DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 352

[Docket No. FDA–1978–N–0018; formerly Docket No. 1978N–0038]

RIN 0910–ZA40

Sunscreen Drug Products for Over-the-Counter Human Use; Request for Data and Information Regarding Dosage Forms

AGENCY: Food and Drug Administration, HHS.

ACTION: Advance notice of proposed rulemaking; request for data and information.

SUMMARY: We (Food and Drug Administration or FDA) are asking sunscreen manufacturers and other interested parties to submit data on over-the-counter (OTC) sunscreen drug products marketed without approved applications that are formulated in certain dosage forms. These data are necessary to address questions about these dosage forms. For spray dosage forms, we are requesting data to resolve specific questions about both effectiveness and safety. We are also inviting comment on possible labeling and testing requirements for spray dosage forms. This information will be used in establishing monograph conditions, including dosage forms, for sunscreens that are generally recognized as safe and effective (GRASE) and not misbranded.

DATES: Submit data and information either electronically or in writing by September 15, 2011.

ADDRESSES: You may submit comments, identified by docket number FDA–1978–N–0018 (formerly Docket No. 1978N–0038) and/or RIN number 0910–ZA40, by any of the following methods:

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.

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.

Instructions: All submissions received must include the agency name and docket number FDA–1978–N–0018 and RIN 0910–ZA40 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided if not marked as confidential.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov,* insert the docket numbers, 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: Reynold Tan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Mail Stop 5411, Silver Spring, MD 20993, 301–796–2090.

SUPPLEMENTARY INFORMATION:

I. Purpose of This Document

FDA is requesting additional data necessary to establish monograph conditions for sunscreens, including specification of certain dosage forms. In this document, we discuss those dosage forms that we consider currently to be part of the OTC Drug Review, and thus eligible for potential inclusion in a sunscreen monograph, and those dosage forms that we do not consider eligible. For the dosage forms that are eligible, we seek to ensure that the record is complete, so as to support a future monograph identifying conditions, including dosage forms and appropriate testing and labeling, for sunscreens to be GRASE and not misbranded. Finally, as explained below, sunscreens in certain dosage forms such as wipes, towelettes, powders, body washes, and shampoos are not currently considered eligible for inclusion in the sunscreen monograph, and even if their eligibility were established, they lack a sufficient record to support inclusion in the sunscreen monograph.

Although spray dosage forms are among those dosage forms we consider potentially eligible for inclusion in the final sunscreen monograph, they currently lack a record comparable to other dosage forms that could be included in the sunscreen monograph. Considering the greatly increasing number of sunscreen products formulated as sprays, it is critical that the safety and effectiveness of this dosage form be adequately supported. From their existing marketing of spray sunscreens, manufacturers may have the necessary data, but to date these data have not been submitted to FDA. To further encourage submission of data and allow us to move to a proposed rule as quickly as possible, we have developed possible labeling and testing specific to sprays, for which we solicit comment.

Although at this time we expect to receive the necessary data, if we do not obtain sufficient data to support monograph conditions for sunscreen products formulated in certain dosage forms, these products may not be included in the future OTC sunscreen monograph. Any sunscreen product not included in a future final monograph could obtain approval to market by submitting new drug applications (NDAs) under section 505 of the Federal Food, Drug, and Cosmetic Act (FD&C Act). These products might in the future be able to submit NDA deviations in accordance with 21 CFR 330.11, limiting the scope of review necessary to obtain approval. It should be noted that, where a final monograph exists, the content of an NDA that deviates only in limited respects from the monograph may omit all information except that pertinent to the deviation.

II. Enforcement Policy

In the absence of an effective final monograph for OTC sunscreen products, questions may arise regarding FDA's enforcement policy for OTC sunscreen products in various dosage forms that are marketed without approved applications. For clarification, we are issuing a draft guidance document that explains the Agency's intended enforcement policy on the various dosage forms for OTC sunscreen products that are marketed during the absence of an effective sunscreen final monograph. This draft guidance document is being published elsewhere in this issue of the **Federal Register**. We are also publishing elsewhere in this issue of the **Federal Register** a final rule for OTC sunscreen products containing certain ingredients and marketed without approved applications that specifies labeling and testing requirements, without regard to dosage form.

III. Dosage Forms Currently Eligible for Inclusion in a Sunscreen Monograph

We have not explicitly stated in previous rulemakings which dosage forms of OTC sunscreen drug products we would consider to be GRASE and not misbranded. However, in 21 CFR 352.52(d), we identified several dosage forms, including sprays, for the purposes of labeling: ''(*e.g.,* cream, gel,

lotion, oil, spray, *etc.*).'' In 21 CFR 352.72(e), we further identified oils, lotions, creams, gels, butters, and pastes and ointments for the purposes of testing. We also identified sticks in the August 25,1978, advanced notice of proposed rulemaking (ANPR) (43 FR 38206 at 38207, 38223, 38224, 38229, and 38239) as lip protectants, which are allowed to contain sunscreen active ingredients and are formulated as sticks (existing 21 CFR 352.60).

For a drug product to be eligible for review, the drug product must either be a product that can be substantiated to have been marketed OTC before the OTC Drug Review began in 1972, or it must be determined to be eligible through submission of a time and extent application (21 CFR 330.14). With respect to OTC sunscreen drug products, the following dosage forms are eligible for review and potential inclusion in the monograph:

- Oils
- Lotions
- Creams
- Gels
- Butters
- Pastes
- Ointments
- Sticks
- Sprays

On the existing record, we anticipate that all of these listed dosage forms, except sprays, would be included in the future OTC sunscreen monograph as GRASE and not misbranded under the labeling and testing established in new 21 CFR 201.327. However, the record does not yet contain comparable safety and effectiveness data and information for spray dosage forms.

Although we have information about how sunscreens in eligible dosage forms other than sprays are applied, including data on the amounts of oils, creams, and lotions consumers typically apply (Refs. 1 and 2), spray dosage forms are sufficiently different from other eligible dosage forms identified during the course of development of the sunscreen monograph that the data and information for these dosage forms are not directly applicable. The nature of other eligible dosage forms identified during the course of development of the sunscreen monograph (oils, creams, lotions, gels, butters, pastes, ointments, sticks) requires that consumers dispense the product into their hand or directly onto their skin and rub these products into the skin to some extent, with most of the amount dispensed applied. Sprays, however, in particular aerosolized sprays, are dispensed in a more diffuse manner even when applied directly to the body. Due to the different modes of dispensing and application between sprays and the other dosage forms, we do not know if consumers obtain the same protection with sprays as these other dosage forms. With sprays, we also do not know how much of the typical dispensed amount is effectively transferred to the skin. Adequate, uniform coverage of sprays may also be difficult to assess, because some sprays are applied in a thin, clear layer which is more difficult to visualize than other dosage forms. Some spray products are similarly meant to be rubbed into the skin, but we do not know if consumers typically rub these spray products into the skin. Thus, upon review of the record, we have determined that additional data or information (as outlined below) are necessary, and must be sufficient to support appropriate monograph conditions (e.g., testing and labeling specific to sprays) to be included in the future final monograph. Thus, we are soliciting data to address the following questions to build a record comparable to other dosage forms such as lotions:

- What amounts of sunscreen spray do consumers typically dispense and what amounts are effectively transferred to the skin?)
- How uniform is the sunscreen application across the sun-exposed area of skin?
- How frequently do consumers reapply the product?
- If a product is labeled with a direction to rub it into the skin, do consumers typically follow this direction?
- How does rubbing the product into the skin change the effectiveness?
- How do the protection levels (SPF values) when typical amounts are applied compare with those under laboratory conditions?
- Should the SPF and broad spectrum tests be modified to address sprays? If so, how?

In addition to answering these questions for spray dosage forms, it would be useful if studies also directly compared spray dosage forms to the other eligible dosage forms previously identified during the course of development of the sunscreen monograph. We are interested in whether use of sunscreen sprays differs enough from use of other eligible sunscreen dosage forms that the SPF values on sunscreen sprays are not comparable to those on other sunscreens. We are also interested in whether use differs among sunscreen spray products. Some sunscreen sprays are dispensed by pumps rather than as aerosolized sprays. Other sprays may turn into a foam upon contact with the skin. We would be interested in data and information that helps us assess how our concerns about sunscreen sprays in general apply to different types of sunscreen sprays. (See section *V. ''Submission of Data and Information''* for information on submitting these data.)

As we have done previously for other spray OTC products, we are also requesting data to understand the possibility and consequences of unintentional inhalation of spray sunscreens, an issue not presented by the other eligible dosage forms because they are applied directly to the skin:

- What are the risks associated with inhalation of sunscreen active ingredients and propellants?
- What are typical particle size distributions for sunscreen spray products?
- Are animal toxicity studies necessary for determining the potential for toxicity resulting from inhalation?
- Is the labeling discussed in this document adequate to prevent unintentional inhalation? If not, please provide alternative labeling.

In responding to the first question, (What are the risks associated with inhalation of sunscreen active ingredients and propellants?), we request submission of any reports of adverse events associated with unintentional inhalations of currently marketed sunscreen spray products.

To encourage submission and in anticipation of receiving this necessary data/information, we have used the available data and information on sprays to develop possible labeling and testing for comment. To address the possibility that inhalation of aerosolized particulates could cause adverse health effects, we are considering proposing a warning for sunscreen spray products that reads:

- ''*When using this product* keep away from face to avoid breathing it.''

We are also considering specific directions for sunscreen spray products that read:

- ''hold container 4 to 6 inches from the skin to apply''
- ''do not spray directly into face. Spray on hands then apply to face.''
- ''do not apply in windy conditions''
- ''use in a well-ventilated area''

Sunscreen spray products would be required to be labeled with these warnings and directions in addition to the other warnings and directions required for all sunscreen products.

We are also considering a proposal to modify a directions statement to ensure that sunscreen products in spray dosage forms are applied comparably to sunscreen products in other dosage forms. The sun protection factor (SPF)

and broad spectrum test procedures in the 2011 final rule (published elsewhere in this issue of the **Federal Register**) require that test products be applied in an amount of 2 milligrams per square centimeter (mg/cm^2) and 0.75 mg/cm^2, respectively, and then spread evenly by hand (21 CFR 201.327(i)(4)(iii) and (j)(2)). Comparable product application during testing, as required by these standard testing conditions, is necessary to ensure consistent and comparable test values between sunscreen products. However, valid comparison of SPF test values and broad spectrum test results between products further requires comparable product application during actual use. Therefore, we are considering proposing directions for the application of sprays to more closely follow the way they are applied in SPF and broad spectrum testing. The modified directions statement would read:

- ''spray [select one of the following: 'liberally' or 'generously'] and spread evenly by hand 15 minutes before sun exposure.''

We invite comment on all of the labeling statements we are considering. If there are other labeling statements that should be considered, in order for us to propose them for inclusion in a final monograph, we will need adequate data supporting the alternative labeling, just as we are requesting data to support the labeling we have already developed for consideration. In developing any alternative labeling for consideration, we advise submitters that the directions for application should reflect how the SPF and broad spectrum test procedures are performed.

We are considering adding the following sentence to the SPF and broad spectrum test procedures (21 CFR 201.327(i) and (j), respectively) to require the following regarding application of test material: ''For spray formulations, dispense the product into a weighing vessel and then apply the appropriate weight of liquid.'' This revision is based upon the one public test modification for a sunscreen spray product that we are aware of (Ref. 3). However, the information regarding the test method did not contain validation of the test as it relates to sprays. To support proposing this modification as a monograph condition, we need data to validate the modified test method; we also remain open to any other testing alternative that is supported by sufficient data to demonstrate that it would be an appropriate monograph condition for sprays. To support a testing alternative, data would need to show that testing a spray product according to the alternative test produces SPF and broad spectrum test results that can be validly compared to SPF and broad spectrum test results for other dosage forms. We solicit comment on whether this test modification would be appropriate for all spray dosage forms and whether modifications are needed to address differences in dispensing and application between spray dosage forms. For example, some current spray labels direct the user to spray directly onto skin and some also direct the user to rub in. As noted, we are soliciting comment on directions calling for spray products to be spread by hand, as is done under the current test method. If spray manufacturers instead seek labeling indicating that spray application is alone sufficient (*e.g.,* ''no-rub'' labeling), we seek validated testing to support this labeling. We invite manufacturers to discuss possible methods and validations with us.

The foregoing discussion concentrates on specific dosage forms that we have concluded are eligible for potential inclusion in the sunscreen monograph. Although we particularly solicit specific data regarding sprays, we welcome the submission of any additional information relevant to the safety and effectiveness of other eligible dosage forms. We also invite submitters to identify any additional dosage forms that may be eligible for inclusion in the OTC monograph based on marketing prior to the outset of the OTC drug review in 1972, and to provide information to support their eligibility. If eligible, any additional dosage forms will also require a sufficient record to support finding them to be generally recognized as safe and effective if they are to be proposed for inclusion in the OTC sunscreen monograph. See 21 CFR 330.10 for information regarding the types of information to be submitted to support eligibility and inclusion in an OTC drug monograph.

IV. Dosage Forms Not Eligible for Inclusion in a Sunscreen Monograph

In response to the August 27, 2007, proposed rule for OTC sunscreen products (72 FR 49070), several submissions recommended that we include the following dosage forms in the final sunscreen monograph (Ref. 4):

- Wipes
- Towelettes
- Powders
- Body washes
- Shampoos

We currently do not consider these dosage forms eligible for review under the OTC monograph process. We were unable to identify any sunscreen products in wipe, towelette, powder, body wash, or shampoo dosage forms that were marketed OTC before the OTC Drug Review began. To determine eligibility for the OTC Drug Review, we must have actual product labeling or a facsimile of labeling that documents the conditions of marketing of the product prior to May 1972 (21 CFR 330.10(a)(2)). Conditions include active ingredient, dosage form, dosage strength, route of administration, and specific OTC use of the product (21 CFR 330.14(a)). These are the same criteria used to establish that OTC drugs initially marketed in the United States after the OTC Drug Review began or without U.S. marketing experience meet the ''material extent'' or ''material time'' provisions of the FD&C Act's ''new drug'' definition (21 U.S.C. part 201, section 201(p)(2)) and are eligible for the OTC Drug Review (21 CFR 330.14(c)(3)). We also have not received any time and extent applications for OTC sunscreen products formulated as wipes, towelettes, powders, body washes or shampoos. Therefore, sunscreens formulated as wipes, towelettes, powders, body washes, or shampoos are not currently eligible for review under the OTC sunscreen monograph. If their eligibility is to be established, the required information must be submitted in the form of a time and extent application (21 CFR 330.14). Determination of eligibility would not itself be sufficient for inclusion in the OTC sunscreen monograph. As discussed in 21 CFR 330.14(e), we would publish a notice of eligibility if the dosage form was found eligible and then we would request data to demonstrate the safety and effectiveness of the dosage form for its intended OTC use (21 CFR 330.14(f)).

V. Submission of Data and Information

Interested persons may submit data and information as described under the **ADDRESSES** heading at the beginning of this document. Submit a single copy of electronic submissions or two paper copies of any mailed submissions, except that individuals may submit one paper copy. Submissions are to be identified with the docket number found in brackets in the heading of this document. Received submissions may be viewed electronically at *http://www.regulations.gov* or by visiting the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

VI. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**), under docket number FDA–1978–N–0018

(formerly Docket No. 1978N–0038) unless otherwise noted, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Neale *et al., Archives of Dermatology,* 138:1319–25, 2002.

2. Autier *et al., British Journal of Dermatology,* 144:288–91, 2001.

3. Docket No. FDA–1978–N–0018 (formerly Docket No. 1978N–0038): C712, Schering Plough.

4. Docket No. FDA–1978–N–0018 (formerly Docket No. 1978N–0038): FDA List of Docket Submissions Regarding Dosage Forms Issues: C683, C712, C716, EC2720.

This ANPR is issued under 21 U.S.C. 321, 331, 351, 352, 353, 355, 358, 360, 360b, 360gg–360ss, 371, 374, 379e; 42 U.S.C. 216, 241, 262, 264 and under the authority of the Commissioner of Food and Drugs.

Dated: June 9, 2011.

Leslie Kux,

Acting Assistant Commissioner for Policy.

[FR Doc. 2011–14768 Filed 6–14–11; 8:45 am]

BILLING CODE 4160–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 201

[Docket No. FDA–1978–N–0018; formerly Docket No. 1978N–0038]

RIN 0910–AF43

Revised Effectiveness Determination; Sunscreen Drug Products for Over-the-Counter Human Use

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to limit the maximum labeled SPF value for over-the-counter (OTC) sunscreen drug products to ''50+.'' We are issuing this proposed rule after reviewing data and information we received on the safety and effectiveness of OTC sunscreen drug products after publication of our 2007 proposed rule. The record does not currently contain sufficient data to indicate that there is additional clinical benefit above SPF 50. This proposal is part of FDA's ongoing review of these products to ensure their safety and effectiveness.

DATES: Submit either electronic or written comments on the proposed rule by September 15, 2011. Submit comments on information collection issues under the Paperwork Reduction Act of 1995 (the PRA) by July 18, 2011, (see the ''Paperwork Reduction Act of 1995'' section of this document). See section VII of this document for the proposed effective date of a final rule based on this proposal.

ADDRESSES: You may submit comments, identified by Docket No. FDA–1978–N–0018 and RIN number 0910–AF43, by any of the following methods, except that comments on information collection issues under the PRA must be submitted to the Office of Regulatory Affairs, Office of Management and Budget (OMB) (see the ''Paperwork Reduction Act of 1995'' section of this document).

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the instructions for submitting comments.

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.

Instructions: All submissions received must include the Agency name, Docket No. FDA–1978–N–0018, and RIN 0910–AF43 for this rulemaking. All comments received may be posted without change to *http://www.regulations.gov,* including any personal information provided.

Docket: For access to the docket to read background documents or comments received, go to *http://www.regulations.gov,* insert the docket numbers, 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: Reynold Tan, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 5411, Silver Spring, MD 20993–0002, 301–796–2090.

SUPPLEMENTARY INFORMATION:

Table of Contents

I. Overview of This Document

A. Summary of Proposal

This document proposes to specify one of the conditions under which OTC sunscreen products are considered to be generally recognized as safe and effective (GRASE) and not misbranded. We are proposing a maximum labeled sun protection factor (SPF) value of ''50+'' for all monograph sunscreen products. In a final monograph issued in 1999, and stayed prior to becoming effective, we determined that the maximum SPF permitted under the monograph should be ''30+'' (64 FR 27666 at 27674 through 27675, May 21, 1999). In a 2007 proposed rule, we proposed to amend the sunscreen monograph in part 352 to permit products marketed under the monograph to be labeled with SPF values up to ''50+,'' and we expressed particular concern that sunscreen products with SPF test values above 50 could not be tested with acceptable accuracy and reproducibility (72 FR 49070 at 49085 through 49087, August 27, 2007) (the 2007 proposed rule). Although submissions in response to the 2007 proposed rule demonstrated the accuracy and reproducibility of such tests at values as high as SPF 80, we are again proposing a maximum labeled SPF value of ''50+'' for sunscreen products marketed without approved applications, because the record continues to lack data demonstrating that sunscreen products with SPF values above 50 provide additional clinical benefit compared to SPF 50 products. In this document, we are inviting the submission of data demonstrating additional clinical benefit provided by sunscreen products with SPF values greater than 50.

B. Enforcement Policy

Elsewhere in this issue of the **Federal Register**, we are issuing a final regulation establishing effectiveness