



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

TESTIMONY OF

U.S. FOOD AND DRUG ADMINISTRATION

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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BEFORE THE

SUBCOMMITTEE ON HEALTH

COMMITTEE ON ENERGY AND COMMERCE

U.S. HOUSE OF REPRESENTATIVES

“Improving Predictability and Transparency in DEA and FDA Regulation”

APRIL 7, 2014

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INTRODUCTION

Mr. Chairman, Ranking Member Pallone, and Members of the Subcommittee, I am Dr. Janet Woodcock, Director of the Center for Drug Evaluation and Research at the Food and Drug Administration (FDA or the Agency), which is part of the Department of Health and Human Services (HHS). Thank you for the opportunity to be here today to discuss the important issues concerning sunscreen ingredients, over-the-counter (OTC) drug monographs, and the Time and Extent Application (TEA) process.

Background

The Federal Food, Drug, and Cosmetic Act (FD&C Act) requires FDA to review and approve a new drug application (NDA) or abbreviated new drug application (ANDA) for all new drugs before they can be marketed in the United States. To avoid “new drug” status as defined in the FD&C Act, a drug must be generally recognized as safe and effective (GRASE) and also must have been marketed to a material extent and for a material time under the conditions described in its labeling (the material time-and-extent standard), 21 U.S.C. 321(p).

An OTC drug monograph is an FDA regulation that describes the conditions, including specified active ingredients, that various categories of OTC drugs (such as sunscreens) must meet to be determined GRASE and not misbranded. The monograph process is intended to create a pathway for FDA to review and identify OTC drug ingredients that are GRASE. Products using these ingredients can reach the market without using the NDA process. However, the process of establishing an OTC drug monograph requires multiple stages of notice-and-comment rulemaking, and can be both lengthy and complex. A drug product that complies with an

applicable OTC monograph and the general requirements for OTC drugs can be marketed without an NDA or ANDA. FDA's GRASE determinations must be supported by publicly available data that satisfy the requirements and evidentiary standards specified in FDA's OTC drug regulations.

The TEA process, established by regulations finalized in 2002 (21 CFR 330.14(g)), expanded the scope of the OTC Drug Review. This process provides a potential pathway to OTC monograph status for newer active ingredients and other conditions; primarily, those with no U.S. marketing history. The TEA process enables sponsors to establish that a condition satisfies the threshold eligibility requirement of a "material time and extent" of OTC marketing, based on historic marketing data other than the date of U.S. market entry (TEA eligibility requirements).

Active ingredients and other conditions that satisfy the TEA eligibility requirements are subject to the same GRASE standard and evidentiary requirements that apply to other active ingredients and conditions under the OTC monograph process. Like the OTC monograph process, the TEA process requires multi-step, notice-and-comment rulemaking procedures, before a new ingredient is officially included in an OTC drug monograph.

To elaborate, the TEA process begins with the submission of a TEA application containing data documenting the OTC marketing history of the active ingredient or other condition(s) for which monograph consideration is sought. FDA reviews the application and determines whether the sponsor's marketing data establish a material time and extent of OTC marketing, as set forth in the TEA eligibility requirements. If not, the application is denied. If the marketing data satisfy the TEA eligibility criteria, FDA publishes a *Federal Register* notice announcing that the active ingredient or other condition is being considered for OTC monograph status and calling for

submissions of safety and efficacy data. If FDA’s review of the submitted data (together with any other data from the published scientific literature) supports a tentative GRASE determination, the Agency will publish a proposed rule to include the active ingredient or other condition in the appropriate OTC monograph. If the evidentiary record does not support a tentative GRASE determination, the regulations provide for FDA to issue “feedback” letters to data submitters and the public docket, in which the Agency details its evaluation of the available data and may identify remaining data gaps and invite further data submissions. If additional data are not forthcoming or do not adequately support GRASE status, FDA will publish a proposed rule declaring that the active ingredient or other condition may be marketed only under an approved NDA or ANDA. If the supplemented record supports GRASE status, FDA will issue a proposed rule adding the active ingredient to the OTC monograph. In each of the cases, where FDA publishes a proposed rule, this will be followed by a public comment period, review of comments, and issuance of a final rule.

Current Scientific Considerations

Human exposure to sunscreens has increased significantly since the 1970s, when the examination of sunscreens in the OTC Drug Review began. Back then, sunscreens were used primarily on a seasonal basis to prevent sunburn. Accordingly, when evaluating the safety of sunscreen drug products, the OTC sunscreen advisory panel anticipated that consumers would be exposed to sunscreen active ingredients in modest amounts and for short, intermittent time periods. Sunscreen ingredients also were not thought to penetrate beyond the surface of the skin, so that potential systemic exposure to sunscreen active ingredients was not a concern. As a result, the advisory panel’s safety evaluation focused primarily on ensuring that sunscreen products caused minimal skin irritation and sensitivity.

Today, sunscreens are used on a routine basis by a large percentage of the population, with labeling that instructs consumers to apply sunscreens in generous amounts and to reapply, often resulting in an extent and duration of exposure to sunscreen ingredients that is orders of magnitude greater than it was in the 1970s, both for individual consumers and for the public at large. There is also increasing evidence that some sunscreen ingredients can be absorbed through the skin, leading to systemic exposures to these agents, not previously anticipated. The shift in sunscreen use, together with advances in scientific understanding and in safety evaluation methods during the same period, have given rise to new questions about what information is necessary and available to support general recognition of safety and effectiveness for sunscreens.

In order for FDA to propose to amend the OTC sunscreen monograph to include a new active ingredient as GRASE, we must also make an initial determination, based on appropriate scientific evidence, that any sunscreen product that could be formulated using the new active ingredient in the concentrations, permitted combinations, or other applicable limitations specified in the monograph, would be GRASE for use under the conditions prescribed, recommended, or suggested in its labeling. In other words, inclusion of a new ingredient in the monograph requires more than a general assessment of the ingredient, followed by adding it to the list of ingredients in the monograph. In some cases, it may require amending the monograph, not only in terms of specifying the concentration of the allowed active ingredient, but also to lay out any other limitations on its use that are needed for its safe and effective use as well as new labeling that would apply to products that included the ingredient.

FDA has been actively examining the important scientific questions for the sunscreen ingredients currently proposed in TEAs, and significant efforts have resulted in FDA recently sending letters to sponsors providing feedback on safety and efficacy data submitted in support of TEA ingredients. These letters are publicly available in the docket, in accordance with the TEA regulation. The letters that have been issued for the TEA ingredients amiloxate and diethylhexyl butamido triazone describe FDA's review of the scientific record for these sunscreen active ingredients (consisting of material submitted by the TEA sponsors and others, and information identified by FDA from the medical literature), and provide initial determinations that the record is insufficient to establish that either ingredient is GRASE for OTC sunscreen use. As described in these letters, given the expansion of sunscreen use and scientific advances since the OTC sunscreen evaluation began, our safety evaluation of these ingredients must consider, not only short term concerns (such as skin sensitivity), but also long-term concerns (such as the results of systemic exposure), about which little scientific data has been provided.

FDA's efforts on the remaining six TEA sunscreen ingredients are actively continuing, and we expect to reach our initial determinations soon. Unfortunately, we cannot say anything further on this topic until we issue our initial determinations. FDA will be holding a public meeting to discuss the information provided in the TEA letters and provide an opportunity to further clarify FDA's thinking about the data required to support a GRASE determination for sunscreens. Another public hearing relevant to the sunscreens and the TEA process was held last week (on March 25 and 26, 2014) to discuss the need to modernize the OTC monograph system in general. Our discussions about modernizing the overall OTC process will continue. However, given the public health benefits of sunscreen use, we are committed to finding ways to facilitate the marketing of additional OTC sunscreen active ingredients independent of

discussion about the overall OTC process, but must do so with appropriate assurances of both their safety and effectiveness.

While evaluating the safety and effectiveness of potential new sunscreen active ingredients has been an important task for FDA, it is not the only major effort regarding sunscreens that FDA has undertaken in the last several years. In 2011, we took several regulatory actions on a number of important sunscreen issues. First, we finalized rules that updated the efficacy testing requirements and related labeling, which applies to sunscreens currently available in the U.S.¹ This final rule prescribes new, improved labeling, including updated Drug Facts labeling. The final rule also establishes two effectiveness tests, one that must be done to support the sun protection factor (SPF) of the product, and another if a product claims to be broad spectrum (protecting against both UVA and UVB).

We issued a proposed rule proposing a maximum labeled SPF value of “50+” for all monograph sunscreen products. We also issued an advance notice of proposed rulemaking (ANPR) to seek additional information on the safety and effectiveness of sunscreens formulated as sprays and to address additional questions related to other specific dosage forms of sunscreens.

Subsequent rulemaking activity is needed for each of these topics, and FDA has dedicated resources to ensure diligent follow-up.

¹ The new requirements, and several proposed changes to regulations, are discussed in four regulatory documents that include a final rule, proposed rule, an ANPR, and draft guidance for industry. Links to each of these documents are included below:

-Final Rule, Labeling and Effectiveness Testing, <http://www.gpo.gov/fdsys/pkg/FR-2011-06-17/pdf/2011-14766.pdf>

-Proposed Rule, Revised Effectiveness Determination, <http://www.gpo.gov/fdsys/pkg/FR-2011-06-17/pdf/2011-14769.pdf>

-ANPR, Dosage Forms for Sunscreens, <http://www.gpo.gov/fdsys/pkg/FR-2011-06-17/pdf/2011-14767.pdf>

-Draft guidance for industry, Enforcement Policy – OTC Sunscreen Drug Products Marketed Without an Approved Application,

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM259001.pdf>

CONCLUSION

FDA agrees that the review process for TEA submissions has taken too long. However, it is important to note that we have taken important steps to ensure the safety and effectiveness of all sunscreen products, and we are working diligently to complete the pending TEA proceedings.

We can work with the Committee to improve the timeliness and predictability of the TEA process while ensuring that any changes maintain the integrity of the review process.

I am happy to answer any questions you may have.