

paragraphs 85 through 91 of the preamble to the procedures for classification of OTC drug products (May 11, 1972, 37 FR 9464 at 9471 to 9472) and in paragraph 1 of the preamble to the TFM in the present proceeding (47 FR 36492 at 36493).

(Comment 2) Three comments disagreed with the agency's proposed definition of an antiperspirant: "A drug product that, when applied topically to the underarm, will reduce the production of perspiration (sweat) at that site," (47 FR 36492 at 36503). One comment contended it was unduly restrictive and unnecessary to limit use only in the underarm area because it is not the only area of the body upon which these products could potentially be applied. The comment asked the agency to modify the definition to parallel the pharmacologic activity of the active ingredients and suggested: "A drug product that, when applied topically, will reduce the production of perspiration (sweat) at that site."

A second comment stated that the definition limiting use to the underarm only would adversely affect its products labeled for use on the hands and for use with orthotic and prosthetic appliances (to keep appliance-skin contact areas dry). Noting that the agency and the Panel recognized the similarities and differences between axillary and foot perspiration, a third comment stated that ingredients effective in the underarm area are probably effective to control foot perspiration.

The agency agrees with the first comment that it is not necessary to specify the area of use on the body in the definition of an antiperspirant because that information is included in the product's labeling. Accordingly, the agency is deleting the phrase "to the underarm" from the definition of an antiperspirant in § 350.3 (21 CFR 350.3) of this final monograph to read: "*Antiperspirant*. A drug product applied topically that reduces the production of perspiration (sweat) at that site." The use of an antiperspirant on other areas of the body, as mentioned by the second and third comments, is discussed in section II.A, comment no. 4 and section II.C, comment 14 of this document.

(Comment 3) One comment stated that the TFM for OTC antiperspirant drug products was substantively and procedurally defective because it failed to address adequately the Panel's Category III recommendations concerning "enhanced duration of effect" and "problem perspiration" and failed to state what testing was required to substantiate these claims. The comment requested that FDA issue a

new or amended TFM to address these issues.

The agency has determined that there is no need to withdraw, amend, or initiate a new TFM. Since the Panel's report was published in 1978, the procedural regulations for the OTC drug review were revised to comply with the Court ruling in *Cutler v. Kennedy*, 475 F. Supp. 838 (D.D.C. 1979). The revised regulations (46 FR 47730, September 29, 1981) provide that TFMs and final monographs will no longer contain recommended testing guidelines. The agency is not required by statute or regulation to include testing guidelines as part of OTC panel reports or TFMs. The agency stated in proposed § 350.60 of the TFM (47 FR 36492 at 36504) and states in § 350.60 of this final monograph (21 CFR 350.60) that "To assure the effectiveness of an antiperspirant, the Food and Drug Administration is providing guidelines that manufacturers may (emphasis added) use in testing for effectiveness."

The "enhanced duration of effect" and the "problem perspiration" issues are discussed in section II.C, comments 10 and 12 of this document. Extended duration of effect claims have been placed in Category I based on data submitted by other comments (see also comment 12). The agency has determined that claims for problem perspiration are outside the scope of this monograph because no data were submitted to support such claims (see also comment 10).

(Comment 4) One comment contended that the proposed monograph would have a disastrous economic effect on its company, which markets an antiperspirant product first formulated in 1902 and labeled for excessive perspiration, including keeping the hands free of perspiration (labeled for use on the hands for tennis, racquetball, bowling, football, and other sporting uses), and marketed for prosthesis and orthotic use (for amputees to keep their appliance contact areas dry).

To qualify for exemption from the "new drug" definition under the 1938 grandfather clause of the act, the drug product must have been subject to the Food and Drug Act of 1906, prior to June 25, 1938, and at such time its labeling must have contained the same representations concerning the conditions of its use (21 U.S.C. 321(p)(1)). Under the 1962 grandfather clause of the act, a drug product which on October 9, 1962 was: (1) Commercially used or sold in the United States; (2) not a "new drug" as defined in the 1938 act; and (3) not covered by an effective NDA under the 1938 act, would not be subject to the

added requirement of effectiveness "when intended solely for use under conditions prescribed, recommended, or suggested in labeling with respect to such drug on that day." (Public Law 87-781, section 107(c)(4), 76 Stat. 788, note following 21 U.S.C. 321).

The person seeking to show that a drug comes within a grandfather exemption must prove every essential fact necessary for invocation of the exemption. See *United States v. An Article of Drug \* \* \* "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied*, 412 U.S. 938 (1973). Furthermore, the grandfather clause will be strictly construed against one who invokes it. See *id.*; *United States v. Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir.), *cert. denied*, 385 U.S. 899 (1966). A change in composition or labeling precludes the applicability of the grandfather exemption. See *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655, 663 (1973).

Although the comment stated that its drug products have been marketed since 1902 with hand perspiration labeling claims, no evidence was submitted to show that the labeling and composition of the products have remained unchanged since either 1938 or 1962, so that they qualify as grandfathered products. The agency requested product labeling from these years on several occasions (Refs. 1, 2, and 3), but none was ever provided. Without such evidence, the products do not qualify for either grandfather exemption. The burden of proof with respect to the grandfather exemption is not on FDA, but on the person seeking the exemption. See *An Article of Drug \* \* \* "Bentex Ulcerine," supra*.

The 1938 and 1962 grandfather clauses apply only to the new drug provisions of the act (see 21 CFR 314.200(e)) and not to the adulteration and misbranding provisions. The OTC drug review was designed to implement both the misbranding and the new drug provisions of the act. (See § 330.10 (21 CFR 330.10), 37 FR 9464 at 9466.) The grandfather clauses do not preclude the agency from reviewing any currently marketed OTC drug product, regardless of whether it has grandfather protection from the new drug provisions, in order to ensure that it is not misbranded.

Although the comment claimed this final rule would have a disastrous economic effect on its company if antiperspirants can be labeled only for underarm use, it provided no documentation about this impact. The agency notes that while the company's products would need to be relabeled to bear different indications, as long as the monograph conditions are met, the