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Food and Drug Administration

21 CFR Part 350

[Docket No. 1978N–0064]

RIN 0910–AC89

Antiperspirant Drug Products for Over-the-Counter Human Use; Final Monograph; Partial Stay; Reopening of the Administrative Record

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; partial stay; reopening of the administrative record.

SUMMARY: The Food and Drug Administration (FDA) is staying part of the final monograph (FM) for over-the-counter (OTC) antiperspirant drug products that published in the **Federal Register** on June 9, 2003 (68 FR 34273). The FM established conditions under which OTC antiperspirant drug products are generally recognized as safe and effective (GRASE) and not misbranded. This partial stay applies only to the labeling claims for enhanced duration in § 350.50(b)(3) and (b)(5) (21 CFR 350.50(b)(3) and (b)(5)). In addition, FDA is reopening the administrative record for the rulemaking on OTC antiperspirant drug products to allow for comment and data specifically on the information requested in this document. FDA is taking this action in response to a citizen petition containing data demonstrating that FDA's effectiveness testing guidelines for OTC antiperspirant drug products may support an enhanced duration claim greater than 24 hours. This action is part of FDA's ongoing review of OTC drug products.

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DATES: This rule is effective December 9, 2004 ~~[insert date 30 days after date of publication in the **Federal Register**]~~. The limitation of the enhanced duration claim to 24 hours (21 CFR 350.50(b)(3) and (b)(5)) is stayed until further notice.

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Submit written or electronic comments and data by [*insert date 180 days after date of publication in the* **Federal Register**]. The administrative record will remain open until [*insert date 180 days after date of publication in the* **Federal Register**].

ADDRESSES: You may submit comments, identified by Docket No. 1978N–0064 by any of the following methods:

- Federal eRulemaking Portal: *http://www.regulations.gov*. Follow the instructions for submitting comments.
- Agency Web site: *http://www.fda.gov/dockets/ecomments*. Follow instructions for submitting comments on the agency Web site.
- E-mail: *fdadockets@oc.fda.gov*. Include Docket No. 1978N–0064 in the subject line of your e-mail message.
- FAX: 301–827–6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]: Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Instructions: All submissions received must include the agency name and Docket No. 1978N–0064. All comments received will be posted without change to *http://www.fda.gov/dockets/ecomments*, including any personal information provided. For detailed instructions on submitting comments and additional information on the rulemaking process, see the "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/dockets/ecomments* and/or the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Xin Zhou, Center for Drug Evaluation and Research (HFD–560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2222.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of October 10, 1978 (43 FR 46694), FDA published an advance notice of proposed rulemaking (ANPRM) to establish a monograph for OTC antiperspirant drug products, together with the recommendations of the Advisory Review Panel on OTC Antiperspirant Drug Products (the Panel), which evaluated the data on these products. The Panel classified claims for enhanced duration of effect as Category III (more data needed) because the Panel did not receive any scientific data to support a claim of prolonged or enhanced duration of effect (43 FR 46694 at 46728).

In the **Federal Register** of August 20, 1982 (47 FR 36492), FDA issued a proposed rulemaking or tentative final monograph (TFM) for OTC antiperspirant drug products. To standardize the antiperspirant drug product effectiveness test, FDA also issued guidelines for effectiveness testing of antiperspirant drug products (47 FR 36492 at 36504). However, FDA did not include testing recommendations for an enhanced duration claim in these guidelines because the Panel had not recommended such guidelines and FDA received no comments on this subject in response to publication of the ANPRM.

In response to the TFM, FDA received data from 15 studies to support enhanced duration claims. FDA found the studies supportive of a 24-hour or all day protection claim and included such a claim in § 350.50(b)(3) and (b)(5) of the FM. However, FDA stated that claims of enhanced duration for more than 24 hours are nonmonograph because FDA had not received any data to demonstrate antiperspirant effectiveness for more than 24 hours according to the Panel's criteria (68 FR 34273 at 34278).

II. Partial Stay of Part 350

Following publication of the antiperspirant FM, a drug manufacturer and an association representing manufacturers submitted citizen petitions disagreeing with FDA's decision to limit the enhanced duration claim to 24 hours (Refs. 1 and 2). Neither petition contained any effectiveness testing data to support enhanced duration claims beyond 24 hours. However, the manufacturer subsequently submitted such data from two studies (Ref. 3).

FDA evaluated the data and the results demonstrate that a roll-on and a solid stick antiperspirant drug product are extra effective for 48 hours duration (i.e., sweat was reduced by at least 30 percent in the majority of subjects up to 48 hours after antiperspirant application). The protocol in the two studies followed FDA's testing guidelines, with no significant deviations from those guidelines. The antiperspirant drug products used in the studies contained an active ingredient at a concentration allowed under the antiperspirant FM (§ 350.10 (21 CFR 350.10)). Thus, FDA believes the study results suggest that FDA's testing guidelines can be used to test enhanced duration claims of up to 48 hours. Accordingly, FDA is staying the enhanced duration claim limitation of 24 hours (in § 350.50(b)(3) and (b)(5)) so that products labeled for enhanced duration claims greater than 24 hours and up to 48 hours can

continue to be marketed while FDA reviews additional data on such claims. Manufacturers making such claims for their products should have supporting test data in their files. FDA will consider allowing enhanced duration claims of greater than 48 hours after it receives and evaluates data supporting such claims. This stay will remain in effect until further documentation is provided in a future issue of the **Federal Register**.

To the extent that 5 U.S.C. 553 applies to this action, it is exempt from notice and comment because it constitutes a rule of procedure under 5 U.S.C. 553(b)(3)(A). Alternatively, FDAs implementation of this action without opportunity for public comment comes within the good cause exceptions in 5 U.S.C. 553(b)(3)(B) and (d)(3) in that obtaining public comment is impracticable, unnecessary, and contrary to the public interest. FDA is staying the enhanced duration claim limitation of 24 hours in § 350.50(b)(3) and (b)(5) because FDA received and is reviewing data demonstrating an enhanced duration claim greater than 24 hours. FDA is also reopening the administrative record and inviting the submission of additional comments and data related to the effectiveness of antiperspirant drug products for more than 24 hours. Following evaluation of submitted comments and data, FDA will propose amendments to § 350.50(b)(3) and (b)(5) and possibly other sections of part 350. Thus, there will be an opportunity for public comment on enhanced duration claims greater than 24 hours within proposed amendments to part 350. In this final rule, FDA is providing an opportunity for comment on whether this partial stay should be modified or revoked.

III. Information Requested

In the antiperspirant FM, FDA stated that claims of enhanced duration for more than 24 hours are nonmonograph because FDA did not receive any data

to demonstrate antiperspirant effectiveness for more than 24 hours (68 FR 34273 at 34278). Because FDA has now received data demonstrating antiperspirant product effectiveness for 48 hours, FDA is reopening the administrative record to provide for additional submission of data and comments on enhanced duration effectiveness claims for antiperspirant drug products. FDA would like to evaluate additional data demonstrating antiperspirant effectiveness beyond 24 hours before including enhanced duration claims for longer time periods (e.g., 48 hours) in the FM. FDA will only include enhanced duration claims in the FM for time periods for which appropriate data have been submitted to demonstrate effectiveness.

A. Testing Conditions

To determine whether enhanced duration claims of effectiveness beyond 24 hours are GRASE, FDA strongly encourages manufacturers to submit data that meet the following six conditions. First, studies should be conducted according to the testing guidelines referenced in 21 CFR 350.60, which are on file in the Division of Dockets Management (see **ADDRESSES**). These guidelines are available at *http://www.fda.gov/cder/otc/index.htm.*

Second, studies should be conducted using antiperspirant drug products that contain active ingredients listed in § 350.10. The test product ingredient and strength must be identified in the data submitted to FDA.

Third, FDA encourages interested parties to conduct enhanced duration effectiveness tests using different active ingredients and dosage forms. These data will demonstrate that enhanced duration claims determined by the testing guidelines are applicable to multiple active ingredient and dosage forms. Fourth, FDA would like data submitted from different testing laboratories.

Ideally, the same antiperspirant drug product will be tested at multiple laboratories, to validate the reproducibility of the testing results.

Fifth, FDA believes that the test subject panel composition should reflect consumer demographics (Ref. 4) although the testing guidelines do not specify the panel composition. Although the testing guidelines do not specify the panel composition, FDA would like data from roughly equal numbers of men and women. It would also be informative if submitted studies also identified race or ethnicity of subjects. FDA would like to assure that the submitted study results demonstrate enhanced duration of effectiveness for the entire consumer population, not just a subset of the population.

Sixth, FDA is interested in reviewing data for antiperspirant drug products with standard effectiveness as well as products with extra effectiveness. FDA would like to determine whether enhanced duration claims are limited to extra effective antiperspirant drug products or whether enhanced duration claims also apply to standard (effectiveness) antiperspirant drug products.

B. Labeling Questions

In addition to data demonstrating an enhanced duration claim beyond 24 hours, FDA requests comments on labeling related to products having such a claim. Currently, products demonstrating enhanced duration are allowed to contain a statement such as "last 24 hours" (§ 350.50(b)(3) and (b)(5)) to inform consumers about the duration of effectiveness. However, there are no specific direction statements about how frequently to apply the product. The directions in § 350.50(d) simply state "apply to underarms only." For products demonstrating effectiveness for greater than 24 hours (one day), additional or alternative labeling may be necessary. FDA would like comments regarding labeling, such as the following:

• how often to apply the product,

• the effect of bathing or showering before the duration of effect period ends, and

• whether any other special labeling should apply to products with a duration of effect greater than 24 hours.

FDA also requests comments on whether there should be any limit on the enhanced duration claim and whether there are any potential safety issues if a product with enhanced duration of action is reapplied more frequently than directed (e.g., an antiperspirant labeled as providing 48 hours of sweat protection applied every 24 hours).

IV. Analysis of Impacts

The economic impact of the FM was discussed in the final rule (68 FR 34273 at 34289). This partial stay of the labeling claims for enhanced duration in § 350.50(b)(3) and (b)(5) does not change the economic impact on industry described in the final rule.

FDA has examined the impacts of this final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (2 U.S.C. 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant economic impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Section 202(a) of the Unfunded Mandates Reform Act requires that agencies prepare a written statement of anticipated costs and

benefits before proposing any rule that may result in an expenditure in any one year by State, local, and tribal governments, in the aggregate, or by the private sector, of $100 million (adjusted annually for inflation). The current inflation adjusted statutory threshold is about $110 million.

FDA concludes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive order and in these two statutes. The final rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. FDA has determined that the final rule does not have a significant economic impact on a substantial number of small entities. The Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs and benefits for this final rule, because this final rule is not expected to result in any 1-year expenditure that would exceed $100 million adjusted for inflation.

The purpose of this final rule is to stay the effective date of one part of the antiperspirant FM: The limitation of the enhanced duration claim to 24 hours (§ 350.50(b)(3) and (b)(5)). The partial stay will allow manufacturers who have supporting data to include greater than 24 hour duration claims in the labeling of OTC antiperspirant drug products while FDA evaluates data to support such claims using FDA's effectiveness test. FDA has learned that one manufacturer has approximately 40 stockkeeping units (SKUs) and another manufacturer has several SKUs with labels indicating effectiveness for more than 24 hours. These manufacturers will not have to revise the existing "enhanced duration" portion of their labeling when the FM becomes effective on December 9, 2004. Accordingly, FDA certifies that this final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

V. Paperwork Reduction

This final rule contains no collections of information. Therefore, clearance by the Office of Management and Budget under the Paperwork Reduction Act of 1995 is not required.

VI. Environmental Impact

FDA has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, FDA has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

VIII. Request for Comments

Interested persons may submit written or electronic comments regarding this rule to the Division of Dockets Management (see **ADDRESSES**). Three copies of all written comments are to be submitted. Individuals submitting written comments or anyone submitting electronic comments may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IX. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**) under Docket No. 1978N–0064 and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Comment No. PRC1.

2. Comment No. PRC2.

3. Comment No. SUP4.

4. Comment No. C54.

X. Authority

This final rule (partial stay) is issued under sections 201, 501, 502, 503, 505, 510, and 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, and 371) and under authority delegated to the Commissioner of Food and Drugs.

Dated: 10/6/04
October 6, 2004.

Jeffrey Shuren,
Assistant Commissioner for Policy.

[FR Doc. 04–????? Filed ??–??–04; 8:45 am]

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