

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 347 and 352

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RIN 0910-AF43

Sunscreen Drug Products for Over-the-Counter Human Use; Proposed Amendment of Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a proposed rule that would amend the final monograph (FM) for over-the-counter (OTC) sunscreen drug products as part of FDA's ongoing review of OTC drug products. This amendment addresses formulation, labeling, and testing requirements for both ultraviolet B (UVB) and ultraviolet A (UVA) radiation protection. FDA is issuing this proposed rule after considering public comments and new data and information that have come to FDA's attention. This rule proposes to lift the stays of 21 CFR 347.20(d) and 21 CFR Part 352 when FDA publishes a final rule based on this proposed rule.

DATES: ~~Submit written or electronic comments on the proposed avobenzone combinations by [insert date 60 days after date of publication in the Federal Register].~~ Submit written or electronic comments ~~on all other parts of the proposed regulation~~ by [insert date 90 days after date of publication in the Federal Register]. Submit written or electronic comments on FDA's economic impact determination by [insert date 90 days after date of publication in the

8/23/07
A. Corbin
(per M. Helman)

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Federal Register]. Please see section X of this document for the effective and compliance dates of any final rule that may publish based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. 1978N–0038 and RIN number 0910–AF43, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.
- Agency Web site: <http://www.fda.gov/dockets/ecomments>. Follow the instructions for submitting comments on the agency Web site.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301–827–6870.
- Mail/Hand delivery/Courier (for paper, disk, or CD–ROM submissions):
Division of Dockets Management (HFA–305), Food and Drug Administration,
5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described in the *Electronic Submissions* portion of this paragraph.

Instructions: All submissions received must include the agency name, docket number and regulatory information number (RIN) for this rulemaking. All comments received may be posted without change to <http://www.fda.gov/ohrms/dockets/default.htm>, including any personal information provided. For additional information on submitting comments, see the “Request for

Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.fda.gov/ohrms/dockets/default.htm> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Matthew R. Holman, Office of Nonprescription Products, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 5414, Silver Spring, MD 20993, 301-796-2090.

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I. Background

In the **Federal Register** of May 12, 1993 (58 FR 28194), FDA published a notice of proposed rulemaking in the form of a tentative final monograph (TFM) for OTC sunscreen drug products. In the TFM, FDA proposed the conditions under which OTC sunscreen drug products would be considered generally recognized as safe and effective (GRASE), under section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)), and not misbranded, under section 502 of the act (21 U.S.C. 352).

In the **Federal Register** of April 5, 1994 (59 FR 16042), FDA reopened the administrative record until July 31, 1994, to allow additional submissions on UVA-related issues and announced a public meeting for May 12, 1994, to discuss UVA testing procedures. As explained in that **Federal Register** notice, the TFM included proposed UVB (i.e., 290–320 nm) testing and labeling. The sun protection factor (SPF) test and corresponding labeling reflects the level of protection against sunburn, which is caused primarily by UVB radiation. The TFM also explained the importance of protection against UVA radiation (i.e., 320–400 nm), the other UV component of sunlight (58 FR 28194 at 28232 and 28233). The TFM referenced published UVA test methods but did not propose a method (58 FR 28194 at 28248 to 28250). Rather, the TFM stated that a product could be labeled as “broad spectrum” or a similar claim if it protected against UVA radiation. Thus, FDA held the 1994 public meeting to gather further information about an appropriate UVA test method and labeling.

In the **Federal Register** of June 8, 1994 (59 FR 29706), FDA proposed to amend the TFM (and reopened the comment period until August 22, 1994) to remove five proposed sunscreen ingredients from the TFM because of lack

of interest in establishing United States Pharmacopeia—National Formulary (USP–NF) monographs. FDA also reiterated that all sunscreen ingredients must have a USP–NF monograph before being included in the FM for OTC sunscreen drug products.

In the **Federal Register** of August 15, 1996 (61 FR 42398), FDA reopened the administrative record until December 6, 1996, to allow additional submissions on zinc oxide and titanium dioxide as well as sunscreen photostability. FDA also announced a public meeting for September 19 and 20, 1996, to discuss the safety and efficacy of these two ingredients and photostability of sunscreens in general.

In the **Federal Registers** of September 16, 1996 (61 FR 48645) and October 22, 1998 (63 FR 56584), FDA amended the TFM to add the UVA-absorbing sunscreen ingredients avobenzone and zinc oxide to the proposed list of monograph ingredients. FDA also proposed indications for these ingredients. As a result of this amendment to the TFM, in the **Federal Register** of April 30, 1997 (62 FR 23350), FDA announced an enforcement policy allowing interim marketing of OTC sunscreen drug products containing avobenzone.

On November 21, 1997, Congress enacted the Food and Drug Administration Modernization Act of 1997 (FDAMA). Section 129 of FDAMA stated that “Not later than 18 months after the date of enactment of this Act, the Secretary of Health and Human Services shall issue regulations for over-the-counter sunscreen products for the prevention or treatment of sunburn.” FDA identified the UVB portions of the monograph (and related provisions on water resistant test methods and cosmetic labeling) as items that could be finalized within the timeframe set by FDAMA. Because of outstanding issues

related to the development of testing standards and labeling for UVA radiation protection, FDA deferred final action on these items.

Therefore, in the **Federal Register** of May 21, 1999 (64 FR 27666), FDA published the FM for OTC sunscreen drug products in part 352 (21 CFR part 352) with an effective date of May 21, 2001, but deferred UVA testing and labeling for future regulatory action. FDA stated that more time was required to review comments from interested parties on active ingredients, labeling, and test methods for products intended to provide UVA protection. This proposed amendment to the FM for OTC sunscreen drug products will complete the FM by addressing both UVB and UVA testing and labeling.

In the **Federal Register** of June 8, 2000 (65 FR 36319), FDA reopened the administrative record of the rulemaking for OTC sunscreen drug products to allow for specific comment on high SPF and UVA radiation testing and labeling. FDA also extended the effective date for the FM to December 31, 2002.

In the **Federal Register** of December 31, 2001 (66 FR 67485), FDA stayed the December 31, 2002, effective date of the FM for OTC sunscreen drug products in part 352 until we provided further notice in a future issue of the **Federal Register**. FDA took this action because we planned to amend part 352 to address formulation, labeling, and testing requirements for both UVB and UVA radiation protection. This document proposes such changes. This document also proposes an effective date related to publication of an amended FM (see section X of this document). The existing stay of the effective date for part 352 remains in effect at this time.

In the **Federal Register** of June 20, 2002 (67 FR 41821), FDA published a technical amendment to change the names of four sunscreen active

ingredients in § 352.10 of the monograph to be consistent with name changes that appeared in USP 24. The new names, which are simpler and more convenient, are meradimate for menthyl anthranilate, octinoxate for octyl methoxycinnamate, octisalate for octyl salicylate, and ensulizole for phenylbenzimidazole sulfonic acid. Because the names became official on March 1, 2001, manufacturers could begin using them at any time after that date.

In the **Federal Register** of June 4, 2003 (68 FR 33362), FDA issued a final rule establishing conditions under which OTC skin protectant products are generally recognized as safe and effective and not misbranded. This final rule lifted the stay of 21 CFR part 352 to amend the final monograph for OTC sunscreen drug products to include sunscreen-skin protectant combination drug products. This final rule concluded by placing a stay on both part 352 and on § 347.20(d). The proposed rule that is the subject of this document provides UVA testing and labeling that is necessary on sunscreen and sunscreen-skin protectant combination drug products. This proposed rule, therefore, proposes that the stays of both part 352 and § 347.20(d) be lifted when this rule is finalized. These stays will be maintained until a final rule based on this proposed rule becomes effective.

In the **Federal Register** of September 3, 2004 (69 FR 53801), FDA delayed the implementation date for OTC sunscreen drug products subject to the final rule that established standardized format and content requirements for the labeling of OTC drug products (i.e., Drug Facts rule). FDA explained that we postponed the Drug Facts implementation date because we did not expect to complete the final amendment of the sunscreen monograph to include UVA testing and labeling by the Drug Facts implementation date of May 16, 2005

(64 FR 13254 at 13273 and 13274, March 17, 1999). Thus, FDA delayed the implementation date of the Drug Facts rule with respect to OTC sunscreen drug products until further notice to avoid issuing successive relabeling requirements for sunscreen drug products at two closely related time intervals, as required by the Drug Facts rule and the final amendment to the sunscreen monograph.

II. Summary of Major Changes to the FM

In response to the TFM and FM, FDA received substantial data and information regarding UVA and UVB active ingredients, claims, and testing procedures, as well as on other issues addressed in this document. FDA summarizes these issues and proposed changes to the FM in this section.

A. Ingredients

FDA proposes to add combinations of avobenzone with zinc oxide and avobenzone with ensulizole as permitted combinations of active sunscreen ingredients in the FM (see section III.C, comment 7 of this document).

B. UVB (SPF) Labeling

The FM allowed specific labeled SPF values up to, but not exceeding, 30. OTC sunscreen drug products with SPF values greater than 30 could be labeled with the collective term “30+.” In this amendment, FDA proposes to increase the specific labeled SPF value to 50 and revise the collective term to “50+.” FDA will consider higher specific labeled SPF values upon receipt of adequate, validated data (see section III.F, comment 15 of this document).

In addition, FDA proposes to revise the following FM labeling:

- The phrase “sun protection” to “sunburn protection” where used in §§ 352.3(b)(1), (b)(2), (b)(3), and (d) and 352.52(e)(1)(i), (e)(1)(ii), and (e)(1)(iii) (see section III.D, comment 10 of this document); and

- Section 352.50(a) to include the term “UVB” before the term “SPF” on the principal display panel (PDP), along with the product category designation (PCD) (see section III.E, comment 14 of this document).

FDA also proposes to revise the PCD SPF ranges in § 352.3(b)(1), (b)(2), and (b)(3) (proposed § 352.3(c)(1) through (c)(4)) to reflect the following:

- The current standard public health message concerning use of sunscreens,
- The proposed increase of the labeled SPF value to “50+,” and
- The proposed addition of the term “UVB” before the word “sunburn.”

Proposed § 352.3(c)(4) contains a new PCD of “highest UVB sunburn protection product” for products that provide an SPF value over 50. FDA further proposes to revise current § 352.3(b)(1) and (b)(2) to replace the current category descriptors of “minimal” and “moderate” with the terms “low” and “medium,” respectively. FDA considers the new terms to be simpler and uniform with the proposed UVB and UVA “Uses” statements. Proposed changes to PCDs and category descriptors also occur in proposed § 352.52(e)(1) (see section III.D, comment 13 and section III.G, comment 16 of this document). In addition, FDA proposes optional UVB radiation protection statements (see proposed § 352.52(e)(2) and (e)(3)).

C. UVA Labeling

FDA proposes new labeling to designate the level of UVA protection on the PDP of OTC sunscreen drug products. FDA proposes the use of symbols (“stars”) in conjunction with a descriptor (i.e., “low,” “medium,” “high,” or “highest”). FDA also proposes to add new § 352.50(b) specifying the required PDP labeling for OTC sunscreen products tested in accordance with the

proposed UVA testing procedures in §§ 352.71 and 352.72 (see section III.E, comment 14 and section III.N, comment 45 of this document).

D. Indications

The FM allowed the following two UVB indications in § 352.52(b)(1):

- “helps prevent sunburn”
- “higher SPF gives more sunburn protection”

In this amendment, FDA proposes to revise the first statement to read “low,” “medium,” “high,” or “highest” “UVB sunburn protection” in proposed § 352.52(b)(1)(i) through (b)(1)(iv). FDA is proposing to revise the additional indications in § 352.52(b)(2) to reflect the new PCD ranges in proposed § 352.3(c) (e.g., SPF of 2 to under 12 becomes SPF of 2 to under 15) and create the new PCD range over SPF 50. These proposed revisions are based upon the revised PCD categories in proposed § 352.3(c) (see section III.G, comment 16 of this document). FDA proposes that the second statement in current § 352.52(b)(1) (“higher SPF gives more sunburn protection”) no longer be required and proposes an additional indication regarding UVA protection (see proposed § 352.52(b)(2)(v)).

In proposed § 352.52(b)(2)(v), FDA includes a new indication for UVA protection that involves selection of the appropriate descriptor (“low,” “medium,” “high,” or “highest”) to describe the level of protection. In proposed § 352.52(b)(2)(vi), FDA includes a modified version of the sunburn “Uses” statement required by proposed § 352.52(b)(1)(i) through (b)(1)(iv) when the additional statement in proposed § 352.52(b)(2)(v) is used and bears the same category descriptor as the SPF value (e.g., medium UVA/UVB protection from sunburn) (see section III.G, comment 17 of this document).

E. Warnings

FDA is proposing to shorten the warning in § 352.52(c)(1)(ii) (proposed § 352.52(c)(3)) under the subheading “Stop use and ask a doctor if” from “[bullet] rash or irritation develops and lasts” to “[bullet] skin rash occurs.”

FDA proposes removing the optional “sun alert” product performance statement (current § 352.52(e)(2)) and requiring a revised “sun alert” statement in the “Warnings” section (proposed § 352.52(c)(1)). FDA proposes that this revised statement be required on all OTC sunscreen drug products except lip cosmetic-drug and lip protectant-sunscreen products subject to § 352.52(f), which are not required to include this statement under proposed § 352.52(f)(1)(v) and (f)(1)(vi) (see section III.G, comment 19 of this document). The statement in proposed § 352.52(c)(1) reads as follows: “UV exposure from the sun increases the risk of skin cancer, premature skin aging, and other skin damage. It is important to decrease UV exposure by limiting time in the sun, wearing protective clothing, and using a sunscreen.” FDA proposes that the statement appear in bold type as the first statement in the “Warnings” section.

F. Directions

FDA proposes changes to the directions to reduce the likelihood that OTC sunscreen drug products are underapplied. Section 352.52(d)(1)(i) currently provides manufacturers the option to select one or more of the following terms: “liberally,” “generously,” “smoothly,” or “evenly.” FDA is proposing to allow the choice of one of two required terms (i.e., “liberally” or “generously”) and to include “evenly” as an additional optional term. FDA is proposing to eliminate the term “smoothly” because it is vague.

FDA also proposes to add a new direction “apply and reapply as directed to avoid lowering protection” (proposed § 352.52(d)(1)(ii)). Because new

information demonstrates the importance of sunscreen reapplication, FDA also proposes to make the optional directions in paragraph (d)(2) a requirement. As a result of this change, FDA is proposing to remove the current language in paragraph (d)(3) because it is no longer necessary. Instead, FDA is proposing, in paragraph (d)(3), required information for products that do not satisfy the water resistant testing procedures in § 352.76. FDA is also proposing a required reapplication statement in § 352.52(d)(1)(ii). The reapplication information in current § 352.52(d)(2) appears in proposed § 352.52(d)(2) and (d)(3) of this document (see section III.H, comment 22 of this document).

G. UVB Testing

FDA is proposing to revise the SPF (UVB) testing procedure (see section III, paragraphs I through L of this document) and to move the SPF testing procedure currently in §§ 352.70 through 352.73 to proposed § 352.70. FDA proposes a padimate O/oxybenzone sunscreen standard in § 352.70 that will be required for testing sunscreen products with SPF values over 15. Manufacturers may use either this padimate O/oxybenzone standard or the homosalate standard to test products with SPF values of 2 to 15. FDA proposes a high pressure liquid chromatography (HPLC) method to replace the spectrophotometric method used to assay the homosalate and padimate O/oxybenzone standards.

FDA proposes the following modifications to the SPF testing procedure:

- Specifications for the solar simulator in § 352.71 (proposed § 352.70(b)),
- Instructions for the application of test materials and response criteria in § 352.72 (proposed § 352.70(c)), and
- Doses and determination of minimal erythema dose (MED) in § 352.73 (proposed § 352.70(d)).

FDA proposes to continue requiring a finger cot to be used in the application of sunscreen standard and test product as specified in § 352.72(e) (proposed § 352.70(c)(5)). However, FDA now proposes that the finger cot be pretreated. These two proposed UVB testing changes also apply to UVA in vivo testing.

H. UVA Testing

FDA proposes a combination of spectrophotometric (in vitro) and clinical (in vivo) UVA test procedures in proposed §§ 352.71 and 352.72, respectively. To assure UVA protection for “water resistant” and “very water resistant” sunscreen products, FDA proposes that the in vivo UVA test be conducted after the appropriate water immersion period for OTC sunscreen drug products making a UVA claim. Therefore, FDA proposes modification of § 352.76 to state that the water resistance claim applies to the SPF and, if appropriate, UVA values determined after the appropriate water immersion period as described in proposed § 352.70 and, if appropriate, proposed § 352.72.

III. FDA’s Tentative Conclusions on the Comments

A. General Comments on OTC Sunscreen Drug Products

(Comment 1) Several comments asked that FDA provide more time to comply with requirements of the FM in order to avoid an adverse economic impact on the sun care industry and consumers. The comments described the seasonal dynamics of the sun care industry (i.e., products are sold in two marketing cycles over a period of 18 months) and stated that the industry would need more time to develop products that meet the FM requirements and allow for shipment of the previous year’s returns. The comments mentioned times from 2 to 3 years after publication of the FM as appropriate or necessary for implementation. Several of these comments added that the

date should be in the June/July time period because the shipping season is practically over at that time and manufacturing for the next season is just beginning.

FDA understands the seasonal nature of the sunscreen industry and the time required for product testing and relabeling. FDA is also aware that more than 1 year may be needed for implementation. FDA is proposing an 18- to 24-month implementation date and will try to have it coincide with the June/July time period (see section XI of this document).

(Comment 2) One comment requested that FDA and the Federal Trade Commission (FTC) take steps to make sure that sunscreen manufacturers provide information to the American public to help them understand and use the Ultraviolet Index (UVI) to determine their risk of sunburn.

The National Weather Service, the Environmental Protection Agency (EPA), and the Centers for Disease Control and Prevention (CDC) developed the UVI, which has been in use since 1995. This index is an indication of the amount of UV radiation reaching the surface of the earth as a function of ozone data, atmospheric pressure, temperature, and cloudiness and is generated for 58 cities around the United States.

Usage information required by the OTC sunscreen drug product monograph applies regardless of the UVI value. Therefore, FDA believes that UVI information need not be required in the monograph for the safe and effective use of these products and should not be included in the “Drug Facts” labeling. However, manufacturers who wish to do so may voluntarily include such information in their labeling outside the “Drug Facts” box.

(Comment 3) One comment requested that FDA make clear, through either the FM for skin protectant or sunscreen drug products, or both, that

combination products containing sunscreen and skin protectant ingredients may be lawfully marketed.

Section 347.20(d) of the skin protectant FM (21 CFR 347.20(d)), which published in the **Federal Register** of June 4, 2003 (68 FR 33362), provides for combinations of sunscreen ingredients and specific skin protectant ingredients. The final rule for OTC skin protectant drug products also included an amendment to the sunscreen FM, adding new § 352.20(b), which allows combinations of sunscreen and skin protectant active ingredients. Thus, both monographs now state the same conditions for lawfully marketing these combination products. The existing language in §§ 347.20(d) and 352.20(b) would include the two new combinations that FDA is proposing to add to the sunscreen monograph (see section II.A, comment 7 of this document).

B. Comments on Tanning and Tanning Preparations

(Comment 4) One comment requested that the effective date of § 740.19 (21 CFR 740.19) be extended to December 31, 2002, consistent with the delay of the effective date for § 310.545(a)(29) and (d)(31), part 352, and § 700.35 (65 FR 36319). The comment stated that singling out § 740.19 to become effective earlier might constitute an arbitrary and capricious decision by FDA.

The May 21, 1999, final rule set a 2-year effective date (May 21, 2001) for § 310.545(a)(29) and (d)(31), part 352, and § 700.35. In the **Federal Register** of June 8, 2000 (65 FR 36319), FDA extended the effective date for compliance with § 310.545(a)(29) and (d)(31), part 352, and § 700.35 until December 31, 2002, to provide time for completion of a more comprehensive UVA/UVB FM for OTC sunscreen drug products. On December 31, 2001, FDA then stayed the effective date of part 352 (but not § 310.545(a)(29) and (d)(31), and § 700.35) until further notice (66 FR 67485). FDA took this action because we are

amending part 352 to address formulation, labeling, and testing requirements for both UVA and UVB radiation protection. The May 21, 1999, final rule also set a 1-year effective date (May 22, 2000) for new § 740.19, which addresses a warning statement for cosmetic suntanning preparations that do not contain a sunscreen active ingredient. These products are not subject to the monograph for OTC sunscreen drug products in part 352. FDA considered this warning to be sufficiently important for safety reasons when we issued the final rule (64 FR 27666 at 27669) to require a 12-month effective date as opposed to the 24-month effective date for the other sections of the rule. Further, FDA's primary reason for extending the effective date of those other sections to December 31, 2002, and then staying part 352 to address formulation, labeling, and testing requirements for both UVA and UVB protection, was to allow FDA to develop a comprehensive UVB/UVA final monograph. This reason does not apply to § 740.19. Accordingly, FDA did not extend the effective date for § 740.19, and § 740.19 is in effect at this time. FDA concludes that this decision is not arbitrary and capricious, but is based on valid health concerns related to the products subject to the warning requirement in § 740.19.

(Comment 5) One comment requested that FDA and FTC take steps to ensure sunscreen manufacturers inform consumers that their natural skin pigmentation provides protection from sunlight. The comment stated that these adaptive individuals might not require a daily application of a sunscreen. Another comment submitted a copy of a patent for an electronic sensor device to measure solar radiation. The comment stated that the personal device could alert consumers to their level of UV exposure so they could either come out of the sun or apply a sunscreen to avoid sunburn and skin cancer.

FDA has no objection to sunscreen manufacturers informing consumers that their natural skin pigmentation provides protection from sunlight. However, FDA has no basis to require such information as part of the required labeling for OTC sunscreen drug products. Thus, manufacturers may include this information in labeling outside of the “Drug Facts” box, but are not required to include this information. FDA considers the comment regarding the UV measuring device to be outside the scope of this rulemaking, which evaluates the safety, effectiveness, and labeling of OTC drug products.

C. Comments on Specific Sunscreen Active Ingredients

(Comment 6) Several comments requested that dihydroxyacetone (DHA) be added to the monograph as a single active ingredient for UVA protection. The comments claimed that DHA alone provides an SPF of 2 to 4. One comment claimed that a 15 percent topical solution of DHA provided a photoprotective factor of 10 in the UVA region. Other comments contended that the brown color produced by DHA, resembling melanin, should potentiate the action of sunscreens. Another comment stated that DHA alone is not a sunscreen, but forms a sunscreen when combined with lawsone. The comment cited unpublished observations by two independent investigators that the melanoidins of DHA-induced skin pigment resemble melanin in that they absorb UVB strongly, with decreasing absorbance through the UVA region and into visible light. The comment added that, because DHA alters the structure of the skin surface, it is, by definition, a drug.

One comment provided information on the safety and UVA effectiveness of DHA alone (Ref. 1). Safety studies included the following:

- Oral and dermal toxicity studies,
- A chronic skin painting carcinogenicity study in mice,

- Comedogenicity tests in rabbits,
- Repeated insult patch test in humans, and
- Photoallergy tests.

Effectiveness studies consisted of published articles using either humans or photosensitized rats. Another comment discussed investigations with DHA on psoriasis patients sensitized with 8-methoxypsoralen (8-MOP).

FDA is not proposing to include DHA in the monograph as a single active ingredient in OTC sunscreen products. Although there were no product submissions to the Advisory Review Panel on Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Panel) using DHA as a sunscreen ingredient, the Panel discussed available scientific evidence for DHA as a single sunscreen ingredient. The Panel concluded that DHA is not a sunscreen but a cosmetic; it is a sunscreen only when used with lawsone (43 FR 38206 at 38215 to 38216, August 25, 1978). Although one comment stated that DHA alters the structure of the skin, it did not provide data to support this claim. Thus, at this time, FDA agrees with the Panel that DHA is a cosmetic.

FDA acknowledges that DHA is the subject of an approved color additive petition and its safety as a color additive has been established. However, the submitted chronic (life-span) skin painting study in mice does not support the safe use of DHA as a sunscreen because no group of mice was included in the study to determine the possible photocarcinogenic effect of DHA. This effect needs to be studied because DHA is associated with carbonyl compounds known to react with pyrimidine bases in the presence of UV radiation, and it appears to be a potent inducer of thymine dimers, premutagenic deoxyribonucleic acid (DNA) lesions. Therefore, its safety, in terms of the type,

extent, and location of photo-induced DNA damage, is of concern and should be determined. Whether DHA contributes or promotes UV carcinogenesis is not known.

The submitted studies on the effectiveness of DHA as a single UVA sunscreen ingredient add only qualitative information. Many of the studies utilized animal models; few included human subjects. One study involved only five subjects, three with erythropoietic protoporphyria and two with polymorphic light eruptions. Another study involved six subjects sensitized with 8-MOP. In both studies, too few subjects were enrolled, and the study subjects were not representative of the average sunscreen user.

Well-controlled clinical trials with DHA alone are lacking. Although some investigations described by the comments suggest that DHA may help protect the normal skin of psoriasis patients, concerns remain about the usefulness of DHA products in the OTC market. For example, one comment stated that photoprotection provided by DHA depends upon the way the product polymerizes in the stratum corneum and that polymerization depends on the skin of each individual. Therefore, the photoprotection provided by DHA varies from person to person and has to be determined for each person by diffuse reflectance spectroscopy. Given these statements, it is not clear how appropriate OTC drug product labeling could be written to aid consumers in proper selection and use of a DHA sunscreen.

FDA concludes that current information is inadequate to include DHA in the monograph as a single sunscreen ingredient. None of the comments provided information to establish the appropriate number of consecutive product applications and the timing of these applications (how far apart or how soon before sun exposure) that are necessary to achieve the desired

protection using products containing various concentrations of DHA. In two submitted studies, a preparation containing 3 percent DHA was applied six times prior to sun exposure and a preparation containing 15 percent DHA preparation was applied one time 24 hours prior to sun exposure, respectively (Ref. 1). The comments did not include any information on appropriate regimens for various skin types, which is necessary because the level of photoprotection provided by DHA is dependent on skin type. Therefore, based upon this lack of information, it is not clear how to state appropriate label directions for consumer use. FDA needs additional information from clinical studies to determine the effective concentration of DHA in sunscreen product formulations and the frequency and timing of product application.

(Comment 7) One comment submitted data to support the combination of avobenzone with ensulizole and avobenzone with zinc oxide (Ref. 2). The safety data included the following:

- A repeat insult patch test,
- A phototoxicity study, and
- A photoallergy study.

The effectiveness data involved a clinical study using the in vitro “critical wavelength” (CW) method and the in vivo “protection factor A” (PFA) method to support the UVA radiation protection potential of the combination products. The PFA test data were from a double blind clinical study using five sunscreen formulations.

The safety studies demonstrated that the following combinations of active ingredients have a low potential for irritation, allergenic sensitization, and phototoxicity:

- 3 percent or less avobenzone with 2 percent ensulizole

- 3 percent or less avobenzone with 5 percent zinc oxide

The data further suggested that the photoallergenic potential of avobenzone is not augmented by its combination with either ensulizole or zinc oxide.

The clinical study using the PFA in vivo method demonstrated that the following combinations of active ingredients are significantly more effective than 1.5 percent ensulizole or 3 percent zinc oxide alone in protecting against UVA radiation:

- 3 percent avobenzone with 1.5 percent ensulizole
- 3 percent avobenzone with 4 percent zinc oxide

FDA's detailed comments on the safety and effectiveness studies are on file in the Division of Dockets Management (Ref. 3).

FDA considers the data submitted by the comment sufficient to support the safety and effectiveness of avobenzone with ensulizole and avobenzone with zinc oxide when used in the concentrations established for each ingredient in § 352.10 of the sunscreen monograph. Accordingly, FDA is proposing to amend § 352.20(a)(2) by adding ensulizole and zinc oxide.

Marketing of products containing avobenzone with ensulizole and avobenzone with zinc oxide will not be permitted unless and until the following three actions occur:

1. The comment period specific to this proposal closes.
2. FDA has evaluated all comments on these combination products submitted in response to the proposal.
3. FDA publishes a **Federal Register** notice announcing our determination to permit the marketing of OTC sunscreen drug products containing these combinations.

D. General Comments on the Labeling of Sunscreen Drug Products

(Comment 8) One comment agreed that the labeling modifications allowed by the FM in § 352.52 for OTC sunscreen products marketed as a lipstick or labeled for use only on specific small areas of the face (e.g., lips, nose, ears, and/or around eyes) are appropriate for these products. Based on the labeling in § 352.52, the comment proposed eight additional modifications for all other OTC sunscreen products regardless of package size:

1. Delete “Drug Facts” title because it is inappropriate and unnecessary for sunscreens.
2. Omit “Purpose” because it is repetitive of the statement of identity on the PDP and “Uses” information.
3. Revise “higher SPF gives more sunburn protection” in “Uses” to read “higher SPF products give more sun protection, but are not intended to extend the time spent in the sun,” and require this statement only on products with an SPF value over 30.
4. Omit “For external use only” warning because it is self-evident for sunscreen products.
5. Revise “When using this product [bullet] keep out of eyes. Rinse with water to remove” to read “Keep out of eyes.”
6. Revise “Stop use and ask a doctor if [bullet] rash or irritation develops and lasts” to read “Stop use if skin rash occurs.”
7. Omit barlines, hairlines, and box enclosure.
8. Allow the option to list inactive ingredients in a different location on the label or in labeling accompanying the product.

The comment stated that these modifications would allow reduced Drug Facts labeling for all OTC sunscreen drug products.

The comment contended that sunscreen products meet all of FDA's criteria for reduced labeling (64 FR 13254 at 13270):

- Packaged in small amounts,
- High therapeutic index,
- Extremely low risk in actual consumer use situations,
- A favorable public health benefit,
- No specified dosage limitation, and
- Few specific warnings and no general warnings (e.g., pregnancy or overdose warnings).

The comment added that OTC sunscreen products are a unique category substantially different from most other types of OTC drug products because they are recommended for use on a daily basis to prevent serious disease. The comment concluded that FDA's rationale for standardized labeling format and content requirements does not necessarily transfer to OTC sunscreen products and specifically not to drug-cosmetic products with a sunscreen.

When FDA created the standardized labeling format and content requirements (i.e., "Drug Facts" labeling) for OTC drug products, we recognized that some product packages were too small to accommodate all of the required labeling. Therefore, under § 201.66(d)(10) (21 CFR 201.66(d)(10)), FDA allows labeling format modifications for all OTC drug products sold in small packages. In the final rule establishing "Drug Facts" labeling, FDA also stated that we may allow reduced labeling requirements beyond those specified under § 201.66(d)(10) for OTC drug products that meet the criteria listed in the preceding paragraph (see section III.D, comment 9 of this document).

In the final rule for OTC sunscreen drug products (64 FR 27666 at 27681 to 27682), FDA recognized that some OTC sunscreen drug products meet these

criteria for reduced labeling. Specifically, FDA identified OTC sunscreen drug products that qualify for the small package specifications in § 201.66(d)(10) and are labeled for use only on specific small areas of the face as meeting the criteria for reduced labeling. Therefore, FDA allows content and format modifications for these products under § 352.52(f). FDA allows further modifications for lip products containing sunscreen because these products for small areas of the face are sold in even smaller packages than the other sunscreen products marketed under § 352.52(f) (68 FR 33362 at 33371; 64 FR 13254 at 13270). FDA believes that sunscreen products labeled for use only on small areas of the face, including lip products containing sunscreen, serve an important public health need and FDA does not want to discourage manufacturers from marketing these products (64 FR 13254 at 13270).

FDA does not find it appropriate to extend the labeling modifications for OTC sunscreen drug products marketed under § 352.52(f) to all OTC sunscreen drug products. FDA disagrees with the comment's argument that all sunscreen products meet the criteria for reduced Drug Facts labeling (64 FR 13254 at 13270), because most sunscreen products are not sold in small packages. Therefore, because sunscreen products do not generally meet all of the criteria for reduced Drug Facts labeling, FDA is not proposing reduced labeling for all OTC sunscreen products.

FDA does not consider sunscreens as a unique category substantially different from other types of OTC drug products because they are recommended for use on a daily basis to prevent serious disease, as argued by the comment. Other OTC drug products are used on a daily basis, some to prevent serious disease and some for other reasons. For example, anticaries drug products are used daily to prevent dental caries. Antiperspirant drug

products can be used daily to reduce underarm wetness. FDA has concluded that these various products should generally be labeled using the standardized content and format in § 201.66. The standardized labeling allows consumers to more easily recognize that these products are, in fact, drug products and to more easily read and understand the labeling information.

The same principle applies when the product is a drug cosmetic product (e.g., sunscreen moisturizer or antiperspirant deodorant). Consumers need to be informed that the product has a drug effect, and the uniform Drug Facts labeling for all OTC drug and drug cosmetic products helps convey this message. FDA applied this rationale when it finalized the requirements in the final rule that established § 201.66.

FDA agrees that some OTC sunscreen drug products meet the criteria for reduced information for safe and effective use (64 FR 13254 at 13270, 64 FR 27666 at 27681 to 27682). However, FDA disagrees with most of the modifications proposed by the comment for all package sizes of OTC sunscreen products. FDA disagrees with deletion of the “Drug Facts” title and the “Purpose” information because many sunscreen products do not meet the parameters for reduced Drug Facts labeling.

FDA disagrees that the “Purpose” information is repetitive and, therefore, disagrees that it may be omitted where there is sufficient labeling space. The “Purpose” section is a standard part of Drug Facts labeling and is intended to inform consumers which ingredients are sunscreens in a product. This information is even more important when a sunscreen is marketed in a combination product. For example, in a sunscreen skin protectant drug product, the “Purpose” section informs consumers which ingredients are sunscreens and which are skin protectants.

FDA has revised the “Uses” section and deleted the statement “higher SPF gives more sunburn protection” (see section III.G, comment 16 of this document). FDA disagrees with omitting the “For external use only” warning for all OTC sunscreen drug products. FDA finds no basis to exclude all OTC sunscreen products from this requirement. Likewise, FDA finds no reason to omit the two standard subheadings that accompany the warning statements, as proposed by the comment. Further, FDA disagrees with the comment’s suggestion to omit the statement “Rinse with water to remove.” This is useful information if a sunscreen product gets into the eyes. FDA agrees with part of the proposed shortened warning for OTC sunscreen drug products to “Stop use if skin rash occurs” in place of “Stop use and ask a doctor [bullet] if rash or irritation develops and lasts.” Therefore, FDA is proposing to amend § 352.52(c)(1)(ii) (proposed § 352.52(c)(3)) to state: “Stop use and ask a doctor if [bullet] skin rash occurs.”

FDA finds no reason to omit barlines, hairlines, or the box enclosure for all OTC sunscreen drug products regardless of package size. These labeling formats help consumers identify a product as a drug and help make labeling information easier to read and understand. Thus, they should be included when package size allows. The FM already allows horizontal barlines and hairlines and the box enclosure to be omitted if a small package meets the criteria in §§ 352.52(f) and 201.66(d)(10).

Finally, FDA has no basis to provide an option for sunscreen products to list inactive ingredients in labeling that accompanies the products. FDA interprets section 502(e)(1)(A)(iii) of the act (21 U.S.C. 352(e)(1)(A)(iii)) as requiring the inactive ingredients to be listed on the outside container of a retail package or on the immediate container if there is no outside container

or wrapper (§ 201.66(c)). Because this information, by law, must appear either on the outside container or immediate container of the product, FDA does not find a basis for allowing an option to list the inactive ingredients in a different location, such as other labeling accompanying the product. In accordance with § 201.66(c)(8), the inactive ingredients must be listed on the product label in the “Drug Facts” box.

(Comment 9) Two comments supported extending the labeling in § 352.52(f) for products intended for use only on specific small areas of the face and sold in small packages to all OTC sunscreen products. The comments contended that all OTC sunscreen drug products meet most of FDA’s criteria for products that require minimal information for safe and effective use (64 FR 13254 at 13270) (see section III.G, comment 8 of this document).

The first comment added that FDA should permit the labeling modifications in § 352.52(f) for the following products:

- Makeup products (as defined in 21 CFR 720.4(c)(7)) with sunscreen, and
- Lotions and moisturizers for the hands or face with sunscreen in containers of 2 ounces (oz) or less (by weight or liquid measure).

The comment added that most facial makeup products are typically packaged in small containers. The comment stated that to meet any of FDA’s concerns that lotions and moisturizers sold in larger packages may be used over the entire body despite labeling that restricts use to the face or hands, FDA could limit the flexible labeling to containers of 2 oz or less. Furthermore, the comment added that containers of 2 oz or less could not feasibly include the full OTC drug labeling.

The second comment contended that the modified labeling in § 352.52(f) is particularly compelling for color cosmetic products for the face that contain

sunscreens (i.e., “facial makeups with sunscreen”). The comment added that these products and OTC sunscreen drug products for use only on specific small areas of the face have the same overall safety profile, and, therefore, FDA should allow these products to be labeled similarly.

A third comment strongly disagreed with a specific labeling exemption for makeup with sunscreen and moisturizer products for use on the face and hands. The comment contended that an exemption would not be in the best interest of consumers. The comment also argued that consumer confusion and subsequent misuse of sunscreen products, particularly failure to apply adequate amounts of sunscreen or to reapply a product after certain activities, will occur if FDA permits reduced labeling for these products. The comment added that many consumers use face and hand cosmetic products with sunscreen as their primary and only source of UV radiation protection for those areas of the body. Moreover, consumers are more likely to use these products properly if they contain full sunscreen drug labeling. The comment concluded that makeup foundations, tints, blushes, rouges, and moisturizers that are intended to be used on a daily or frequent basis to protect against the adverse health and skin aging effects of acute and chronic sun exposure must be labeled as drugs similar to other OTC sunscreen products.

FDA is not proposing to extend the labeling modifications in § 352.52(f), which is specific for products used only on small areas of the face and sold in small packages, to all OTC sunscreen products. FDA has determined that most OTC sunscreen products should have full drug labeling information using the standardized content and format in § 201.66 to ensure the safe and effective use of these products. In establishing the labeling modifications in § 352.52(f), FDA determined how the labeling information for sunscreen drug products,

including drug cosmetic products, could best be presented on products with limited labeling space and still provide consumers with adequate information to use these products safely and effectively. Although any sunscreen products sold in small packages that meet the criteria in § 201.66(d)(10) are allowed the format exemptions under that section, FDA is also proposing content exemptions for sunscreen products marketed under § 352.52(f). FDA is proposing these exemptions under § 352.52(f) because sunscreen products labeled for use only on small areas of the face and sold in small packages are generally sold in packages substantially smaller than other sunscreen products, even those sunscreen products labeled for other uses that meet the criteria in § 201.66(d)(10).

FDA continues to believe that requiring full Drug Facts labeling on sunscreen products used only on specific small areas of the face and sold in small packages (i.e., § 352.52(f)) would discourage manufacturers from marketing some of these products for drug use. Many of these products, such as sunscreen-lip protectant products, are sold in extremely small packages that cannot accommodate the required labeling even with the format exemptions allowed under § 201.66(d)(10). As explained in a number of rulemakings (64 FR 27666 at 27681 to 27682; 68 FR 33362 at 33371; 64 FR 13254 at 13270), these products meet the criteria for additional reduced labeling. Removal of these products from the OTC market would have a negative impact on public health. FDA believes that the benefit of UV radiation protection provided by these products outweighs the need for manufacturers to include all sunscreen labeling information. In contrast, FDA believes manufacturers of sunscreen products that are not within the scope of § 352.52(f) will continue to market their products even though full Drug Facts labeling is required. Unlike

sunscreen products that meet § 352.52(f), the package size of products that do not meet § 352.52(f) will accommodate full Drug Facts labeling.

Although FDA is not extending the labeling modifications in § 352.52(f) to all OTC sunscreen products, as requested by the first and second comments, we are allowing these labeling modifications for certain makeup with sunscreen products. Specifically, these labeling modifications would apply to makeup with sunscreen products that are labeled for use only on specific small areas of the face and that meet the criteria in § 201.66(d)(10). However, FDA does not agree that these labeling modifications should apply to all makeup products identified in § 720.4(c) (21 CFR 720.4(c)) that contain sunscreen, because most are not sold in small packages and, therefore, do not meet all of the criteria for reduced labeling (64 FR 13254 at 13270). Thus, most of these products can accommodate full Drug Facts labeling, and FDA finds no reason to extend the labeling modifications in § 352.52(f) to all makeup with sunscreens products.

As explained in the previous paragraph, the labeling modifications in § 352.52(f) apply to makeup with sunscreen products labeled for use only on specific small areas of the face and sold in small packages. FDA also believes that any sunscreen products that are used only on specific small areas of the face and sold in small packages meet FDA's reduced labeling criteria regardless of whether they are drug or drug-cosmetic products. Therefore, FDA is proposing to amend the heading of § 352.52(f) to read as follows: "Products, including cosmetic-drug products, containing any ingredient identified in § 352.10 labeled for use only on specific small areas of the face (e.g., lips, nose, ears, and/or around the eyes) and that meet the criteria established in § 201.66(d)(10) of this chapter."

In addition, FDA is proposing to extend the labeling exemptions, with some modifications, currently allowed for lipsticks in § 352.52(f)(1)(vi) to the following lip products with sunscreen, as defined in § 720.4(c):

- Lipsticks,
- Lip products to prolong wear of lipstick,
- Lip gloss, and
- Lip balm.

FDA has identified lip products to prolong wear of lipstick as “makeup fixatives” under § 720.4(c)(7)(viii). Lip gloss and lip balm fall under “other makeup preparations” in § 720.4(c)(7)(ix). As long as these lip products with sunscreen are used only on specific small areas of the face and are sold in small packages (i.e., meet the criteria in § 201.66(d)(10)), they would meet FDA’s reduced labeling criteria. As discussed earlier in this comment, FDA believes not allowing Drug Facts labeling exemptions for these products would discourage manufacturers from marketing some of these products for drug use. In proposed § 352.52(f)(1)(vi), FDA is proposing to extend the labeling modifications for lipsticks to other lip cosmetic products containing sunscreen and clarifying that the labeling modifications in § 352.52(f) apply to both sunscreen and makeup with sunscreen products. Furthermore, because lip products with sunscreen have substantially less labeling space than the nonlip products with sunscreen used only on specific small areas of the face and sold in small packages, proposed § 352.52(f)(1)(vi) allows more labeling exemptions for lip products with sunscreen than other products that are within the scope of § 352.52(f).

(Comment 10) Several comments recommended changing the acronym “SPF” from “sun protection factor” to “sunburn protection factor” because the

latter definition is more descriptive of the use of OTC sunscreen drug products and avoids giving consumers the impression of solar invincibility and a false sense of security.

FDA agrees. In § 352.52(b) of the sunscreen FM, FDA included only indications for sunburn protection (e.g., “helps prevent sunburn”) (64 FR 27666 at 27691). In this document, FDA is proposing to change the word “sun” to “sunburn” in § 352.3(b)(1), (b)(2), (b)(3), and (d) and § 352.52(e)(1)(i), (e)(1)(ii), and (e)(1)(iii).

Manufacturers can continue to use existing labeling until the compliance dates of a final rule based on this proposal. However, FDA encourages manufacturers to revise any labeling that states “sun protection” attributed to sunscreen active ingredient(s) to the new term “sunburn protection” as early as possible.

(Comment 11) Some comments questioned the constitutionality of the FM’s labeling provisions. Specifically, the comments contended that the FM’s prohibition on the labeling of SPF products over 30, its restrictions on skin aging claims, and its limitation of the indications for use for OTC sunscreen drug products all violate the first amendment to the U.S. Constitution. The comments asserted that these bans on allegedly truthful labeling in the FM go well beyond constitutionally permissible restrictions on commercial free speech.

One comment contended that FDA had failed to meet its burden to demonstrate that the claims at issue are misleading or that the restrictions on speech directly advance any substantial governmental purpose. In addition, the comment claimed that any interest FDA has asserted in restricting the speech

at issue is served equally well, if not better, by regulations that do not restrict speech to the same extent as FDA's regulations.

FDA disagrees with the comments for the following reasons. OTC drug monographs establish conditions under which ingredients for certain OTC uses are generally recognized as safe and effective (GRASE) and are not misbranded. General recognition of safety and effectiveness in an OTC drug monograph means that experts qualified by scientific training and experience recognize the conditions as safe and effective for OTC marketing for the use recommended or suggested in the product's labeling. An OTC drug monograph establishes, among other things, specific indications that are appropriate for the safe and effective use of a drug. An OTC drug product with labeled indications different than those set forth in an applicable OTC drug monograph would not be considered GRASE.

OTC drug monographs allow manufacturers to market those products satisfying the monograph standard without requiring the specific approval of the product by means of a new drug application (NDA) under section 505 of the act. FDA has issued numerous OTC drug monographs for certain categories of OTC drug products. If an OTC drug product subject to a final monograph is labeled for indications that differ from those set forth in the monograph, then it would be a "new drug" under section 201(p) of the act. In order to be legally marketed and distributed in interstate commerce, the drug manufacturer would be required to obtain approval from FDA for that product, and those conditions varying from the monograph, in an NDA under section 505 of the act.

All OTC drug monographs place limits on the conditions that have been found acceptable for inclusion in the monograph by an administrative

rulemaking process based on scientific data. Here, FDA set certain limits on the labeling of sunscreen drug products in the final rule, such as the prohibition on specific SPF values over 30, certain skin aging claims, and other indications for use. FDA is maintaining similar labeling restrictions in this proposed rule with respect to skin aging claims and other indications proposed by the comments. Also, as described elsewhere in this document, the revised “sun alert” in the “Warnings” section does not include any skin aging claims (see section III.G, comment 19 of this document). However, FDA is proposing to increase the SPF labeling limit from 30 to 50, based on additional data that was submitted subsequent to the issuance of the FM. FDA is also proposing that the term “SPF 50+” can be used, rather than the term “SPF 30+” allowed in the FM. This increase in the SPF labeling limit addresses, in part, the comments’ request that FDA allow specific labeled SPF values over 30.

Elsewhere in this document, FDA explains the reasons for the specific labeling proposals, such as the required SPF labeling, revised “sun alert” in the “Warnings” section of the Drug Facts box, and indications for use (see section III.F, comment 15 and section III.G, comments 16, 17, and 19 of this document). FDA also explains our denial of specific labeling claims suggested by the comments, including the prohibition on specific SPF values over a certain threshold (SPF 50), skin aging claims, and additional indications for use (see section III.F, comments 15 and 17 of this document). As noted earlier in this comment, any variation from these labeling conditions in the monograph, if finalized, would cause an OTC sunscreen drug product to be a new drug requiring an approved NDA before it could be legally marketed in the United States.

The labeling requirements in this proposed rule would not violate the first amendment. FDA's requirements for the disclosure of information in the labeling of OTC sunscreen drug products are constitutionally permissible because they are reasonably related to the Government's interest in promoting the health, safety, and welfare of consumers and because they are not an "unjustified or unduly burdensome" disclosure requirement that offends the first amendment (see *Zauderer v. Office of Disciplinary Counsel*, 471 U.S. 626, 651 (1985); see also *Ibanez v. Florida Dep't of Bus. and Prof'l Regulation*, 512 U.S. 136, 146 (1994)). The reasonable relationship between the required labeling disclosures proposed herein and the Government's interest is plain here.

The proposed labeling disclosures addressed by the comments, such as the SPF value, indications for use, and revised "sun alert," would contribute directly to the safe and effective use of OTC sunscreen drug products. The SPF value and indications for use are critical components of labeling that allow consumers to understand more clearly a sunscreen product's use in preventing sunburn and relative level of UVA/UVB protection. As explained elsewhere in this document, the revised "sun alert" we propose to require in the "Warnings" section would help consumers understand more clearly the role of sunscreens as part of a comprehensive sun protection program (see section III.F, comment 19 of this document). The greater consumer understanding resulting from all of these labeling conditions would promote directly the proper use of sunscreens, which, in turn, would better ensure the protection of public health.

In addition, it would not be "unduly burdensome" to sunscreen manufacturers to require these labeling disclosures. Finally, it is important to

note that a sunscreen manufacturer could pursue alternative labeling conditions for its product by filing an NDA with the appropriate evidence demonstrating the product's safety and effectiveness under the proposed conditions.

In any event, FDA believes that the labeling requirements outlined in this proposed rule would pass muster when analyzed under the four-part test for restrictions on commercial speech set forth by the Supreme Court in *Central Hudson Gas & Electric Corporation v. Public Service Commission*, 447 U.S. 557 (1980). Under the test, the first question is whether the commercial speech at issue is false, misleading, or concerns unlawful activity, because such speech is beyond the first amendment's protection and may be prohibited. If the speech is truthful, nonmisleading, and concerns lawful activity, the Government may nonetheless regulate it if the government interest asserted to justify the regulation is substantial, the regulation directly advances the asserted governmental interest, and the regulation is no more extensive than necessary to serve the government interest (*Id.* at 566). The Supreme Court has explained that the last element of the test is not a "least restrictive means" requirement but, rather, requires narrow tailoring (i.e., "a fit that is not necessarily perfect, but reasonable" between means and ends) (*Board of Trustees of the State Univ. of N.Y. v. Fox*, 109 S.Ct. 3028, 3032–35 (1989)). In subsequent decisions, the Court has also clarified that "misleading" in the first element of the test refers to speech that is inherently or actually misleading. Thus, if the speech to be regulated concerns lawful activity and is not inherently or actually misleading, the remainder of the test applies (see *In re R.M.J.*, 455 U.S. 191, 203 (1982)).

Based on the data currently available, FDA believes that the labeling statements proposed by the comments (i.e., specific SPF values above FDA's established threshold, skin aging claims, and certain other indications) would not be protected speech and may be prohibited under the first prong of the *Central Hudson* test. FDA has tentatively determined that these proposed labeling statements would be inherently misleading on OTC sunscreen products sold and, thus, misbrand the products under section 502(a) and 201(n) of the act. Because FDA believes these labeling statements are inherently misleading, they would not be subject to protection under the first prong of the *Central Hudson* test.

With respect to the labeling limitations for SPF values, based on current data, FDA believes that the labeling of sunscreens with specific SPF values greater than 50 would be inherently misleading. As discussed elsewhere in this document, FDA is concerned with the accuracy and reproducibility of test results showing protection greater than SPF 50 due to the lack of adequate validation data (see section III.F, comment 15 of this document). FDA had the same concern with SPF values above 30 when we published the FM in 1999. At that time, FDA had only received data demonstrating that the SPF test produces accurate results for products with SPF values of 30 or less. Since publication of the FM, FDA has received additional SPF testing data for sunscreen products with SPF values between 30 and 50 (Ref. 13). However, FDA has not received any data for sunscreen products with SPF values greater than 50. The data submitted to FDA indicate that the SPF test is accurate and reproducible for sunscreen products with SPF values up to 50 (Ref. 13). However, these data cannot be extrapolated to SPF values above 50. Thus, FDA is proposing to allow specific labeled SPF values only up to 50.

Increasing variability in test results is likely with increasing SPF values. If there is large variability in test results, then the SPF value determined from the test is not accurate (i.e., an SPF 60 product may not actually be an SPF 60 product). The submitted data demonstrated that variability is not an issue for sunscreen products with SPF values up to 50. However, FDA is concerned that variability will become an issue for sunscreen products with SPF values over 50.

For those sunscreens with SPF values above 50, FDA is proposing that the labeling can denote such values by a “50+” designation. As discussed elsewhere in this document, FDA has sufficient assurance that a result over 50 from the required SPF test is, in fact, greater than 50 and can be labeled “50+” (see section III. F, comment 15 of this document). Thus, FDA believes that the term “50+” is truthful and nonmisleading on the label of OTC sunscreen drug products for which the SPF test in the monograph has indicated an SPF value greater than 50. However, without proper validation of specific SPF values above 50, there is no assurance that the specific values themselves are in fact truthful and not misleading. Thus, labeling of specific values above SPF 50 without appropriate validation (which FDA currently lacks) would be inherently misleading. As noted elsewhere, FDA invited any interested parties to submit such validation data for consideration by FDA and possible inclusion of specific values above SPF 50 in the FM.

With respect to anti-aging, skin cancer, and sun damage claims proposed by the comments, as discussed elsewhere in this proposed rule, FDA is concerned that these statements would be false or misleading due to lack of sufficient data in support of these claims (see section III.F, comment 17 of this document). FDA has reviewed the submitted articles concerning UV-induced

skin damage (i.e., premature aging and cancer) along with the articles obtained from a search of scientific literature (Refs. 26 through 34). As discussed elsewhere, although FDA has concluded that the studies support the conclusion that exposure to UV rays increase the risk of premature skin aging, the study data fails to show that sunscreen use alone helps prevent premature skin aging and skin cancer for several reasons (see section III. F., comment 17 of this document).

First, with respect to premature skin aging, the studies have not completely defined the action spectrum for the majority of UV radiation-induced effects on human skin. Second, the inability to identify the exact UVB and UVA wavelengths that induce each histological change in skin derives from the study designs. Without knowing which UVB and UVA wavelengths induce each histological change in the skin, FDA is unable to determine which wavelengths are most important to causing skin aging and cannot determine the action spectrum for aging. Third, the studies did not examine the chronic, long-term consequences of UV radiation exposure in human skin. Fourth, although the studies that examined the ability of sunscreens to protect against UV radiation-induced histological changes in the skin provide useful data, it is difficult for FDA to conclude that sunscreen use alone helps prevent skin aging based on these studies.

Likewise, FDA is not aware of data demonstrating that sunscreen use alone helps prevent skin cancer. Like skin aging, these are studies examining the effects of sunscreen drug products on short-term factors for skin cancer, such as sunburn and other cellular damage. However, it is difficult to extrapolate these short-term adverse effects of UV radiation to a long-term, chronic effect

such as skin cancer. In addition, like skin aging, the complete action spectrum for skin cancer is not known at this time.

For all these reasons, FDA has tentatively concluded that the available evidence fails to show that sunscreen use alone helps prevents skin cancer or premature skin aging. Thus, the anti-aging, skin cancer, and sun damage claims proposed by the comments would be false or misleading due to lack of sufficient data in support of these claims. For example, the statement proposed by one comment that sunscreen use “may help prevent sun-induced skin damage, such as premature skin aging” would be inherently misleading to consumers by suggesting that sunscreen use alone may help prevent premature skin aging. As explained in this response, the available data fail to show that sunscreen use alone helps prevent premature skin aging and skin cancer.

As described elsewhere, FDA is proposing a revised “sun alert” so that the labeling of OTC sunscreen drug products include the most accurate information, based on the available scientific evidence, concerning the relationship of sunscreen use to the prevention of sunburn, skin cancer, and premature skin aging caused by UV exposure (see section III.F, comment 19 of this document). The revised “sun alert” also includes a statement about limiting sun exposure and wearing protective clothing because FDA has tentatively determined that it is critical for consumers to understand the role of sunscreen use in a comprehensive sun protection program. As FDA has explained, the available evidence strongly suggests that consumers rely more heavily on sunscreens alone without taking other protective measures against sunlight, particularly when the labeling of products indicates the potential for greater protection (see section III.F, comment 19 of this document). By

indicating the potential for greater protection than is supported by the available evidence, the proposed anti-aging, skin cancer, and other related claims would mislead consumers into relying more heavily on sunscreens alone. Such excessive reliance would undermine consumers' protection from the sun and, thus, FDA's public health mission.

FDA has also preliminarily determined that the proposed labeling statements would concern unlawful activity which are not protected speech under the first prong of the *Central Hudson* test.

FDA is proposing specific conditions in the monograph under which OTC sunscreen drug products would be GRASE. Elsewhere, FDA explains how the labeling statements proposed by the comments would not be appropriate monograph indications for these sunscreen products (see section III.G, comment 17 of this document). Thus, the proposed labeling statements outside the proposed indications of the final monograph, as FDA proposes to revise it, would promote a sunscreen drug product for use as an unapproved new drug, which is illegal. In addition, any variation in the statements in a "Warnings" section of a final monograph, such as the revised "sun alert" statement in this proposed rule, would be outside the monograph conditions and, thus, would promote the product as an unapproved new drug. The marketing and distribution in interstate commerce of an OTC sunscreen drug product with such labeling variations would be prohibited under sections 301(d) and 505(a) of the act. Speech promoting such an illegal activity may be restricted without violating the first amendment (*Central Hudson*, 447 U.S. at 563–564).

If a manufacturer could circumvent the requirements and restrictions imposed by a final monograph by including nonmonograph labeling

statements, or excluding required monograph statements, based on its own assertions of the alleged appropriateness and truthfulness of the statements, then such activity would significantly undermine the monograph system and FDA's assurance that OTC drugs are safe and effective for their labeled conditions. FDA has assessed the labeling statements proposed by the comments and preliminarily determined that they are not justified by the available scientific evidence as GRASE conditions for the monograph. Instead, in order to legally market a sunscreen drug product with such labeling statements, an interested manufacturer would have to submit an NDA to FDA with the appropriate evidence to show the safety and effectiveness of the drug under the proposed nonmonograph labeling conditions. Requiring premarket FDA review and authorization of such nonmonograph drug claims ensures that such claims will be evaluated by a public health agency that has scientific and medical expertise so that only products that are safe and effective will be permitted to be sold for therapeutic purposes.

Although this preliminary-determination that the labeling statements at issue would be inherently misleading and would concern unlawful activity would obviate the need for FDA to address the other three prongs of the *Central Hudson* test, we believe that the labeling requirements proposed in this document would satisfy each of the parts of this test. With respect to the second prong, FDA's interest in the required labeling disclosures and prohibitions addressed by the comments would contribute directly to the safe and effective use of these OTC sunscreen drug products, which is critical for the protection of public health. FDA's interest in protecting the public health has been previously upheld as a substantial government interest under *Central*

Hudson (see *Pearson v. Shalala*, 164 F.3d 650, 656 (D.C. Cir. 1999) (citing *Rubin v. Coors Brewing Co.*, 514 U.S. 476, 484–485 (1995))).

The proposed labeling requirements would directly advance this interest, thereby satisfying the third prong of the *Central Hudson* test. By requiring labeling disclosure of the SPF value, the proposed revised “sun alert,” and indications for use, FDA can better assure that consumers understand more clearly the use of sunscreens in preventing sunburn, their relative UVA/UVB protection, and their role as part of a comprehensive sun protection program. The greater consumer understanding resulting from all of these labeling conditions would promote directly the proper use of sunscreens, which, in turn, would better ensure the protection of the public health.

Likewise, this proposed rule’s exclusion from the monograph of the labeling statements proposed by the comments also directly advances FDA’s public health interest. FDA has preliminarily determined from the available evidence that these statements would not be appropriate conditions for OTC use under the monograph. Thus, the statements would directly undermine the protection of public health. In addition, it is important to note that the *Pearson* court, in assessing whether the specific dietary supplement regulations at issue directly advanced FDA’s stated public health goals under the third prong of the *Central Hudson* test, explained that its findings under this prong did not apply to drugs, where “the potential harm is presumably much greater” than other products (*Pearson*, 164 F. 3d at 656, n 13).

Finally, under the fourth prong of the *Central Hudson* test, there are not numerous and obvious (*Cincinnati v. Discovery Network*, 507 U.S. 410, 418 n. 13 (1993)) alternatives to the required labeling statements or labeling prohibitions proposed herein. Consumers are accustomed to using the label

as their primary source of information about a drug product's contents and use. Neither a public education campaign, nor encouraging OTC drug product manufacturers to provide information, such as that in the proposed revised "sun alert," to consumers by other means, would ensure that people have the information they need about sunscreen products at the point of sale or use. Likewise, with respect to the alternative labeling statements proposed by the comments, FDA's proposed indications and revised "sun alert" present the relevant public health information to consumers in the clearest and most direct manner. Thus, FDA's proposed indications and prohibition of other labeling statements are not more extensive than necessary. In this way, the required labeling disclosures and prohibitions proposed in this document would meet the fourth prong of the test.

Furthermore, the proposed prohibition of claims in a final monograph does not prevent such claims from being approved in an NDA. As explained previously, a final monograph sets forth those conditions, including labeling, under which an OTC drug product would be considered GRASE and not misbranded. In issuing monographs, FDA considers whether the available scientific evidence demonstrates that OTC drug products within a therapeutic category are GRASE. A final monograph does not constitute an FDA decision regarding an NDA for an OTC drug proposing variations in these conditions. Thus, FDA's proposals in this document would not prohibit any interested manufacturer from filing an NDA, with the appropriate evidence, for any variations from the monograph labeling conditions. Because of this significant available option to manufacturers for proposing alternative labeling statements, FDA's proposed labeling requirements and prohibitions are not more extensive than necessary.

In conclusion, FDA believes it has complied with its burdens under the first amendment to support the labeling requirements of this proposed rule.

(Comment 12) One comment stated that voluntary professional labeling can be provided to physicians that will allow them to select or recommend sunscreen products for their patients' needs, based on more detailed information describing the quantity (protection factor) and the range of UV protection (e.g., UVB, UVA, or UVB/UVA protection). Another comment stated that FDA should not require professional labeling because complete and accurate product labeling should be available to all consumers, not just to their health care providers.

FDA defines professional labeling in OTC drug monographs as labeling that is provided to health professionals but not to the general public (i.e., not directly to consumers) (for example, see § 331.80 (21 CFR 331.80)). In the final rule, FDA stated that it would consider professional labeling, such as protection against photosensitization reactions, if data were received (64 FR 22666 at 27674). FDA has not received any data to date. Therefore, FDA is not proposing any professional labeling in this document. FDA will consider professional labeling for OTC sunscreen drug products in the future if specific supportive data are provided.

(Comment 13) Some comments objected to the ranges of SPF values that define the product category designations (PCDs) in § 352.3(b). Stating that standard public health messages recommend use of a sunscreen with at least an SPF of 15, the comments contended that the "moderate" PCD (SPF values of 12 to under 30) may cause consumers to believe that SPF values of less than 15 provide adequate protection. One comment further stated that if the PCD range is from SPF 12 to 29, manufacturers will only produce the minimum

SPF value as they can use less active ingredients and get the same PCD classification.

As discussed in the final rule (64 FR 27666 at 27681), the PCD ranges in § 352.3(b) and § 352.52(e) reflect a modified, simpler, combined version of the previously proposed five PCDs and the “Recommended Product Guide.” However, FDA agrees with the comments that the current standard public health message from public health organizations generally recommends use of a sunscreen with an SPF value of at least 15 (see section III.G, comment 19 of this document). We also agree that allowing SPF values below 15 in any but the lowest PCD range may appear to contradict this message. Therefore, FDA is proposing to modify the PCD SPF value range in proposed § 352.3(c)(1) from “2 to under 12” to “2 to under 15” and in proposed § 352.3(c)(2) from “12 to under 30” to “15 to under 30.” FDA is also proposing to replace the PCD terms “minimal” and “moderate” with the simpler terms “low” and “medium,” respectively, and to use these simpler terms for the UVA radiation protection categories (see section III.E, comment 14 of this document). These labeling changes will provide consumers with familiar and consistent terms describing both UVA and UVB radiation protection.

FDA disagrees with the comment contending that manufacturers will only produce the minimum SPF value in a given PCD range because they can use less active ingredients and get the same PCD classification. Section 352.50 of the current FM requires the SPF value to appear on a sunscreen product’s PDP. This proposed rule would not change that requirement. Thus, while the PCD provides additional information about the SPF value, consumers seeking higher SPF values can readily identify such products by the SPF value stated on a sunscreen product’s PDP.

E. Comments on the Labeling of Sunscreen Drug Products With UVA Protection

(Comment 14) Many comments discussed ways to categorize, phrase, and display UVA/UVB radiation protection on an OTC sunscreen drug product label. All of the comments stated that the SPF value should retain preeminence on the label's PDP and be the consumers' criteria for choosing an OTC sunscreen product. Some comments recommended that UVA radiation protection be stated on the PDP in descriptive words or simple phrases, rather than numbers or symbols, for the following reasons:

- Simplicity,
- Clarity,
- To avoid confusion with SPF, and
- To maximize consumer comprehension.

Some comments referenced consumer research, discussed in subsequent paragraphs, to support this recommendation (Refs. 4 and 5).

One comment suggested the following labeling statements:

- "Protects against UVA rays"
- "screens out UVA rays"
- "shields from UVA rays"
- "broad spectrum sunscreen"
- "UVA/UVB protection"
- "provides protection against both UVB and UVA rays"
- other truthful and nonmisleading statements describing a quantification

of the product's UVA radiation protection

The comment stated that quantification of the UVA radiation protection should be allowed in labeling, but not required, so that consumers can have additional product performance information to help them select appropriate products.

Another comment stated that UVA radiation protection should be labeled only as grades of effectiveness (multiple levels) for the following reasons:

- UVA radiation irritation induces various skin reactions (e.g., erythema, pigment darkening, skin cancer, and photodermatitis), and
- Some action spectra of damages have not been determined.

This comment referred to The Japan Cosmetic Industry Association (JCIA) Measurement Standards for UVA Protection Efficacy (Ref. 6), which recommend labeling UVA protection as three grades: (1) PA+, (2) PA++, or (3) PA+++.

Several comments recommended two categories of UV protection labeling based on the ratio of UVA radiation protection factor to SPF value:

- “with UV protection” if ratio equals 0.20
- “with extra UV protection” if ratio equals 0.25

The proposed ratio is based on the UVA radiation protection factor as determined by the persistent pigment darkening (PPD) test method (see section III.N, comment 46 of this document). These comments stated that, because the ratio of damage from solar UVB radiation to that of solar UVA radiation is 80:20 over a day, a sunscreen must protect against an 80:20 ratio of UVB to UVA radiation. The comments also recommended that products labeled “with UV protection” or “with extra UV protection” exhibit absorbance of 360 nanometers (nm) and longer wavelengths.

Another comment suggested two categories to state overall UV radiation protection: “regular” and “broad spectrum.” The comment proposed that the ratio of a sunscreen product’s SPF value to its UVA protection factor be the single criterion for the “broad spectrum” designation, with the maximum ratio

no greater than 4:1. For example, an SPF 16 product would need to provide a UVA protection factor of at least 4 to be designated “broad spectrum.”

One comment disagreed with the previous comment, stating that there is no supportable scientific basis for the relevance of the 4:1 ratio. The comment argued that the ratio inappropriately combines, in the same equation, SPF values obtained with a solar simulator and solar irradiance values at low sun angles.

Another comment suggested that sunscreen products with an SPF value of 2 or greater must have a UVA protection factor of at least 2 to be labeled “UVA/UVB” or “broad spectrum protection.” The comment stated that products with SPF values of at least 15 and UVA protection factors of at least 4 may be labeled “extra (or extended or enhanced) UVA protection.” The comment stated that these criteria are independent of test method and should apply to any of the proposed UVA radiation test methods.

Another comment proposed establishing PCDs based on the UVA radiation protection value obtained by the PPD test method. The comment suggested four PCDs that would enable consumers to choose the desired levels of protection:

- “moderate”
- “high”
- “very high”
- “extra”

Another comment recommended three PCDs:

- “low UVA protection”
- “moderate UVA protection”
- “maximum UVA protection”

Another comment suggested using the five PCDs proposed in the TFM (58 FR 28194 at 28295) and added a UVA protection factor number for each PCD based on the immediate pigment darkening (IPD) test method.

Two comments recommended a four-star rating system to describe UVA radiation protection. The comments stated that this system, based on the ratio of UVA to UVB radiation absorbance, would provide a simple method for consumers to determine the protective nature of an OTC sunscreen drug product. The absorbance ratio would range from 0 for products exhibiting no protection against UVA radiation to 1 for products exhibiting equal absorption at all wavelengths throughout the UVA/UVB radiation spectrum. Using this ratio, products would be classified in one of the following five categories:

- 0 to < 0.2 = no UVA radiation protection claim
- 0.2 to < 0.4 = Moderate (★)
- 0.4 to < 0.6 = Good (★★)
- 0.6 to < 0.8 = Superior (★★★)
- 0.8 plus = Maximum (★★★★)

Another comment recommended a five point rating system using the “critical wavelength” (CW) (λ_c) test method. This system uses a scale analogous to the star rating system to assign products a “broad spectrum” rating as follows:

- $\lambda_c < 325$ = “0”
- $325 < \lambda_c < 335$ = “1”
- $335 < \lambda_c < 350$ = “2”
- $350 < \lambda_c < 370$ = “3”
- $370 < \lambda_c$ = “4”

Several comments supported a single claim, such as “provides broad spectrum protection against UVB and UVA radiation,” based on determining a sunscreen pass/fail CW (λ_c). Comments that supported this “broad spectrum protection” claim stated that, in combination with SPF, it provides simple and accurate labeling that is easily understood by consumers. The comments referred to a research study that suggested this approach to UVA radiation protection labeling was superior for consumer comprehension and ease of product selection (Ref. 7). Other comments provided consumer research data, discussed elsewhere in this comment, suggesting this approach was least preferred by consumers (Refs. 4 and 8).

One comment stated that UVA radiation protection claims should be allowed for sunscreen products with SPF values of 4 and higher. The comment added that, for products claiming to protect against UVA and UVB radiation, a minimum UVA protection factor of 2 should be required if the SPF value is less than or equal to 12.

Several comments stated that sunscreen drug products labeled as “full spectrum” or “broad spectrum” should protect consumers from substantially all of the harmful effects of the sun, including sunburn associated with UVA radiation. According to one comment, sunscreen drug products labeled “full spectrum” or “broad spectrum” that do not protect against nearly all UVB and UVA radiation wavelengths seriously risk misleading consumers into believing they are fully and completely protected from the dangers of the sun. One comment recommended using the claim “full spectrum” rather than “broad spectrum” to describe products that attenuate more than 90 percent of UVA radiation and are at least SPF 15. The comment suggested no UVA radiation protection claims be allowed if the product is below SPF 15.

In support of their proposed UVA labeling, a number of comments provided results from consumer research studies that assessed consumer labeling preferences for stating UVA radiation protection. One comment described a 1996 survey (Ref. 4) in which 275 subjects compared two labeling systems:

- 3-level descriptive (“light,” “intermediate,” or “extended” “UVA protection”) and
- Grapho/numerical (a bar graph indicating a level, 0, 4, 8, or 12, with the corresponding number appearing alongside the graph).

The comment stated that the survey data suggested that, while equally able to understand both types of labels, the panelists preferred the grapho/numerical system over the descriptive system.

Another comment described two consumer research studies, conducted in 1994 and 1995 (Ref. 9), in which 235 subjects compared three potential UVA radiation labeling options:

- Numerical (2, 3, or 5),
- Symbolic (4 stars with 1, 2, 3, or 4 stars filled), and
- 3-level descriptive (labeled blank if no UVA radiation protection provided or labeled “UVA and UVB Protection” or “UVB Plus Extended UVA Protection,” depending on the level of UVA radiation protection provided).

The studies included focus group discussions and indepth interviews. The comment stated that the data suggested that a numeric designation for UVA radiation protection (in addition to the SPF value) created confusion for consumers and that symbols (i.e., stars) misled consumers into giving equal or greater importance to the UVA radiation rating compared to the SPF value. The comment concluded that a descriptive approach better conveyed to

consumers the added benefit of UVA protection without detracting from the SPF value.

Another comment described two consumer research studies conducted in 1999 (Ref. 7) in which 2,238 consumers assessed three sunscreen product labeling systems:

- A pass/fail descriptive (labeled blank if no UVA protection provided (i.e., fails) or labeled “Broad Spectrum UVA and UVB Protection” if UVA radiation protection provided (i.e., passes)),
- A 3-level descriptive (labeled blank if no UVA radiation protection provided or labeled “UVA and UVB Protection” or “UVB Plus Extended UVA Protection,” depending on the level of UVA radiation protection provided), and
- A 3-level grapho/numerical (a bar graph indicating a level, 4, 8, or 12, with the corresponding number appearing alongside the graph).

The comment stated that the data suggested the pass/fail descriptor, “broad spectrum,” was significantly superior to the other labels and recommended that FDA use this labeling to designate UVA radiation protection.

Another comment described a consumer research study conducted in 2000 (Ref. 8) at 20 urban and suburban shopping malls in which 1,921 subjects ranked four labeling systems:

- 4-level numerical,
- 4-level symbolic,
- 4-level descriptive, and
- Pass/fail descriptive (“with/without broad spectrum UVA/UVB protection”).

The numerical labeling system was shown as Arabic numerals “1, 2, 3, 4” with the number “2” highlighted. The descriptor labeling system was shown as the words “Minimum, Moderate, High, Maximum” with the word “Moderate” highlighted. The symbolic labeling system was shown as a picture of four stars with two stars highlighted.

The comment concluded that the subjects had a significant preference for a labeling system based on descriptive words or numbers because of clarity, specificity, and ease of comprehension. Subjects least preferred the pass/fail system because they found it unclear, nonspecific, and lacking sufficient information to compare sunscreen products. This study also revealed that the numerical labeling system was one of the top two choices because numbers were “clearer, more specific, and easier to understand.” Age, gender, and educational or ethnic background were reported as not affecting the study results.

In the TFM for OTC sunscreen drug products (58 FR 28194 at 28233), FDA proposed to allow claims relating to “broad spectrum protection” or “UVA radiation protection” for OTC sunscreen products that meet the following two criteria:

1. Contain sunscreen active ingredients with absorption spectra extending to 360 nm or above, and
2. Demonstrate meaningful UVA radiation protection using appropriate testing procedures to be developed.

In the FM for OTC sunscreen drug products (64 FR 27666 at 27672), FDA stated that UVA radiation labeling of OTC sunscreen drug products could continue in accordance with the TFM and its amendments until addressed in a future issue of the **Federal Register**. Elsewhere in this document, FDA is proposing

test methods for determining the UVA radiation protection potential of an OTC sunscreen drug product (see section III.N, comment 46).

FDA believes that the existing data do not clearly define the relationship between UVA radiation and skin damage. The principal reason for not better understanding this relationship is that the action spectra for specific types of UVA radiation-induced skin damage (i.e., which wavelengths of UVA cause which types of skin damage) have not been established. However, most scientific data demonstrate that UVA radiation is harmful to the skin. Thus, until these action spectra are known, FDA believes that more protection against UVA radiation damage is better for consumers' health. Therefore, FDA believes it is important, as with the SPF value, to designate UVA radiation protection in a straightforward manner that consumers clearly understand.

FDA proposes that the UVA radiation protection of an OTC sunscreen drug product determined from these UVA test methods be designated on the PDP using a combination of category descriptors (i.e., "low," "medium," "high," or "highest") and stars (i.e., symbols) similar to those described by some of the comments. The category descriptors and stars will designate relative levels of UVA radiation protection as measured by the UVA radiation test methods. The level of UVA radiation protection identified on the label reflects the following:

- A numerical "UVA protection factor" (from the clinical test), and
- A numerical ratio of UVA I (340 to 400 nm) radiation absorption to UVB/UVA (290 to 400 nm) radiation absorption (from the in vitro test).

The test that indicates the lowest level of UVA radiation protection determines the level identified on the label. For example, if the clinical test indicates "low" protection and the in vitro test indicates "medium" protection for a

product, the product is labeled as providing “low” UVA radiation protection. This system comprises four categories of UVA radiation protection as described in table 1 of this document.

TABLE 1.—OVERALL UVA PROTECTION OF A SUNSCREEN DRUG PRODUCT

Star category	Category descriptor
☆☆☆☆	Low
☆☆☆☆	Medium
☆☆☆☆	High
☆☆☆☆	Highest

Some of the comments argued that the UVB radiation protection labeling is more important than UVA radiation protection and should be emphasized in the labeling over UVA radiation protection. FDA disagrees with the comments and proposes that the UVA radiation protection designation appear on the PDP along with the SPF value in an equally prominent manner that does not conflict with the SPF value. Because action spectra for UV-induced skin damage have not been clearly defined, FDA is unable to specify labeling for OTC sunscreen drug products that indicates what ranges of UV radiation are most harmful to consumers. In other words, FDA cannot conclude whether UVB or UVA radiation is more harmful to humans based on the scientific data collected to date. Therefore, FDA considers both UVB and UVA radiation protection equally important at this time because scientific data demonstrates that both have harmful effects on the skin.

So that consumers consider UVB and UVA radiation protection equally in selecting an OTC sunscreen drug product, FDA is proposing a number of labeling requirements. Under this proposal, the font size of the stars and category descriptors for UVA radiation protection must be the same size as the SPF value and its descriptors. All four stars must appear and be preceded by the term “UVA” and followed by the appropriate category descriptor (e.g., UVA ★★☆☆ High). All star borders and the color inside a solid star must be

the same while the color of “empty” stars must be lighter and distinctively different than solid stars. The color inside a solid star must be distinctively different than the background color. The stars must be filled in starting with the first star on the left and must appear in a straight horizontal line.

As requested by some comments, an OTC sunscreen drug product that does not provide the minimum UVA protection, as determined by the proposed UVA test methods, may only display an SPF value on the PDP. An OTC sunscreen drug product is not required to provide UVA protection and may bear only a sunburn (UVB/SPF) protection claim. However, FDA is proposing that a sunscreen product that does not provide at least a “low” level of UVA protection include the following statement on the PDP: “no UVA protection.” This statement must be the same font size as the SPF value and its descriptor. FDA is not proposing four empty stars because we are concerned that consumers may confuse products providing no UVA protection (i.e., four empty stars) with those providing the highest UVA protection (i.e., four filled stars).

In developing this UVA radiation protection labeling, FDA has particularly considered the label comprehension studies (Refs. 4, 7, 8, and 9). These studies used multiple methodologies and report a diverse range of preferences for each labeling system:

- Category descriptors,
- Graphics,
- Symbols,
- Numerics, and
- “Pass/fail” descriptors.

The diverse results and varying methodology make it difficult to identify a clear preference for one labeling system. However, the studies indicate an overall preference for category descriptors.

In agreement with the studies, FDA is proposing category descriptors to indicate the relative level of UVA radiation protection. As discussed in preceding paragraphs, FDA believes consumers should consider UVB and UVA radiation protection equally when selecting an OTC sunscreen drug product. For this reason, FDA is proposing that stars be used with category descriptors. FDA believes that the category descriptor and star labeling for UVA radiation protection will give it equal prominence with UVB radiation protection (i.e., category descriptor and SPF) on the PDP.

FDA is not proposing grapho/numeric labeling because we are concerned that consumers may be confused by a second number on the PDP (i.e., in addition to the SPF value). FDA is also not proposing any of the simple two-category designations suggested by the comments:

- With/without UVA protection,
- With UVA protection/with extra UVA protection, or
- Regular/broad spectrum protection.

FDA agrees with one of the comments, which argued that these types of statements are misleading. FDA does not consider this labeling as providing consumers with enough information about the magnitude of UVA protection offered by an OTC sunscreen product. However, FDA does not object to the use of the following four statements for OTC sunscreen drug products that satisfy the requirements of proposed § 352.73 for a labeled UVA protection value:

- “broad spectrum sunscreen”,

- “provides [select one of the following: ‘UVB and UVA,’ or ‘broad spectrum’] protection”,
- “protects from UVB and UVA [select one of the following: ‘rays’ or ‘radiation’]”, and
- [select one of the following: “absorbs” or “protects”] “within the UVA spectrum”.

These statements may appear elsewhere in product labeling outside the “Drug Facts” box or enclosure but not intermixed with the information required on the PDP under § 352.50. FDA agrees with some comments that these statements, by themselves, may be misleading by implying that a sunscreen protects against nearly all UVB and UVA radiation. However, FDA does not believe these optional statements will be misleading in the context of the entire label, because the relative level of UVB and UVA protection must be stated on sunscreen product labels (alongside these more general statements).

Although none of the studies combined labeling systems as proposed in this document, FDA believes the studies support use of category descriptors and symbols together. One study suggested that symbols may imply importance over SPF values (Ref. 9). However, FDA believes consumers will not place greater importance on UVA protection because we are proposing a required statement to inform consumers about the importance of both UVB and UVA protection. We are proposing to require one of the following statements on the PDP of all OTC sunscreen drug products:

- “UV rays from the sun are made of UVB and UVA. It is important to protect against both UVB & UVA rays.”

- “UV rays from the sun are made of UVB and UVA. It is important to protect against both UVB & UVA rays to prevent sunburn and other skin damage.”

FDA believes that the use of one of these statements, along with the proposed UVB and UVA radiation protection labeling, including the format requirements described in preceding paragraphs, will lead consumers to view UVB and UVA radiation protection as equally important.

In addition, this statement will educate consumers about UVA radiation, which will be a new term and concept to many consumers. The proposed statement should help consumers better understand the new UVB and UVA labeling when it is initially introduced to the OTC market. Thus, FDA believes that the consumer label comprehension studies, along with the proposed educational statement about UVB and UVA radiation, support the stars and descriptor UVA radiation protection labeling proposed in this document. Moreover, a similar “star rating system” for UVA radiation protection (i.e., the Boots Star System) has been used to label sunscreen products throughout Europe for over 10 years.

To prevent consumer confusion about UV radiation protection, FDA is proposing changes to UVB radiation protection labeling (i.e., the SPF value). SPF values indicate how effective a sunscreen product is in protecting against sunburn. By displaying the relative level of sunburn protection on the sunscreen drug product PDP in terms of an SPF value, consumers can choose their desired level of UVB radiation protection. To further improve consumers’ understanding of the sunburn protection level provided by a certain sunscreen product, FDA is proposing to require descriptive terms of relative sunburn protection (i.e., “low,” “medium,” “high,” and “highest”) to accompany the

SPF value on the PDP. FDA is further proposing that the SPF value must be preceded by the term “UVB” to further differentiate the SPF value from the UVA symbol/descriptor on the PDP. FDA believes that numerical labeling for UVB protection, symbolic labeling for UVA protection, and the same descriptive labeling for UVB and UVA protection will allow consumers to easily understand and choose from relative levels of UVB and UVA radiation protection.

FDA is aware that consumers have used and become accustomed to choosing OTC sunscreen drug products based on the SPF value for many years. Likewise, FDA believes that, over a period of time, consumers will similarly become accustomed to the proposed labeling using symbols and descriptors to designate relative UVA radiation protection. Furthermore, FDA believes consumer familiarity with similar star rating systems (e.g., movies, hotels, and restaurants) used for many years in the United States provide a basis for consumers’ understanding of this proposed labeling for OTC sunscreen drug products.

FDA is providing a number of examples of how the UVA/UVB protection designations could appear on the PDP.

UVB SPF 30 High	UVA ★★★★ Medium
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UVB SPF 30 High

UVA
★★★★
Medium

UVB
SPF
30
High

UVA
★★★★
Medium

UVB
SPF
30
High

UVA
★★★★
Medium

FDA believes that, as with SPF values, identifying the relative level of UVA radiation protection provides the most useful information for consumers. Consumers who desire more protection from the sun will be able to identify products with higher UVB (SPF) and UVA radiation protection. FDA agrees with the comments that a product must provide at least some minimum level of UVA radiation protection (as with SPF values) to be labeled as providing UVA radiation protection. Therefore, FDA is proposing minimum criteria for the lowest UVA category in its proposed test procedures (see section III.N, comment 46 of this document).

F. Comments on the Labeling of Sunscreen Drug Products With High SPF Values

(Comment 15) Several comments objected to FDA limiting specific labeled SPF values “up to but not above 30.” The comments stated that data and information supplied to FDA since publication of the sunscreen FM demonstrate that SPF values over 30 can be safely tested with accuracy. The comments also argued that removing the limit will not lead to consumers spending more time in the sun when using high SPF sunscreens in comparison to low SPF sunscreens. To address that point, one comment proposed labeling to help reduce potential consumer misuse of sunscreens with SPF values over 30: “higher SPF products give more sun protection, but are not intended to extend the time spent in the sun.” Another comment noted that the SPF value, in addition to proper sunscreen application and reapplication, is only part of a comprehensive sun protection program.

Other comments explained the need for high SPF sunscreen products. The comments contended that consumers and physicians are familiar with and want the many currently marketed sunscreens that are labeled as “SPF 45, SPF

50, etc.” Thus, the comments argued that U.S. consumers will be at a disadvantage within the international community, because products providing SPF values over 30 are available in other countries. In addition, the comments stated that many prominent medical authorities maintain the need for high SPF sunscreens for individuals at “high risk” based on medical and/or occupational concerns and individuals who desire increased protection from photoaging and lengthy/intensive sun exposure situations. The comments argued that the need for high SPF sunscreens is supported by findings that UV exposures in several cities are considerably higher than previously recognized and because high SPF products can reduce cumulative UV exposure. The comments stated that consumer desire for high SPF products is demonstrated by sales data showing that products with an SPF value of 45 are one of the fastest growing segments of the total sunscreen market.

The remaining comments discussed the consequences of limiting the specific labeled SPF value. For example, one comment noted that if manufacturers cannot state the SPF level above 30, they will no longer have an incentive to fund research for better sunscreens. In addition, manufacturers may reformulate products to reduce active ingredients and, thus, reduce the level of UV protection. A comment argued that another adverse consequence results from most consumers failing to achieve the labeled SPF value because they do not apply enough sunscreen and/or reapply it too infrequently. Because high SPF products can help make up for such improper use, limiting the specific labeled SPF value to 30 has a negative impact on UV protection.

A foreign industry organization suggested an upper limit for labeled SPF values of 50+ and provided three reasons:

- Unreasonably high SPF values will lead consumers to expect “too much effectiveness” from sunscreen products.

- Higher concentrations of sunscreen active ingredients are not “in the interest of safety.”

- Higher SPF values will invite excessive, meaningless competition in the industry.

The comment explained that competition would be meaningless because the amount of UV protection provided by products with SPF values above 50 is not significantly greater than products with an SPF of 50.

Another comment from a sunscreen manufacturer agreed with FDA’s concern about the possibility of increasing variability when testing high SPF sunscreens. The comment suggested a modified “binomial” test method and labeling requirements for SPF values over 20 that would allow for high SPF products.

Another comment submitted a published survey of 208 sunbathers on Miami’s South Beach during July 2001 with the goal of measuring UV radiation exposure and probable injury (Ref. 10). The “worst case” scenario identified by the survey was based on sunbathers with Type I skin (persons most sensitive to sunlight who burn easily and never tan) exposed to UV radiation near the longest day and highest sun angle of the year at the “southern-most major beach” in the United States. The survey was a followup to one conducted in 1993 with 62 sunbathers and evaluated by FDA in the FM (64 FR 27666 at 27674). The 2001 survey determined MEDs absorbed by the following three steps:

1. Measuring incident UV radiation (using three dosimeters),

2. Multiplying by an adjusting factor for skin type (using a 30 percent increase in sensitivity between skin types), and
3. Dividing by the SPF worn by the sunbather.

The survey suggests that sunbathers with Type I skin might receive a cumulative dose of 49.5 MEDs with 8 hours of exposure. The comment concluded that, while SPF values up to, and including, 50 are warranted, values over 50 are unwarranted in any condition for sunburn protection.

Two comments submitted testing data for sunscreens with SPF values between 30 and 50 using the test method in the FM. The comments concluded that the test method was valid for these high SPF values. In addition, one comment indicated that a very water resistant test for an SPF 45 to 50 sunscreen would take nearly 4.5 hours using the skin types of subjects in the SPF testing procedures in the FM (i.e., skin types I, II, and III) (Ref. 13). The comment concluded that it is beyond the practical endurance capabilities of many people in the test to spend more than 5 to 6 hours in front of a UV radiation lamp and that fatigue can lead to errors in test results. The comment also noted that the potential for intra and interlaboratory variability in test results increases as sunscreen SPF values increase.

FDA concluded in the FM (64 FR 27666 at 27675) that test methods supported specific SPF label values up to 30. FDA invited interested persons to submit data in support of high SPF test methods and to consider proposed methods for communicating the level of protection in labeling. Data and information on high SPF testing and labeling were submitted to FDA at, and following, public meetings on July 22, 1999, and October 26, 1999, and after reopening of the administrative record (65 FR 36319) (see section III.I, comment 24 of this document) (Refs. 11 and 12).

FDA continues to be aware that many OTC sunscreen products with specific labeled SPF values over 30 are currently marketed, both nationally and internationally, and are increasingly used by consumers and recommended by health professionals (64 FR 27666 at 27675). FDA agrees that these products should be available for those sun-sensitive consumers who require such products based upon personal knowledge, planned sun exposure, geographical location, or advice of a health professional. FDA previously noted the lack of any known safety problems for sunscreen products with SPF values greater than 30 (64 FR 27666 at 27675). The comment that argued higher concentrations of sunscreen active ingredients are not “in the interest of safety” did not supply any new data to support its contention. FDA will continue to monitor adverse drug experience reports for sunscreen drug products reported to its Medwatch program and in the medical literature.

As noted by one comment, some researchers have raised the concern that sunscreen use may lead to increased sun exposure. The “compensation hypothesis” states that consumers who use high SPF sunscreens spend more time in the sun and/or use less protective clothing. The only double blind, randomized trial that addressed this issue showed a significant increase in sun-exposure time when comparing use of SPF 30 to SPF 10 (Ref. 14). In addition, two retrospective survey studies showed that sun exposure time is longer when using sunscreen compared to not using sunscreen (Refs. 15 and 16). Other studies cited by the comment to support the premise that the “compensation hypothesis” is incorrect and either did not provide data about the length of sun exposure or the study method did not allow for data interpretation (Refs. 17 through 20). Based on all of this data, FDA believes that some consumers may increase total UV exposure through over-reliance on sunscreens. The

apparent divergent results on the validity of the “compensation hypothesis” between studies may indicate that sun protection behaviors vary greatly for each person. More specifically, there is a spectrum of attitudes about the sun, from those individuals who seek dark suntans to those who seek to avoid the sun and consequent UV skin damage (Ref. 21). Such evidence underscores the need for adequate labeling so consumers can make informed decisions regarding their use of OTC sunscreen drug products.

FDA agrees that the SPF value is one factor in a comprehensive sun protection program. However, the SPF is only a measure of protection from erythema (i.e., UVB radiation-induced sunburn) and does not measure protection from other UV skin damage, such as that induced by UVA radiation. While increased short wavelength UVA radiation protection generally increases with increasing SPF values, studies using in vivo or in vitro UVA radiation testing methods demonstrate that sunscreen products with the same SPF values can have markedly different levels of UVA protection, especially for long wavelength UVA radiation (Refs. 22 and 23). These studies also indicate that a specific high SPF product can provide much less UVA radiation protection than a product with a much lower SPF value. Elsewhere in this document, FDA is proposing UVA radiation testing methods and labeling that will categorize the relative levels of protection provided by the SPF and UVA values of the sunscreen product (see section III.E, comment 14 and section III.N, comment 45 of this document), allowing consumers to compare products and choose the levels of UVB and UVA radiation protection desired.

An SPF 30 sunscreen product may provide adequate sunburn protection for many consumers. However, FDA believes that appropriately tested and labeled high SPF value sunscreen products should be available for consumers

who desire or need high levels of UV protection, in particular, those who burn easily. Such products would do the following:

- Help compensate for inadequate application and/or reapplication,
- Provide additional sunburn protection during intense UV radiation conditions,
- Help reduce cumulative UV radiation exposure (when used in conjunction with other measures to reduce overall sun exposure), and
- Generally provide consumers incremental increases in sunburn protection.

FDA agrees that SPF values should be supported by scientific evidence. In the FM, FDA limited the specific labeled SPF value to 30. At that time, FDA had only received data demonstrating that the SPF test produces accurate results for products with SPF values of 30 or less. Since publication of the FM, FDA has received additional SPF testing data for sunscreen products with SPF values between 30 and 50 (Ref. 13). However, FDA has not received any data for sunscreen products with SPF values greater than 50. The data submitted to FDA indicate that the SPF test is accurate and reproducible for sunscreen products with SPF values up to 50 (Ref. 13). However, these data cannot be extrapolated to SPF values above 50. Thus, FDA proposes to allow specific labeled SPF values up to 50.

FDA agrees with the sunscreen manufacturer that increasing variability in test results is likely with increasing SPF values. If there is large variability in test results, then the SPF value determined from the test is not accurate (i.e., an SPF 50 product may not actually be an SPF 50 product). The submitted data demonstrate that variability is not an issue for sunscreen products with

SPF values up to 50. However, FDA is concerned that variability will become an issue for sunscreen products with SPF values over 50.

FDA recognizes that future data may demonstrate that variability may not be a problem for sunscreen products with SPF values over 50. Therefore, FDA will consider specific SPF values greater than 50 upon receipt of data demonstrating that accurate and reproducible results can be obtained from the SPF test for sunscreen products with SPF values over 50. Generally, such data should include results from multiple laboratories using the same sunscreen formulations and using the SPF test proposed in this document, along with a statistical analysis of the overall results. In addition, FDA believes that the modified “binomial” test method submitted by one comment has merit for high SPF sunscreens and is requesting others’ views on this method during the comment period for this rulemaking (see section III.I, comment 24 of this document).

In the FM (64 FR 27666 at 27675), FDA disagreed with the comment that manufacturers would have no incentive to fund research for better sunscreens and may reformulate to less protective products if there is an upper limit to specific labeled SPF values. Although FDA would not want to decrease research incentive, FDA is more concerned about valid scientific data demonstrating the ability of multiple laboratories to accurately and reproducibly determine SPF values. However, FDA does not believe it is necessary to arbitrarily limit specific labeled SPF values. To the contrary, both in the FM and in this proposal, FDA has specifically stated that high SPF sunscreens should be available for those individuals desiring such products. The maximum allowable specific labeled SPF value, both in the FM and in this proposal, is based upon the review of data and information submitted to

FDA. FDA purposely did not limit labeled SPF values at 30 in the FM. Instead, FDA used the value of “30+,” pending the receipt of adequate data to support any higher specific label values.

Similarly, in this document, FDA is proposing the collective value “50+.” FDA has sufficient assurance that a result over 50 from the required SPF test is, in fact, greater than 50 and can be labeled “50+.” Thus, FDA believes that the term “SPF 50+” is truthful and nonmisleading on the label of OTC sunscreen drug products for which the SPF test in the monograph has indicated an SPF value greater than 50. FDA believes that allowing manufacturers to label sunscreens as “SPF 50+” may encourage further research in human skin photobiology and the development of safe and effective sunscreen drug products with specific SPF values over 50. As explained earlier in this comment, FDA is not proposing that the specific value over 50 be stated in the labeling because there is no data, at this time, demonstrating the accuracy and reproducibility of the specific value over 50. Based upon the proposed labeling, improvements to SPF testing methods, and specific high SPF test data, FDA is proposing to modify the labeled SPF values in current § 352.50(a)(1) and (a)(2) by changing the SPF values from “30” to “50.”

G. Comments on Indications for Sunscreen Drug Products

(Comment 16) One comment requested that the “Uses” statement, “higher SPF gives more sunburn protection,” be omitted except for products with an SPF over 30. This and other comments suggested that FDA’s labeling concerns regarding high SPF sunscreens could be alleviated if the following statement was required on sunscreens over SPF 30: “Higher SPF products give more sun protection, but are not intended to extend the time spent in the sun.”

FDA is proposing to revise the sunscreen FM “Uses” statement “helps prevent sunburn” and delete the “Uses” statement “higher SPF gives more sunburn protection” in current § 352.52(b). The first indication, “helps prevent sunburn,” is being revised to one of the following, which would be required on all sunscreens:

- “low UVB sunburn protection”
- “medium UVB sunburn protection”
- “high UVB sunburn protection”
- “highest UVB sunburn protection”

The relative level of sunburn protection is determined from the SPF value:

- low = SPF 2 to under 15
- medium = SPF 15 to under 30
- high = SPF 30 to 50
- highest = SPF over 50

Thus, relative descriptors (low, medium, high, and highest) describe SPF values, which are relative and not absolute levels of sunburn protection intended to help consumers determine differences in sunburn protection offered by different sunscreen products (see section III.I, comment 23 of this document).

FDA considers it important that consumers be made aware of the relative level of sunburn protection provided by a product in addition to its indication for sunburn protection. Individuals may select a low, medium, high, or highest sunburn protection product to meet their specific needs. The descriptor “UVB” is included to describe the predominant rays that are screened. The phrase “helps prevent” is being deleted because it is duplicative and no longer necessary. This phrase would only lengthen the “Uses” statement.

Furthermore, consumers will now be able to equate a product's UVB radiation protection rating (i.e., SPF value) directly to the relative level of sunburn protection.

The second indication "higher SPF gives more sunburn protection" is no longer needed because the relative level of sunburn protection is provided in the new "Uses" statements. In addition, without clarification, the statement may encourage consumers to spend more time in the sun. Clarification is necessary because, as discussed in comment 19 of this document, surveys reveal that consumers spend more time in the sun with increasingly higher SPF sunscreen products (Refs. 14, 15, and 16). Therefore, FDA is not allowing this statement in the "Uses" section. However, under proposed § 352.52(e)(2), FDA is proposing the following optional statement under "Other information" or anywhere outside of the "Drug Facts" box or enclosure: "higher SPF products give more sun protection, but are not intended to extend the time spent in the sun." The phrase "but are not intended to extend the time spent in the sun" is additional information not included in the FM indication. FDA believes this revised indication statement will discourage consumers from spending more time in the sun when using a higher SPF product.

FDA is proposing additional revisions in "Uses" in § 352.52(b)(1) to include UVA claims and other information (see section III.G, comments 17 and 18 of this document). The proposed revisions will help consumers to more fully understand the uses and expected results for individual sunscreen products. These changes are necessary because the PDP for a sunscreen product will now include two performance ratings (see section III.E, comment 14 of this document):

- The well-accepted SPF value and new descriptor rating for UVB radiation protection, and

- A new star/descriptor rating for UVA radiation protection.

Consequently, FDA considers it important that the “Uses” statements in the “Drug Facts” box accurately reflect product claims related to specific indications, UVA and UVB radiation, and the level of anticipated protection (low, medium, high, or highest) determined by the UVA and UVB product ratings. As with the introduction of SPF labeling years ago, it will take the combined efforts of government, manufacturers, consumer organizations, and the health care community to educate consumers to fully understand these labeling initiatives to enhance their safe and effective use of sunscreen products.

(Comment 17) One comment stated that FDA’s “sun alert” statement in the FM recognized that sun-induced skin damage can contribute to photoaging and increase the risk of skin cancer. This statement reads: “Sun alert: Limiting sun exposure, wearing protective clothing, and using sunscreens may reduce the risks of skin aging, skin cancer, and other harmful effects of the sun.” The comment urged FDA to allow other truthful use statements, such as the following:

- “helps protect against skin damage caused by the sun”
- “helps protect against skin aging caused by the sun”
- “regular use helps protect against certain forms of skin cancer caused by the sun”
- “helps protect against fine lines and wrinkles caused by the sun”
- “helps protect against pigmentary changes due to sun exposure”

Another comment urged FDA to include the first three use statements suggested by the first comment, as well as “helps protect against the harmful effects of the sun” and “helps protect against (select one: ‘casual,’ ‘incidental,’ ‘intermittent,’ or ‘daily’) sun exposure.” The comment contended that, when used effectively as part of a sun protection program, sunscreens may prevent very serious disease conditions.

Another comment provided citations from the medical literature to support its contention that claims of sunscreens preventing skin cancer induction may be false, deceptive, misleading, and unsubstantiated. The comment mentioned an article by Garland (Ref. 25) that states the following: “No epidemiological studies were identified that showed a protective effect of use of chemical sunscreen on risk of melanoma or other cutaneous malignancies in humans.” The comment also mentioned an article by Gasparro (Ref. 24) that states the following: “Although some have promoted daily use (of sunscreen) for the prevention of premature aging of the skin and the prevention of skin cancer, actual data are lacking to support these recommendations.”

FDA has reviewed the submitted articles concerning UV-induced skin damage (i.e., premature aging and cancer) along with articles obtained from a search of the scientific literature (Refs. 26 through 34). Many of the articles involved preclinical data, which can be difficult to extrapolate to consumer (human) actual use conditions. FDA believes that the articles with clinical data provide more meaningful results, as they can be easily extrapolated to consumer actual use conditions. Therefore, FDA is focusing discussion in this document on the clinical studies. In agreement with Garland (Ref. 25) and

Gasparro (Ref. 24), FDA does not believe, as a whole, that the studies demonstrate that sunscreens alone help prevent skin aging or skin cancer.

Some of the clinical studies examined the role of UVB and UVA radiation in producing histological changes indicative of skin aging due to the sun. Lowe et al. demonstrated that high doses of UVA radiation (320 to 400 nm) increased melanization of human skin more than lower doses of UVA or solar simulating UV radiation at 290 to 400 nm (Ref. 26). Seite et al. demonstrated that melanization of human skin increased with exposure to UVB/UVA radiation at 290 to 400 nm (Ref. 32) and UVA radiation at 330 to 440 nm (Ref. 27). Seite et al. also showed that human skin hydration decreased after chronic exposure to UV radiation at the wavelengths studied.

Five studies revealed stratum corneum thickening produced by both UVB and UVA radiation (Refs. 26 through 29 and 32). Stratum granulosum thickening was transiently induced after 6 weeks of exposure to UV radiation (UVB/UVA) at 290 to 400 nm (Ref. 32). The same effects were seen with solar simulated radiation and high and low doses of UVA radiation after 12 weeks of exposure (Ref. 26). Viable epidermal thickening was seen after 6 weeks of exposure to UV radiation at 290 to 400 nm in one study (Ref. 32) and after 9 days of exposure to UVA radiation at 335 to 345 nm in another study (Ref. 31).

Inflammation and lysozyme deposition along the dermal elastic fibers were increased more in human skin exposed to UVA than UVB radiation (Refs. 26, 28, 29, and 31). Sunburn cell appearance, a typical response to UVB radiation, was also found to be present after exposure to different UVA radiation regimens in two studies (Refs. 28 and 31) but not found in a third study (Ref.

27). Thus, FDA concludes that these studies demonstrated that both UVB and UVA radiation induce histological changes associated with skin aging.

Four of these studies focused on the histological changes within the skin induced by UVB and UVA radiation and explored the ability of sunscreens to protect human skin against these changes (Refs. 29, 30, 32, and 33). The first study suggested that an SPF 29 sunscreen prevented the development of solar elastosis, a condition in which skin loses its elasticity after chronic exposure to the sun (Ref. 33). However, these method and data analyses raise questions about the validity of the reported conclusion:

- Discrepancies were noted concerning demographic characteristics of subjects, sunscreen application, and compliance rates.
- Skin biopsy data at all three time points in the study were available from only 10 of the 35 subjects.
- The only statistically significant difference between the sunscreen and placebo treatment groups was achieved in a computerized evaluation of solar elastosis at baseline and 24 months.

The second study demonstrated significant contribution of a sunscreen in preventing UV radiation-induced skin damage (Ref. 32). The use of sunscreens with absorption spectra covering the 290 to 400 nm range prevented all of the effects of chronic exposure (6 weeks) to UV radiation evaluated in the study. The third study showed a photoprotective effect of an SPF 15 sunscreen product from damage induced by short term exposure to UVB radiation (Ref. 30). The fourth study showed that a UVB only sunscreen did not provide protection against chronic exposure to UVA radiation (Ref. 29).

The studies provide evidence that both UVB and UVA radiation induce histological changes in the skin consistent with skin aging. Thus, the studies

support the conclusion that exposure to UV rays increases the risk of premature skin aging. However, the study data fails to show that sunscreen use alone helps prevent premature skin aging for several reasons. First, the studies have not completely defined the action spectrum for the majority of UV radiation-induced effects on human skin. While studies demonstrate that a given histological change, such as thickening of the stratum corneum, is induced by certain wavelengths within the UVB and UVA region, studies have not examined the ability of the remaining UVB and UVA regions outside of these wavelengths to induce the same change. For example, studies may have shown that 290 nm to 310 nm and 360 nm to 400 nm radiation induce stratum corneum thickening, but it is not known whether 311 nm to 359 nm radiation induces the same histological change.

Second, the inability to identify the exact UVB and UVA wavelengths that induce each histological change in the skin derives from the study designs. Each study differed in the following parameters:

- UV radiation wavelengths,
- UV exposure regimens,
- Sunscreen doses,
- Sunscreen application techniques, and
- Endpoints.

Therefore, FDA cannot combine all of the data from these studies to define a complete action spectrum for each histological change in the skin.

Furthermore, the action spectrum for each histological change would need to be combined to define a single action spectrum for skin aging, which is a cumulation of these histological changes. Without knowing which UVB and UVA wavelengths induce each histological change in the skin, FDA is unable

to determine which wavelengths are most important in causing skin aging and cannot determine the action spectrum for aging.

Third, the studies did not examine the chronic, long-term consequences of UV radiation exposure in human skin. Thus, it is not possible for FDA to extrapolate the data to longer time points at which the short-term histological changes may cumulate to produce visible signs of skin aging.

Fourth, although the studies that examined the ability of sunscreens to protect against UV radiation-induced histological changes in the skin provide useful data, it is difficult for FDA to conclude that sunscreens alone help prevent skin aging based on these studies. The number of participants in each study was relatively small, with only 10 to 35 subjects per study. Different sunscreen formulations, with differing absorption spectra, were used in each study. As explained previously, these studies do not identify exactly which UVB and UVA wavelengths contribute the most to skin aging (i.e., the studies do not define the skin aging action spectrum). For all of these reasons, the studies do not prove that sunscreens alone help prevent premature skin aging.

Likewise, FDA is not aware of data demonstrating that sunscreens alone help prevent skin cancer. It has been known for many years that UV radiation increases the risk of skin cancer. It has also been known for many years that a higher incidence of sunburn earlier in life corresponds to a higher incidence of skin cancer later in life. However, FDA is not aware of any studies demonstrating that the use of sunscreens alone decreases the risk of skin cancer. Like skin aging, there are studies examining the effects of sunscreens on short-term factors for skin cancer, such as sunburn and other cellular damage. However, it is difficult to extrapolate these short-term adverse effects of UV radiation to a long-term, chronic effect such as skin cancer. In addition,

like skin aging, the complete action spectrum for skin cancer is not known at this time.

Unlike skin cancer and premature skin aging, FDA has evidence that sunscreens alone help prevent sunburn. The SPF test measures the effectiveness of sunscreens with sunburn (erythema) as the endpoint. Thus, the impact of sunscreens on sunburn can be measured directly. In contrast, it is difficult to measure directly the impact of sunscreens on skin cancer or premature skin aging because these are long-term, cumulative adverse effects of UV exposure.

Thus, for all of the reasons discussed in this comment, FDA concludes that the available evidence fails to show that sunscreens alone help prevent skin cancer or premature skin aging. Based on this conclusion, FDA is not proposing the indication statements proposed by the first and second comments, because these claims are for protection from premature skin aging, skin cancer, and related factors (e.g., “helps protect against skin aging caused by the sun”). FDA also is not proposing claims that sunscreens protect against “casual, incidental, intermittent, or daily” sun exposure, as proposed by the second comment, because the studies do not support these claims. Furthermore, FDA considers these terms as lacking sufficient meaning to be useful to consumers.

As described elsewhere in this document (see section III.G, comment 19), FDA is proposing to require a revised “sun alert” statement in the form of a new warning. The new warning statement is based on FDA’s review of the available evidence concerning UV exposure and skin cancer, premature skin aging, and other skin damage. The new warning statement clarifies that UV exposure from the sun increases the risk of skin cancer, premature skin aging,

and other skin damage. In addition, the new warning statement specifies that consumers should use complementary sun protection measures along with sunscreen (i.e., limit sun exposure and wear protective clothing). FDA has concluded from the available evidence that it is important to adopt a complete sun protection program (sunscreen, sun avoidance, and protective clothing) to decrease UV exposure. In fact, the second comment argued for new indication statements by considering the sunscreen use as part of such a sun protection program (i.e., in conjunction with limiting time in sun and wearing protective clothing). Thus, the second comment, along with the third comment, seemed to agree with FDA's conclusions in this proposed rule concerning the need for consumers to use sunscreens in conjunction with other sun protection measures.

In addition, the reference in the new warning statement to sunscreen use combined with limiting sun exposure and wearing protective clothing is consistent with recommendations by other public health organizations. For example, the World Health Organization's International Agency for Research on Cancer (IARC) (Ref. 21) makes the following assessments and recommendations:

- There is inadequate evidence in humans for a cancer preventative effect of sunscreens against basal cell or malignant melanoma cancers.
- There is only limited evidence for a preventive effect of sunscreens against squamous cell cancer.
- Sunscreens should not be the first choice for skin cancer prevention or used as the sole agent for protection against UV radiation.

Likewise, the CDC recommends that sunscreens be used as a complementary measure in an overall sun protection program (Ref. 35).

FDA believes that additional information from controlled clinical studies is needed to better understand the role of sunscreens in preventing premature skin aging and skin cancer. Studies examining premature skin aging (using solar radiation or simulated solar radiation) are needed to determine the following in humans:

- Measurable skin properties such as elasticity, collagen/elastin ratios and properties, wrinkling, pigmentation changes and visual grades, leading to accepted quantitative definitions of chronological and sun-induced skin aging;
- The relationship between sunlight exposure and skin aging, stratified by skin type;
- An action spectrum for photoaging of skin;
- A dose response for UV radiation-induced skin aging;
- Quantitative estimates of realistic “worst case,” long-term exposures to sunlight in relevant UVA and UVB radiation spectral ranges (i.e., the level of UVB and UVA protection needed); and
- How UV radiation-induced processes that occur at a given wavelength affect UV radiation-induced processes that occur at other wavelengths.

Similar information is needed for skin cancer, except that studies should examine the different types of skin cancer, rather than examining different skin properties. In addition, IARC has provided recommendations for research on skin cancer prevention and sunscreens. These recommendations can also be used as a guide in designing studies to examine the role of sunscreens in preventing premature skin aging due to the sun (Ref. 21). FDA encourages interested parties to submit study protocols to FDA for review to ensure that studies are as informative as possible. FDA also invites comments by interested parties on the feasibility and validity of surrogate endpoints for studies to

determine whether the use of sunscreens alone help prevent skin cancer, premature skin aging, or other skin damage.

(Comment 18) As discussed in section III.E of this document, FDA received several comments discussing ways to categorize, phrase, and display UVA/UVB radiation protection on an OTC sunscreen drug product label. In the amendment to include avobenzone in the monograph (61 FR 48645 at 48655), FDA proposed the following indications for UVB and UVA radiation protection by sunscreen drug products containing avobenzone:

1. “Broad spectrum sunscreen”;
2. “Provides” (select one of the following: “UVB and UVA,” or “broad spectrum”) “protection”;
3. “Protects from UVB and UVA” (select one of the following: “Rays” or “radiation”);
4. (Select one of the following: “Absorbs,” “Protects,” “Screens,” or “Shields”) “throughout the UVA spectrum”; and
5. “Provides protection from the UVA rays that may contribute to skin damage and premature aging of the skin”.

Likewise, in the amendment to include zinc oxide in the monograph (63-FR 56584 at 56588), FDA proposed similar labeling for UVA and UVB radiation protection for products containing zinc oxide (substituting the word “within” for the word “throughout” in the fourth statement). FDA did not include these indications in the FM but has allowed their use until the UVA portion of the monograph is established.

FDA has reconsidered these UVA protection indications. FDA is proposing to allow all of them except the fifth statement. In proposed § 352.52(e), the first four statements are optional statements allowed for products that

demonstrate UVA protection according to the proposed testing (see section III.N, comment 45 of this document). The statements can only be included in labeling outside of the “Drug Facts” box. Within the “Drug Facts” box, FDA is proposing one of the following UVA indication statements, depending on the level of UVA protection provided by a product:

- “low UVA protection”
- “medium UVA protection”
- “high UVA protection”
- “highest UVA protection”

The level of protection (i.e., low, medium, high, or highest) is determined from the UVA rating obtained from product testing (see section III.N, comment 45 of this document). Manufacturers who wish to combine the “Uses” statements about UVA protection and UVB sunburn protection may do so if the descriptors (i.e., levels of protection) are the same. For example, if the levels of UVA and UVB protection are medium, the “Use” may read: “medium UVA/UVB sunburn protection”.

FDA is not including the fifth indication because FDA does not consider “skin aging” or “skin damage” claims adequately supported at this time. As discussed elsewhere in this document (see section III.G, comment 19), FDA is proposing a statement in the “Drug Facts” box that informs consumers that sunscreens may reduce the risks of skin aging, skin cancer, and other harmful effects from the sun when used in a regular program that relies upon limiting sun exposure and wearing protective clothing. Therefore, FDA believes the fifth indication statement would mislead consumers by not discussing sun exposure and protective clothing.

(Comment 19) As discussed in section III.G of this document, FDA received several comments concerning the “sun” alert statement. In § 352.52(e)(2) of the FM, FDA included the optional statement: “Sun alert: Limiting sun exposure, wearing protective clothing, and using sunscreens may reduce the risks of skin aging, skin cancer, and other harmful effects of the sun.” This statement’s emphasis of the need for a comprehensive sun protection program (64 FR 27666 at 27679) was based on the findings of numerous groups, including the following:

- The American Academy of Dermatology (AAD),
- The CDC,
- The Australian Government; and
- The New Zealand Government.

These groups have recommended that sunscreens be considered an adjunct to other UV protection strategies, such as avoiding the sun near midday, seeking shade, and wearing protective clothing and hats.

The FM provided that the “sun alert” appear under the heading “Other information” or anywhere outside of the “Drug Facts” box or enclosure. At that time, FDA encouraged manufacturers to **voluntarily include this statement** in labeling, make it available at the point of purchase, and/or make it available through consumer education programs.

FDA is now proposing a revised “sun alert” statement be required in the “Warnings” section of the “Drug Facts” box. FDA is proposing the statement to read as follows: “UV exposure from the sun increases the risk of skin cancer, premature skin aging, and other skin damage. It is important to decrease UV exposure by limiting time in the sun, wearing protective clothing, and using a sunscreen. FDA is proposing that the statement appear in bold type as the

first statement in the “Warnings” section. FDA believes the statement is most appropriate in the “Warnings” section because it warns consumers that effective protection from the sun does not involve only the application of sunscreens, as many consumers believe. In addition, it warns consumers that UV radiation not only increases the risk of sunburn but also increases the risk of skin cancer and premature skin aging, which many consumers may not know. FDA believes the new warning will encourage consumers to use sunscreen, limit time in the sun, and wear protective clothing to reduce UV exposure. Because of the importance of warning statements and the need for consumers to receive a uniform message concerning such warnings, no variations in wording are allowed under § 330.1(c)(2).

FDA acknowledges that the new warning statement differs from the wording of the voluntary “sun alert” in the FM. These differences are based on FDA’s assessment of the additional evidence available since publication of the FM in 1999. As explained in comment 17 of this document, FDA does not believe that the available data support a claim concerning the use of sunscreen and a reduction in the risk of premature skin aging and skin cancer. The revised wording of the statement more accurately reflects the scientific conclusions that can be drawn from this evidence.

FDA is proposing the warning because we continue to be concerned about adequate consumer understanding of a sun protection program that includes sun avoidance and wearing protective clothes along with sunscreen use. This proposed rule provides for even higher SPF values and a new rating system for UVA protection. Consumers may believe that sunscreens with higher SPF values (especially with UVA protection) provide complete UV radiation protection. Subsequently, consumers may prolong sun exposure because they

think higher SPF values equate to longer times in the sun without burning. FDA is aware of a double-blind, randomized clinical study that showed a significant increase in sun exposure time of persons using high SPF sunscreens compared to persons using low SPF sunscreens (Ref. 14). In addition, two questionnaire-based surveys showed that sun exposure time is prolonged for persons using sunscreens compared to persons not using sunscreens (Refs. 15 and 16). By educating consumers about a sun protection program, we believe requiring this new proposed warning will decrease the likelihood of consumers spending more time in the sun when using a sunscreen.

The new proposed warning also informs consumers that use of sunscreens alone is not the sole measure of protection from UV exposure, even with the use of high SPF products that provide UVA protection. Although it is well established that sunscreens protect against UV radiation, the following factors affect the level of protection provided by a sunscreen for each individual:

- Variations between individuals,
- UV radiation absorption,
- Ability of sunscreens to adhere to and be absorbed by the skin,
- Exposure conditions, and
- Conditions of use (e.g., inadequate application amount or reapplication frequency).

Therefore, FDA agrees with the numerous groups that promote sunscreen use as part of a total sun protection program.

FDA reviewed the relationship between sunscreen use and skin cancer incidence in the scientific literature and did not find confirmatory evidence that sunscreens alone protect against the development of skin cancer. The incidence of skin cancer continues to rise in the United States. The incidence

of the most serious form of skin cancer, malignant melanoma, grew 6.1 percent per year during the 1970s (Refs. 14 and 36). The rate is still rising an average 2.8 percent annually, with a rate of 14.3 percent per 100,000 persons in 1997. Melanoma is one of the top 10 cancers, by incidence, for persons with white skin. The American Cancer Society (ACS) estimated the following statistics concerning skin cancer in 2007 (Ref. 37):

- More than 1 million new cases of curable basal cell and squamous cell carcinomas would be detected,
- Approximately 59,940 new cases of malignant melanoma would be diagnosed, and
- An estimated 8,110 persons would die from melanoma and 2,000 persons would die from other skin cancers.

Skin cancer affects roughly the same number of people as all other cancers combined. In view of the continuing increase in the incidence of all types of skin cancer and the lack of data demonstrating that sunscreens alone prevent skin cancer, FDA considers the new warning important for the protection of the public health.

FDA is proposing that the new warning be required on all OTC sunscreen drug products except lip cosmetic-drug and lip protectant-sunscreen products subject to § 352.52(f). FDA continues to believe that all sunscreen products should have labeling to ensure that consumers are adequately protected against overexposure to UV radiation (64 FR 27666 at 27673). Thus, sunscreen products labeled for use only on specific small areas of the face and sold in small packages (i.e., sunscreen products subject to § 352.52(f)) must include the new warning. The only sunscreen products not required to include the new warning are those lip cosmetic-drug and lip protectant-sunscreen products

subject to § 352.52(f), as proposed in § 352.52(f)(1)(ii). FDA is making this proposal because lip cosmetic and lip protectant products are often sold in packages that are substantially smaller than those of other products that fall under § 352.52(f). FDA believes requiring the new warning on lip cosmetic-sunscreen and lip protectant-sunscreen products may discourage manufacturers from marketing these products because it requires a significant amount of labeling space.

FDA has limited labeling requirements as much as possible for sunscreen products subject to § 352.52(f). However, FDA believes consumers are at great risk for UV-induced skin damage, including cancer, on the face. Therefore, consumers who purchase products specifically for use on the face need to be informed about the information contained in the new warning. Although these products are marketed in small package sizes, FDA has determined that the products' labeling needs to include this important information in order to protect consumers.

(Comment 20) One comment stated that consumers who use color cosmetics or facial moisturizers with sunscreens make the informed decision to purchase them as an additional benefit to their cosmetic use. The comment contended that a significant number of people with dark skin types, who do not burn easily, purchase sunscreens to provide protection from the sun damage that is not immediately recognizable. For these reasons, the comment requested claims such as the following:

- “helps protect against casual or incidental or intermittent daily sun exposure”
- “helps protect against the harmful effects of the sun”

Another comment acknowledged that facial makeups with sunscreen provide protection from sunburn, but that is not the primary reason why consumers use these products. The comment contended that requiring the “sunburn” indication would be inappropriate and misleading labeling for most facial makeups with sunscreen. The comment, instead, requested a claim such as “protects against the harmful rays of the sun.”

FDA notes that the second comment acknowledged that facial makeups with sunscreen provide protection from sunburn. Not every consumer who uses color cosmetics or facial makeups with sunscreen meets the following criteria:

- Has a dark skin type, or
- Uses these products solely to provide protection from sun damage that is not immediately recognizable.

As noted in section III.D, comment 9 of this document, many consumers use facial products with sunscreen as their primary and only source of sunscreen protection for that area of the body. As discussed in section III.G, comment 16 of this document, sunscreen products will be required to bear a claim of low, medium, high, or highest UVB sunburn protection. FDA does not consider it inappropriate or misleading for color cosmetic or facial makeup products containing sunscreens to have this sunburn protection claim of low, medium, high, or highest.

Sunscreen products that provide UVA radiation protection may also bear a claim about the level of protection. In addition, all OTC sunscreen products, except lip cosmetic-drug and lip protectant-sunscreen products subject to § 352.52(f), will be required to bear the revised “sun alert” statement, which is now included in the “Warnings” section of the “Drug Facts” box. FDA

considers the information in this new “Warnings” statement much more beneficial to consumers than the statements proposed by the comments. FDA rejected the terms “casual, incidental, and intermittent,” as explained in section III.G, comment 17 of this document.

H. Comments on Directions for Sunscreen Drug Products

(Comment 21) Several comments requested alternative directions for makeup with sunscreen products. One comment requested “apply smoothly or evenly before sun exposure and/or as needed.” The comment added that “before sun exposure” may not always be appropriate as these makeup products are not exclusively or even primarily used for protection against sun exposure. A second comment requested “apply smoothly or evenly before sun exposure and reapply as needed.” A third comment did not suggest any specific language, but requested flexibility to recognize the product’s primary use as a makeup, while providing adequate information about the sunscreen component. This comment added that the direction to consult a doctor for children under 6 months of age was clearly unnecessary for facial makeup with sunscreen because these products cannot reasonably be expected to be used on children that age.

FDA agrees that flexibility is appropriate for the directions for makeup with sunscreen products. Elsewhere in this document, FDA is proposing to allow labeling modifications for makeup with sunscreen products used only on specific small areas of the face and sold in small packages (see section III.D, comment 9 of this document). Those modifications include modified directions for cosmetic lip products containing sunscreen that are within the scope of proposed § 352.52(f). FDA is not extending the proposed modifications to all makeup with sunscreen products. Makeup with sunscreen products not labeled

only for specific small areas of the face may be applied to a large area of the face or other areas of the body. As explained later in this comment, FDA would have concerns with the modifications being applied to these products.

Whether intentional or not, makeup with sunscreen products may be the primary sunscreen for many consumers. A recent study examined sunscreen use patterns (Ref. 48). Participants were instructed to apply sunscreen every day. Of those who used sunscreen infrequently, the majority spent some time outdoors with 11 percent spending the majority of their time outdoors. These same participants explained that they did not believe sunscreen was necessary because of their planned activities. The authors cited this finding in advocating educating consumers on the need for sunscreen for frequent incidental sun exposure in addition to intentional sun exposure, such as sunbathing.

For these reasons, FDA considers it important that consumers using makeup with sunscreen products not labeled for use only on specific small areas of the face recognize that these products are sunscreens and use them appropriately to maximize UV protection. Therefore, FDA is not proposing modified directions for these makeup with sunscreen products.

(Comment 22) One comment requested that FDA require sunscreen manufacturers to provide accurate and appropriate instructions about how much sunscreen should be applied to the body. The comment also suggested that a warning about the dangers of sunburn from applying suboptimal amounts be included in sunscreen product labeling. A second comment stated that it was not aware of any study indicating that consumers use adequate amounts of sunscreen. The comment supplied data and other information concerning the dependency of the SPF value on the total quantity of sunscreen applied (Ref. 49).

Section 352.52(d)(1) currently provides manufacturers the option to select one or more of the following application terms for a sunscreen product:

“liberally, generously, smoothly, or evenly.” Manufacturers may also include optional directions that state “[bullet] reapply as needed or after towel drying, swimming, or (select one of the following: ‘sweating’ or ‘perspiring’).” In the final rule, FDA had concluded that the directions in § 352.52(d)(1) to apply “liberally” or “generously” convey the appropriate message to ensure that consumers adequately apply the sunscreen (64 FR 27666 at 27679).

Several studies suggest that, in practice, consumers may apply amounts of sunscreen below the density of 2 milligrams/square centimeter (mg/cm^2), which is the amount of product required for the SPF determination in § 352.72(e) (proposed § 352.71(e)). These data suggest that consumers may apply as little as 0.5 to 1.0 mg/cm^2 (Refs. 50 through 54). One comment reported that, to achieve the rated protection over the whole body, a typical adult with a surface area of 1.73 square meters (m^2) would need to apply 35 milliliters (mL) of sunscreen, roughly one-third of a 4 oz bottle per application (Ref. 55). Studies indicate that SPF values determined at an application rate of 1 mg/cm^2 are approximately 50 percent of those determined at 2 mg/cm^2 , and when applied at 0.65 mg/cm^2 , the SPF values are 20 to 30 percent of those determined at 2 mg/cm^2 (Refs. 49, 50, and 51). Gasparro notes that statements such as “apply liberally and frequently” are too vague to be informative (Ref. 24).

FDA is concerned that, in practice, consumers may be getting less protection than the labeled SPF value and believes that further information should be included in the labeling for sunscreen drug products to reduce the likelihood of underapplication. FDA believes that this information is better

communicated as revised product directions rather than a warning. FDA is, therefore, proposing to revise § 352.52(d)(1). The directions will continue to state that OTC sunscreen drug products should be applied “liberally” or “generously” because it would be cumbersome to specify quantitative amounts for all possible body areas and the various uses on the label. However, FDA is proposing to make optional the directions in § 352.52(d)(1)(i) to apply “evenly.” FDA believes that this term, if used alone, may not convey the appropriate message to ensure that consumers apply sufficient sunscreen. In addition, FDA is proposing to remove the term “smoothly” from § 352.52(d)(1)(i) because FDA considers that term to be vague and it may have different meanings to different consumers. FDA also believes this term is more likely to result in product underapplication.

In addition to labeling directing consumers to apply sufficient amounts of sunscreen, FDA is also proposing to revise the labeling requirements concerning reapplication of the sunscreen product. In § 352.52(d) of the FM, the general reapplication statement “and as needed” was the only required information. FDA made specific reapplication directions in § 352.52(d)(2) of the FM optional in an effort to equalize requirements between sunscreens with and without water resistant claims (64 FR 27666 at 27681). FDA now believes that more detailed reapplication directions must be included on all OTC sunscreen products, because sunscreens may be underapplied as suggested by the comments.

FDA came to this conclusion after reviewing studies concerning sunscreen reapplication as well as recommendations of public health organizations. Wright, et al. suggests that inadvertent sunburn may be due to the failure to use and reapply sunscreen appropriately (Ref. 56). Study subjects who

reapplied sunscreen every 1 to 2 hours and after swimming did not report sunburn. Rigel et al. reported that, even under intense solar conditions, those reapplying an SPF 15 sunscreen every 2 hours or sooner were five times less likely to sunburn compared to those who reapplied every 2.5 or more hours (Ref. 57). The AAD (Refs. 38, 58, and 59), the ACS (Ref. 60), and the EPA (Ref. 40) recommend reapplying sunscreens every 2 hours or sooner and also recommend application to all exposed areas of the body (Refs. 60, 61, and 62).

Because the frequency of application appears to be critical for proper protection, FDA is proposing to add the statement “apply and reapply as directed to avoid lowering protection.” In addition, FDA is proposing to further revise the directions in § 352.52(d) to include the following reapplication statement: “reapply at least every 2 hours.” Likewise, for those products making a water resistant claim, FDA is proposing to include the number of minutes (i.e., 40 or 80) that the product maintains its water resistance before the “swimming/sweating” term. FDA believes these additional proposed directions will alert consumers about the hazards of using insufficient amounts of sunscreen product and encourage reapplication after the appropriate time. FDA considers these specific, informative reapplication statements, instead of “and as needed,” to be necessary on all OTC sunscreen products. FDA is also proposing the optional direction “apply to all skin exposed to the sun.” FDA is proposing that this direction be optional because we believe most consumers know to apply sunscreen to all exposed skin. However, if a sunscreen product can accommodate this direction, it will serve to remind consumers that all exposed skin is susceptible to UV damage. These proposed directions, as a whole, should serve to better protect consumers, particularly those who tend to underapply sunscreen, from overexposure to the sun.

Accordingly, FDA is proposing to change § 352.52(d) to read as follows:

(d) *Directions.* * * *

(1) *For products containing any ingredient in § 352.10.* (i) The labeling states “[bullet] apply [select one of the following: ‘liberally’ or ‘generously’] [and, as an option: ‘and evenly’] [insert appropriate time interval, if a waiting period is needed] before sun exposure”.

(ii) The labeling states “[bullet] apply and reapply as directed to avoid lowering protection”.

(iii) As an option, the labeling may state “[bullet] apply to all skin exposed to the sun”.

(iv) The labeling states “[bullet] children under 6 months of age: ask a doctor”.

(2) *For products that satisfy the water resistant or very water resistant testing procedures identified in § 352.76.* The labeling states “[bullet] reapply after [select one of the following: ‘40 minutes of’ or ‘80 minutes of’ for products that satisfy either the water resistant or very water resistant test procedures in § 352.76, respectively] swimming or [select one of the following: ‘sweating’ or ‘perspiring’] and after towel drying. Otherwise, reapply at least every 2 hours”.

(3) *For products that do not satisfy the water resistant or very water resistant testing procedures identified in § 352.76.* The labeling states “[bullet] reapply at least every 2 hours and after towel drying, swimming, or [select one of the following: ‘sweating’ or ‘perspiring’]”.

As discussed in the FM (64 FR 27666 at 27679), manufacturers who have data to support different reapplication directions based on specific substantiation information may submit the information for approval of those directions via an NDA deviation as provided in § 330.11 (21 CFR 330.11).

I. General Comments on SPF Testing Procedure

(Comment 23) One comment suggested that the SPF test incorporate an amount of product that more closely reflects the amount applied by consumers. More specifically, the comment requested that FDA replace the 2 mg/cm² required in § 352.72(e) (proposed § 352.70(c)(5)) to a value between 0.5 and 1.0 mg/cm². The comment argued that the protection afforded during actual usage may be only one-quarter to one-half the labeled SPF value (see section III.H, comment 22 of this document). The comment also suggested that SPF could be stated using descriptive terms, such as “light,” “moderate,” or “heavy” protection, instead of a numerical value.

FDA is not proposing the suggested change in test method at this time. This issue was discussed in detail in the TFM (58 FR 28194 at 28264 to 28266). The majority of comments advocated continuing the use of an application density of 2 mg/cm². The current comment did not provide data demonstrating the suitability of a smaller test amount. FDA is concerned that a uniform distribution of sunscreen over the test area might be difficult using a smaller amount of sunscreen. Further, the standard application density used worldwide in the SPF test is 2 mg/cm² (Ref. 63).

FDA agrees that SPF values do not reflect exact levels of sunburn protection that consumers receive under actual use conditions. The required SPF test is a clinical test conducted with strict control over factors such as product application density. However, under actual use conditions, these factors are not controlled and vary greatly. The actual level of sunburn protection under consumer use conditions is affected by a number of factors. Some of the key factors are

- Application density,

- Reapplication frequency,
- Skin type (e.g., burns easily versus never burns),
- Time of day during sun exposure, and
- Geographical location during sun exposure.

Thus, SPF values reflect relative and not absolute levels of sunburn protection.

Although SPF values do not convey actual levels of sunburn protection, when comparing multiple sunscreen products, SPF values enable consumers to determine which products provide the most sunburn protection. For example, FDA believes most consumers would correctly identify an SPF 20 product as providing more sunburn protection than an SPF 10 product. Thus, lowering the sunscreen application density would not be necessary to more accurately reflect the degree of relative sunburn protection.

FDA agrees that, in addition to bringing SPF values closer to representing absolute levels of protection, lowering the sunscreen application density might also reduce some of the inaccuracies and limitations encountered when testing high SPF sunscreen products. Thus, FDA invites interested parties to submit data supporting a smaller application density for SPF testing of all sunscreen dosage forms in accordance with § 352.77. However, developing a single global method and labeling would require a coordinated effort between the regulatory agencies in many countries around the world. Because FDA does not have data to validate the SPF test using a lowering sunscreen density, FDA is proposing directions that we believe will encourage consumers to apply greater densities of sunscreen (i.e., closer to 2 mg/cm²) (see section III.H, comment 22 of this document).

FDA does not find that there are sufficient benefits for using descriptors instead of numerical values for SPF on the PDP. Consumers are familiar with

numerical SPF values from over 20 years of usage. As described in section III.G, comment 16 of this document, FDA believes that the use of descriptors in combination with numerical values on the PDP may be beneficial to consumer understanding of the level of sunburn protection provided by a product. Thus, as explained in comment 16, FDA is proposing to include a descriptive term of relative sunburn protection (i.e., low, medium, high, or highest) with the proposed sunburn protection statement in the “Uses” section and on the PDP. The intent of this dual descriptive and numerical sunburn protection measure is to allow consumers to more easily differentiate the level of sunburn protection provided by different sunscreen products. In addition, this proposed labeling for sunburn protection is similar to the proposed UVA protection labeling (see section III.G, comment 14 of this document).

FDA is also aware of sunscreen drug products marketed in dosage forms that may not be addressed by current SPF testing procedures. The SPF testing procedure described in § 352.72 (proposed § 352.70) references oils, lotions, creams, gels, butters, pastes, and ointments. FDA invites interested parties to submit SPF testing modifications for new dosage forms (e.g., mousses, foams, and towelettes) in accordance with § 352.77.

(Comment 24) One comment recommended a pass/fail (binomial) test to determine SPF values (Ref. 49). The test would demonstrate that subjects have no reaction to a quantity of UV energy equivalent to an expected SPF value (for products passing the test). For example, subjects being tested with a product with an expected SPF value of 30 would be dosed only at the SPF 30 level, and the product would either pass or fail. A product passing this test would actually have an SPF value of 30 or over, whereas a product failing this test would have an SPF value below 30. The comment argued that while