

ingestion for most individuals. However, individuals with renal dysfunction or immature renal function (i.e., infants) are at a higher risk from any exposure to aluminum. Further, ingestion of the various inactive ingredients present in these products may make young children ill or cause other undesirable consequences. Without adequate proof of safety if accidental ingestion were to occur, the agency has no basis to exempt OTC antiperspirant drug products from the accidental ingestion warning.

Although aerosol antiperspirant drug products are unlikely to be accidentally ingested by most consumers, the agency notes that the product containers are similar to those used for some food products. Spraying an aerosol into the mouth and ingesting it could be more hazardous than ingesting other dosage forms of the product because of the aerosol propellants. The warnings required under § 369.21, for those drugs in dispensers pressurized by gaseous propellants, are not related to ingestion, but state the following: "Avoid spraying in the eyes. Do not puncture or incinerate. Do not store at temperatures above 120 °F. Keep out of reach of children." The agency does not consider these warnings a basis to exempt aerosol antiperspirants from the accidental ingestion warning required by § 330.1(g) for topical drug products. The last statement of the warning required by § 369.21 and the first warning required by § 330.1(g) (i.e., "Keep out of reach of children.") are identical as of March 17, 1999 (64 FR 13254 at 13294). Section 350.50(c)(4)(ii) of the final monograph requires aerosol antiperspirant drug products to bear the language in § 369.21. These products do not have to repeat the first general warning required by § 330.1(g) but need to have the accidental ingestion warning required by § 330.1(g).

(Comment 8) Two comments objected to the proposed warning in § 350.50(c) for aerosol antiperspirants, which states: "Avoid excessive inhalation." The comments argued that the warning duplicates and gives less information than the current warning required for aerosol drug products under § 369.21.

Section 369.21 requires the following warning statement for a drug packaged in a self-pressurized container in which the propellant consists in whole or in part of a halocarbon or hydrocarbon: "Use only as directed. Intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal." The agency does not consider this warning (which addresses deliberate misuse) as being the same as a general statement warning people to

avoid excessive inhalation. There are many people who would not deliberately misuse the product who should be alerted to keep away from their face and mouth and to avoid excessive inhalation. The warning appears in the final monograph in more consumer friendly language and in the new labeling format as follows: "When using this product [bullet] keep away from face and mouth to avoid breathing it." (See § 201.66(b)(4) for description of a "bullet.")

C. Comments on Category III Effectiveness Testing

(Comment 9) Several comments objected to user perception testing to substantiate Category III effectiveness claims. (See comment 24, 47 FR 36492 at 36499.) The comments contended that the user perception test is not reliably indicative of product effectiveness and offers at best a crude index of activity that is difficult to employ for precise qualitative and quantitative evaluations. The comments considered objective gravimetric sweat collection procedures more reliable than user perception testing to assess antiperspirant activity levels and requested that user perception testing be deleted. Three comments submitted data on user perception testing of Category III claims, including extra effective, 24-hour duration, emotional sweating, and foot perspiration (see section II.C, comments 11 through 14 of this document).

The agency has determined that user-perception test data support emotional sweating, 24-hour protection, and extra effective claims. Accordingly, the agency concludes that there are sufficient data on user perception tests (including both user and independent observer perception tests) for use of antiperspirants for the underarm. No further user perception tests are necessary if an underarm antiperspirant shows at least 20 percent sweat reduction by gravimetric tests for emotional sweating and 24-hour protection claims or 30 percent sweat reduction for extra effective claims. Adequate user perception tests have not been conducted for parts of the body other than the underarms, such as the hands or feet. The agency will still require user perception and other effectiveness data to support use of antiperspirants on the hands and feet (see section II.A, comment 4 and section II.C, comment 14 of this document).

(Comment 10) Several comments objected to the Category III status of the claims "problem perspiration" and "especially troublesome perspiration." One comment contended these claims

are not inherently misleading or untruthful and many people who do not perspire heavily may, at times, consider themselves to have "problem" or "troublesome" perspiration.

Other comments objected to the agency's definition of problem perspiration as affecting the upper 5 percent of perspirers, contending that a more realistic approach would be to let consumers define the meaning of these words by running efficacy studies on people who identify themselves as having problem or especially troublesome perspiration. One comment objected to the economic consequences of testing the top 5 percent of the population to establish a "problem perspiration" claim, because this could raise the price for one efficacy evaluation from the current \$5,000 to \$10,000 up to \$200,000. The comment requested a hearing on this issue if FDA did not revise its approach.

No data were submitted to the agency to show that any OTC antiperspirant drug product is effective in reducing "problem" or "especially troublesome" perspiration. The agency is not aware of any products that currently qualify as effective for those conditions. If products are found to be effective in the future, the agency will include a definition and labeling for "problem" or "especially troublesome" perspiration in the monograph. The agency proposed in the tentative final monograph that a 30 percent reduction in sweat production in the upper 5 percent of perspirers is necessary for a "problem perspiration claim" (47 FR 36492 at 36500). As discussed in section II.C, comment 9 of this document, gravimetric testing is sufficient to prove these claims. The agency would find acceptable an antiperspirant effectiveness study on a population of individuals who perceive themselves to have "problem perspiration," as one comment suggested. Based on changes in the testing to support these claims, the agency concludes that a hearing is not needed.

(Comment 11) Several comments objected to the agency's proposed Category II classification of the claims "extra strength," "extra effective," or any other comparative effectiveness claims (see comment 19, 47 FR 36492 at 36498). The comments argued that if manufacturers can demonstrate by appropriate testing and methods of statistical analysis that one product is more effective than another, they should be permitted to so inform consumers. The comments noted that the agency had approved an NDA for an acetaminophen "extra strength" product and allowed sunscreen products to label