available in the FDA laboratory, and (2) a single HPLC column was used instead of the prescribed two-column system, because satisfactory separation of the components of interest could be obtained with one column.

Using its methodology for NMPABAO detection, the agency performed duplicate analyses of each sample and obtained good agreement between analyses of the same samples. The recovery of added NMPABAO using the FDA method ranged from 39 to 83

percent, with an overall average of 58 percent. The same samples were analyzed using the modified proposed alternative method. Recovery of added NMPABAO ranged from 56 to 93 percent, with an overall average of 77 percent. Using its own method, the manufacturer reported recoveries ranging from 79 to 100 percent, with an overall average of 86 percent. The agency concludes that NMPABAO was more efficiently recovered from the sunscreen matrix by the proposed alternative method than by the FDA method. Data obtained by the proposed alternative method in both laboratories were in good agreement throughout the entire NMPABAO fortification range.

The agency has determined that partial losses of NMPABAO by the FDA method occurred by premature elution of the N-nitrosamine during the petroleum ether wash of the silica gel column. Similar losses previously observed using the FDA method were found to be caused by inactivation of the silica gel by samples containing significant water levels. The FDA method was modified to improve recovery efficiency of NMPABAO from samples containing substantial amounts of water. Reanalysis of the sunscreen samples by the modified FDA method resulted in recoveries of NMPABAO ranging from 78 to 88 percent, with an average of 83 percent.

The agency concludes that the proposed alternative method, as modified by FDA, and the FDA method, modified to accommodate matrices with high levels of water, result in comparable recoveries of NMPABAO from a sunscreen drug product. Although the proposed alternative method provides the most accurate recoveries of NMPABAO, either method can successfully detect NMPABAO in sunscreen drug products without artifact formation.

3. Photostability Data

One comment submitted data (Ref. 13) that included the results of photostability studies of NMPABAO. The results show that NMPABAO, even in films containing UV absorbers, is extremely unstable when exposed to UV light. When added to sunscreen lotions of both low (SPF 4) and high (SPF 25) photoprotection levels, NMPABAO decomposed rapidly. After exposure to radiation for 1 minute, approximately 50 percent of the NMPABAO in the SPF 25 product and 80 percent of the NMPABAO in the SPF 4 product were degraded. After exposure for 4 minutes, the extent of NMPABAO decomposition was 91 percent for the SPF 25 product and 97 percent for the SPF 4 product.

The agency also conducted a study designed to investigate the photodecomposition of NMPABAO in a model system and in a commercial sunscreen drug product with an SPF of 15 (Ref. 17). The model system consisted of dimethyl silicone as the carrier base, approximately 3,000 ppb NMPABAO, and either 0 or 4 percent padimate O. The commercial sunscreen drug product contained padimate O and approximately 14,000 ppb NMPABAO. Samples of the model system and the sunscreen product were exposed to UV radiation from a high intensity solar simulator for periods of up to 60 minutes, with 1 minute of exposure being approximately equivalent to 0.2 MED. The samples were spread on glass plates as films of approximately 20 micrometer (μm) for the model system and approximately 150 μm for the commercial product. NMPABAO concentrations were determined by HPLC separation and Thermal Energy Analyzer detection before and after UV radiation exposure. NMPABAO in the model system was totally decomposed following exposure of 1 minute (i.e., radiation equivalent to approximately 0.2 MED) even in the presence of 4 percent padimate O. The decomposition of the NMPABAO in the commercial sample was found to follow first order reaction kinetics; the half-life was 2.6 minutes, i.e., approximately 0.5 MED. The results of this study indicate that NMPABAO decomposes upon exposure to UV radiation and corroborate the photodegradation results submitted to the agency (Ref. 13).

4. Conclusions

Two analytical methods with which NMPABAO contamination of OTC sunscreen drug products can be accurately determined are available: (1) The agency's method (Refs. 1 and 14), and (2) the method submitted by one of the comments (Ref. 12). Either method can successfully detect NMPABAO in OTC sunscreen drug products.

Regarding the safety concerns associated with the presence of NMPABAO in padimate O-containing sunscreen drug products, the agency notes that the toxicological data available to the agency at this time indicate that NMPABAO does not have mutagenic or carcinogenic potential. Although the agency does not contemplate additional toxicological testing at this time, it cannot be stated with certainty that NMPABAO is not carcinogenic. This can only be resolved by a carcinogenic bioassay. The agency is not planning any such studies nor is it aware of any such studies currently in progress. However, the agency believes

that the risk associated with NMPABAO contamination of sunscreen drug products is very low. For example, in addition to low mutagenicity and carcinogenicity potential, photostability studies done with NMPABAO demonstrate that the nitrosamine decomposes rapidly when exposed to UV radiation (Refs. 13 and 17).

The agency believes that padimate O, if formulated in a sunscreen drug product properly, is a safe and effective sunscreen ingredient. The presence of NMPABAO in padimate O-containing sunscreen drug products is the result of poor manufacturing practices, and demonstrates that the product has not been formulated properly. For example, the agency recently analyzed 25 commercially available sunscreens for NMPABAO (Ref. 18). NMPABAO was found in 11 samples at levels up to 21,020 ppb. Four of these samples also contained 2-bromo-2-nitro-1,3-propanediol, an indirect nitrosating agent. If these products were formulated without the nitrosating agent, there would be no nitrosamine contamination.

According to § 330.1(a), OTC sunscreen drug products must be manufactured in compliance with current good manufacturing practices, as established in 21 CFR Parts 210 and 211. The agency believes that the presence of NMPABAO in sunscreen drug products indicates that the product has not been manufactured under current good manufacturing practices, and therefore, the product is adulterated under section 501(a) of the act (21 U.S.C. 351(a)). The agency is considering establishing limits for the amount of NMPABAO that may be present in a sunscreen drug product. If these limits were surpassed, the product would be considered to be adulterated. Although not proposed in this tentative final monograph, the agency is including for comment a proposal that OTC sunscreen drug products must contain less than 500 ppb of NMPABAO.

As stated above, the agency believes that padimate O is a safe and effective OTC sunscreen ingredient. Therefore, in this tentative final monograph, padimate O remains in Category I.

References

- (1) Chou, H. J., R. L. Yates, and J. A. Wenninger, "2-Ethylhexyl 4-(N-methyl-N-nitrosoamino) Benzoate in Commercial Sunscreen Preparations," Comment No. REF001, Docket No. 78N-0038, Dockets Management Branch.
- (2) "Report on Testing of RH-III-30112-5-8 in the Ames Assay," OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(3) "Summary of Mutagenicity Data for NPABAO," draft of an unpublished study, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(4) "Mouse Lymphoma Assay (L5178Y TK +/-)," draft of an unpublished study, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(5) Letter from D. Hoffman, America Health Foundation, to J. A. Wenninger, FDA, dated June 13, 1989, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(6) "Evaluation of 4-(Methylnitro-soamino) benzoic acid-2-ethylhexylester (MNBEHE) [also known as MNPABAO] and Padimate O by Autoradiographic Measurements of Unscheduled DNA Synthesis (UDS) in the Rat Hepatocyte Primary Culture/DNA Repair Test," draft of unpublished study, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(7) Butterworth, B. E., et al., "A Protocol and Guide for the In Vitro Rat Hepatocyte DNA/Repair Assay," *Mutation Research*, 189:113-121, 1987.

(8) Swierenga, S. H. H., et al., "Recommended Protocols Based on Survey of Current Practice in Genotoxicity Testing Laboratories: I. Unscheduled DNA Synthesis Assay in Rat Hepatocyte Cultures," *Mutation Research*, 246:235-253, 1991.

(9) Linjinsky, W., "Structure-activity Relations in Carcinogenesis by N-nitroso compounds," *Cancer and Metastasis Reviews*, 6:301-356, 1987.

(10) Letter from W. E. Gilbertson, FDA, to E. Kavanaugh, The Cosmetic, Toiletory and Fragrance Association, dated July 25, 1989, coded LET030 in Docket No. 78N-0038, Dockets Management Branch.

(11) Letter from W. E. Gilbertson, FDA, to J. Cope, Nonprescription Drug Manufacturers Association, dated July 25, 1989, coded LET029 in Docket No. 78N-0038, Dockets Management Branch.

(12) Letter from J. M. Clayton, Schering-Plough Corporation, to J. A. Wenninger, FDA, dated July 10, 1989, coded C100 in Docket No. 78N-0038, Dockets Management Branch.

(13) Letter from E. E. Kavanaugh, The Cosmetic, Toiletory and Fragrance Association, to W. E. Gilbertson, FDA, dated April 30, 1990, coded RPT4 in Docket No. 78N-0038, Dockets Management Branch.

(14) "Evaluation of the FDA Method for Determination of 2-Ethylhexyl-P-(N-Nitroso-N-Methylamino) Benzoate in Commercial Sunscreen Products," coded RPT3 in Docket No. 78N-0038, Dockets Management Branch.

(15) Letter from J. A. Wenninger, FDA, to J. M. Clayton, Schering-Plough Corporation, dated June 1, 1990, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(16) "Comparative Study of FDA's and Schering-Plough's Analytical Methods for the Determination of NMPABAO in Sunscreen Products," draft of unpublished study, OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

(17) "Study of the Photodecomposition of N-Nitroso-N-Methyl-p-Aminobenzoic Acid Octyl Ester on Exposure to Ultraviolet Light," coded RPT3 in Docket No. 78N-0038, Dockets Management Branch.

(18) "Technical Plan Project Quarterly Report," draft of unpublished study, OTC

Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.

B. Sunless Tanning/Tanning Accelerator Products

The agency is aware of several sunless tanning/tanning accelerator products that are available commercially (Ref. 1). These products include various ingredients that are purported to either: (1) Give the user the appearance of a tan by coloring the skin, or (2) accelerate the actual tanning process.

In the first case, the tanning effect is accomplished either by an externally applied dye such as dihydroxyacetone or by orally ingested carotenoid dyes (tanning pills) such as canthaxanthin. Products containing dihydroxyacetone rely upon a Schiff Base formation between dihydroxyacetone (or its glyceraldehyde tautomer) and amino or imino moieties associated with the keratin of the stratum corneum. These Schiff Bases then undergo condensation-polymerization reactions to yield dark-colored melanoidins (Ref. 2). Dihydroxyacetone is approved for use in externally applied drugs and cosmetics to impart color to the human body. (See 21 CFR 73.1150 and 73.2150.) Dihydroxyacetone may also be combined with lawsone as a Category I sunscreen ingredient in this tentative final monograph.

The Panel concluded that lawsone in conjunction with dihydroxyacetone is safe and effective for OTC use as a sunscreen. The Panel reviewed a marketed product composed of two lotions packaged together and labeled to be applied separately and in sequence. The Panel recommended that when the two ingredients are used separately and sequentially, the combination can be classified as Category I (43 FR 38206 at 38235). Each ingredient when used alone cannot be classified as a Category I sunscreen. The submitted data indicated that the two-solution product provides sunscreen protection which varies considerably among individuals, depending on such factors as susceptibility of the skin to fixing of the active ingredients, thickness of the keratin layer where the sunscreen resides, number of daily applications, degree of individual photosensitivity, and amount of UV radiation received (43 FR 38235). The Panel recommended Category I labeling for sunscreen active ingredients and the following warnings: (i) "This is a two lotion product. Do not mix the contents of the two solutions. Use both solutions, for use of one alone will not provide protection." (ii) "Use only on skin free of rash and abrasions." (iii) "May stain clothing when freshly applied."

Canthaxanthin, which has been used in tanning pills, enters the blood stream after ingestion and is partially deposited in skin tissue, giving the skin a tan-like color. Although this compound is approved for use at very low levels as a color additive in some foods and drugs (see 21 CFR 73.75 and 73.1075), it is not approved at any level for use in tanning pills to impart color to the human body. Tanning pills containing canthaxanthin or any other carotenoid additives are considered adulterated cosmetics and, consequently, may not be legally marketed. See, e.g., *U.S. v. Eight Unlabeled Cases of an Article of Cosmetic*, 888 F.2d 945 (2nd Cir. 1989). Some reports of adverse reactions associated with "tanning pills" have mentioned aplastic anemia, allergic reactions, stomach cramps, hepatitis, nausea, diarrhea, and deposition of the color in the retina of the eye (Refs. 3, 4, and 5).

In the case of acceleration, the tanning process is supposedly hastened by stimulating the production of melanin by ingredients such as tyrosine or tyrosine derivatives. These derivatives supposedly increase the substrate available for tyrosinase enzyme action. Tyrosinase is a key enzyme in melanogenesis (Ref. 6). The use of tyrosine is based upon the presumption that it penetrates the skin, increases the tyrosine content of the melanocytes, and thus enhances melanin formation. This effect has not been convincingly substantiated in the scientific literature. The agency notes that any product purporting to "accelerate the tanning process" or "stimulate the production of melanin" is claiming to affect the structure and function of the body and, therefore, is a drug. The agency is not aware of any data demonstrating that tyrosine or its derivatives are effective in stimulating the production of melanin. Thus, any product containing tyrosine or its derivatives and claiming to accelerate the tanning process is an unapproved new drug.

The agency is concerned about the health hazards associated with using products labeled for tanning purposes that do not contain sunscreen ingredients. The agency tentatively finds that the majority of consumers expect sunburn protection from suntanning products, whether the product contains a sunscreen ingredient or not. Because of the serious consequences of overexposure to the sun, the agency considers it important for consumers to know whether a suntanning product, including sunless tanning products, contains a sunscreen ingredient or not. Therefore, in conjunction with this tentative final

monograph, the agency is proposing to amend the cosmetic regulations in 21 CFR part 700 by adding § 740.19 as follows: "Suntanning preparations. The labeling of suntanning preparations that do not contain a sunscreen ingredient must display the following warning: 'Warning—This product does not contain a sunscreen and does not protect against sunburn.'" This warning also applies to sunless tanning lotions.

References

- (1) Memorandum from S. Milstein to J.E. Bailey, dated June 25, 1991, in OTC Vol. 06ATFM, Dockets Management Branch.
- (2) "Artificial Suntan Preparations" in "Harry's Cosmetology" in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (3) Fenner, L. "The Tanning Pill, a Questionable Inside Dye Job," in OTC Vol. 06ATFM, Docket No. 78N-0038, Dockets Management Branch.
- (4) Rousseau, A., et al., "Canthaxanthine Deposits in the Eye; *Journal of the American Academy of Dermatology*, 8:123-124, 1983.
- (5) Bluhm, R., et al., "Aplastic Anemia Associated with Canthaxanthin Ingested for Tanning Purposes," *Journal of the American Medical Association*, 264:1141-1142, 1990.
- (6) Duggan, M., J. Wilmott, and A. Znaiden, Tyrosinase * * * The Enzyme Behind the Tan," *Cosmetics and Toiletries*, 102:97-101, 1987.

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 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). Therefore, this sunscreen proposed rule, which applies only to a single drug category, does not require a regulatory impact analysis or a regulatory flexibility analysis.

The agency recognizes, however, that some products currently marketed by manufacturers as cosmetics would be affected by this rulemaking, e.g., suntanning products, and daily use make-up preparations and skin lotions that contain sunscreens or make drug claims. The presence of a sunscreen ingredient in such products and labeling that includes a drug claim would cause

these products to be drugs under the act. While all affected firms are currently subject to general regulatory requirements under the act, some companies would be subject, for the first time, to current good manufacturing practices (CGMP) for drugs, as established in 21 CFR Parts 210 and 211. The agency has limited data but believes that most major manufacturers of sunscreen-containing products already follow these procedures and are familiar with agency regulations for manufacturing drug products. In addition, some states, including California and New York, regulate cosmetic products as drugs and conduct on-site inspections of manufacturing facilities.

Nonetheless, some clear differences exist between cosmetic and drug regulations. For example, current agency regulations allow for the voluntary registration of cosmetic manufacturers, while registration is compulsory for drug manufacturers. The agency attempts to inspect each drug manufacturer every two years, whereas cosmetic inspections are done less frequently. Therefore, many current cosmetic plants can expect more frequent inspection as drug manufacturers.

The agency has attempted to define the possible economic consequences of this proposal but has been hindered by the paucity of data concerning the manufacture of these products. The industry segment that currently manufactures sunscreen-containing lipsticks, skin lotions, and make-up preparations that would be covered by this regulation would need either to: (1) Reformulate and/or relabel these products to eliminate sunscreen ingredients and omit drug claims, or (2) comply with drug regulations if they do not already do so. The agency will continue to gather economic information and solicit industry comment on the extent of any additional costs of compliance, or other regulatory burdens, that would be associated with this proposed rule.

In addition, the agency specifically invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC sunscreen drug products or on manufacturers who elect to reformulate or relabel their product(s) so that the products' status would continue to be cosmetics. Types of impact may include, but are not limited to, costs associated with product testing, relabeling, repackaging, reformulating, or costs related to conversion to drug manufacturing capabilities to meet CGMPs. Comments regarding the 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 sunscreen drug products, a period of 180 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 under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Interested persons may, on or before November 8, 1993, submit to the Dockets Management Branch 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. Written comments on the agency's economic impact determination may be submitted on or before November 8, 1993. 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 May 12, 1994, 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 July 12, 1994. 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. 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 July 12, 1994. 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.

List of Subjects in 21 CFR

Part 352

Labeling, Over-the-counter drugs, Sunscreen drug products.

Part 700

Cosmetics, Packaging and containers.

Part 740

Cosmetic product warning statements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR Chapter I be amended as follows:

1. Part 352 is added to read as follows:

PART 352—SUNSCREEN DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.

352.1 Scope.

352.3 Definitions.

Subpart B—Active Ingredients

352.10 Sunscreen active ingredients.

352.20 Permitted combinations of active ingredients.

Subpart C—Labeling

352.50 Principal display panel of all sunscreen drug products.

352.52 Labeling of sunscreen drug products.

352.60 Labeling of permitted combinations of active ingredients.

Subpart D—Testing Procedures

352.70 Standard sunscreen.

352.71 Light source (solar simulator).

352.72 General testing procedures.

352.73 Determination of SPF value.

352.76 Determination if a product is water resistant or very water resistant.

352.77 Test Modifications.

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

Subpart A—General Provisions

§ 352.1 Scope.

(a) An over-the-counter sunscreen drug product in a form suitable for topical 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 of this chapter.

(b) References in this part to regulatory sections of the Code of Federal Regulations are to Chapter I of Title 21 unless otherwise noted.

§ 352.3 Definitions.

As used in this part: (a) *Minimal erythema dose (MED)*. The smallest dose of ultraviolet (UV) radiation (expressed as Joules per meter squared) that produces redness reaching the borders of the exposure site.

(b) *Product category designation (PCD)*. A labeling designation for sunscreen drug products to aid in selecting the type of product best suited to an individual's complexion (pigmentation) and desired response to UV radiation.

(1) *Minimal sun protection product*. A sunscreen product that provides a sun protection factor (SPF) value of 2 to under 4, and offers the least protection, but permits suntanning.

(2) *Moderate sun protection product*. A sunscreen product that provides an SPF value of 4 to under 8, and offers moderate protection from sunburning, but permits some suntanning.

(3) *High sun protection product*. A sunscreen product that provides an SPF value of 8 to under 12, offers high protection from sunburning, and permits limited suntanning.

(4) *Very high sun protection product*. A sunscreen product that provides an SPF value of 12 to under 20, offers very high protection from sunburning, and permits little or no suntanning.

(5) *Ultra high sun protection product*. A sunscreen product that provides an SPF value of 20 to 30, offers the most protection from sunburning, and permits no suntanning.

(c) *Sunscreen active ingredient*. An active ingredient that absorbs at least 85 percent of the radiation in the UV range at wavelengths from 290 to 320 nanometers, but may or may not transmit radiation at wavelengths longer than 320 nanometers.

(d) *Sunscreen opaque sunblock*. An opaque sunscreen active ingredient that reflects or scatters all light in the UV and visible range at wavelengths from 290 to 777 nanometers and thereby prevents or minimizes suntan and sunburn.

(e) *Sun protection factor (SPF) value*. The UV energy required to produce an MED on protected skin divided by the UV energy required to produce an MED on unprotected skin, which may also be defined by the following ratio: $SPF \text{ value} = MED (\text{protected skin (PS)}) / MED (\text{unprotected skin (US)})$, where MED (PS) is the minimal erythema dose for protected skin after application of 2 milligrams per square centimeter of the final formulation of the sunscreen product, and MED (US) is the minimal erythema dose for unprotected skin, i.e., skin to which no sunscreen product has been applied. In effect, the SPF value is the reciprocal of the effective transmission of the product viewed as a UV radiation filter.

Subpart B—Active Ingredients

§ 352.10 Sunscreen active ingredients.

The active ingredient of the product consists of any of the following when used in the concentration established for each ingredient, and the finished product provides a minimum sun protection factor value of not less than 2 as measured by the testing procedures established in subpart D of this part:

- (a) Aminobenzoic acid up to 15 percent.
- (b) Cinoxate up to 3 percent.
- (c) Diethanolamine methoxycinnamate up to 10 percent.
- (d) Digalloyl trioleate up to 5 percent.
- (e) Dioxibenzene up to 3 percent.
- (f) Ethyl 4-[bis(hydroxypropyl)]aminobenzoate up to 5 percent.
- (g) Glyceryl aminobenzoate up to 3 percent.
- (h) Homosalate up to 15 percent.
- (i) Lawsone up to 0.25 percent with dihydroxyacetone up to 3 percent.
- (j) Menthyl anthranilate up to 5 percent.
- (k) Octocrylene up to 10 percent.
- (l) Octyl methoxycinnamate up to 7.5 percent.
- (m) Octyl salicylate up to 5 percent.
- (n) Oxybenzone up to 6 percent.
- (o) Padimate O up to 8 percent.
- (p) Phenylbenzimidazole sulfonic acid up to 4 percent.
- (q) Red petrolatum up to 100 percent.
- (r) Sulisobenzene up to 10 percent.
- (s) Titanium dioxide up to 25 percent.
- (t) Trolamine salicylate up to 12 percent.

§ 352.20 Permitted combinations of active ingredients.

(a) *Combinations of sunscreen active ingredients*.

(1) Two or more sunscreen active ingredients identified in § 352.10 may be combined when used in the concentrations established for each

ingredient in paragraph (a)(2) of this section and the finished product has a minimum sun protection factor value of not less than 2 as measured by the testing procedures established in subpart D of this part.

(2) Sunscreen active ingredients shall be used within the following concentrations when used in combination with another sunscreen or when the combination is used with any other permitted active ingredient:

- (i) Aminobenzoic acid 5 to 15 percent.
- (ii) Cinoxate 1 to 3 percent.
- (iii) Diethanolamine methoxycinnamate 8 to 10 percent.
- (iv) Digalloyl trioleate 2 to 5 percent.
- (v) Dioxybenzone 3 percent.
- (vi) Ethyl 4-[bis(hydroxypropyl)]aminobenzoate 1 to 5 percent.
- (vii) Glyceryl aminobenzoate 2 to 3 percent.
- (viii) Homosalate 4 to 15 percent.
- (ix) Lawsone 0.25 percent with dihydroxyacetone 3 percent.
- (x) Menthyl anthranilate 3.5 to 5 percent.
- (xi) Octocrylene 7 to 10 percent.
- (xii) Octyl methoxycinnamate 2.0 to 7.5 percent.
- (xiii) Octyl salicylate 3 to 5 percent.
- (xiv) Oxybenzone 2 to 6 percent.
- (xv) Padimate 0.14 to 8 percent.
- (xvi) Phenylbenzimidazole sulfonic acid 1 to 4 percent.
- (xvii) Red petrolatum 30 to 100 percent.
- (xviii) Sulisobenzene 5 to 10 percent.
- (xix) Titanium dioxide 2 to 25 percent.
- (xx) Trolamine salicylate 5 to 12 percent.

(b) *Sunscreen and skin protectant combinations.*

(1) Any single sunscreen active ingredient when used in the concentration established in § 352.10 may be combined with one or more skin protectant active ingredients identified in § 347.10(a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in Subpart D of this part and provided the product is labeled according to § 352.60.

(2) Two or more sunscreen active ingredients when used in the concentrations established in § 352.20(a)(2) may be combined with one or more skin protectant active ingredients identified in § 347.10(a), (d), (e), (f), (h), (i), and (j) of this chapter, provided the finished product has a minimum SPF value of not less than 2 as measured by the testing procedures established in subpart D of this part and provided the product is labeled according to § 352.60.

(c) *For sunscreen and skin bleaching combinations.* See § 358.50 of this chapter.

Subpart C—Labeling

§ 352.50 Principal display panel of all sunscreen drug products.

In addition to the statement of identity required in § 352.52, the following labeling statements shall be prominently placed on the principal display panel:

(a) *For products that do not satisfy the water resistant or very water resistant sunscreen product testing procedures in § 352.76.* "SPF (insert tested SPF value of the product up to 30)."

(b) *For products that satisfy the water resistant sunscreen product testing procedures in § 352.76.*

- (1) "Water Resistant."
- (2) "SPF=(insert SPF value before water resistant testing) before" (select one of the following: "sweating" or "perspiring") "or going into the water. SPF=(insert SPF value resulting from water resistant testing) after 40 minutes of" (select one of the following: "sweating" or "perspiring") "or activity in the water."

(c) *For products that satisfy the very water resistant sunscreen product testing procedures in § 352.76.*

- (1) "Very Water Resistant."
- (2) "SPF=(insert SPF value before very water resistant testing) before" (select one of the following: "sweating" or "perspiring") "or going into the water. SPF=(insert SPF value resulting from very water resistant testing) after 80 minutes of" (select one of the following: "sweating" or "perspiring") "or activity in the water."

§ 352.52 Labeling of sunscreen 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 "sunscreen."

(b) *Indications.* The labeling of the product states, under the heading "Indications" any of the phrases listed in paragraph (b) of this section, as appropriate. Other truthful and nonmisleading statements, describing only the indications for use that have been established and listed in this paragraph, may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *For products containing any ingredient identified in § 352.10—*(i) "Sunscreen to help prevent sunburn."

(ii) (Select one of the following: "Filters" or "Screens") "out the sun's" (select one of the following: "burning" or "harsh and often harmful") "rays to prevent sunburn."

(iii) "Allows you to stay in the sun up to (insert SPF of product up to 30) times longer than without sunscreen protection."

(iv) "Provides up to (insert SPF of product up to 30) times your natural protection from sunburn."

(v) (Select one of the following: "Filters" or "Screens") "out the" (select one of the following: "sun's rays," "sun's harsh rays," or "sun's harmful rays") "to help prevent" (select one or more of the following: "lip damage," "skin damage," "freckling," or "uneven coloration").

(vi) (Select one of the following: "Protects from" or "Shields from") (select one of the following: "the harmful rays of the sun" or "the sun") "to help prevent" (select one or more of the following: "lip damage," "skin damage," "freckling," or "uneven coloration").

(2) *Additional indications.* In addition to the indications provided above in § 352.52(b)(1), the following may be used:

(i) *For products containing any ingredient in § 352.10 that provide an SPF of 2 to under 4, any of the following labeling statements may be used—*(A) (Select one of the following: "Provides minimal," "Provides minimum," "Minimal," or "Minimum") "protection against sunburn."

(B) "Prolongs exposure time before sunburn occurs."

(C) "Permits" (select one of the following: "tanning" or "suntanning") "and" (select one of the following: "reduces chance of" or "minimizes") "sunburning."

(D) "Helps prevent sunburn on limited exposure of untanned skin."

(E) "Helps to protect the skin against sunburn while permitting tanning."

(ii) *For products containing any ingredient in § 352.10 that provide an SPF of 4 to under 8, any of the following labeling statements may be used—*(A) (Select one of the following: "Provides moderate" or "Moderate") "protection against sunburn."

(B) "Prolongs exposure time before sunburn occurs."

(C) "Permits" (select one of the following: "tanning" or "suntanning") "and" (select one of the following: "reduces chance of" or "minimizes") "sunburning."

(D) "Helps prevent sunburn on moderate exposure of untanned skin."

(iii) *For products containing any ingredient in § 352.10 that provide an SPF of 8 to under 12, any of the following labeling statements may be used—*(A) (Select one of the following: "Provides high" or "High") "protection against sunburn."

(B) "Prolongs exposure time before sunburn occurs."

(C) "Permits" (select one of the following: "tanning" or "suntanning") "and" (select one of the following: "reduces chance of" or "minimizes") "sunburning."

(D) "Helps prevent sunburn."

(E) "For sun-sensitive skin."

(F) "High protection against sunburn for blondes, redheads, and fair-skinned persons."

(iv) *For products containing any ingredient in § 352.10 that provide an SPF of 12 to under 20, any of the following labeling statements may be used—*(A) (Select one of the following: "Provides very high" or "Very high") "protection against sunburn."

(B) "Prevents sunburn and limits tanning."

(C) "For sun-sensitive skin."

(D) "Very high protection against sunburn for blondes, redheads, and fair-skinned persons."

(v) *For products containing any ingredient in § 352.10 that provide an SPF of 20 to 30, any of the following labeling statements may be used—*(A) (Select one of the following: "Provides the most" or "The most") "protection against sunburn."

(B) "Prevents tanning and sunburn."

(C) "For highly sun-sensitive skin."

(D) "The most protection against sunburn for blondes, redheads, and fair-skinned persons."

(E) "Provides the highest degree of" (select one of the following: "sunburn" or "sunscreen") "protection and permits no tanning."

(3) *For products containing the active ingredient identified in § 352.10(s) that provide an SPF of 12 to 30, the following labeling statement may be used.*

"Reflects the burning rays of the sun."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings:"

(1) *For products containing any ingredient in § 352.10—*(i) "For external use only, not to be swallowed."

(ii) "Avoid contact with the eyes. If contact occurs, rinse eyes thoroughly with water."

(iii) "Discontinue use if signs of irritation or rash appear. If irritation or rash persists, consult a doctor."

(2) *For products containing the ingredient identified in § 352.10(i)—*(i)

"This product consists of two solutions. Do not mix the contents of the two solutions. Use both solutions; one alone will not provide protection."

(ii) "Use only on skin free of rash and abrasions."

(iii) "May stain clothing when freshly applied."

(3) *For products containing any ingredient identified in § 352.10 formulated as a lip balm or lipstick.* The warning in paragraph (c)(1)(i) of this section is not required.

(4) *For products containing any ingredient identified in § 352.10 formulated as a lipstick.* The warning in paragraph (c)(1)(ii) of this section is not required.

(d) *Directions.* The labeling of the product contains the following information under the heading "Directions." More detailed directions applicable to a particular product formulation (e.g., cream, gel, lotion, oil, spray, etc.) may also be included.

(1) *For products containing any ingredient in § 352.10 that do not satisfy the water resistant or very water resistant testing procedures in § 352.76.*

"Adults and children 6 months of age and over: Apply" (select one or more of the following, as applicable: "liberally," "generously," "smoothly," or "evenly") "before sun exposure. Reapply after swimming, excessive" (select one of the following: "sweating," or "perspiring,") "or anytime after towel drying. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

(2) *For products containing any ingredient in § 352.10 that satisfy the water resistant or very water resistant testing procedures in § 352.76.* "Adults and children 6 months of age and over: Apply" (select one or more of the following, as applicable: "liberally," "generously," "smoothly," or "evenly")

"(insert appropriate time interval, if a waiting period is needed) before sun or water exposure. Reapply after" [select one of the following: "40 minutes" (if water resistant) or "80 minutes" (if very water resistant)] "of swimming or excessive" (select one of the following: "sweating" or "perspiring") "or anytime after towel drying. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

(3) *For products containing the ingredient identified in § 352.10(i).* Products are composed of two separate formulations. Solution 1 contains 3 percent dihydroxyacetone and Solution 2 contains 0.25 percent lawsone.

"Adults and children 6 months of age

and over: Apply liberally before sun exposure as follows: *First application.* The evening prior to sun exposure: Apply Solution 1. Wait 15 minutes then apply Solution 2 to the same areas of skin. Wait until dried. Then repeat application of solutions alternately as before until a total of three applications of both solutions have been applied. Leave on skin without washing. *Repeated application.* After first day, apply one application of each solution. Reapply after swimming or after excessive" (select one of the following: "sweating" or "perspiring") "or anytime after towel drying. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

(4) *For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52 (b)(1)(v) and/or (b)(1)(vi) and formulated as a make-up preparation or lipstick.* "Apply liberally as often as necessary."

(5) *For products containing any ingredient identified in § 352.10 labeled with only the indications in § 352.52(b)(1)(v) and/or (b)(1)(vi) and formulated as a lip balm or skin preparation.* "Adults and children 6 months of age and over: Apply liberally as often as necessary. Children under 2 years of age should use sunscreen products with a minimum SPF of 4. Children under 6 months of age: consult a doctor."

(e) *Statement on product performance—*(1) *For products containing any ingredient identified in § 352.10, the following PCD labeling claims may be used—*(i) *For products containing active ingredient(s) that provide an SPF value of 2 to under 4.* "Minimal Sun Protection Product."

(ii) *For products containing active ingredient(s) that provide an SPF value of 4 to under 8.* "Moderate Sun Protection Product."

(iii) *For products containing active ingredient(s) that provide an SPF value of 8 to under 12.* "High Sun Protection Product."

(iv) *For products containing active ingredient(s) that provide an SPF value of 12 to under 20.* "Very High Sun Protection Product."

(v) *For products containing active ingredient(s) that provide an SPF value of 20 to 30.* "Ultra High Sun Protection Product."

(2) *For products containing any ingredient in § 352.10 that satisfy the water resistant testing procedures identified in § 352.76, any of the following labeling statements may be used—*(i) "Retains its sun protection for at least 40 minutes in the water."

(ii) "Resists removal by" (select one of the following: "perspiring" or "sweating".)

(iii) (Select one of the following: "Sweat" or "Perspiration") "resistant."

(3) For products containing any ingredient in § 352.10 that satisfy the very water resistant testing procedures identified in § 352.76, any of the following labeling statements may be used—(i) "Retains its sun protection for at least 80 minutes in the water."

(ii) "Resists removal by" (select one of the following: "perspiring" or "sweating".)

(iii) (Select one of the following: "Sweat" or "Perspiration") "resistant."

(4) For products containing any ingredient identified in § 352.10, the following compilation of skin types and SPF's shall be appropriately included in labeling as a guide.

RECOMMENDED SUNSCREEN PRODUCT GUIDE

Sunburn and tanning history	Recommended sun protection product
Always burns easily; rarely tans.	SPF 20 to 30.
Always burns easily; tans minimally.	SPF 12 to under 20.
Burns moderately; tans gradually.	SPF 8 to under 12.
Burns minimally; always tans well.	SPF 4 to under 8.
Rarely burns; tans profusely.	SPF 2 to under 4.

(5) For products containing the active ingredient identified in § 352.10(s) that provide an SPF of 12 to 30, the following labeling statement may be used. "Sunblock."

(6) For products containing any ingredient identified in § 352.10, the following labeling statement shall be used. "SUN ALERT: The sun causes skin damage. Regular use of sunscreens over the years may reduce the chance of skin damage, some types of skin cancer, and other harmful effects due to the sun."

(7) For products containing any ingredient identified in § 352.10. Any variation of the statement in § 352.52(e)(6) that does not relate skin aging or skin cancer as being "due to the sun" will cause the product to be misbranded under section 502 of the Federal Food, Drug, and Cosmetic Act.

(f) The word physician may be substituted for the word doctor in any of the labeling statements in this part.

§ 352.60 Labeling of permitted combinations of active ingredients.

Statement of identity, indications, warnings, and directions for use,

respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) *Statement of identity.* For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs. For a combination drug product that does not have an established name, the labeling of the product states the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs, unless otherwise stated below.

(b) *Indications.* The labeling of the product states under the heading "Indications," the indication(s) for each ingredient in the combination as established in the indications sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph. Other truthful and nonmisleading statements, describing only the indications for use that have been established in the applicable OTC drug monographs or listed in this paragraph, may also be used, as provided by § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act. In addition to the required information identified in this paragraph, the labeling of the product may contain any of the "other allowable statements" that are identified in the applicable monographs, 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 conspicuousness than the required information.

(1) For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). In addition to any or all of the indications for sunscreens in § 352.52(b), the indication for skin protectants in § 347.50(b)(2) of this chapter should be used.

(2) [Reserved]

(c) *Warnings.* The labeling of the product states, under the heading "Warnings," the warning(s) for each

ingredient in the combination, as established in the warnings section of the applicable OTC drug monographs unless otherwise stated in this paragraph.

(1) For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The warning for skin protectants in § 347.50(c)(3) of this chapter is not required.

(2) [Reserved]

(d) *Directions.* The labeling of the product states, under the heading "Directions," directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph. When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not contain any dosage that exceeds those established for any individual ingredient in the applicable OTC drug monograph(s), and may not provide for use by any age group lower than the highest minimum age limit established for any individual ingredient.

(1) For permitted combinations containing a sunscreen and a skin protectant identified in § 352.20(b). The directions for sunscreens in § 352.52(d) should be used.

(2) [Reserved]

Subpart D—Testing Procedures

§ 352.70 Standard sunscreen.

(a) *Laboratory validation.* A standard sunscreen shall be used concomitantly in the testing procedures for determining the sun protection factor value of a sunscreen drug product to ensure the uniform evaluation of sunscreen drug products. The standard sunscreen shall be an 8-percent homosalate preparation with a mean SPF value of 4.47 (standard deviation = 1.279). In order for the SPF determination of a test product to be considered valid, the SPF of the standard sunscreen must fall within the standard deviation range of the expected SPF (i.e., 4.47 ± 1.279) and the 95-percent confidence interval for the mean SPF must contain the value 4.

(b) *Preparation of the standard homosalate sunscreen.* The standard homosalate sunscreen is prepared from two different preparations (preparation A and preparation B) with the following compositions:

COMPOSITION OF PREPARATION A AND PREPARATION B OF THE STANDARD SUNSCREEN

Ingredients	Percent by weight
Preparation A:	
Lanolin	5.00
Homosalate	8.00
White petrolatum	2.50
Stearic acid	4.00
Propylparaben	0.05
Preparation B:	
Methylparaben	0.10
Edetate disodium	0.05
Propylene glycol	5.00
Triethanolamine	1.00
Purified water U.S.P.	74.30

Preparation A and preparation B are heated separately to 77 to 82 °C, with constant stirring, until the contents of each part are solubilized. Add preparation A slowly to preparation B while stirring. Continue stirring until the emulsion formed is cooled to room temperature (15 to 30 °C). Add sufficient purified water to obtain 100 grams of standard sunscreen preparation.

(c) *Assay of the standard homosalate sunscreen.* Assay the standard homosalate sunscreen preparation by the following method to ensure proper concentration:

(1) *Preparation of the assay solvent.* The solvent consists of 1 percent glacial acetic acid (V/V) in denatured ethanol. The denatured ethanol should not contain a UV absorbing denaturant.

(2) *Preparation of a 1-percent solution of the standard homosalate sunscreen preparation.* Accurately weigh 1 gram of the standard homosalate sunscreen preparation into a 100-milliliter volumetric flask. Add 50 milliliters of the assay solvent. Heat on a steam bath and mix well. Cool the solution to room temperature (15 to 30 °C). Then dilute the solution to volume with the assay solvent and mix well to make a 1-percent solution.

(3) *Preparation of the test solution (1:50 dilution of the 1-percent solution).* Filter a portion of the 1-percent solution through number 1 filter paper. Discard the first 10 to 15 milliliters of the filtrate. Collect the next 20 milliliters of the filtrate (second collection). Add 1 milliliter of the second collection of the filtrate to a 50-milliliter volumetric flask. Dilute this solution to volume with assay solvent and mix well. This is the test solution (1:50 dilution of the 1-percent solution).

(4) *Spectrophotometric determination.* The absorbance of the test solution is measured in a suitable double beam spectrophotometer with the assay

solvent and reference beam at a wavelength near 306 nanometers.

(5) *Calculation of the concentration of homosalate.* The concentration of homosalate is determined by the following formula which takes into consideration the absorbance of the sample of the test solution, the dilution of the 1-percent solution (1:50), the weight of the sample of the standard homosalate sunscreen preparation (1 gram), and the standard absorbance value (172) of homosalate as determined by averaging the absorbance of a large number of batches of raw homosalate: Concentration of homosalate = absorbance $\times 50 \times 100 \times 172$ = percent concentration by weight.

§ 352.71 Light source (solar simulator).

A solar simulator used for determining the SPF of a sunscreen drug product should be filtered so that it provides a continuous emission spectrum from 290 to 400 nanometers similar to sunlight at sea level from the sun at a zenith angle of 10°; it has less than 1 percent of its total energy output contributed by nonsolar wavelengths shorter than 290 nanometers; and it has not more than 5 percent of its total energy output contributed by wavelengths longer than 400 nanometers. In addition, a solar simulator should have no significant time-related fluctuations in radiation emissions after an appropriate warm-up time, and it should have good beam uniformity (within 10 percent) in the exposure plane. To ensure that the solar simulator delivers the appropriate spectrum of UV radiation, it must be measured periodically with an accurately-calibrated spectroradiometer system or equivalent instrument.

§ 352.72 General testing procedures.

(a) *Selection of test subjects (male and female).* Only fair-skin volunteers with skin types I, II, and III using the following guidelines shall be selected:

Selection of Fair-skin Subjects

Skin Type and Sunburn and Tanning History (Based on first 30 to 45 minutes sun exposure after a winter season of no sun exposure.)

- I—Always burns easily; never tans (sensitive).
- II—Always burns easily; tans minimally (sensitive).
- III—Burns moderately; tans gradually (light brown) (normal).
- IV—Burns minimally; always tans well (moderate brown) (normal).
- V—Rarely burns; tans profusely (dark brown) (insensitive).
- VI—Never burns; deeply pigmented (insensitive).

A medical history shall be obtained from all volunteers with emphasis on the effects of sunlight on their skin. To be ascertained are the general health of the individual, the individual's skin type (I, II, or III), whether the individual is taking medication (topical or systemic) that is known to produce abnormal sunlight responses, and whether the individual is subject to any abnormal responses to sunlight, such as a phototoxic or photoallergic response.

(b) *Test site inspection.* The physical examination shall determine the presence of sunburn, suntan, scars, active dermal lesions, and uneven skin tones on the areas of the back to be tested. The presence of nevi, blemishes, or moles will be acceptable if in the physician's judgment they will not interfere with the study results. Excess hair on the back is acceptable if the hair is clipped or shaved.

(c) *Informed consent.* Legally effective written informed consent must be obtained from all individuals.

(d) *Test site delineation—(1) Test site area.* A test site area serves as an area for determining the subject's MED after application of either the sunscreen standard or the test sunscreen product, or for determining the subject's MED when the skin is unprotected (control site). The area to be tested shall be the back between the beltline and the shoulder blade (scapulae) and lateral to the midline. Each test site area for applying a product or the standard sunscreen shall be a minimum of 50 square centimeter, e.g., 5 $\times$ 10 centimeter. The test site areas are outlined with ink. If the person is to be tested in an upright position, the lines shall be drawn on the skin with the subject upright. If the subject is to be tested while prone, the markings shall be made with the subject prone.

(2) *Test subsite area.* Each test site area shall be divided into at least three test subsite areas that are at least 1 square centimeter. Usually four or five subsites are employed. Each test subsite within a test site area is subjected to a specified dosage of UV radiation, in a series of UV radiation exposures, in which the test site area is exposed for the determination of the MED.

(e) *Application of test materials.* To ensure standardized reporting and to define a product's SPF value, the application of the product shall be expressed on a weight basis per unit area which establishes a standard film. Both the test sunscreen product and the standard sunscreen application shall be 2 milligrams per square centimeter. For oils and most lotions, the viscosity is such that the material can be applied with a volumetric syringe. For creams,

heavy gels, and butters, the product shall be warmed slightly so that it can be applied volumetrically. On heating, care shall be taken so as not to alter the product's physical characteristics, especially separation of the formulations. Pastes and ointments shall be weighed, then applied by spreading on the test site area. A product shall be spread by using a finger cot. If two or more sunscreen drug products are being evaluated at the same time, the test products and the standard sunscreen, as specified in § 352.70, should be applied in a blinded, randomized manner. If only one sunscreen drug product is being tested, the testing subsites should be exposed to the varying doses of UV radiation in a randomized manner.

(f) *Waiting period.* Before exposing the test site areas after applying a product, a waiting period of at least 15 minutes is required.

(g) *Number of subjects.* A test panel shall consist of not more than 25 subjects with the number fixed in advance by the investigator. From this panel, at least 20 subjects must produce valid data for analysis.

(h) *Response criteria.* In order that the person who evaluates the MED responses does not know which sunscreen formulation was applied to which site or what doses of UV radiation were administered, he/she

must not be the same person who applied the sunscreen drug product to the test site or administered the doses of UV radiation. After UV radiation exposure to the solar simulator is completed, all immediate responses shall be recorded. These include several types of typical responses such as the following: an immediate darkening or tanning, typically greyish or purplish in color, fading in 30 to 60 minutes, and attributed to photo-oxidation of existing melanin granules; immediate reddening, fading rapidly, and viewed as a normal response of capillaries and venules to heat, visible and IR radiation; and an immediate generalized heat response, resembling prickly heat rash, fading in 30 to 60 minutes, and apparently caused by heat and moisture generally irritating to the skin's surface. After the immediate responses are noted, each subject shall shield the exposed area from further UV radiation for the remainder of the test day. The MED is determined 22 to 24 hours after exposure. The erythema responses of the test subject should be evaluated under the following conditions: the source of illumination should be either a tungsten light bulb or a warm white fluorescent light bulb that provides a level of illumination at the test site within the range of 450 to 550 lux, and the test subject should be in the same

position used when the test site was irradiated. Testing depends upon determining the smallest dose of energy that produces redness reaching the borders of the exposure site at 22 to 24 hours postexposure for each series of exposures. To determine the MED, somewhat more intense erythemas must also be produced. The goal is to have some exposures that produce absolutely no effect, while of those exposures that produce an effect, the maximal exposure should be no more than twice the total energy of the minimal exposure.

(i) *Rejection of test data.* Test data shall be rejected if the exposure series fails to elicit an MED response on either the treated or unprotected skin sites or if the responses on the treated sites are randomly absent, which indicates the product was not spread evenly or if the subject was noncompliant (e.g., subject withdraws from the test due to illness or work conflicts, subject does not shield the exposed testing sites from further UV radiation until the MED is read, etc.).

§ 352.73 Determination of SPF value.

(a) The following erythema action spectrum shall be used to calculate the erythema effective exposure of a solar simulator:

$$V_i(\lambda) = 1.0(250 < \lambda < 298 \text{ nm})$$

$$V_i(\lambda) = 10^{0.094(298-\lambda)}(298 < \lambda < 328 \text{ nm})$$

$$V_i(\lambda) = 10^{0.015(139-\lambda)}(328 < \lambda < 400 \text{ nm})$$

The data contained in this action spectrum are to be used as spectral weighting factors to calculate the erythema effective exposure of a solar simulator as follows:

$$E = \sum_{250}^{405} V_i(\lambda) * I(\lambda)$$

where:

E=Erythema Effective Exposure (dose)
V_i=Weighting Factor (Erythema Action Spectrum)

I=Spectral Irradiance (Watts per meter squared per nanometers)

(b) *Determination of MED of the unprotected skin.* A series of UV radiation exposures expressed as Joules per meter squared (adjusted to the erythema action spectrum calculated according to § 352.73(a)) is administered to the subsite areas on each volunteer with an accurately calibrated solar simulator. A series of five exposures shall be administered to the untreated,

unprotected skin to determine the subject's inherent MED. The doses selected shall be a geometric series represented by (1.25ⁿ), wherein each exposure time interval is 25 percent greater than the previous time to maintain the same relative uncertainty (expressed as a constant percentage), independent of the subject's sensitivity to UV radiation, regardless of whether the subject has a high or low MED. Usually, the MED of a person's unprotected skin is determined the day prior to testing a product. This MED(US) shall be used in the determination of the series of UV radiation exposures to be administered to the protected site in subsequent testing. The MED(US) should be determined again on the same day as the standard and test sunscreens and this MED(US) should be used in calculating the SPF.

(c) *Determination of individual SPF values.* A series of UV radiation exposures expressed as Joules per meter squared (adjusted to the erythema action spectrum calculated according to § 352.73(a)) is administered to the subsite areas on each subject with an accurately-calibrated solar simulator. A series of seven exposures shall be administered to the protected test sites to determine the MED of the protected skin (MED(PS)). The doses selected shall consist of a geometric series of five exposures, where the middle exposure is placed to yield the expected SPF plus two other exposures placed symmetrically around the middle exposure. The exact series of exposures to be given to the protected skin shall be determined by the previously established MED(US) and the expected SPF of the test sunscreen. For products with an expected SPF less than 8, the

exposures shall be the MED(US) times 0.64X, 0.80X, 0.90X, 1.00X, 1.10X, 1.25X, and 1.56X, where X equals the expected SPF of the test product. For products with an expected SPF between 8 and 15, the exposures shall be the MED(US) times 0.69X, 0.83X, 0.91X, 1.00X, 1.09X, 1.20X, and 1.44X, where X equals the expected SPF of the test product. For products with an expected SPF greater than 15, the exposures shall be the MED(US) times 0.76X, 0.87X, 0.93X, 1.00X, 1.07X, 1.15X, and 1.32X, where X equals the expected SPF of the test product. The MED is the lowest dose of radiation that produces uniform redness reaching the borders of the exposure site at 22 to 24 hours postexposure. The SPF value of the test sunscreen is then calculated from the dose of UV radiation required to produce the MED of the protected skin and from the dose of UV radiation required to produce the MED of the unprotected skin (control site) as follows:

SPF value = the ratio of erythema effective exposure (Joules per meter squared) (MED(PS)) to the erythema effective exposure (Joules per meter squared) (MED(US)).

(d) *Determination of the test product's SPF value and PCD.* Use data from at least 20 test subjects with n representing the number of subjects used. First, for each subject, compute the SPF value as stated in § 352.73 (b) and (c). Second, compute the mean SPF value, $\bar{x}$, and the standard deviation, s, for these subjects. Third, obtain the upper 5-percent point from the t distribution table with n - 1 degrees of freedom. Denote this value by t. Fourth, compute $ts/\sqrt{n}$. Let this quantity be denoted by A (i.e., $A = ts/\sqrt{n}$). Fifth, calculate the SPF value to be used in labeling as follows: the label SPF equals the largest whole number less than $\bar{x} - A$. Sixth and last, the drug product is classified into a PCD as follows: if $20 + A < \bar{x}$, the PCD is Ultra High; if $12 + A < \bar{x} < 20 + A$, the PCD is Very High; if $8 + A < \bar{x} < 12 + A$, the PCD is High; if $4 + A < \bar{x} < 8 + A$, the PCD is Moderate; if $2 + A < \bar{x} < 4 + A$, the PCD is Minimal; if $\bar{x} < 2 + A$, the product shall not be labeled as a sunscreen drug product and may not display an SPF value.

§ 352.76 Determination if a product is water resistant or very water resistant.

The general testing procedures in § 352.72 should be used as part of the following tests, except where modified in this section. An indoor fresh water pool, whirlpool, and/or jacuzzi maintained at 23 to 32 °C shall be used in these testing procedures. Fresh water is clean drinking water that meets the standards in 40 CFR Part 141. The pool

and air temperature and the relative humidity shall be recorded.

(a) *Procedure for testing the water resistance of a sunscreen product.* If the sunscreen product retains the same PCD after 40 minutes of water immersion as it had before water immersion, the claim of "water resistant" may be made.

The following procedure shall be used for the water resistance test:

(1) Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).

(2) 20 minutes moderate activity in water.

(3) 20-minute rest period.

(4) 20 minutes moderate activity in water.

(5) Conclude water test (air dry test sites without toweling).

(6) Begin solar simulator exposure to test site areas as described in § 352.73.

(b) *Procedure for testing a very water resistant sunscreen product.* If the sunscreen product retains the same PCD after 80 minutes of water immersion as it had before water immersion, the claim of "very water resistant" may be made. The following procedure shall be used for the very water resistant test:

(1) Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).

(2) 20 minutes moderate activity in water.

(3) 20-minute rest period.

(4) 20 minutes moderate activity in water.

(5) 20-minute rest period.

(6) 20 minutes moderate activity in water.

(7) 20-minute rest period.

(8) 20 minutes moderate activity in water.

(9) Conclude water test (air dry test sites without toweling).

(10) Begin solar simulator exposure to test site areas as described in § 352.73.

§ 352.77 Test modifications.

The formulation or mode of administration of certain products may require modification of the testing procedures in this subpart. In addition, alternative methods (including automated or in vitro procedures) employing the same basic procedures as those described in this subpart may be used. Any proposed modification or alternative procedure shall be submitted as a petition under the rules established in § 10.30 of this chapter. The petition should contain data to support the modification or data demonstrating that an alternative procedure provides results of equivalent accuracy. All information submitted will be subject to

the disclosure rules in Part 20 of this chapter.

PART 700—GENERAL

4. The authority citation for 21 CFR Part 700 continues to read as follows:

Authority: Secs. 201, 301, 502, 505, 601, 602, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 352, 355, 361, 362, 371, 374).

5. Section 700.35 is added to subpart B to read as follows:

§ 700.35 Cosmetics containing sunscreens.

(a) A product that includes a sunscreen active ingredient and the term "sunscreen" in its labeling or in any other way represents or suggests that it is intended to prevent, cure, treat, or mitigate disease or to affect a structure or function of the body comes within the definition of a drug in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act. Sunscreen active ingredients affect the structure or function of the body by screening, reflecting, or scattering the harmful, burning rays of the sun, thereby altering the normal physiological response to solar radiation. These ingredients also help to prevent diseases such as sunburn and reduce the chance of premature skin aging or skin cancer due to the sun. Moreover, when consumers see the term "sunscreen" on the label of a product, they expect the product to protect them in some way from the harmful effects of the sun, irrespective of other labeling statements.

Consequently, the use of the term "sunscreen" in a product's labeling normally makes that product a drug. However, sunscreen ingredients may also be used in some cosmetic products for nontherapeutic uses. In order to avoid consumer misunderstanding, if a cosmetic product uses the term "sunscreen" anywhere in its labeling, the term "sunscreen" must be qualified by describing the cosmetic benefit provided by the sunscreen. For example: "This product contains a sunscreen that assists in protecting the hair from damage by the sun."

(b) Any information describing the purpose of the sunscreen in the product shall appear in direct conjunction with the term "sunscreen."

PART 740—COSMETIC PRODUCT WARNING STATEMENTS

6. The authority citation for 21 CFR Part 740 continues to read as follows:

Authority: Secs. 201, 301, 502, 505, 601, 602, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 352, 355, 361, 362, 371, 374).

7. Section 740.19 is added to subpart B to read as follows:

§ 740.19 Suntanning preparations.

The labeling of suntanning preparations that do not contain a

sunscreen ingredient must display the following warning:

Warning—This product does not contain a sunscreen and does not protect against sunburn.

Dated: February 3, 1993.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 93-10888 Filed 5-11-93; 8:45 am]

BILLING CODE 4160-01-P

Federal Register

Wednesday
May 12, 1993

Part IV

Department of Labor

Office of Labor-Management Standards

29 CFR Parts 402 and 403
Labor Organization Annual Financial
Reports and Abbreviated Annual
Financial Reports for Small Labor
Organizations; Final Rule

DEPARTMENT OF LABOR

Office of Labor-Management Standards

29 CFR Parts 402 and 403

RIN 1215-AA86

Labor Organization Annual Financial Reports and Abbreviated Annual Financial Reports for Small Labor Organizations

AGENCY: Office of Labor-Management Standards, Employment Standards Administration, Labor.

ACTION: Final rule; postponement of effective date.

SUMMARY: This final rule postpones the effective date of revisions to the regulations pertaining to the filing, by labor organizations, of annual financial reports required by the Labor-Management Reporting and Disclosure Act of 1959, as amended (LMRDA). The rule postpones the effective date of final rules published in the *Federal Register* on October 30, 1992, which revised Forms LM-2 and LM-3 and issued the new Form LM-4. The effective date of the October 30 final rules was December 31, 1993, which would have required covered labor organizations filing financial reports for fiscal years beginning January 1, 1993, and thereafter to file the newly revised Form LM-2 or LM-3, or the new Form LM-4. This final rule postpones the effective date from December 31, 1993, to December 31, 1994, because of problems encountered by labor organizations and the Department in connection with efforts to implement the revised reporting forms and because further study of the revisions is necessary, including evaluating whether modification or rescission of some or all of the revisions may be appropriate. As a result of this extension, labor organizations filing financial reports for fiscal years ending before December 31, 1994, will continue to file reports on the preexisting Form LM-2 or LM-3.

EFFECTIVE DATE: The rules amending 29 CFR Parts 402 and 403 published at 57 FR 49282 and 49356 will be effective December 31, 1994.

FOR FURTHER INFORMATION CONTACT: Kay H. Oshel, Chief, Division of Interpretations and Standards, Office of Labor-Management Standards, Employment Standards Administration, U.S. Department of Labor, 200 Constitution Avenue NW., room N-5605, Washington, DC 20210, (202) 219-7373. This is not a toll-free number.

SUPPLEMENTARY INFORMATION:

I. Background and Overview

Section 201(b) of the Labor-Management Reporting and Disclosure Act of 1959, as amended (LMRDA) (Pub. L. 86-257, 73 Stat. 519), requires each covered labor organization to file annually with the Secretary of Labor a financial report, signed by its president and treasurer or corresponding principal officers, containing information in the detail necessary to disclose accurately its financial condition and operations for the preceding fiscal year. The Secretary of Labor has delegated his authority under the LMRDA to the Assistant Secretary for Employment Standards. See Secretary's Order No. 9-92 (57 FR 53514, 57 FR 56641).

The requirements of LMRDA section 201 apply to all labor organizations in the private sector including those representing employees under the provisions of the National Labor Relations Act, as amended, and the Railway Labor Act, as amended. Section 1209(b) of the Postal Reorganization Act made the LMRDA applicable to labor organizations representing employees of the U.S. Postal Service. Section 701 of the Civil Service Reform Act of 1978 (CSRA) and section 1017 of the Foreign Service Act of 1980 (FSA), as implemented by Department of Labor regulations at 29 CFR parts 457-459, extended the LMRDA reporting requirements to labor organizations representing certain employees of the Federal government.

Section 208 of the LMRDA authorizes the Secretary to issue rules prescribing the form and publication of the annual financial reports required by section 201, and to provide a simplified report for labor organizations for whom the Secretary finds that by virtue of their size a detailed report would be unduly burdensome. Under the preexisting regulations issued pursuant to section 208, the Secretary has prescribed Form LM-2 for labor organizations with total annual receipts of \$100,000 or more, and the simplified Form LM-3 for labor organizations with total annual receipts of less than \$100,000. (The preexisting regulations at 29 CFR 403.4(b) also provide that for a labor organization which is not in trusteeship and which has no assets, liabilities, receipts, or disbursements, the parent national or international may fulfill that organization's reporting obligation by filing basic information on its behalf in a simplified format.)

On October 30, 1992, the Department published final rules revising the annual financial reporting Forms LM-2 and LM-3 and issuing a new abbreviated

annual financial reporting Form LM-4 (57 FR 49282 and 49356). The effective date of these final rules was December 31, 1993. The revised financial reporting Forms LM-2 and LM-3, among other things, added a requirement that labor organizations report expenditures by functional categories, provided the option of completing the reporting forms on the cash or accrual basis of accounting, and raised the annual receipts ceiling for use of the simplified Form LM-3 from \$100,000 to \$200,000. A new abbreviated Form LM-4 for use by small labor organizations with total annual receipts of less than \$10,000 was also issued. Since the annual financial reports disclose details of each labor organization's financial condition and operations for the preceding year, labor organizations filing reports for fiscal years ending on or after the December 31, 1993, effective date would have had to begin maintaining records to comply with the new functional reporting requirement on or shortly after the beginning of their fiscal year, which for the majority of labor organizations was January 1, 1993. The addition of the functional reporting requirement to Forms LM-2 and LM-3 would have also required many labor organizations to modify their recordkeeping systems in order to collect and report the required information. The December 31, 1993, effective date of the final rule thus would have compelled labor organizations to begin implementing new procedures as early as January 1, 1993, only two months after the publication of the final rules on October 30, 1992.

During the formal comment period prior to the issuance of the October 30, 1992, final rules, the Department received a number of comments stating that a lead time of less than one year would be insufficient to establish and operate new accounting systems needed to comply with the proposed functional requirements. In addition, the Department has continued to receive comments and inquiries from labor organizations and accounting firms regarding difficulties in interpreting and applying the new rules. Reexamination of the initial comments the Department received on the proposed effective date, the Department's own difficulties in adequately responding to labor organizations' inquiries regarding the final rule, and labor organizations' continuing problems in preparing to comply with the new functional reporting requirements led the Department to propose extending the effective date of the final rules until December 31, 1994 (*Federal Register*, 58

FR 9418, February 19, 1993). The purpose of the postponement is to alleviate these compliance problems and allow for reevaluation of these new rules, including whether modification or rescission of some or all of the revisions may be appropriate.

Public comment on the proposed rule was invited, with the comment period ending on March 22, 1993. The comments, the Department's responses, and the Department's decision are discussed in detail below.

For the reasons discussed below, the Department has decided to extend, for one year, the effective date of the two final rules published on October 30, 1992. As a result of this extension, labor organizations filing financial reports for fiscal years ending before December 31, 1994, will continue to file reports on the preexisting Form LM-2 or LM-3.

II. Comments on the Proposal and the Department's Responses and Decision

Forty-six timely comments were received from the public; forty-one from labor organizations, four from accounting firms, and one from another organization. Ten of the comments from labor organizations were identical. Additionally, five identical comments were submitted by various officers of one labor organization.

The AFL-CIO and the following national and international labor organizations commented on the proposed rule:

- Utility Workers;
- Chemical Workers;
- Aluminum, Brick and Glass Workers;
- Ladies Garment Workers;
- Laundry and Dry Cleaning;
- Postal Workers;
- Service Employees;
- Auto Workers;
- Food and Commercial Workers;
- Teachers;
- Bricklayers;
- Steelworkers;
- Letter Carriers;
- Iron Workers;
- Machinists.

Other labor organizations which commented on the proposal are:

- Local 278, Electrical Workers, IBEW;
- Local 1031, Electrical Workers, IBEW;
- District 14, Steelworkers;
- Local 604-605, Postal Workers;
- Local 512, Transport Workers;
- Local 218, Sheet Metal Workers;
- Local 293, Plumbers;
- Local 589, Operating Engineers;
- Local 150, Operating Engineers;
- Local 383, Plumbers;
- Local 18, Operating Engineers;
- Local 204, Electrical Workers, IBEW;
- Local 82, Electrical Workers, IBEW (five comments);

- Washington County Central Labor Council;
- Local 2327, Electrical Workers, IBEW;
- Local 336, Electrical Workers, IBEW;
- Local 383, Electrical Workers, IBEW;
- Local 99, Plumbers;
- Local 7200, Communications Workers;
- Local 95, Electrical Workers, IBEW;
- Local 280, Electrical Workers, IBEW.

Accounting firms which commented on the proposal are:

- Daniel A. Winters and Company;
- Potter and Company (on behalf of seven client labor organizations);
- Damore, Hamric and Schneider;
- Winkler and Forner.

The one other organization which commented on the proposed rule is:

- The National Right to Work Legal Defense Foundation.

The Department has carefully reviewed and considered all statements made in the comments in developing this final rule. The following is a summary of the comments and the Department's responses.

A. Discussion of the Comments

Thirty comments specifically support the extension. Sixteen of these addressed why the organizations believed the extension is necessary, arguing generally that:

- A two-month implementation period was inadequate to make necessary revisions to international union records and to train local union officers;
- The Department should review and evaluate the soundness of the October 30, 1992, revisions.

The other fourteen comments which supported the extension did not provide specific reasons but expressed opposition to the October 30, 1992, revisions.

Fifteen comments did not specifically address the extension but only expressed opposition to the October 30, 1992, revisions.

One organization, the National Right to Work Legal Defense Foundation, opposed the extension, arguing generally that:

- The two-month lead time for implementation of the revised forms was adequate to make the necessary internal recordkeeping revisions and resolve compliance difficulties;
- There is no need for the Department to further review and examine the soundness of the October 30, 1992, revisions.

1. Revision of Internal Union Records

Nine of the organizations which supported the extension stated that the

two-month implementation period was inadequate because the revised reporting requirements necessitate extensive revision of unions' internal records prior to the beginning of their fiscal year to accurately compile the necessary data to complete the revised Form LM-2 or LM-3 at the end of the fiscal year.

One international union (Ladies Garment Workers) noted that any necessary revisions to its recordkeeping procedures should have been in place on December 31, 1992, but stated the Union "struggled to develop the necessary internal procedures in the early months of 1993, but has not yet succeeded * * *. The Union's staff will be required to maintain detailed time records, geared to the LM reports, so that their salaries may be allocated to each of the respective functions * * *. Literally hundreds of questions arise in the development of such a system, and it is impossible to resolve them overnight and then adequately train staff throughout the nation." This union also stated that "it is unclear whether [the time records supporting officer and employee payments] would also support the functional allocation for the other required line items. In particular, the Union has many unanswered questions concerning the proper allocation of office and administrative expenses." The Ladies Garment Workers also noted that in January 1993, they sought advice from the Department and learned that the Department was in the process of developing compliance assistance programs for unions but had not had sufficient time to complete such programs.

Another international union (Bricklayers) stated that: "(A)t the very least, the proposed extension of effective date will give labor organizations an opportunity to become familiar with and adjust to the new reporting requirements by implementing necessary accounting changes and modifying recordkeeping systems. Without the extension, unions are afforded inadequate lead time to prepare for these revised reporting methods."

On other international (Letter Carriers) which supported the extension indicated that the two-month implementation period was "not sufficient to accommodate required revisions to [the Union's] computerized accounting system. An extension * * * would permit [the Union] to identify the appropriate allocation methods based on the definitions of the functional categories and make the necessary revisions to its computerized accounting system."

One local union (Local 383, Electrical Workers, IBEW) provided comments on its attempts to revise internal procedures to comply with the revised forms. This union stated that "(t)he amount of time required to process the vouchers each month increased as it was necessary to establish a separate data base to cover the salary/salary reimbursement allocations. My accounting system was able to accommodate the expense allocation, however, the amount of paper involved in each month's activities more than doubled." Local 383, Electrical Workers, IBEW also pointed out that "there was no one who was able to explain where to post day to day office administration of the Union, including such things as the time spent processing the salary and expense vouchers, membership records and the monthly meetings of the Executive Board, etc., etc., etc."

The AFL-CIO comments cited a survey (prepared on its behalf) of accounting firms that work extensively with labor organizations. According to the survey, "(m)any of the accountants surveyed add that the 60-day lead-time * * * has substantially exacerbated the inherent difficulties of coming into compliance with these complex bookkeeping and recordkeeping requirements."

The comment opposing the extension (National Right to Work Legal Defense Foundation) stated that "(f)unctional reporting simply means that paid officers and staff must keep contemporaneous records of their time in certain categories. *Those categories are defined by the Rules, themselves* * * *. (T)he design of a form for officers and employees to record time by function cannot reasonably take two hours, never mind two weeks, or two months." This comment also cited the Department's statement in the October 30, 1992, final rule that, "(a)fter reviewing these comments [seeking a longer implementation period], the Department has decided that the effective date will be December 31, 1993 * * *. In the Department's judgment, this should provide sufficient time for labor organizations to adapt to the new reporting requirements" (57 FR 49286).

2. Training on Revised Internal Recordkeeping Procedures

Seven of the comments from organizations which supported the extension also argued that the two-month implementation period was inadequate because national and international unions must provide training to local union officers on the

necessary revisions to internal recordkeeping procedures.

One comment (Ladies Garment Workers) stated that "it is foolhardy to race headlong into a complicated new reporting system without adequate guidance and training on its proper implementation. To properly comply with the new requirement for functional reporting, the Union must first develop an appropriate record-keeping system and must then conduct multiple training sessions around the country to educate its staff on the new record-keeping requirements, answer questions, and make modifications where necessary."

Another international union (Auto Workers) indicated that it has 1200 locals and 200 related entities which must file Form LM-2 or LM-3 and that 70 percent of the officers who will be responsible for completing the revised forms are part-time financial officers who are not trained in accrual accounting nor do they know what is intended by the functional categories. The Auto Workers also stated that "whatever * * * unions may be able to achieve with time and training, it is patently unreasonable for the Government to impose such duties without long lead time * * *."

One other union (Bricklayers) stated that "(t)his International Union had insufficient time to educate its own staff and field representatives about the new requirements or to prepare and circulate educational material on the subject to our approximately 500 affiliates. These new requirements inequitably affect the majority of our local unions which have very limited accounting background or experience and lack the resources to hire accountants to set up the necessary recordkeeping system required for this functional reporting."

Another comment (Letter Carriers) noted that time to train local officers is necessary, observing that many of their 600 locals cannot afford accounting assistance and that the international will have to consider developing a national training program to assist local officials.

3. Department of Labor Implementation Difficulties

The Department of Labor's Office of Labor-Management Standards (OLMS) determined that proper implementation of the revised reporting requirements would require OLMS to train its field staff, respond to inquiries on the revisions, develop compliance assistance materials for union officials, and change internal operations to accommodate the revised reporting forms.

During November and December, 1992, OLMS developed procedures for notifying unions prior to the beginning of their fiscal year of the revised reporting requirements, prepared summary sheets for labor organizations highlighting the major revisions, and sent notification letters to approximately 21,000 unions. Preliminary plans were developed for: Printing and distributing the revised forms; redesigning OLMS' computer data base system to align with the new reports; revising internal procedure and enforcement manuals; and revising existing pamphlets and publications. In addition, OLMS began developing staff training and compliance assistance materials and programs for union officials. OLMS' experience demonstrated that it would not be possible to complete all necessary actions to implement the revised forms in the allotted time.

After the final rules were published in the Federal Register on October 30, 1992, OLMS received numerous requests from its field staff seeking guidance and raising issues related to the accrual and functional reporting requirements. OLMS also received many interpretative and technical questions from union officials and accountants, which arose as they began to revise their internal recordkeeping systems to comply with the revised reporting requirements. Examples of issues raised include: the proper allocation of expenses on multi-purpose business trips by union officials, the reasonableness of using a sample period for allocating officer and staff time for the entire reporting period, and the proper allocation of general overhead expenses.

OLMS was unable to provide adequate guidance on many interpretative and technical issues because of insufficient time to analyze all the relevant factors and develop policy positions. Three of the comments noted that the inability of the Department to provide guidance prior to the beginning of the affected reporting period exacerbated the difficulties labor organizations were experiencing in revising their internal reporting requirements.

One comment (National Right To Work Legal Defense Foundation) opposed the extension arguing that the Department's statement concerning its implementation difficulties "proceeds on a false premise. It assumes that there was a 'short time for implementation' and, therefore, that OLMS personnel had no reasonable time within which to determine responses to reasonable compliance inquiries. This is simply not

the case. The basic form which provided the basis for the Modern Forms [i.e., revised forms] was initially developed within OLMS (then Labor-Management Services Administration) in 1983 * * *. The Modern Forms are not naked, with OLMS and reporting labor organizations left to grope for instructions on their completion. To the contrary, there are thirty one (31) pages of instructions for completion of the LM-2 * * *. Thus, there is no absence of instructive educational material concerning completion of the Modern Forms."

4. Reevaluation of the Revised Rules

Forty-two of the comments urged the Department to review and rescind the revised reporting requirements. These comments supported reevaluation or rescission because of the increased recordkeeping and financial burden caused by the revisions.

The AFL-CIO indicated that its initial comments opposing the October 30 revisions were "based in significant part on the material showing that the proposed changes would impose bookkeeping, recordkeeping and reporting burdens on unions out of all proportion to any possible gain in the information made available to the Labor Department and to union members." The AFL-CIO also submitted a December 1992 study (completed on its behalf) on the cost to unions of complying with the revised reports. This study suggests that "the first year compliance costs imposed on unions * * * will be \$58 million over and above what would have been spent on reporting under the LM-2/LM-3 regime previously in effect * * *. This figure includes \$28 million in start-up costs to institute recordkeeping systems necessary to compile the data required by the revised LM forms and \$30 million in annual increased costs for filling out the revised forms." This comment also asserts that the Department's burden hours and associated cost figures for the revised forms significantly understate the burden associated with the revised reports.

A CPA firm (Daniel A. Winters & Company) submitted comments recommending that the revisions be reevaluated because the "time and effort required to submit the additional information is wasteful and counterproductive." The comment argued that since no method is prescribed for the functional allocation of expenses, "some unions will undoubtedly choose to maintain records of time spent by union officials and employees to provide a basis of allocation. Some unions will probably

estimate broad across-the-board percentages * * *. Accordingly, the information which the government will receive will not be useful or meaningful on a micro or macro level and * * * the cost of providing this information will be great to individual unions and to the unionized community in the aggregate."

Two comments suggested that the initial comments submitted prior to the publication of the October 30 final rule were not given proper consideration by the Department and reevaluation is necessary.

Thirteen comments stated that, contrary to what was stated in the preamble to the October 30 final rule, they believed that the functional allocation requirement was an attempt to further implement the Supreme Court's decision in *Communications Workers of America v. Beck*, 487 U.S. 735 (1988) and that requiring all unions to report in this manner is an unreasonable and unnecessary burden.

Two comments indicated that some local unions which are required to prepare special reports for agency fee payers are now required to maintain an additional set of records to fulfill the functional reporting requirement.

The comment opposing the extension (National Right To Work Legal Defense Foundation) stated that "complete evaluation by OLMS has already taken place; it resulted in the New Forms. There is no need for 'modification * * * of some * * * of the revisions', and no case has been made for such action. There is no need, either, for 'rescission of * * * all of the revisions'."

B. The Department's Responses and Decision

After considering the comments and the Department's difficulties in attempting to implement the reporting revisions, the Department has concluded that an effective date of December 31, 1993, which, in effect, allowed only a two-month implementation period was insufficient. Therefore, the Department has decided to extend the effective date of the final rules to December 31, 1994.

The comments which supported the extension as discussed above have convinced the Department that the implementation period for the revised reports must allow adequate time for labor organizations to revise their internal records and accounting systems in order to properly classify financial transactions prior to the beginning of the fiscal year for which the revised reporting forms must be used. The Department recognizes that national and international unions often develop

recordkeeping and reporting procedures for their subordinate unions so that, as a first step to implementing major revisions to the reporting process, the national or international must revise the formats of their internal records to coincide with the revised reporting categories on Forms LM-2 and LM-3.

Additionally, the comments concerning the need to train union officers who will be required to maintain the revised internal union records and ultimately to complete the revised Form LM-2 or LM-3, have demonstrated the need for the one-year extension. The Department's own experiences in attempting to develop and conduct training for its staff as well as to develop associated compliance assistance materials for use by union officials further support the need for the extension.

Finally, the comments urging the Department to reevaluate the revisions, the questions and requests for assistance directed to the Department, and the Department's own implementation difficulties suggest the need to reevaluate the revisions. During the extension period, the Department will reevaluate the October 30 final rules and determine whether modification or rescission of some or all of the revisions may be appropriate.

The Department is not persuaded by the comments of the National Right To Work Legal Defense Foundation opposing the extension. Listed below are the Foundation's principal arguments and the Department's response:

(1) Additional "lead" time is not necessary because functional reporting only requires paid union officers and staff to keep contemporaneous records of their time in certain categories.

Functional reporting not only requires maintaining time records for officers and staff but also requires unions to make determinations concerning the proper allocation categories for various activities of officers and staff. Additionally, functional reporting will require labor organizations to allocate expenditures for administrative items such as rent, office supplies, and utilities and several other types of expenditures to functional categories. As illustrated in the discussion of the comments and the Department's experience in preparing to implement the revised forms, labor organizations must revise their internal reporting records prior to the beginning of the fiscal year to which the revisions apply in order to properly allocate expenditures during the reporting period. Additionally, the Department has a responsibility to provide the

regulated organizations with adequate guidance for making those allocations. The record illustrates that a two-month implementation period was not sufficient.

(2) Compliance difficulties could not have been "serious and substantial" since they were not specified in the February 19 proposed extension, and, in any case, "(e)xperience confirms that the best means to ferret out the 'difficulties', if any, caused by the reporting requirements of the Modern Forms is to require the reporting in accordance with the present deadline."

It is clear from the above discussion of the comments that serious compliance difficulties exist. The Department has decided that implementing the revised forms without adequate time to answer questions, resolve issues, and provide sufficient guidance to affected labor organizations would result in the submission of reports which may be so fraught with errors that the functional information reported would be misleading and/or of little value to union members and others.

The Department also notes that both the Department and the reporting labor organizations will have to alter internal operating systems and procedures to implement the revised reports. It would be a waste of taxpayers' and union members' monies to expend funds to revise computer systems, accounting systems, training programs, etc., only to determine at the end of the first reporting period that there may be serious flaws in the reports necessitating further revisions.

(3) There is no need for additional guidance as the revised forms contain numerous pages of instructions and, in any event, the Department should not need additional time to develop responses to inquiries since "(t)he basic form which provided the basis for the Modern Forms was initially developed within OLMS * * * in 1983."

Although the reporting instructions identify what information is to be reported on the forms, the Department must be able to provide guidance on the application of the instructions to specific circumstances in individual reporting organizations. In addition, while it is true that a preliminary draft form was developed by OLMS in 1982-83, that draft contained a substantially different version of functional reporting.

Moreover, that proposal was never approved by the Department and the project was terminated in 1983.

(4) There is no need for reevaluation of the revisions as all necessary review

and evaluation was conducted prior to the publication of the October 30 final rules.

The experience of the labor organizations required to file the revised reports and the Department's experience during the implementation period as described in the comments and discussion above illustrate the need to reevaluate the revisions. The Department will determine whether modification or rescission of the revised rules is appropriate after reevaluating the revisions.

III. Comments on the October 30, 1992, Revisions

Forty-two comments expressed opposition to some or all of the revisions contained in the October 30 final rule, fifteen comments recommended rescission of all changes, and twenty-seven recommended rescission of the functional reporting requirement. However, four comments supported raising the annual receipts ceiling for use of the simplified Form LM-3 from \$100,000 to \$200,000 or higher, and five expressed support for the abbreviated Form LM-4.

During the postponement period, the Department will reexamine the October 30 rules and, if it is determined that these rules should be revised, a Notice of Proposed Rulemaking requesting comments on proposed changes will be published in the *Federal Register*. Comments concerning any proposed changes will be considered at that time.

IV. Administrative Requirements

A. Effective Date

This document will become effective upon publication pursuant to 5 U.S.C. 553(d). The undersigned have determined that good cause exists for waiving the customary requirement for delay in the effective date of a final rule for 30 days following its publication. As a result of this final rule, labor organization financial reports for fiscal years beginning January 1, 1993, and thereafter through December 31, 1993, will be filed on the preexisting Form LM-2 or LM-3 rather than the revised Form LM-2 or LM-3 or the new Form LM-4. Because of the significant differences in the information required to be reported on the preexisting and revised forms, and because the postponement relieves the obligation of labor organizations to revise their recordkeeping systems for the above-mentioned fiscal years, it is appropriate to have this postponement become effective upon publication.

B. Executive Order 12291

The Department of Labor has determined that this rule is not a major rule as defined by Executive Order 12291 in that it will not have an annual effect on the economy of \$100 million or more, not cause a major increase in costs or prices, and not have an adverse effect on competition in the marketplace. Therefore, a regulatory impact analysis is not required.

C. Regulatory Flexibility Act

In accordance with section 605(b) of the Regulatory Flexibility Act (5 U.S.C. 601 et seq.), the Department certifies that this rule will not have a significant economic impact on a substantial number of small entities. The rule will only apply to labor organizations, and the Department has determined that labor organizations regulated pursuant to the statutory authority granted under the LMRDA do not constitute small entities. Therefore, a regulatory analysis is not required.

D. Paperwork Reduction Act

The Final Rule has resulted in a one-year continuation of the pre-existing approved labor organization reporting requirements. The burden hour estimate of 250,185 remains unchanged. Therefore, it is not subject to section 3504(h) of the Paperwork Reduction Act, 44 U.S.C. 3504(h).

List of Subjects in 29 CFR Parts 402 and 403

Labor unions, Reporting and recordkeeping requirements.

Postponement of Effective Date of Final Rules

In consideration of the foregoing, the Department of Labor postpones the effective date for the final rules published in the *Federal Register* on October 30, 1992, 57 FR 49282 and 49356, which revised Forms LM-2 and LM-3, issued Form LM-4, and amended 29 CFR parts 402 and 403, from December 31, 1993, until December 31, 1994.

Signed in Washington, DC, this 7th day of May, 1993.

Robert B. Reich,
Secretary of Labor.

John R. Fraser,
Acting Assistant Secretary for Employment Standards.

[FR Doc. 93-11241 Filed 5-11-93; 8:45 am]

BILLING CODE 4510-86-M

Federal Register

Wednesday
May 12, 1993

Part V

**Department of
Health and Human
Services**

Office of Community Services

**Request for Application Under the Office
of Community Services' Fiscal Year 1993
Job Opportunities for Low-Income
Individuals Program (Demonstration
Projects); Notice**

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of Community Services

[Program Announcement No. OCS-93-3]

Request for Applications Under the Office of Community Services' Fiscal Year 1993 Job Opportunities for Low-Income Individuals Program (Demonstration Projects)

AGENCY: Administration for Children and Families (ACF), DHHS.

ACTION: Announcement of availability of funds and request for applications under the Office of Community Services' FY 1993 Job Opportunities for Low-Income Individuals Programs (Demonstration Projects).

SUMMARY: The Administration for Children and Families (ACF), Office of Community Services (OCS), announces that competing applications will be accepted for new grants pursuant to the Secretary's discretionary authority under section 505 of the Family Support Act of 1988. This Program Announcement consists of eight parts:

Part I covers information on legislative authorities, eligible applicants, definition of terms used in the Program Announcement and describes the purpose of the program;

Part II describes the types of projects that will be considered for funding;

Part III provides details on application requirements, funds available, limitations on grant amounts, project and budget periods, mobilization of resources, who should benefit from the programs, partnership agreement, prohibition and restrictions on the use of funds and multiple submittals, third-party evaluation, economic development strategy, and maintenance of effort;

Part IV describes the criteria used in the assessment of applications;

Part V describes the application procedures, including the availability of forms, where and how to submit an application and the intergovernmental review. It also includes the initial screening, pre-rating review and factors considered in the selection process;

Part VI provides instructions for completing the SF-424.

Note: OCS has included specific instructions for completing Section B of the SF-424;

Part VII describes the contents of the application package, how the project narrative should be ordered and presented and the receipt process; and

Part VIII details post-award information and reporting requirements.

CLOSING DATE: The closing date for submission of applications is June 28, 1993.

FOR FURTHER INFORMATION CONTACT: Office of Community Services, Administration for Children and Families, 370 L'Enfant Promenade SW., Washington, DC 20447, Telephone (202) 401-2333, Contact: Margaret Washnitzer.

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Part I—Preamble

A. Legislative Authority

The FY 1993 Senate Appropriations Committee's recommendation includes \$5,000,000 for job creation demonstration activities authorized under section 505 of the Family Support Act of 1988. No funds were included in the budget request for these projects. These grants provide technical and

financial assistance to businesses that agree to target new jobs and enterprise opportunities to welfare individuals at or below 100 percent of the poverty threshold. The Committee directs that the funds for section 505 be administered by the Office of Community Services within HHS and that funds be made available on a priority basis to community development corporations with a record of achievement in job and business for low-income people. Section 505 of the Family Support Act of 1988 also authorizes the Secretary to enter into agreements with not less than 5 nor more than 10 nonprofit organizations for the purpose of conducting demonstration projects to create employment and business opportunities for certain low-income individuals.

B. Eligible Applicants

The organization eligible to apply for funding under this program is any nonprofit organization (including community development corporations) that is exempt from taxation under Section 501(a) of the Internal Revenue Code of 1986 by reason of paragraph (3) or (4) of section 501(c) of such Code.

C. Definition of Terms

For purposes of this Program Announcement the following definitions apply:

—**Budget Period:** The interval of time into which a multi-year period of assistance (project period) is divided for budgetary and funding purposes.

—**Community-Level Data:** Key information to be collected by each grantee that will allow for a national-level analysis of common features of JOLI projects. This includes data on the population of the target area, the percentage on public assistance, the percentage whose incomes fall below the poverty line, the unemployment rate, the number of new business starts and business closings, and a description of the major employers and average wage rates.

—**Community Development Corporation:** A private, locally initiated, nonprofit entity, governed by a board consisting of residents of the community and business and civic leaders, which has a record of implementing economic development projects or whose Articles of Incorporation and/or By-Laws indicate that it has a focus in the area of economic development.

—**Hypothesis:** An assumption made in order to test its validity. It should assert a cause-and-effect relationship between a program intervention and its expected result. Both the

intervention and result must be measured in order to confirm the hypothesis. For example: Eighty hours of classroom training in small business planning will be sufficient for participants to prepare a successful loan application. In this example, data would be obtained on the number of hours of training actually received by participants (the intervention), and the quality of loan applications (the result).

- Intervention:** Any planned activity within a project that is intended to produce changes in the target population and/or the environment and can be formally evaluated. For example, assistance in the preparation of a business plan and loan package are planned interventions.
- Job Creation:** To bring about, by activities funded under this program, new jobs, that is jobs that were not in existence before the start of the project. These activities can include self-employment/entrepreneurial training, the development of new businesses or the expansion of existing businesses.
- Non-profit organizations:** Any organization (including a community development corporation) exempt from taxation under section 501(a) of the Internal Revenue Code of 1986 by reason of paragraph (3) or (4) of section 501(c) of such Code.
- Private employers:** Third-party private non-profit organizations or third-party for-profit businesses operating in the same community as the applicant.
- Process evaluation:** The ongoing examination of the implementation of a program. It focuses on the effectiveness and efficiency of the program's activities and interventions (for example, methods of recruiting participants, quality of training activities, or usefulness of follow-up procedures). It should answer questions such as: "Who is receiving what services?", "Are the services being delivered as planned?", and "Are client competencies improving?" It is also known as "formative" evaluation because it gathers information that can be used to improve the way a program is in progress.
- Program participant/beneficiary:** Any individual eligible to receive Aid to Families with Dependent Children under Part A of Title IV of the Social Security Act and any other individual whose income level does not exceed 100 percent of the official poverty line as found in the most recent Annual Revision of Poverty Income Guidelines published by the

Department of Health and Human Services. (See Attachment A.)

- Project Period:** The term "project period" refers to the total time a project is approved for support, including any extensions.
- Self-Sufficiency:** A condition where an individual or family, by reason of employment, does not need and is not eligible for public assistance.

D. Purpose

The purpose of this program is to demonstrate and evaluate ways of creating new employment and business opportunities for certain low-income individuals through the provision of technical and financial assistance to private employers in the community. A low-income individual eligible to participate in a project conducted under this program is any individual eligible to receive Aid to Families with Dependent Children (AFDC) under Part A of Title IV of the Social Security Act and any other individual whose income level does not exceed 100 percent of the official poverty line. (See Attachment A.) Within these categories, emphasis should be on individuals who are unemployed, those residing in public housing, and those who are homeless.

Part II—Program Priority Areas

A. General Projects 1.0

The Congressional Conference Report on the FY 1992 appropriations for the Departments of Labor, Health and Human Services, and Education and related agencies directs the ACF to require economic development strategies as part of the application process to ensure that highly qualified organizations participate in the demonstration. H.R. Conf. Rep. No. 282, 102d Cong., 1st Sess. 39 (1991). The inclusion of these strategies was a valuable addition to the application materials and will be continued this year. Proposed projects should demonstrate how their program will impact the overall community/communities served by the applicant. OCS will only fund projects that create new jobs and/or business opportunities for eligible program participants. Projects funded under this program must demonstrate how the proposed project will enhance the participants' ability and skills in their progress toward self-sufficiency. Therefore, proposed projects must show promise toward progress of achieving self-sufficiency among the target population. OCS expects that the jobs and/or business/self employment opportunities to be created under this program will contribute to the goal of self-sufficiency.

The employment opportunities should provide hourly wages that exceed the minimum wage and also provide benefits such as health insurance, transportation, child care, career development opportunities, etc.

Applicants must show that the proposed project will create a significant number of new full-time permanent jobs through the expansion of a pre-identified business or new business development and by providing opportunities for self-employment to eligible participants.

While projected employment in future years may be included in the application, it is essential that the focus of employment opportunities concentrate on new full-time, permanent jobs to be created during the duration of the grant project period and/or on the creation of new business development opportunities for low-income individuals.

In creating self-employment business opportunities for eligible participants, the applicant must detail how it will work with private employers in identifying potential entrepreneurs. The assistance to be provided to potential entrepreneurs must include, at a minimum, technical assistance in basic business planning and management concepts, and assistance in preparing a business plan (see Part IV, Criterion III for requirements) and loan application.

Any funds that are used for training purposes must be limited to providing specific job-related training to eligible participants who have been selected for employment and/or self-employment business opportunities.

In the review process, favorable consideration will be given to applicants with a demonstrated record of achievement in promoting job and enterprise opportunities for low-income people. Favorable consideration also will be given to those applicants who show the lowest cost-per-job created for low-income individuals. For this program, OCS views \$15,000 as the maximum amount for the creation of a job and, unless there are extenuating circumstances, will not fund projects where the cost-per-job in OCS funds exceeds this amount. Only those jobs created and filled by low-income people will be counted in the cost-per-job formula. (See Part IV, Criterion IV)

Technical assistance should be specifically addressed to the needs of the private employer in creating new jobs to be filled by eligible individuals and/or to the individuals themselves such as skills training, job preparation, self-esteem building, etc. Financial assistance also may include assistance to the private employer as well as

assistance to the individual. If the technical and/or financial assistance is to be provided to pre-identified businesses that will be expanded or franchised, written comments from the businesses must be included with the application.

The creation of a revolving loan fund with funds received under this program is an allowable activity. However, OCS encourages the use of funds from other sources for this purpose. Points will be awarded in the review process to those applicants who leverage funds from other sources. (See Part IV, Criterion VI.) Loans made to eligible beneficiaries for business development activities must be at or below market rate.

(Note: Interest accrued on revolving loan funds may be used to continue or expand the activities of the approved project)

Grant funds received under this program may not be used for construction.

A formal, cooperative relationship between the applicant and the agency (State IV-A agency) responsible for administering the Job Opportunities and Basic Skills (JOBS) training program (as provided for under title IV-A of the Social Security Act) in the area served by the project is a requirement for funding. The application must include a signed, written agreement between the applicant and the State IV-A agency, or a letter of commitment (contingent only on receipt of OCS funds), which describes the cooperative relationship, including specific activities and/or actions each of these entities proposes to carry out over the course of the grant period in support of the project. The agreement, at a minimum, must cover activities that will be provided to the target population and which are related to one or more of the mandatory or optional components offered by the appropriate State's JOBS program. The mandatory activities offered by the States' JOBS programs consist of the following components: Basic education activities, job skills training, job readiness activities, job development and job placement. The optional components offered by the States' JOBS programs include: group and individual job search counseling and training on job seeking skills; on-the-job-training; work supplementation; and community work experience.

(Note: A signed written agreement or a signed letter of commitment between the applicant and the State IV-A agency must be submitted with the application in order to be reviewed and evaluated competitively.)

Projects also must include an independent, methodologically sound evaluation of the effectiveness of the

activities carried out with the grant in creating new jobs and business opportunities. (See Part IV, Criterion V).

Applications should include a plan for disseminating the results of the project after expiration of the grant period. Applicants may budget up to \$1,000 for dissemination purposes.

Priority will be given to applications proposing to serve those areas containing the highest percentage of individuals receiving Aid to Families with Dependent Children under Title IV-A of the Social Security Act. (See Part IV, Criterion II.)

Applicants must be aware that it is expected that projects will be operational by the end of the project period, i.e. that the jobs and/or businesses that the applicant committed itself in the application to creating will be in place, and low-income individuals will actually be employed in those jobs and/or businesses.

See Part IV, Criterion III for special instructions on developing a work program.

B. Community Development Corporations Set-Aside 2.0

For Fiscal Year 1993, a set-aside fund of \$1 million will be included for community development corporations. A set-aside fund is a private, non-profit entity which has a record of implementing economic development projects or, whose Articles of Incorporation and/or By-Laws indicate that it has a focus in the area of economic development, and which has a tax exempt determination under Section 501(a) of the Internal Revenue Code of 1986 by reason of paragraph (3) or (4) of Section 501(c) of such code.

Such projects must conform to the purposes, requirements, and prohibitions applicable to those submitted under Part II, General Projects 1.0.

Applications for these set-aside funds which are not funded due to the limited amount of funds available will also be considered competitively within the larger pool of eligible applicants.

Part III—Application Requirements

A. Background Information

1. Availability of Funds and Grant Amounts

The Office of Community Services expects to award approximately \$5,000,000 by September 30, 1993 for new grants under this program.

A maximum of \$500,000 for the three-year project period will be awarded to selected organizations under this program in FY 93. OCS will award no less than 5 and no more than 10 grants

under this program. Due to the limited funds available under this program only one grant will be allowed to any organization.

2. Project and Budget Periods

Project and budget periods will be 36 months. Full funding of the three-year project and budget periods in FY 93 assures stability for these 36 months.

3. Mobilization of Resources

OCS will give favorable consideration in the review process to applicants who mobilize cash and/or third-party in-kind contributions for direct use in the project. (See Part IV, Criterion VI.)

4. Program Participants/Beneficiaries

Projects proposed for funding under this announcement must result in direct benefits to low-income people as defined in the most recent Annual Revision of Poverty Income Guidelines published by DHHS and individuals eligible to receive Aid to Families with Dependent Children under Part A of Title IV of the Social Security Act.

Attachment A to this announcement is an excerpt from the guidelines currently in effect. Annual revisions of these guidelines are normally published in the *Federal Register* in February or early March of each year. Grantees will be required to apply the most recent guidelines throughout the project period. These revised guidelines also may be obtained at public libraries, Congressional offices, or by writing the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402.

No other government agency or privately-defined poverty guidelines are applicable for the determination of low-income eligibility for this program.

5. Cooperative Partnership Agreement

A signed written agreement or letter of commitment between the applicant and the State IV-A agency must be submitted with the application in order to be reviewed and evaluated competitively. The agreement/letter must describe the cooperative relationship and include specific activities and/or actions that each of the entities proposes to carry out over the course of the grant period in support of the project. (Please review section IIA for additional specific information related to this agreement.)

6. Prohibition and Restrictions on the Use of Funds

The use of funds for new construction or the purchase of real property is prohibited. Costs incurred for rearrangement and alteration of facilities

required specifically for the grant program are allowable when specifically approved by ACF in writing.

If the applicant is proposing a project which will affect a property listed in, or eligible for inclusion in the National Register of Historic Places, it must identify this property in the narrative and explain how it has complied with the provisions of section 106 of the National Historic Preservation Act of 1966 as amended. If there is any question as to whether the property is listed in or eligible for inclusion in the National Register of Historic Places, the applicant should consult with the State Historic Preservation Officer. (See Attachment D: SF-424B, Item 13 for additional guidelines.) The applicant should contact OCS early in the development of its application for instructions regarding compliance with the Act and data required to be submitted to the Department of Health and Human Services. Failure to comply with the cited Act must result in the application being ineligible for funding consideration.

7. Multiple Submittals

Due to the limited number of grants which will be made under this program, only one proposal from an eligible applicant will be funded by OCS for either the general project fund or the community development corporation set-aside fund.

8. Third-Party Project Evaluation

Projects also must include an independent, methodologically sound evaluation of the effectiveness of the activities carried out with the grant in creating new jobs and business opportunities.

9. Economic Development Strategy

Applicants must include an economic development strategy in accordance with the legislative reference cited in Part II, Section A.

10 Maintenance of Effort

The application must include an assurance that activities funded under this program announcement are in addition to, and not in substitution for, activities previously carried on without Federal assistance.

Part IV—Application Review Criteria

Applications which pass the pre-rating review will be assessed and scored by reviewers. Each reviewer will give a numerical score for each application reviewed. These numerical scores will be supported by explanatory statements on a formal rating form describing major strengths and

weaknesses under each applicable criterion published in the announcement.

The in-depth assessment and review process will use the following criteria coupled with the specific requirements described in Part III. Scoring will be based on a total of 100 points.

(Note: the following review criteria reiterate the collection of information requirements contained in Part VI of this announcement. These requirements are approved under OMB Control Number 0970-0062 expiration 09-30-93.)

A. Criteria for Review and Assessment of Applications in Priority Areas 1.0 and 2.0

Criterion I: Organizational Experience in Program Area and Staff Responsibilities (Maximum: 10 points)

(i) *Organizational experience in program area.* Documentation provided indicates that projects previously undertaken have been relevant and cost-effective and have provided permanent benefits to the low-income population.

The organization has detailed competence in the specific program area and as a deliverer with expertise in the area of technical assistance. The applicant has demonstrated the ability to implement major activities in such areas as human development, business development, economic development or financial services; the ability to mobilize funds from sources such as the private sector (corporations, banks, etc.), foundations, the public sector, including State and local governments, or individuals; that it has a sound organizational structure and proven organizational capability; and an ability to develop and maintain a stable program in terms of business or job creation activities that will provide needed permanent jobs and/or business development opportunities.

(Note: The maximum number of points will be given only to those organizations with a demonstrated record of achievement in promoting job creation and enterprise opportunities for low-income people.)

(ii) *Staff skills, resources and responsibilities.* The application describes in brief resume form the experience and skills of the project director who is not only well qualified, but his/her professional capabilities are relevant to the successful implementation of the project. If the key staff person has not yet been identified, the application contains a comprehensive position description which indicates that the responsibilities to be assigned to the project director are relevant to the successful

implementation of the project. The assigned responsibilities of the staff are appropriate to the tasks identified for the project and sufficient time of senior staff will be budgeted to assume timely implementation and cost effective management of the project.

The applicant has included the minimum qualifications for the third-party evaluator (independent entity, i.e. an entity organizationally distinct from, and not under the control of the applicant). A third-party evaluator must have knowledge about and have experience in conducting process and outcome evaluations, evaluating issues in the job creation field, expansion of businesses and the creation of self-employment and small business opportunities for low-income neighborhoods and understands the complexity of the problems the target population faces. The competitive procurement regulations (45 CFR part 74, appendix G) apply to service contracts such as those for evaluators when the costs of such service will exceed \$5,000.

The applicant should include an adequate position description for the third-party evaluator.

The applicant has described the facilities and resources (i.e. space, equipment, etc.) that it has available to carry out the project.

Criterion II: Analysis of Need (Maximum: 10 points)

The applicant includes a description of the geographic area and population to be served as well as a discussion of the nature and extent of the problem to be solved. It should indicate what the unemployment rates are in the geographic areas to be served and (to the extent practicable) cites how the proposed businesses and subsequent jobs will impact on the nature and extent of the problem. It should also include documentation regarding the number and percentage of individuals receiving Aid to Families with Dependent Children and the total number of individuals which make up the population in the area where the project will operate.

Criterion III: Work Program (Maximum: 25 points)

The work plan and business plan(s), where appropriate, are both sound and feasible. If the applicant is proposing to use project funds to provide technical and/or financial assistance to a third-party private employer to develop or expand a pre-identified business, the application must include a complete business plan. An application that does not include a business plan where one

is appropriate may be disqualified and returned to the applicant.

The project is responsive to the needs identified in the Analysis of Need.

(i) *Work plan.* The work plan includes a hypothesis or hypotheses that is significant and that includes the key interventions and permits measurement of the extent to which the target population can achieve greater self-sufficiency as a result of its involvement in the project. The key interventions should include the types of technical and financial assistance to be provided the recipients, the level of effort, as well as other activities. If the technical and/or financial assistance is to be provided to pre-identified businesses that will be expanded or franchised, written commitments from the businesses are included with the application. The work program sets forth realistic quarterly time targets by which the various work tasks will be completed. Critical issues or potential problems that might impact negatively on the project are defined and the project objectives can be reasonably attained despite such potential problems. The application provides a description of the process evaluation which will culminate in the development of a policies and procedures manual.

(ii) *Business plan.* The business plan, where appropriate, is one of the major components that will be evaluated by OCS to determine the feasibility of a Jobs Opportunities project. It must be well prepared and address all the major issues noted herein.

Because the guidelines were written to cover a variety of possibilities, rigid adherence to them is not possible nor even desirable for all projects. For example, a plan for a service business would not require a discussion of manufacturing nor product design.

The business plan should include the following:

—*The Business and its Industry.* This section should describe the nature and history of the business if the proposal is an expansion of an existing business, including the following:

1. Products and services;
2. Market research and evaluation (show that the product or service has a substantial market and can achieve sales in the face of competition);
3. Marketing plan (including the estimated market share and sales)
4. Manufacturing and operations plan (describe the kind of facilities, plant location, space, capital equipment and labor force [part and/or full-time wage structure] that are

required to provide the company's product or service).

5. Critical risk and assumptions (include a description of the risks and critical assumptions relating to the industry, the venture, its personnel, the product's market appeal, and the timing and financing of the venture).
6. Community benefits (identify low-income individuals to be employed); and
7. A financial plan (In developing the financial plan, the following exhibits must be prepared for the first three years of the business' operation: (a) Profit and Loss Forecasts—for each year; (b) Cash Flow Projections—for each year; (c) pro forma balance sheets—for each year; (d) initial uses of project funds; and (e) any future capital requirements and sources.

(iii) *Facilities.* If the rearrangement or alteration of facilities will be required in implementing the project, the applicant has described and justified such changes.

Criterion IV: Significant and Beneficial Impact (Maximum: 25 points)

(i) *Quality of JOBS/business opportunities.* The proposed project is expected to produce permanent and measurable results that will reduce the incidence of poverty in the community. Expected results are quantifiable in terms of the creation of permanent, full-time jobs or business opportunities developed. In developing business opportunities and self-employment for low-income individuals the applicant proposes, at a minimum, to provide basic business planning and management concepts, and assistance in preparing a business plan and loan package. The application documents that:

- The business opportunities to be developed for eligible participants will contribute significantly to their progress toward self-sufficiency; and/or
- Jobs to be created for eligible participants will contribute significantly to their progress toward self-sufficiency; they provide, for example, wages that exceed the minimum wage, plus benefits such as health insurance, transportation, child care and career development opportunities.

(ii) *Cost-per-job.* During the project period the proposed project will create new, permanent jobs or business opportunities for low-income residents at a cost-per-job below \$15,000 in OCS funds, (e.g. cost per job is calculated by

dividing the total amount of grant funds requested (\$420,000) divided by the number of jobs to be created (60) equals the cost-per-job (\$7,000)). If any other calculations are used, please include your methodology in this section.

[Note: Except in those instances where independent reviewers identify extenuating circumstances related to business development activities, the maximum number of points will be given only to those applicants proposing cost-per-job created estimates of \$5,000 or less of OCS requested funds. Higher cost-per-job estimates will receive correspondingly fewer points.]

Criterion V: Third-Part Evaluation (Maximum: 10 points)

A plan for a methodological sound third-party (i.e. independent) evaluation of the demonstration project must be included in the application.

The Evaluation Plan:

- includes a specific working definition of "self-sufficiency" (consistent with the broad definition contained in Part I) that permits the measurement of incremental progress of eligible individuals and their families from dependency toward self-sufficiency;
- clearly defines the changes or benefits (outcomes) to be produced, the activities (interventions) that will produce the changes, and the measures of client progress toward self-sufficiency for which information will be collected (for example: Increases in income, decreases in public assistance payments);
- provides for the annual compilation of community-level data on the characteristics of the population in the project area, including percentage on public assistance, percentage below the poverty line, unemployment rate, business starts and failures, and major employers;
- provides for the conduct of a continuing process evaluation. This should include the periodic assessment of the following: Client characteristics, pertinent policies and procedures, staffing, cooperative partnerships with state and local agencies, use of other community resources, client outreach and recruitment, client service delivery, cost of services, and level of technical and financial assistance to employers. The types of data and information, measures and indicators to be used for the process evaluation, as well as the methods and timeframe for collecting and analyzing the required data should be indicated;
- provides for the completion of two interim evaluation reports and a final report. The final evaluation report will describe the program design and

any changes from the original workplan, outreach and recruitment results, interventions, and accomplishments. The measurement instruments, data collection procedures, and analysis techniques should be discussed, and the report should yield conclusions as to how well the program works and why. It should also discuss the program's potential for replication in other communities; and

—includes a realistic plan for disseminating the project findings to other interested organizations and public agencies.

Criterion VI: Public-Private Partnerships (Maximum: 15 points)

—The cooperative partnership arrangements are fully described and clearly relate to the objectives of the proposed project, and the activities include one or more of the mandatory or optional components of the State's JOBS program as described in Part II, Section A.

—The application documents that the applicant will mobilize from public and/or private sources cash and/or third-party in-kind contributions. Applications that document that the value of such contributions will be at least equal to the OCS funds requested, and demonstrate that the cooperative partnership arrangements clearly relate to the objectives of the proposed project, will receive the maximum number of points for this criterion. Lesser contributions will be given consideration based upon the value documented.

—Applicants should note that partnership relationships are not created via service delivery contracts; partners should be responsible for substantive project components or elements.

Criterion VII: Budget Appropriateness and Reasonableness (Maximum: 5 points)

Funds requested are commensurate with the level of effort necessary to accomplish the goals and objectives of the project.

The application includes a detailed budget break-down for each of the budget categories in the SF-424A. The applicant presents a reasonable administrative cost if an indirect cost rate has not been negotiated with the cognizant Federal agency (See Part VI, Section B, Line 6j).

The estimated cost to the government of the project also is reasonable in relation to the anticipated results.

Part V—Application Procedures

A. Availability of Forms

Attachments B, C and D contain all of the standard forms necessary for the application for awards under this OCS program. These attachments and Parts D and F of this announcement contain all of the instructions required for submittal of applications. These forms may be photocopied for the application.

Copies of the *Federal Register* containing this announcement are available at most local libraries and Congressional District Offices for reproduction. If copies are not available at these sources, they may be obtained by writing or telephoning the office listed under the section entitled **FOR FURTHER INFORMATION** at the beginning of this announcement.

The applicant must be aware that in signing and submitting the application for this award, it is certifying that it will comply with the Federal requirements concerning the drug-free workplace and debarment regulations set forth in Attachments E and F.

Part VII, Section A contains instructions for the project narrative.

B. Application Submission

The closing date for submission of applications is June 28, 1993.

1. Deadlines

Applications shall be considered as meeting the deadline if they are either:

a. Received on or before the deadline date at the Department of Health and Human Services, Administration for Children and Families, Division of Discretionary Grants, room 341-F-1, 200 Independence Avenue SW., Washington, DC 20201, or

b. Sent on or before the deadline date and received by the granting agency in time for them to be considered during the competitive review and evaluation process under Chapter 1-62 of the Health and Human Services Grants Administration Manual. (Applicants are cautioned to request a legibly dated U.S. Postal Service postmark or to obtain a legibly dated receipt from a commercial carrier or the U.S. Postal Service. Private metered postmarks are not acceptable as proof of timely mailing.)

2. Applications Submitted by Other Means

Applications which are not submitted in accordance with the above criteria shall be considered as meeting the deadline only if they are physically received before the close of business on or before the deadline date. Hand delivered applications will be accepted at the Department of Health and Human

Services, Administration for Children and Families, Division of Discretionary Grants, room 341-F-1, 200 Independence Avenue, SW., Washington, DC during the normal working hours of 8:30 a.m. to 5 p.m., Monday through Friday.

3. Late Applications

Applications which do not meet one of these criteria are considered late applications. The ACF Division of Discretionary Grants will notify each late applicant that its application will not be considered in this competition.

4. Extension of Deadline

The ACF Office of Community Services may extend the deadline for all applicants because of acts of God such as floods, hurricanes, etc. resulting in a disruption of the mails. However, if the granting agency does not extend the deadline for all applicants, it may not waive or extend the deadline for any applicant. Applicants are responsible to meet deadlines and are encouraged to submit applications as far in advance as possible to avoid unforeseen events which may inhibit their ability to submit an application on the closing date.

Applications once submitted are considered final and no additional materials will be accepted.

One signed original application and four copies should be submitted.

C. Intergovernmental Review

This program is covered under Executive Order 12372.

"Intergovernmental Review of Federal Programs," and 45 CFR part 100, "Intergovernmental Review of Department of Health and Human Services Programs and Activities." Under the Order, States may design their own processes for reviewing and commenting on proposed Federal assistance under covered programs.

All States and Territories except Alabama, Alaska, Idaho, Kansas, Louisiana, Minnesota, Nebraska, Pennsylvania, Oklahoma, Oregon, Virginia, Washington, American Samoa and Palau have elected to participate in the Executive Order process and have established Single Points of Contact (SPOCs).

Applicants from these fourteen jurisdictions need take no action regarding E.O. 12372. Applicants for projects to be administered by Federally-recognized Indian Tribes are also exempt from the requirements of E.O. 12372. Otherwise, applicants must submit any required material to the SPOCs as soon as possible to alert them of the prospective applications and

receive any necessary instructions, so that the ACF can obtain and review SPOC comments as part of the award process. It is imperative that the applicant submit all required materials, if any, to the SPOC and indicate the date of this submittal (or the date of contact if no submittal is required) on the Standard Form 424, item 16a.

Under 45 CFR 100.8(a)(2), a SPOC has 45 days from the application deadline date to comment on proposed new awards. SPOCs are encouraged to eliminate the submission of routine endorsements as official recommendations. Additionally, SPOCs are requested to clearly differentiate between mere advisory comments and those official State process recommendations which they intend to trigger the "accommodate or explain" rule under 45 CFR 100.10.

When comments are submitted directly to ACF, they should be addressed to: Department of Health and Human Services, Administration for Children and Families, Division of Discretionary Grants, 200 Independence Avenue SW., room 341-F-1, Washington, DC 20201.

A list of the Single Points of Contact for each State and Territory is included as Attachment G of this announcement.

D. Application Consideration of OCS Specific Requirements

Applications which meet the screening requirements in Part V item E below will be reviewed competitively. Such applications will be referred to reviewers for a numerical score and explanatory comments based solely on responsiveness to the guidelines and evaluation criteria published in this announcement.

Applications will be reviewed by persons outside of the OCS unit which will be directly responsible for programmatic management of the grant. The results of these reviews will assist the Director and OCS program staff in considering competing applications. Reviewers' scores will weigh heavily in funding decisions but will not be the only factors considered. Applications generally will be considered in order of the average scores assigned by reviewers. However, highly ranked applications are not guaranteed funding since other factors are taken into consideration including, but not limited to, the timely and proper completion of projects funded with OCS funds granted in the last five (5) years; comments of reviewers and government officials; staff evaluation and input; geographic distribution; previous program performance of applicants; compliance with grant terms under previous DHHS

grants; audit reports; investigative reports; and applicant's progress in resolving any final audit disallowances on previous OCS or other Federal agency grants.

OCS reserves the right to discuss applications with other Federal or non-Federal funding sources to ascertain the applicant's performance record.

E. Criteria for Screening Applicants

1. Initial Screening

All timely applicants will receive an acknowledgement with an assigned identification number. This number, along with any identification code, must be referenced in all subsequent communications concerning the application. If an acknowledgement is not received within three weeks after the deadline date, please notify ACF by telephone at (202) 690-8243.

All applications that meet the published deadline for submission will be screened to determine completeness and conformity to the requirements of this announcement. Only those applications meeting the following requirements will be reviewed and evaluated competitively. Others will be returned to the applicants with a notation that they were unacceptable.

a. The applications must contain a Standard Form 424 "Application for Federal Assistance" (SF-424), a budget (SF-424A), and signed "Assurances" (SF-424B) completed according to instructions published in Part VI and Attachments B, C, and D of this Program Announcement.

b. A project narrative must also accompany the standard forms.

c. The SF-424 and the SF-424B must be signed by an official of the organization applying for the grant who has authority to obligate the organization legally.

2. Pre-Rating Review

Applications which pass the initial screening will be forwarded to reviewers and/or OCS staff prior to the programmatic review to verify that the applications comply with this Program Announcement in the following areas:

a. *Eligibility:* Applicant meets the eligibility requirements described in Part I, Section B. Proof of non-profit status must be included in the Appendices to the Project Narrative (See Part VII, Section A, 11).

Applicants must also be aware that the applicant's legal name as required on the SF-424 (Item 5) must match that listed as corresponding to the Employer Identification Number (Item 6).

b. *Target populations:* The application clearly targets the specific outcomes and

benefits of the project to those types of low-income participants and beneficiaries described in Part III, Section A, Program Participants/Beneficiaries.

c. *Grant amount:* The amount of funds requested does not exceed the limits indicated in Part III, Section A., item 1.

d. *Cooperative partnership Agreement.* The application contains a written agreement or letter of commitment that includes, at a minimum, the activities cited in Part II, Section A. The agreement must be signed by an official of the agency responsible for administering the JOBS program in the area to be served.

e. *Third-party project evaluation.* A third-party project evaluation plan is included.

f. *Business plan.* If a third-party private employer is part of the proposed project, a complete business plan is included in the application.

An application will be disqualified from the competition and returned if it does not conform to all of the above requirements.

Part VI—Instructions for Completing Application Package

[Approved by the Office of Management and Budget under Control Number 0970-0062 date of expiration 09-30-93.]

The standard forms attached to this announcement shall be used to apply for funds under this program announcement.

It is suggested that you reproduce the SF-424 and SF-424A, and type your application on the copies. In order to assist applicants in correctly completing the SF-424, and SF-424A. Please prepare your application in accordance with the following:

A. SF-424—"Application for Federal Assistance"

Top of Page

Please enter the single priority area number under which the application is being submitted. An application should be submitted under only one priority area.

Item 1. For the purposes of this announcement, all projects are considered "Applications"; there are no "Pre-Applications."

Prepare your application in accordance with the standard instructions given in Attachments B and C corresponding to the forms, as well as the OCS specific instructions set forth below:

Item 2. "Date Submitted" and "Applicant Identifier"—Date application is submitted to ACF and

applicant's own internal control number, if applicable.

Item 3. "Date Received by State"—N/A

Item 4. "Date Received by Federal Agency"—Leave blank.

Items 5 and 6. The legal name of the applicant must match that listed as corresponding to the Employer Identification Number. Where the applicant is a previous Department of Health and Human Services grantee, enter the Central Registry System Employee Identification Number CRS/EIN) and the Payment Identifying Number, if one has been assigned, in the Block entitled "Federal Identifier" located at the top right hand corner of the form.

Item 7. If the applicant is a non-profit corporation, enter "N" in the box and specify "non-profit corporation" in the space marked "Other." Proof of non-profit status, such as IRS determination, Articles of Incorporation, or By-laws, must be included as an appendix to the project narrative.

Item 8. "Type of Application"—Please indicate the type of application.

Item 9. "Name of Federal Agency"—Enter DHHS-ACF/OCS.

Item 10. "The Catalog of Federal Domestic Assistance number for OCS programs covered under this announcement is 93.561. The title is "Job Opportunities for Low-Income Individuals Program (Demonstration Projects)"

Item 11. In addition to a brief descriptive title of the project, indicate for which priority area funds are being requested. The following letter designations must be used:

JO—General Project
JS—Community Development Corporation Set-Aside

Item 12. "Areas Affected by Project"—List only the largest unit or units affected, such as State, county or city.

Item 13. "Proposed Project"—Enter the desirable starting date for the project and the proposed completion date.

Item 14. "Congressional District of Applicant/Project"—Enter the number of the Congressional District where the applicant's principal office is located and the number of the Congressional district(s) where the project will be located.

Item 15a. For purposes of this Announcement, this amount should reflect the amount requested for the entire project period. This amount should be no greater than the maximum amount specified in the priority area description.

Item 15b-e. These items should reflect both cash and third-party, in-

kind contributions for the total project period.

Item 15f. N/A

Item 15g. Enter the sum of Items 15a-15e.

B. SF-424A—"Budget Information—Non-Construction Programs"

See Instructions accompanying this form as well as the instructions set forth below:

In completing these sections, the "Federal Funds" budget entries will relate to the requested OCS funds only, and "Non-Federal" will include mobilized funds from all other sources—applicant, state, local, and other. Federal funds other than requested OCS funding should be included in "Non-Federal" entries.

Sections A and D of SF-424A must contain entries for both Federal (OCS) and non-Federal (mobilized) funds for the total project period. Section B contains entries for Federal (OCS) funds only.

Section A—Budget Summary

Lines 1-4

Col. (a):

Line 1—Enter "Job Opportunities for Low-Income Individuals".

Col. (b):

Line 1—Catalog of Federal Domestic Assistance number is 93.561.

Col. (c) and (d):

Columns (c) and (d) are not relevant to this program and should not be completed.

Column (e)-(g)

For line 1, enter in columns (e), (f) and (g) the appropriate amounts needed to support the project for the entire project period. (Maximum \$500,000)

Line 5—Enter the figures from Line 1 for all columns completed (e), (f), and (g).

Section B—Budget Categories

Please Note: This information supersedes the instructions provided following SF-424A.

This section (B) should contain entries for OCS funds only.

Columns (1)–(5):

Column 1: Enter the first budget period of 12 months.

Column 2: Enter the second budget period of 12 months.

Column 3: Enter the third budget period of 12 months.

Column 4: Leave blank.

Column 5: Enter the total requirements for Federal funds by the Object Class Categories of this section. Allocability of costs are governed by the cost principles set forth in OMB Circular A-122 and 45 CFR part 74.

Budget estimates for national administrative costs must be supported

by adequate detail for the grants officer to perform a cost analysis and review. Adequately detailed calculations for each budget object class are those which reflect estimation methods, quantities, unit costs, salaries, and other similar quantitative detail sufficient for the calculation to be duplicated. For any additional object class categories included under the object class "other" identify the additional object class(es) and provide supporting calculations.

Supporting narratives and justifications are required for each budget category, with emphasis on unique/special initiatives large dollar amounts; local, regional, or other travels new positions; major equipment purchases and training programs.

A detailed itemized budget with a separate budget justification for each major item should be included as indicated below:

Personnel-line 6a. Enter the total costs of salaries and wages.

Justification: Identify the principal investigator or project director, if known. Specify by title or name the percentage of time allocated the project, the individual annual salaries, and the cost to the project of the organization's staff who will be working on the project. Do not include costs of consultants or personnel costs of delegate agencies or of specific project(s) or businesses to be financed by the applicant.

Fringe benefits-line 6b. Enter the total costs of fringe benefits unless treated as part of an approved indirect cost rate which is entered on line 6j.

Justification: Provide a breakdown of amounts and percentages that comprise fringe benefit costs, such as health insurance, FICA, retirement insurance, taxes, etc.

Travel-line 6c. Enter total costs of all travel by employees of the project. Do not enter costs for consultant's travel.

Justification: Include the total number of traveler(s), total number of trips, destinations, number of days, transportation costs and subsistence allowances. Travel costs to attend two national workshops in Washington, DC by the project director should be included.

Equipment-Line 6d. Enter the total costs of all non-expendable personal property to be acquired by the project. "Non-expendable personal property" means tangible personal property having an acquisition cost per unit of \$500 or more for non-profit organizations and \$5,000 or more for public organizations and having a useful life of one year.

Justification: Only equipment required to conduct the project may be purchased with Federal funds. The

applicant organization or its subgrantees must not have such equipment, or a reasonable facsimile, available for use in the project. The justification also must contain plans for future use or disposal of the equipment after the project ends. An applicant may use its own definition of non-expendable personal property, provided that such a definition would at least include all tangible personal property as defined above. (See Line 21 for additional requirements).

Supplies-line 6e. Enter the total costs of all tangible personal property (supplies) other than that included on line 6d.

Justification: Specify general categories of supplies and their costs.

Contractual-line 6f. Enter the total costs of all contracts, including (1) the estimated cost of the third-party evaluation contract; travel costs for the chief evaluator to attend two national workshops in Washington, DC should be included; (2) procurement contracts (except those which belong on other lines such as equipment, supplies, etc.) and (3) contracts with secondary recipient organizations including delegate agencies and specific project(s) or businesses to be financed by the applicant.

Justification: Attach a list of contractors, indicating the names of the organizations, the purposes of the contracts, the estimated dollar amounts, and selection process of the awards as part of the budget justification. Also provide back-up documentation identifying the name of contractor, purpose of contract, and major cost elements.

Note: Whenever the applicant/grantee intends to delegate part of the program to another agency, the applicant/grantee must submit Sections A and B of this Form SF-424A, completed for each delegate agency by agency title, along with the required supporting information referenced in the applicable instructions. The total costs of all such agencies will be part of the amount shown on Line 6f. Provide draft Request for Proposal in accordance with 45 CFR part 74, appendix H. Applicants who anticipate evaluation procurements that will exceed \$5,000 and are requesting an award without competition should include a sole source justification in the proposal which at a minimum should include the basis for contractor's selection, a description of the survey conducted of other service providers, justification for lack of competition when competitive bids or offers are not obtained and basis for award cost or price.

(Note: Previous or past experience with a contractor is not sufficient justification for sole source.)

For successful applicants, the Notice of Grant Award will cite under Remarks, item 18, approval of this action. Also

include any contracts with organizations for the provision of technical assistance.

Construction-line 6g. Not applicable.

Other-line 6h. Enter the total of all other costs. Such costs, where applicable, may include but are not limited to insurance, food, medical and dental costs (noncontractual), fees and travel paid directly to individual consultants, space and equipment rentals, printing and publication, computer use, training costs, including tuition and stipends, training service costs including wage payments to individuals and supportive service payments, and staff development costs.

Total direct charges-lines 6i. Show the total of Lines 6a through 6h.

Indirect charges-line 6j. Enter the total amount of indirect costs. This line should be used only when the applicant currently has an indirect cost rate approved by the Department of Health and Human Services or another cognizant Federal agency. With the exception of local governments, applicants should enclose a copy of the current rate agreement if it was negotiated with a cognizant Federal agency other than the Department of Health and Human Services. If the applicant organization is in the process of initially developing or renegotiating a rate, it should immediately upon notification that an award will be made, develop a tentative indirect cost rate proposal based on its most recently completed fiscal year in accordance with the principles set forth in the pertinent DHHS Guide for Establishing Indirect Cost Rates, and submit it to the appropriate DHHS Regional Office. Applicants awaiting approval of their indirect cost proposals may also request indirect costs.

It should be noted that when an indirect cost rate is requested, those costs included in the indirect cost pool should not be also charged as direct costs to the grant.

Totals-line 6k. Enter the total amounts of Lines 6i and 6j.

Program income-line 7. Enter the estimated amount of income, if any, expected to be generated from this project. Separately show expected program income generated from OCS support and income generated from other mobilized funds. Do not add or subtract this amount from the budget total. Show the nature and source of income in the program narrative statement.

Justification: Describe the nature, source and anticipated use of program income in the Program Narrative Statement. Column 5: Carry totals from Column 1 to Column 5 for all line items.

Section C—Non-Federal Resources

This section is to record the amounts of "non-Federal" resources that will be used to support the project. "Non-Federal" resources mean those other than OCS funds. Therefore, mobilized funds from other Federal programs should be entered on these lines. Provide a brief listing of the non-Federal resources on a separate sheet and describe whether it is a grantee-incurred cost or a third-party in-kind contribution. The firm commitment of these resources must be documented and submitted with the application in order to be given credit in the Public-Private Partnerships criterion.

Except in unusual situations, this documentation must be in the form of letters of commitment from the organization(s)/individuals from which funds will be received.

Justification: Describe third-party, in-kind contributions, if included.

Grant program-line 8.

Column (a): Enter the project title.

Column (b): Enter the amount of contributions to be made by the applicant to the project.

Column (c): Enter the State contribution. If the applicant is a State agency, enter the non-Federal funds to be contributed by the State other than the applicant.

Column (d): Enter the amount of cash and third-party in-kind contributions to be made from all other sources.

Column (e): Enter the total of columns (b), (c), and (d).

Grant program-lines 9, 10, and 11 should be left blank.

Grant program-line 12. Carry the total of each column of Line 8, (b) through (e). The amount in Column (e) should be equal to the amount on Section A, Line 5, column (f).

Section D—Forecasted Cash Needs

Federal-line 13. Enter the amount of Federal (OCS) cash needed for this grant, by quarter, during the first 12 month budget period.

Non federal-line 14. Enter the amount of cash from all other sources needed by quarter during the first year.

Totals-line 15. Enter the total of Lines 13 and 14.

Section E—Budget Estimates of Federal Funds Needed for Balance of Project(s)

Not applicable.

Section F—Other Budget Information

Direct charges-line 21. Use this space and continuation sheets as necessary to fully explain and justify the major items included in the budget categories shown in Section B. Include sufficient detail to facilitate determination of allowability,

relevance to the project, and cost benefits. Particular attention must be given to the explanation of any requested direct cost budget item which requires explicit approval by the Federal agency. Budget items which require identification and justification shall include, but not be limited to, the following:

A. Salary amounts and percentage of time worked for those key individuals who are identified in the project narrative;

B. Any foreign travel;

C. A list of all equipment and estimated cost of each item to be purchased wholly or in part with grant funds which meet the definition of nonexpendable personal property provided on Line 6d, Section B. Need for equipment must be supported in program narrative;

D. Contractual: major items or groups of smaller items; and

E. Other: group into major categories all costs for consultants, local transportation, space, rental, training allowances, staff training, computer equipment, etc. Provide a complete breakdown of all costs that make up this category.

Indirect charges—line 22. Enter the type of HHS or other cognizant Federal agency approved indirect cost rate (provisional, predetermined, final or fixed) that will be in effect during the funding period, the estimated amount of the base to which the rate is applied and the total indirect expense. Also, enter the date the rate was approved and attach a copy of the rate agreement.

Remarks—line 23. Provide any other explanations and continuation sheets required or deemed necessary to justify or explain the budget information.

C. SF-424B "Assurances-Non-Construction"

All applicants must fill out, sign, date and return the "Assurances" with the application.

Part VII—Contents of Application and Receipt Process

A. Contents of Application

Each application submission should include a signed original and four additional copies of the application. Each application should include the following in the order presented:

1. Table of Contents.

2. Completed Standard Form 424 which has been signed by an Official of the organization applying for the grant who has authority to obligate the organization legally.

[Note: The original SF-424 must bear the original signature of the authorizing representative of the applicant organization]

3. "Budget Information—Non-Construction Programs" (SF-424A).

4. A narrative budget justification for each object class category required under Section B, SF-424A.

5. Filled out signed, and dated "Assurance—Non-Construction Programs" (SF-424B).

6. By signing and submitting this application, the applicant is certifying that it will comply with the Federal requirements concerning debarment regulations set forth in attachments E and F.

7. Restrictions on Lobbying, Certification for Contracts, Grants, Loans, and Cooperative Agreements: fill out, sign and date form found at Attachment H.

8. Disclosure of Lobbying Activities, SF-LLL: Fill out, sign, and date form found at Attachment H, if appropriate.

9. An Executive Summary—not to exceed 300 words.

10. A Project Narrative consisting of the following elements preceded by a consecutively numbered Table of Contents that will describe the project in the following order:

- (i) Eligibility Confirmation
- (ii) Organizational Experience and Staff Responsibilities
- (iii) Analysis of Need
- (iv) Project Design/Work Program
- (v) Business Plan (If appropriate)
- (vi) Third-Party Evaluation
- (vii) Cooperative Partnership Agreement
- (viii) Budget Appropriateness and Reasonableness

11. Appendices, including proof of non-profit status; proof that the organization is a community development corporation, if applying under the CDC Set-aside; commitments from officials of businesses that will be expanded or from franchisees, where applicable; Maintenance of Effort Certification and resumes.

The total number of pages for the entire application package, excluding Appendices, should not exceed 50 pages. Pages should be numbered sequentially throughout, excluding Appendices, beginning with the SF-424 as Page 1.

Applications must be uniform in composition since OCS may find it necessary to duplicate them for review purposes. Therefore, applications must be submitted on white 8½ x 11 inch paper only. They must not include colored, oversized or folded materials. Do not include organizational brochures or other promotional materials, slides, films, clips, etc. in the proposal. They will be discarded if included. The applications should be two-holed punched at the top center and fastened

separately with a compressor slide paper fastener, or a binder clip. The submission of bound applications, or applications enclosed in binders, is specifically discouraged.

Attachment K provides a checklist to applicants in preparing a complete application package.

B. Acknowledgment of Receipt

Applicants who meet the initial screening criteria outlined in part V, section E, 1, will receive an acknowledgment postcard with an assigned identification number. Applicants are requested to supply a self-addressed mailing label with their application which can be attached to this acknowledgment postcard. This number and the program letter code must be referred to in all subsequent communication with OCS concerning the application. If an acknowledgment is not received within three weeks after the deadline date, please notify ACF by telephone (202) 690-8243.

Part VIII—Post Award Information and Reporting Requirements

Following approval of the applications selected for funding, notice of project approval and authority to draw down project funds will be made in writing. The official award document is the Notice of Grant Award which provides the amount of Federal funds approved for use in the project, the project and budget period for which support is provided, the terms and conditions of the award, and the total project period for which support is contemplated.

Project directors and chief evaluators will be required to attend two national evaluation workshops in Washington, DC. A program planning and evaluation workshop will be scheduled shortly after the effective date of the grant. They also will be required to attend, as presenters, the final evaluation workshop on utilization and dissemination to be held at the end of the project period.

Grantees will be required to submit quarterly progress and financial reports (SF 269) as well as a final progress and financial report within 90 days of the expiration of the grant. Interim evaluation reports, along with a written policies and procedures manual based on the findings of the process evaluation, will be due 30 days after the first twelve months, and the second interim evaluation 30 days after the second twelve months, and a final evaluation report will be due 180 days after the expiration of the grant. This final report will cover 36 months of activities related to project participants.

Grantees are subject to the audit requirements in 45 CFR parts 74 (non-profit organization) and OMB Circular A-133.

Section 319 of Public Law 101-121, signed into law on October 23, 1989, imposes new prohibitions and requirements for disclosure and certification related to lobbying on recipients of Federal contracts, grants, cooperative agreements, and loans. It provides limited exemptions for Indian tribes and tribal organizations. Current and prospective recipients (and their subtier contractors and/or grantees) are prohibited from using appropriated funds for lobbying Congress or any Federal agency in connection with the award of a contract, grant, cooperative agreement or loan. In addition, for each award action in excess of \$100,000 (or \$150,000 for loans) the law requires recipients and their subtier contractors and/or subgrantees (1) to certify that they have neither used nor will use any appropriated funds for payment to lobbyists, (2) to submit a declaration setting forth whether payments to lobbyists have been or will be made out of nonappropriated funds and, if so, the name, address, payment details, and purpose of any agreements with such lobbyists whom recipients or their subtier contractors or subgrantees will pay with the nonappropriated funds and (3) to file quarterly up-dates about the use of lobbyists if an event occurs that materially affects the accuracy of the information submitted by way of declaration and certification. The law establishes civil penalties for

noncompliance and is effective with respect to contracts, grants, cooperative agreements and loans entered into or made on or after December 23, 1989. See Attachment H for certification and disclosure forms to be submitted with the applications for this program.

Attachment I indicates the regulations which apply to all applicants/grantees under the Discretionary Grants Program.

Dated: April 9, 1993.

Jacqueline G. Lemire,

Acting Director, Office of Community Services.

ATTACHMENT A—1993 POVERTY INCOME GUIDELINES FOR ALL STATES (EXCEPT ALASKA AND HAWAII) AND THE DISTRICT OF COLUMBIA

Size of family unit	Poverty guideline
1	\$6,970
2	9,430
3	11,890
4	14,350
5	16,810
6	19,270
7	21,730
8	24,190

For family units with more than 8 members, add \$2,460 for each additional member.

POVERTY INCOME GUIDELINES FOR ALASKA

Size of family unit	Poverty guideline
1	\$8,700
2	11,780
3	14,860
4	17,940
5	21,020
6	24,100
7	27,180
8	30,260

For family units with more than 8 members, add \$3,080 for each additional member.

POVERTY INCOME GUIDELINES FOR HAWAII

Size of family unit	Poverty guideline
1	\$8,040
2	10,860
3	13,680
4	16,500
5	19,320
6	22,140
7	24,960
8	27,780

For family units with more than 8 members, add \$2,820 for each additional member.

BILLING CODE 4184-01-M

Attachment B

OMB Approval No. 0348-0043

**APPLICATION FOR
FEDERAL ASSISTANCE**

1. TYPE OF SUBMISSION: Application ☐ Construction ☐ Non-Construction Preapplication ☐ Construction ☐ Non-Construction		2. DATE SUBMITTED	Applicant Identifier																												
3. DATE RECEIVED BY STATE		State Application Identifier																													
4. DATE RECEIVED BY FEDERAL AGENCY		Federal Identifier																													
5. APPLICANT INFORMATION																															
Legal Name:		Organizational Unit																													
Address (give city, county, state, and zip code)		Name and telephone number of the person to be contacted on matters involving this application (give area code)																													
6. EMPLOYER IDENTIFICATION NUMBER (EIN): 		7. TYPE OF APPLICANT: (enter appropriate letter in box) ☐ A. State B. County C. Municipal D. Township E. Interstate F. Intermunicipal G. Special District H. Independent School Dist. I. State Controlled Institution of Higher Learning J. Private University K. Indian Tribe L. Individual M. Profit Organization N. Other (Specify) _____																													
8. TYPE OF APPLICATION: ☐ New ☐ Continuation ☐ Revision If Revision, enter appropriate letter(s) in box(es): ☐ ☐ A. Increase Award B. Decrease Award C. Increase Duration D. Decrease Duration Other (specify): _____		9. NAME OF FEDERAL AGENCY:																													
10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER: 		11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT:																													
12. AREAS AFFECTED BY PROJECT (cities, counties, states, etc.):																															
13. PROPOSED PROJECT: Start Date Ending Date		14. CONGRESSIONAL DISTRICTS OF: a. Applicant b. Project																													
15. ESTIMATED FUNDING: <table border="1" style="width: 100%; border-collapse: collapse; font-size: x-small;"> <tr> <td style="width: 30%;">a. Federal</td> <td style="width: 10%;">\$</td> <td style="width: 10%;"></td> <td style="width: 10%;">.00</td> </tr> <tr> <td>b. Applicant</td> <td>\$</td> <td></td> <td>.00</td> </tr> <tr> <td>c. State</td> <td>\$</td> <td></td> <td>.00</td> </tr> <tr> <td>d. Local</td> <td>\$</td> <td></td> <td>.00</td> </tr> <tr> <td>e. Other</td> <td>\$</td> <td></td> <td>.00</td> </tr> <tr> <td>f. Program Income</td> <td>\$</td> <td></td> <td>.00</td> </tr> <tr> <td>g. TOTAL</td> <td>\$</td> <td></td> <td>.00</td> </tr> </table>		a. Federal	\$		.00	b. Applicant	\$		.00	c. State	\$		.00	d. Local	\$		.00	e. Other	\$		.00	f. Program Income	\$		.00	g. TOTAL	\$		.00	16. IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS? a. YES THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON DATE _____ b. NO ☐ PROGRAM IS NOT COVERED BY E.O. 12372 ☐ OR PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW	
a. Federal	\$		.00																												
b. Applicant	\$		.00																												
c. State	\$		.00																												
d. Local	\$		.00																												
e. Other	\$		.00																												
f. Program Income	\$		.00																												
g. TOTAL	\$		.00																												
17. IS THE APPLICANT DELINQUENT ON ANY FEDERAL DEBT? ☐ Yes If "Yes," attach an explanation. ☐ No																															
18. TO THE BEST OF MY KNOWLEDGE AND BELIEF, ALL DATA IN THIS APPLICATION/PREAPPLICATION ARE TRUE AND CORRECT. THE DOCUMENT HAS BEEN DULY AUTHORIZED BY THE GOVERNING BODY OF THE APPLICANT AND THE APPLICANT WILL COMPLY WITH THE ATTACHED ASSURANCES IF THE ASSISTANCE IS AWARDED																															
a. Typed Name of Authorized Representative		b. Title	c. Telephone number																												
d. Signature of Authorized Representative		e. Date Signed																													

Previous Editions Not Usable

Standard Form 424 (REV 4-88)
Prescribed by OMB Circular A-102

Authorized for Local Reproduction

BILLING CODE 4184-01-C

Instructions for the SF 424

This is a standard form used by applicants as a required facesheet for preapplications and applications submitted for Federal assistance. It will be used by Federal agencies to obtain applicant certification that States which have established a review and comment procedure in response to Executive Order 12372 and have selected the program to be included in their process, have been given an opportunity to review the applicant's submission.

Item and Entry:

1. Self-explanatory.
2. Date application submitted to Federal agency (or State if applicable) & applicant's control number (if applicable).
3. State use only (if applicable).
4. If this application is to continue or revise an existing award, enter present Federal identifier number. If for a new project, leave blank.
5. Legal name of applicant, name of primary organizational unit which will undertake the assistance activity, complete address of the applicant, and name and telephone number of the person to contact on matters related to this application.
6. Enter Employer Identification Number (EIN) as assigned by the Internal Revenue Service.
7. Enter the appropriate letter in the space provided.
8. Check appropriate box and enter appropriate letter(s) in the space(s) provided:
 - "New" means a new assistance award.
 - "Continuation" means an extension for an additional funding/budget period for a project with a projected completion date.
 - "Revision" means any change in the Federal Government's financial obligation or contingent liability from an existing obligation.
9. Name of Federal agency from which assistance is being requested with this application.
10. Use the Catalog of Federal Domestic Assistance number and title of the program under which assistance is requested.
11. Enter a brief descriptive title of the project. If more than one program is involved, you should append an explanation on a separate sheet. If appropriate (e.g., construction or real property projects), attach a map showing project location. For preapplications, use a separate sheet to provide a summary description of this project.
12. List only the largest political entities affected (e.g., State, counties, cities).
13. Self-explanatory.
14. List the applicant's Congressional District and any District(s) affected by the program or project.
15. Amount requested or to be contributed during the first funding/budget period by

each contributor. Value of in-kind contributions should be included on appropriate lines as applicable. If the action will result in a dollar change to an existing award, indicate *only* the amount of the change. For decreases, enclose the amounts in parentheses. If both basic and supplemental amounts are included, show breakdown on an attached sheet. For multiple program funding, use totals and show breakdown using same categories as item 15.

16. Applicants should contact the State Single Point of Contact (SPOC) for Federal Executive Order 12372 to determine whether the application is subject to the State intergovernmental review process.

17. This question applies to the applicant organization, not the person who signs as the authorized representative. Categories of debt include delinquent audit disallowances, loans and taxes.

18. To be signed by the authorized representative of the applicant. A copy of the governing body's authorization for you to sign this application as official representative must be on file in the applicant's office. (Certain Federal agencies may require that this authorization be submitted as part of the application.)

BILLING CODE 4184-01-M

Attachment C

OMB Approval No. 0348-0044

BUDGET INFORMATION — Non-Construction Programs

SECTION A — BUDGET SUMMARY

Grant Program Function or Activity (a)	Catalog of Federal Domestic Assistance Number (b)	Estimated Unobligated Funds		New or Revised Budget		
		Federal (c)	Non-Federal (d)	Federal (e)	Non-Federal (f)	Total (g)
1.		\$	\$	\$	\$	\$
2.						
3.						
4.						
5. TOTALS		\$	\$	\$	\$	\$

SECTION B — BUDGET CATEGORIES

Object Class Categories	GRANT PROGRAM, FUNCTION OR ACTIVITY					Total (5)
	(1)	(2)	(3)	(4)		
a. Personnel	\$	\$	\$	\$		\$
b. Fringe Benefits						
c. Travel						
d. Equipment						
e. Supplies						
f. Contractual						
g. Construction						
h. Other						
i. Total Direct Charges (sum of 6a - 6h)						
j. Indirect Charges						
k. TOTALS (sum of 6i and 6j)	\$	\$	\$	\$	\$	\$
7. Program Income	\$	\$	\$	\$	\$	\$

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Prescribed by OMB Circular A 102

SECTION C - NON-FEDERAL RESOURCES					
(a) Grant Program	(b) Applicant	(c) State	(d) Other Sources	(e) TOTALS	
8.	\$	\$	\$	\$	
9.					
10.					
11.					
12. TOTALS (sum of lines 8 and 11)	\$	\$	\$	\$	
SECTION D - FORECASTED CASH NEEDS					
	Total for 1st Year	1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
	\$	\$	\$	\$	\$
13. Federal		\$	\$	\$	\$
14. Nonfederal					
15. TOTAL (sum of lines 13 and 14)	\$	\$	\$	\$	\$
SECTION E - BUDGET ESTIMATES OF FEDERAL FUNDS NEEDED FOR BALANCE OF THE PROJECT					
(a) Grant Program	FUTURE FUNDING PERIODS (Years)				(e) Fourth
	(b) First	(c) Second	(d) Third		
16.	\$	\$	\$	\$	\$
17.					
18.					
19.					
20. TOTALS (sum of lines 16-19)	\$	\$	\$	\$	\$
SECTION F - OTHER BUDGET INFORMATION (Attach additional Sheets if Necessary)					
21. Direct Charges:	22. Indirect Charges:				
23. Remarks					

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Instructions for the SF-424A**General Instructions**

This form is designed so that application can be made for funds from one or more grant programs. In preparing the budget, adhere to any existing Federal grantor agency guidelines which prescribe how and whether budgeted amounts should be separately shown for different functions or activities within the program. For some programs, grantor agencies may require budgets to be separately shown by function or activity. For other programs, grantor agencies may require a breakdown by function or activity. Sections A, B, C, and D should include budget estimates for the whole project except when applying for assistance which requires Federal authorization in annual or other funding period increments. In the latter case, Sections A, B, C, and D should provide the budget for the first budget period (usually a year) and Section E should present the need for Federal assistance in the subsequent budget periods. All applications should contain a breakdown by the object class categories shown in Lines a-k of Section B.

Section A. Budget Summary—Lines 1–4, Columns (a) and (b)

For applications pertaining to a single Federal grant program (Federal Domestic Assistance Catalog number) and not requiring a functional or activity breakdown, enter on Line 1 under Column (a) the catalog program title and the catalog number in Column (b).

For applications pertaining to a single program requiring budget amounts by multiple functions or activities, enter the name of each activity or function on each line in Column (a), and enter the catalog number in Column (b). For applications pertaining to multiple programs where none of the programs require a breakdown by function or activity, enter the catalog program title on each line in Column (a) and the respective catalog number on each line in Column (b).

For applications pertaining to multiple programs where one or more programs require a breakdown by function or activity, prepare a separate sheet for each program requiring the breakdown. Additional sheets should be used when one form does not provide adequate space for all breakdown of data required. However, when more than one sheet is used, the first page should provide the summary totals by programs.

Lines 1–4, Columns (c) Through (g)

For new applicants, leave Columns (c) and (d) blank. For each line entry in Columns (a) and (b), enter in Columns (e), (f), and (g) the appropriate amounts of funds needed to support the project for the first funding period (usually a year).

For continuing grant program applications, submit these forms before the end of each funding period as required by the grantor agency. Enter in Columns (c) and (d) the estimated amounts of funds which will remain unobligated at the end of the grant funding period only if the Federal grantor agency instructions provide for this. Otherwise, leave these columns blank. Enter in Columns (e) and (f) the amounts of funds needed for the upcoming period. The

amount(s) in Column (g) should be the sum of amounts in Columns (e) and (f).

For supplemental grants and changes to existing grants, do not use Columns (c) and (d). Enter in Column (e) the amount of the increase or decrease of Federal funds and enter in Column (f) the amount of the increase or decrease of non-Federal funds. In Column (g) enter the new total budgeted amount (Federal and non-Federal) which includes the total previous authorized budgeted amounts plus or minus, as appropriate, the amounts shown in Columns (e) and (f). The amount(s) in Column (g) should not equal the sum of amounts in Columns (e) and (f).

Line 5—Show the totals for all columns used.

Section B. Budget Categories

In the column headings (1) through (4), enter the titles of the same programs, functions, and activities shown on Lines 1–4, Column (a), Section A. When additional sheets are prepared for Section A, provide similar column headings on each sheet. For each program, function or activity, fill in the total requirements for funds (both Federal and non-Federal) by object class categories.

Lines 6a–1—Show the totals of Lines 6a to 6h in each column.

Line 6j—Show the amount of indirect cost.

Line 6k—Enter the total of amounts on Lines 6i and 6j. For all applications for new grants and continuation grants the total amount in Column (5), Line 6k, should be the same as the total amount shown in Section A, Column (g), Line 5. For supplemental grants and changes to grants, the total amount of the increase or decrease as shown in Columns (1)–(4), Line 6k should be the same as the sum of the amounts in Section A, Columns (e) and (f) on Line 5.

Line 7—Enter the estimated amount of income, if any, expected to be generated from this project. Do not add or subtract this amount from the total project amount. Show under the program narrative statement the nature and source of income. The estimated amount of program income may be considered by the federal grantor agency in determining the total amount of the grant.

Section C. Non-Federal-Resources

Lines 8–11—Enter amounts of non-Federal resources that will be used on the grant. If in-kind contributions are included, provide a brief explanation on a separate sheet.

Column (a)—Enter the program titles identical to Column (a), Section A. A breakdown by function or activity is not necessary.

Column (b)—Enter the contribution to be made by the applicant.

Column (c)—Enter the amount of the State's cash and in-kind contribution if the applicant is not a State or State agency. Applicants which are a State or State agencies should leave this column blank.

Column (d)—Enter the amount of cash and in-kind contributions to be made from all other sources.

Column (e)—Enter totals of Columns (b), (c), and (d).

Line 12—Enter the total for each of Columns (b)–(e). The amount in Column (e) should be equal to the amount on Line 5, Column (f), Section A.

Section D. Forecasted Cash Needs

Line 13—Enter the amount of cash needed by quarter from the grantor agency during the first year.

Line 14—Enter the amount of cash from all other sources needed by quarter during the first year.

Line 15—Enter the total of amounts on Lines 13 and 14.

Section E. Budget Estimates of Federal Funds Needed for Balance of the Project

Lines 16–19—Enter in Column (a) the same grant program titles shown in Column (a), Section A. A breakdown by function or activity is not necessary. For new applications and continuation grant applications, enter in the proper columns amounts of Federal funds which will be needed to complete the program or project over the succeeding funding periods (usually in years). This section need not be completed for revisions (amendments, changes, or supplements) to funds for the current year of existing grants.

If more than four lines are needed to list the program titles, submit additional schedules as necessary.

Line 20—Enter the total for each of the Columns (b)–(e). When additional schedules are prepared for this Section, annotate accordingly and show the overall totals on this line.

Section F. Other Budget Information

Line 21—Use this space to explain amounts for individual direct object-class costs categories that may appear to be out of the ordinary or to explain the details as required by the Federal grantor agency.

Line 22—Enter the type of indirect rate (provisional, predetermined, final or fixed) that will be in effect during the funding period, the estimated amount of the base to which the rate is applied, and the total indirect expense.

Line 23—Provide any other explanations or comments deemed necessary.

Attachment D**Assurances—Non-Construction Programs**

Note: Certain of these assurances may not be applicable to your project or program. If you have questions, please contact the awarding agency. Further, certain Federal awarding agencies may require applicants to certify to additional assurances. If such is the case, you will be notified.

As the duly authorized representative of the applicant I certify that the applicant:

1. Has the legal authority to apply for Federal assistance, and the institutional, managerial and financial capability (including funds sufficient to pay the non-Federal share of project costs) to ensure proper planning, management and completion of the project described in this application.

2. Will give the awarding agency, the Comptroller General of the United States, and if appropriate, the State, through any authorized representative, access to and the right to examine all records, books, papers, or documents related to the award; and will establish a proper accounting system in accordance with generally accepted accounting standards or agency directives.

3. Will establish safeguards to prohibit employees from using their positions for a purpose that constitutes or presents the appearance of personal or organizational conflict of interest, or personal gain.

4. Will initiate and complete the work within the applicable time frame after receipt of approval of the awarding agency.

5. Will comply with the Intergovernmental Personnel Act of 1970 (42 U.S.C. §§ 4728-4763) relating to prescribed standards for merit systems for programs funded under one of the nineteen statutes or regulations specified in Appendix A of OPM's Standards for a Merit System of Personnel Administration (5 C.F.R. 900, Subpart F).

6. Will comply with all Federal statutes relating to nondiscrimination. These include but are not limited to: (a) Title VI of the Civil Rights Act of 1964 (P.L. 88-352) which prohibits discrimination on the basis of race, color or national origin; (b) Title IX of the Education Amendments of 1972, as amended (20 U.S.C. §§ 1681-1683, and 1685-1686), which prohibits discrimination on the basis of sex; (c) Section 504 of the Rehabilitation Act of 1973, as amended (29 U.S.C. § 794), which prohibits discrimination on the basis of handicaps; (d) the Age Discrimination Act of 1975, as amended (42 U.S.C. §§ 6101-6107), which prohibits discrimination on the basis of age; (e) the Drug Abuse Office and Treatment Act of 1972 (P.L. 92-255), as amended, relating to nondiscrimination on the basis of drug abuse; (f) the Comprehensive Alcohol Abuse and Alcoholism Prevention, Treatment and Rehabilitation Act of 1970 (P.L. 91-616), as amended, relating to nondiscrimination on the basis of alcohol abuse or alcoholism; (g) §§ 523 and 527 of the Public Health Service Act of 1912 (42 U.S.C. 290 dd-3 and 290 ee-3), as amended, relating to confidentiality of alcohol and drug abuse patient records; (h) Title VIII of the Civil Rights Act of 1968 (42 U.S.C. § 3601 et seq.), as amended, relating to nondiscrimination in the sale, rental or financing of housing; (i) any other nondiscrimination provisions in the specific statute(s) under which application for Federal assistance is being made; and (j) the requirements of any other nondiscrimination statute(s) which may apply to the application.

7. Will comply, or has already complied, with the requirements of Titles II and III of the Uniform Relocation Assistance and Real Property Acquisition Policies Act of 1970 (P.L. 91-646) which provide for fair and equitable treatment of persons displaced or whose property is acquired as a result of Federal or federally assisted programs. These requirements apply to all interests in real property acquired for project purposes regardless of Federal participation in purchases.

8. Will comply with the provisions of the Hatch Act (5 U.S.C. §§ 1501-1508 and 7324-7328) which limit the political activities of employees whose principal employment activities are funded in whole or in part with Federal funds.

9. Will comply, as applicable, with the provisions of the Davis-Bacon Act (40 U.S.C. §§ 276a to 276a-7), the Copeland Act (40 U.S.C. § 276c and 18 U.S.C. §§ 874), and the Contract Work Hours and Safety Standards Act (40 U.S.C. §§ 327-333), regarding labor standards for federally assisted construction subagreements.

10. Will comply, if applicable, with flood insurance purchase requirements of Section 102(a) of the Flood Disaster Protection Act of 1973 (P.L. 93-234) which requires recipients in a special flood hazard area to participate in the program and to purchase flood insurance if the total cost of insurable construction and acquisition is \$10,000 or more.

11. Will comply with environmental standards which may be prescribed pursuant to the following: (a) institution of environmental quality control measures under the National Environmental Policy Act of 1969 (P.L. 91-190) and Executive Order (EO) 11514; (b) notification and violating facilities pursuant to EO 11738; (c) protection of wetlands pursuant to EO 11990; (d) evaluation of flood hazards in floodplains in accordance with EO 11988; (e) assurance of project consistency with the approved State management program developed under the Coastal Zone Management Act of 1972 (16 U.S.C. §§ 1451 et seq.); (f) conformity of Federal actions to State (Clear Air) Implementation Plans under Section 176(c) of the Clear Air Act of 1955, as amended (42 U.S.C. § 7401 et seq.); (g) protection of underground sources of drinking water under

the Safe Drinking Water Act of 1974, as amended (P.L. 93-523); and (h) protection of endangered species under the Endangered Species Act of 1973, as amended, (P.L. 90-205).

12. Will comply with the Wild and Scenic Rivers Act of 1968 (16 U.S.C. §§ 1271 et seq.) related to protecting components or potential components of the national wild and scenic rivers system.

13. Will assist the awarding agency in assuring compliance with Section 106 of the National Historic Preservation Act of 1966, as amended (16 U.S.C. 470), EO 11593 (identification and protection of historic properties), and the Archaeological and Historic Preservation Act of 1974 (16 U.S.C. 469a-1 et seq.).

14. Will comply with P.L. 93-348 regarding the protection of human subjects involved in research, development, and related activities supported by this award of assistance.

15. Will comply with the Laboratory Animal Welfare Act of 1966 (P.L. 89-544, as amended, 7 U.S.C. 2131 et seq.) pertaining to the care, handling, and treatment of warm blooded animals held for research, teaching, or other activities supported by this award of assistance.

16. Will comply with the Lead-Based Paint Poisoning Prevention Act (42 U.S.C. §§ 4801 et seq.) which prohibits the use of lead based paint in construction or rehabilitation of residence structures.

17. Will cause to be performed the required financial and compliance audits in accordance with the Single Audit Act of 1984.

18. Will comply with all applicable requirements of all other Federal laws, executive orders, regulations and policies governing this program.

Signature of Authorized Certifying Official

Title

Applicant Organization

Date Submitted

BILLING CODE 4154-01-M

Attachment E

U.S. Department of Health and Human Services
Certification Regarding Drug-Free Workplace Requirements
Grantees Other Than Individuals

By signing and/or submitting this application or grant agreement, the grantee is providing the certification set out below.

This certification is required by regulations implementing the Drug-Free Workplace Act of 1988, 45 CFR Part 76, Subpart F. The regulations, published in the May 25, 1990 Federal Register, require certification by grantees that they will maintain a drug-free workplace. The certification set out below is a material representation of fact upon which reliance will be placed when the Department of Health and Human Services (HHS) determines to award the grant. If it is later determined that the grantee knowingly rendered a false certification, or otherwise violates the requirements of the Drug-Free Workplace Act, HHS, in addition to any other remedies available to the Federal Government, may take action authorized under the Drug-Free Workplace Act. False certification or violation of the certification shall be grounds for suspension of payments, suspension or termination of grants, or governmentwide suspension or debarment.

Workplaces under grants, for grantees other than individuals, need not be identified on the certification. If known, they may be identified in the grant application. If the grantee does not identify the workplaces at the time of application, or upon award, if there is no application, the grantee must keep the identity of the workplace(s) on file in its office and make the information available for Federal inspection. Failure to identify all known workplaces constitutes a violation of the grantee's drug-free workplace requirements.

Workplace identifications must include the actual address of buildings (or parts of buildings) or other sites where work under the grant takes place. Categorical descriptions may be used (e.g., all vehicles of a mass transit authority or State highway department while in operation, State employees in each local unemployment office, performers in concert halls or radio studios.)

If the workplace identified to HHS changes during the performance of the grant, the grantee shall inform the agency of the change(s), if it previously identified the workplaces in question (see above).

Definitions of terms in the Nonprocurement Suspension and Debarment common rule and Drug-Free Workplace common rule apply to this certification. Grantees' attention is called, in particular, to the following definitions from these rules:

"Controlled substance" means a controlled substance in Schedules I through V of the Controlled Substances Act (21 USC 812) and as further defined by regulation (21 CFR 1308.11 through 1308.15).

"Conviction" means a finding of guilt (including a plea of nolo contendere) or imposition of sentence, or both, by any judicial body charged with the responsibility to determine violations of the Federal or State criminal drug statutes;

"Criminal drug statute" means a Federal or non-Federal criminal statute involving the manufacture, distribution, dispensing, use, or possession of any controlled substance;

"Employee" means the employee of a grantee directly engaged in the performance of work under a grant, including: (i) All "direct charge" employees; (ii) all "indirect charge" employees unless their impact or involvement is insignificant to the performance of the grant; and, (iii) temporary personnel and consultants who are directly engaged in the performance of work under the grant and who are on the grantee's payroll. This definition does not include workers not on the payroll of the grantee (e.g., volunteers, even if used to meet a matching requirement; consultants or independent contractors not on the grantee's payroll; or employees of subrecipients or subcontractors in covered workplaces).

The grantee certifies that it will or will continue to provide a drug-free workplace by:

(a) Publishing a statement notifying employees that the unlawful manufacture, distribution, dispensing, possession or use of a controlled substance is prohibited in the grantee's workplace and specifying the actions that will be taken against employees for violation of such prohibition;

(b) Establishing an ongoing drug-free awareness program to inform employees about:

(1) The dangers of drug abuse in the workplace; (2) The grantee's policy of maintaining a drug-free workplace; (3) Any available drug counseling, rehabilitation, and employee assistance programs; and, (4) The penalties that may be imposed upon employees for drug abuse violations occurring in the workplace;

(c) Making it a requirement that each employee to be engaged in the performance of the grant be given a copy of the statement required by paragraph (a);

(d) Notifying the employee in the statement required by paragraph (a) that, as a condition of employment under the grant, the employee will:

(1) Abide by the terms of the statement; and, (2) Notify the employer in writing of his or her conviction for a violation of a criminal drug statute occurring in the workplace no later than five calendar days after such conviction;

(e) Notifying the agency in writing, within ten calendar days after receiving notice under subparagraph (d)(2) from an employee or otherwise receiving actual notice of such conviction. Employers of convicted employees must provide notice, including position title, to every grant officer or other designee on whose grant activity the convicted employee was working, unless the Federal agency has designated a central point for the receipt of such notices. Notice shall include the identification number(s) of each affected grant;

(f) Taking one of the following actions, within 30 calendar days of receiving notice under subparagraph (d)(2), with respect to any employee who is so convicted:

(1) Taking appropriate personnel action against such an employee, up to and including termination, consistent with the requirements of the Rehabilitation Act of 1973, as amended; or, (2) Requiring such employee to participate satisfactorily in a drug abuse assistance or rehabilitation program approved for such purposes by a Federal, State, or local health, law enforcement, or other appropriate agency;

(g) Making a good faith effort to continue to maintain a drug-free workplace through implementation of paragraphs (a), (b), (c), (d), (e) and (f).

The grantee may insert in the space provided below the site(s) for the performance of work done in connection with the specific grant (use attachments, if needed):

Place of Performance (Street address, City, County, State, ZIP Code) _____

Check ☐ if there are workplaces on file that are not identified here.

Sections 76.630(c) and (d)(2) and 76.635(a)(1) and (b) provide that a Federal agency may designate a central receipt point for STATE-WIDE AND STATE AGENCY-WIDE certifications, and for notification of criminal drug convictions. For the Department of Health and Human Services, the central receipt point is: Division of Grants Management and Oversight, Office of Management and Acquisition, Department of Health and Human Services, Room 517-D, 200 Independence Avenue, S.W., Washington, D.C. 20201.

DGMO Form#2 Revised May 1990

Certification Regarding Debarment, Suspension, and Other Responsibility Matters—Primary Covered Transactions

By signing and submitting this proposal, the applicant, defined as the primary participant in accordance with 45 CFR Part 76, certifies to the best of its knowledge and believe that it and its principals:

(a) are not presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from covered transactions by any Federal Department or agency;

(b) have not within a 3-year period preceding this proposal been convicted of or had a civil judgment rendered against them for commission of fraud or a criminal offense in connection with obtaining, attempting to obtain, or performing a public (Federal, State, or local) transaction or contract under a public transaction; violation of Federal or State antitrust statutes or commission of embezzlement, theft, forgery, bribery, falsification or destruction of records, making false statements, or receiving stolen property;

(c) are not presently indicted or otherwise criminally or civilly charged by a governmental entity (Federal, State or local) with commission of any of the offenses enumerated in paragraph (1)(b) of this certification; and

(d) have not within a 3-year period preceding this application/proposal had one or more public transactions (Federal, State, or local) terminated for cause or default.

The inability of a person to provide the certification required above will not necessarily result in denial of participation in this covered transaction. If necessary, the prospective participant shall submit an explanation of why it cannot provide the certification. The certification or explanation will be considered in connection with the Department of Health and Human Services (HHS) determination whether to enter into this transaction. However, failure of the prospective primary participant to furnish a certification or an explanation shall disqualify such person from participation in this transaction.

The prospective primary participant agrees that by submitting this proposal, it will include the clause entitled "Certification Regarding Debarment, Suspension, Ineligibility, and Voluntary Exclusion—Lower Tier Covered Transaction," provided below without modification in all lower tier covered transactions and in all solicitations for lower tier covered transactions.

Certification Regarding Debarment, Suspension, Ineligibility and Voluntary Exclusion—Lower Tier Covered Transactions (To Be Supplied to Lower Tier Participants)

By signing and submitting this lower tier proposal, the prospective lower tier participant, as defined in 45 CFR Part 76, certifies to the best of its knowledge and belief that it and its principals:

(a) are not presently debarred, suspended, proposed for debarment, declared ineligible, or voluntarily excluded from participation in this transaction by any federal department or agency.

(b) where the prospective lower tier participant is unable to certify to any of the

above, such prospective participant shall attach an explanation to this proposal.

The prospective lower tier participant further agrees by submitting this proposal that it will include this clause entitled "Certification Regarding Debarment, Suspension, Ineligibility, and Voluntary Exclusion—Lower Tier Covered Transactions," without modification in all lower tier covered transactions and in all solicitations for lower tier covered transactions.

Attachment G

State Single Points of Contact

Arizona

Ms. Janice Dunn, Arizona State Clearinghouse, 3800 N. Central Avenue, Fourteenth Floor, Phoenix, Arizona 85012, Telephone (602) 280-1315.

Arkansas

Mr. Joseph Gillespie, Manager, State Clearinghouse, Office of Intergovernmental Service, Department of Finance and Administration, P.O. Box 3278, Little Rock, Arkansas 72203, Telephone (501) 371-1074.

California

Glenn Stober, Grants Coordinator, Office of Planning and Research, 1400 Tenth Street, Sacramento, California 95814, Telephone (916) 323-7480.

Colorado

State Single Point of Contact, State Clearinghouse, Division of Local Government, 1313 Sherman Street, Room 520, Denver, Colorado 80203, Telephone (303) 866-2156.

Connecticut

Under Secretary, Attn: Intergovernmental Review Coordinator, Comprehensive Planning Division, Office of Policy and Management, 80 Washington Street, Hartford, Connecticut 06106-4459, Telephone (203) 566-3410.

Delaware

Francine Booth, State Single Point of Contact, Executive Department, Thomas Collins Building, Dover, Delaware 19903, Telephone (302) 736-3326.

District of Columbia

Lovetta Davis, State Single Point of Contact, Executive Office of the Mayor, Office of Intergovernmental Relations, Room 416, District Building, 1350 Pennsylvania Avenue, NW., Washington, DC. 20004, Telephone (202) 727-9111.

Florida

Karen McFarland, Director, Florida State Clearinghouse, Executive Office of the Governor, Office of Planning and Budgeting, The Capitol, Tallahassee, Florida 32399-0001, Telephone (904) 488-8114.

Georgia

Charles H. Badger, Administrator, Georgia State Clearinghouse, 270 Washington

Street, SW., Atlanta, Georgia 30334, Telephone (404) 656-3855.

Hawaii

Mr. Harold S. Masumoto, Acting Director, Office of State Planning, Department of Planning and Economic Development, Office of the Governor, State Capitol—Room 406, Honolulu, Hawaii 96813, Telephone (808) 548-5893, FAX (808) 548-8172.

Illinois

Tom Berkshire, State Single Point of Contact, Office of the Governor, State of Illinois, Springfield, Illinois 62706, Telephone (217) 782-8639.

Indiana

Frank Sullivan, Budget Director, State Budget Agency, 212 State House, Indianapolis, Indiana 46204, Telephone (317) 232-5610.

Iowa

Steven R. McCann, Division for Community Progress, Iowa Department of Economic Development, 200 East Grand Avenue, Des Moines, Iowa 50309, Telephone (515) 281-3725.

Kentucky

Debbie Anglin, State Single Point of Contact, Kentucky State Clearinghouse, 2nd Floor Capital Plaza Tower, Frankfort, Kentucky 40601, Telephone (502) 564-2382.

Maine

State Single Point of Contact, Attn: Joyce Benson, State Planning Office, State House Station #38, Augusta, Maine 04333, Telephone (207) 289-3261.

Maryland

Mary Abrams, Chief, Maryland State Clearinghouse, Department of State Planning, 301 West Preston Street, Baltimore, Maryland 21201-2365, Telephone (301) 225-4490.

Massachusetts

State Single Point of Contact, Attn: Beverly Boyle, Executive Office of Communities & Development, 100 Cambridge Street, Room 1803, Boston, Massachusetts 02202, Telephone (617) 727-7001.

Michigan

Milton O. Waters, Director of Operations, Michigan Neighborhood Builders Alliance, Michigan Department of Commerce, Telephone (517) 373-7111.

Please direct correspondence to: Manager, Federal Project Review, Michigan Department of Commerce, Michigan Neighborhood Builders Alliance, P.O. Box 30242, Lansing, Michigan 48909, Telephone (517) 373-6223.

Mississippi

Cathy Mallette, Clearinghouse Officer, Department of Finance and Administration, Office of Policy Development, 421 West Pascagoula Street, Jackson, Mississippi 39203, Telephone (601) 960-4280.

Missouri

Lois Pohl, Federal Assistance Clearinghouse, Office of Administration, Division of General Services, P.O. Box 809, Room 430, Truman Building, Jefferson City, Missouri 65102, Telephone (314) 751-4834.

Montana

Deborah Stanton, State Single Point of Contact, Intergovernmental Review Clearinghouse, c/o Office of Budget and Program Planning, Capitol Station, Room 202—State Capitol, Helena, Montana 59620, Telephone (406) 444-5522.

Nevada

Department of Administration, State Clearinghouse, Capitol Complex, Carson City, Nevada 89710, ATTN: John B. Walker, Clearinghouse Coordinator.

New Hampshire

Jeffery H. Taylor, Director, New Hampshire Office of State Planning, Attn: Intergovernmental Review Process/James E. Bieber, 2½ Beacon Street, Concord, New Hampshire 03301, Telephone (603) 271-2155.

New Jersey

Barry Skokowski, Director, Division of Local Government Services, Department of Community Affairs, CN 803, Trenton, New Jersey 08625-0803, Telephone (609) 292-6613.

Please direct correspondence and questions to:

Nelson S. Silver, State Review Process, Division of Local Government Services, CN 803, Trenton, New Jersey 08625-0803 Telephone (609) 292-9025

New Mexico

Aurelia M. Sandoval, State Budget Division, DFA, Room 190, Bataan Memorial Building, Santa Fe, New Mexico 87503, Telephone (505) 827-3640, FAX (505) 827-3006.

New York

New York State Clearinghouse, Division of the Budget, State Capitol, Albany, New York 12224, Telephone (518) 474-1605.

North Carolina

Mrs. Chrys Baggett, Director, Intergovernmental Relations, N.C. Department of Administration, 116 W Jones Street, Raleigh, North Carolina 27611, Telephone (919) 733-0499.

North Dakota

William Robinson, State Single Point of Contact, Office of Intergovernmental Affairs, Office of Management and Budget, 14th Floor, State Capitol, Bismarck, North Dakota 58505, Telephone (701) 224-2094

Ohio

Larry Weaver, State Single Point of Contact, State/Federal Funds Coordinator, State Clearinghouse, Office of Budget and Management, 30 East Broad Street, 34th Floor, Columbus, Ohio 43266-0411, Telephone (614) 466-0698.

Rhode Island

Daniel W. Varin, Associate Director, Statewide Planning Program, Department

of Administration, Division of Planning, 265 Melrose Street, Providence, Rhode Island 02907, Telephone (401) 277-2656.

Please direct correspondence and questions to: Review Coordinator, Office of Strategic Planning.

South Carolina

Danny L. Cromer, State Single Point of Contact, Grant Services, Office of the Governor, 1205 Pendleton Street, Room 477, Columbia, South Carolina 29201, Telephone (803) 734-0493.

South Dakota

Susan Comer, State Clearinghouse Coordinator, Office of the Governor, 500 East Capitol, Pierre, South Dakota 57501, Telephone (605) 773-3212.

Tennessee

Charles Brown, State Single Point of Contact, State Planning Office, 500 Charlotte Avenue, 309 John Sevier Building, Nashville, Tennessee 37219, Telephone (615) 741-1676.

Texas

Tom Adams, Governors Office of Budget and Planning, P.O. Box 12428, Austin, Texas 78711, Telephone (512) 463-1778.

Utah

Utah State Clearinghouse, Office of Planning and Budget, ATTN: Carolyn Wright, Room 116 State Capitol, Salt Lake City, Utah 84114, Telephone (801) 538-1535.

Vermont

Bernard D. Johnson, Assistant Director, Office of Policy Research & Coordination, Pavilion Office Building, 109 State Street, Montpelier, Vermont 05602, Telephone (802) 828-3326.

West Virginia

Fred Cutlip, Director, Community Development Division, Governor's Office of Community and Industrial Development, Building #6, Room 553, Charleston, West Virginia 25305, Telephone (304) 348-4010.

Wisconsin

William C. Carey, Federal/State Relations, IGA Relations, 101 South Webster Street, P.O. Box 7864, Milwaukee, Wisconsin 53707, Telephone (608) 266-1741.

Please direct correspondence and questions to:

William C. Carey, Section Chief, Federal/State Relations Office, Wisconsin Department of Administration, (608) 266-0267.

Wyoming

Ann Redman, State Single Point of Contact, Wyoming State Clearinghouse, State Planning Coordinator's Office, Capitol Building, Cheyenne, Wyoming 82002, Telephone (307) 777-7574.

Territories

Guam

Michael J. Reidy, Director, Bureau of Budget and Management Research, Office of the

Governor, P.O. Box 2950, Agaña, Guam 96910, Telephone (671) 472-2285.

Northern Mariana Islands

State Single Point of Contact, Planning and Budget Office, Office of the Governor, Saipan, CM, Northern Mariana Islands 96950.

Puerto Rico

Patria Custodio/Israel Soto Marrero, Chairman/Director, Puerto Rico Planning Board, Minillas Government Center, P.O. Box 41119, San Juan, Puerto Rico 00940-9985, Telephone (809) 727-4444.

Virgin Islands

Jose L. George, Director, Office of Management and Budget, No. 32 & 33 Kongens Gade, Charlotte Amalie, V.I. 00802, Telephone (809) 774-0750.

Attachment H

Certification Regarding Lobbying

Certification for Contracts, Grants, Loans, and Cooperative Agreements

The undersigned certifies, to the best of his or her knowledge and belief, that:

(1) No Federal appropriated funds have been paid or will be paid, by or on behalf of the undersigned, to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with the awarding of any Federal contract, the making of any Federal grant, the making of any Federal loan, the entering into of any cooperative agreement, and the extension, continuation, renewal, amendment, or modification of any Federal contract, grant, loan, or cooperative agreement.

(2) If any funds other than Federal appropriated funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this Federal contract, grant, loan or cooperative agreement, the undersigned shall complete and submit Standard Form—LLL, "Disclosure Form to Report Lobbying," in accordance with its instructions.

(3) The undersigned shall require that the language of this certification be included in the award documents for all subawards at all tiers (including subcontracts, subgrants, and contracts under grants, loans, and cooperative agreements) and that all subrecipients shall certify and disclose accordingly.

This certification is a material representation of fact upon which reliance was placed when this transaction was made or entered into. Submission of this certification is a prerequisite for making or entering into the transaction imposed by section 1352, title 31, U.S. Code. Any person who fails to file the required certification shall be subject to a civil penalty of not less than \$10,000 and not more than \$100,000 for each such failure.

State for Loan Guarantee and Loan Insurance

The undersigned states, to the best of his or her knowledge and belief, that:

If any funds have been paid or will be paid to any person for influencing or attempting to influence an officer or employee of any agency, a Member of Congress, an officer or employee of Congress, or an employee of a Member of Congress in connection with this commitment providing for the United States to insure or guarantee a loan, the undersigned shall complete and submit Standard Form—LLL "Disclosure Form to Report Lobbying," in accordance with its instructions.

Submission of this statement is a prerequisite for making or entering into this transaction imposed by section 1352, title 31, U.S. Code. Any persons who fails to file the required statement shall be subject to a civil penalty of not less than \$10,000 and not more than \$100,000 for each such failure.

Signature _____

Title _____

Organization _____

Date _____

Attachment I

The following DHHS regulations apply to all applicants/grantees under the Job Opportunities for Low-Income Individuals Program:

Title 45 of the Code of Federal Regulations:

Part 16—Procedures of the Departmental Grant Appeals Board

Part 74—Administration of Grants (non-governmental)

Part 74—Administration of Grants (state and local governments and Indian Tribal affiliates):

Sections 74.62(a) Non-Federal Audits, 74.173 Hospitals, 74.174(b) Other Nonprofit Organizations, 74.304 Final Decisions in Disputes, 74.710 Real Property, Equipment and Supplies, 74.715 General Program Income.

Part 75—Informal Grant Appeal Procedures

Part 76—Debarment and Suspension Form Eligibility for Financial Assistance, Subpart F—Drug Free Workplace Requirements

Part 80—Non-discrimination under Programs Receiving Federal Assistance through the Department of Health and Human Services Effectuation of Title VI of the Civil Rights Act of 1964

Part 81—Practice and Procedures for Hearings Under Part 80 of this Title

Part 83—Nondiscrimination on the Basis of Sex in the Admission of Individuals to Training Programs

Part 84—Non-discrimination on the Basis of Handicap in Programs

Part 91—Non-discrimination on the Basis of Age in Health and Human Services Programs or Activities Receiving Federal Financial Assistance

Part 92—Uniform Administrative Requirements for Grants and Cooperative Agreements to State and Local Governments (*Federal Register*), March 11, 1988)

Part 93—New Restrictions on Lobbying

Part 100—Intergovernmental Review of Department of Health and Human Services Programs and Activities

Attachment J**Certification Regarding Maintenance of Effort**

The undersigned certifies that:

(1) activities funded under this program announcement are in addition to, and not in substitution for, activities previously carried on without Federal assistance.

(2) funds or other resources currently devoted to activities designed to meet the needs of the poor within a community, area, or State have not been reduced in order to provide the required matching contributions.

When legislation for a particular block grant permits the use of its funds as match, the applicant must show that it has received a real increase in its block grant allotment and must certify that other anti-poverty programs will not be scaled back to provide the match required for this project.

Organization _____

Authorized Signature _____

Title _____

Date _____

Attachment K**Checklist for Use in Submitting OCS Grant Applications Job Opportunities for Low-Income Individuals (Optional)**

The application should contain:

1. Table of Contents
2. A completed, signed SF-424, "Application for Federal Assistance. The letter code for the priority area (JO) should be in the lower right-hand corner of the page.

3. A completed SF-424A, "Budget Information—Non-Construction"

4. A narrative budget justification for each object class category required under Section B, SF-424A;

5. Filled out signed, and dated "Assurances—Non-Construction Programs" (SF-424B);

6. The applicant should sign Attachments E and F. In so doing, the applicant is certifying that it will comply with the Federal requirements concerning the drug-free workplace and debarment regulations set forth in Attachments E.

7. A signed copy of "Certification Regarding Anti-Lobbying Activities".

8. A completed Disclosure of Lobbying Activities, if applicable.

9. An Executive Summary—not to exceed 300 words;

10. A Project Narrative beginning with a Table of Contents that describes the project in the following order:

(i) Eligibility Confirmation

(ii) Organizational Experience and Staff Responsibilities

(iii) Analysis of Need

(iv) Project Design/Work Program

(v) Business Plan (If appropriate)

(vi) Third-Party Evaluation

(vii) Cooperative Partnership Agreement

(viii) Budget Appropriateness and Reasonableness

11. A signed copy of the Cooperative Partnership Agreement or letter of commitment.

12. Appendices, including proof of non-profit status; proof that the organization is a community development corporation, if applying under the CDC Set-aside; commitments from officials of businesses that will be expanded or from franchises, where applicable; Single Point of Contact comments, if applicable; Maintenance of Effort Certification and resumes.

13. A self-addressed mailing label which can be affixed to a postcard to acknowledge receipts of application.

The application should not exceed a total of 50 pages. It should include one original and four identical copies, printed on white 8½ by 11 inch paper, two-holed punched at the top center and fastened separately with a compressor slide paper fastener, such as an ACCO clip, or a binder clip. The submission of bound applications, enclosed in binders, is specifically discouraged.

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