

indication in § 350.50(b)(4) that states “extra effective”. This claim applies to products that demonstrate 30 percent or more sweat reduction using the guidelines for effectiveness testing of antiperspirant drug products referred to in § 350.60. (See section II.C, comment 11 of this document.) The agency is adding a new additional indication in § 350.50(b)(5) for products that demonstrate extra effectiveness sustained over a 24-hour period: These products may state the claims in §§ 350.50(b)(3) and (b)(4) either individually or combined, e.g., “24 hour extra effective protection,” “all day extra effective protection,” “extra effective protection lasts 24 hours,” or “extra effective protection lasts all day”. (See section II.C, comment 12 of this document.)

4. The agency is revising the “Do not apply * * *” warning in proposed § 350.50(c)(1) to the new labeling format. The warning now reads: “Do not use on broken skin” and “Stop use if rash or irritation occurs”.

5. The agency is including a warning to alert people with renal dysfunction to consult a doctor before using antiperspirants containing aluminum. The warning appears in the new labeling format and states: “Ask a doctor before use if you have kidney disease”. (See section II.F, comment 23 of this document.)

6. The agency has revised the August 1982 Guidelines for Effectiveness Testing. The revised guidelines (dated as of the date of publication of this document) state that “FDA recognizes that alternate methods may be appropriate to qualify an antiperspirant drug product as effective. These guidelines do not preclude the use of alternate methods that provide scientifically valid results, subject to FDA approval.” (See section II.D, comment 15 of this document.)

The agency has revised parts of the test procedures section of the guidelines to delete the requirement that the control formulation be devoid of “any” antiperspirant activity. Therefore, the control formulation no longer needs to be compared to no treatment. (See section II.D, comment 17 of this document.) The agency has changed the permitted relative humidity of the hotroom conditions from 35 to 40 percent to a range of 30 to 40 percent. (See section II.D, comment 16 of this document.) The agency has added a requirement for “baseline perspiration rate” to assure that test subjects sweat adequately during a hotroom test: “Test subjects must produce at least 100 milligrams of sweat from the placebo control axilla in a 20-minute collection

in the controlled environment.” (See comment 16 also.)

Because the final monograph contains 24-hour duration effectiveness claims, the agency has revised section 4(a)(4) of the guidelines to state: “For claims of enhanced duration of effect, the test should be conducted at least two times during the period of the claim, such as 1 hour and 24 hours after the last daily treatment for 24 hour claims.” (See section II.C, comment 12 of this document.) Because the final monograph contains “extra-effective” claims shown by standard gravimetric testing to have a 30-percent or more reduction in sweat, the agency has revised the guidelines to include a section on data treatment to demonstrate, with high probability, at least 50 percent of the target population will obtain a sweat reduction of at least 30 percent. (See section II.C, comment 11 of this document.)

The revised “Guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products” are now dated as of the date of publication of this final rule and are on file in the Dockets Management Branch (address above) and on FDA’s Web site at <http://www.fda.gov/cder/otc/index.htm>. Persons wishing to obtain a copy of the guidelines should submit a Freedom of Information (FOI) request in writing to FDA’s FOI Staff (HFI-35), 5600 Fishers Lane, Rockville, MD 20857. The agency has revised § 350.60 to include this information about the guidelines.

IV. Summary of Changes from the Proposed Rule

1. The agency is modifying the definition of an antiperspirant that was proposed in § 350.3 of the TFM to delete the phrase “to the underarm.” (See section II.B, comment 2 of this document.)

2. The agency is revising the format for listing active ingredients in § 350.10. (See section III.2. of this document.)

3. The agency is expanding the indications for OTC antiperspirant drug products based on new data that support these additional uses (see section III.3. of this document) and is expanding the “Guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products” to address some of these additional uses (see section III.6. of this document).

V. The Agency’s Final Conclusions

The agency is issuing a final monograph establishing conditions under which OTC antiperspirant drug products are generally recognized as safe and effective and not misbranded; 18 ingredients listed in § 350.10 are a

monograph condition. In the **Federal Register** of November 7, 1990 (55 FR 46914), the agency published a final rule in part 310 establishing that certain active ingredients that had been under consideration in a number of OTC drug rulemaking proceedings were not generally recognized as safe and effective. That final rule included the antiperspirant ingredients aluminum bromohydrate, aluminum chloride (alcoholic solutions), aluminum chloride (aqueous solution) (aerosol only), aluminum sulfate, aluminum sulfate buffered (aerosol only), potassium alum, and sodium aluminum chlorohydroxy lactate in § 310.545(a)(4), and was effective on May 7, 1991. In this final rule, the agency is redesignating the text of paragraph (a)(4) as paragraph (a)(4)(i), adding new paragraph (a)(4)(i) heading, and adding new paragraph (a)(4)(ii) to contain aluminum sulfate buffered with sodium aluminum lactate. Any drug product labeled, represented, or promoted for use as an OTC antiperspirant drug that contains any of the ingredients listed in § 310.545(a)(4)(i) or (a)(4)(ii) or that is not in conformance with the monograph (21 CFR part 350) may be considered a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(p)) and misbranded under section 502 of the act (21 U.S.C. 352). Such a drug product can not be marketed for OTC antiperspirant use unless it is the subject of an approved application under section 505 of the act (21 U.S.C. 355) and 21 CFR part 314. An appropriate citizen petition to amend the monograph may also be submitted in accord with 21 CFR 10.30 and § 330.10(a)(12)(i). Any OTC antiperspirant drug product initially introduced or initially delivered for introduction into interstate commerce after the effective date of the final rule for § 310.545(a)(4)(i) or after the compliance dates of this final rule that is not in compliance with the regulations is subject to regulatory action.

Mandating warnings in an OTC drug monograph does not require a finding that any or all of the OTC drug products covered by the monograph actually caused an adverse event, and FDA does not so find. Nor does FDA’s requirement of warnings repudiate the prior OTC drug monographs and monograph rulemakings under which the affected drug products have been lawfully marketed. Rather, as a consumer protection agency, FDA has determined that warnings are necessary to ensure that these OTC drug products continue