The comments concluded that the agency should affirm the safety of quaternary ammonium compounds and reclassify these ingredients in Category I for use as preservatives in OTC vaginal drug products.

Although the comments requested that the agency affirm the safety of quaternary ammonium compounds for use as preservatives and reclassify them as Category I, the agency points out that the OTC drug review is primarily a review of active ingredients, not inactive ingredients. However, because the purpose of the OTC drug review process is to determine the safety and effectiveness of OTC drugs, the OTC advisory review panels occasionally made recommendations with respect to inactive ingredients. These recommendations were made to call attention to those inactive ingredients that could potentially interfere with the safety and effectiveness of the product.

In the case of the quaternary ammonium compounds, the agency agrees with the comments' reasoning that the reports cited by the Panel cannot be used to conclude that the use of these compounds as preservatives in OTC vaginal contraceptive drug products may present a health hazard to normal individuals.

As discussed in section I.A., comment 3 of this document, the agency is proposing that each OTC vaginal contraceptive drug product should be the subject of an approved application prior to marketing. Information regarding the appropriateness of ingredients used in the product as preservatives should be included in the application.

References

1. Forkner, Jr., C. E., ''Pseudomonas Aeruginosa Infections,'' in ''Modern Medical Monographs,'' vol. 22, edited by I. S. Wright and R. H. Orr, Gruen and Stratton, New York, p. 71, 1960.

2. Gardner, H. L. and R. H. Kaufman, ''Nonvenereal Bacterial Vulvovaginitides,'' in ''Benign Diseases of the Vulva and Vagina,'' 2d ed., G. K. Hall Medical Publishers, Boston, p. 306, 1981.

3. Ridley, C. M., ''The Vulva,'' in ''Major Problems in Dermatology,'' vol. 5, edited by A. Rook, W. B. Saunders Co., Philadelphia, p. 99, 1975.

4. Mead, P. B. and D. W. Gump, ''Antibiotic Therapy in Obstetrics and Gynecology,'' in ''Clinical Obstetrics and Gynecology,'' vol. 19, No. 1, edited by H. J. Osofsky and G. Schaefer, Harper and Row, Hagerstown, MD, p. 114, 1976.

6. Several comments disagreed with the Panel's recommendations that inactive ingredients and the quantity of the ingredient be listed in the labeling of OTC vaginal contraceptive drug products. The comments argued that a list of inactive ingredients would be meaningless to all but a few consumers and that such a list might overemphasize the importance of the inactive ingredients; obscure more meaningful information such as warnings, directions for use, and the name and quantity of the active ingredients; and be more confusing than helpful. The comments also stated that if the quantity of the inactive ingredients had to be listed there would be an additional problem and expense of changing the labels whenever the quantity of an inactive ingredient is changed.

The act does not require the identification of all inactive ingredients in the labeling of OTC drug products. Section 502(e) of the act (21 U.S.C. 352(e)) does require disclosure of active ingredients and of certain ingredients, whether included as active or inactive components in a product. Although the act does not require the disclosure of all inactive ingredients in the labeling of OTC drug products, the agency agrees with the Panel that listing of inactive ingredients in OTC drug product labeling would be useful information for some consumers. Consumers with known allergies or intolerances to certain ingredients would then be able to identify substances that they may wish to avoid.

The Nonprescription Drug Manufacturers Association (formerly known as The Proprietary Association), the trade association that represents approximately 85 OTC drug manufacturers who reportedly market between 90 and 95 percent of the volume of all OTC drug products sold in the United States, has established guidelines (Ref. 1) for its member companies to list voluntarily inactive ingredients in the labeling of OTC drug products. Under another voluntary program begun in 1974, the member companies of the Association have been including the quantities of active ingredients on OTC drug labels. The agency is not at this time proposing to require the listing of inactive ingredients in OTC drug product labeling. However, the agency commends these voluntary efforts and urges all other OTC drug manufacturers to similarly label their products.

Reference

1. ''Guidelines for Disclosure of Inactive Ingredients in OTC Medicines,'' The Proprietary Association, Washington, July 12, 1984, in OTC Vol. 11ATFM.

7. One comment urged that the label of OTC vaginal contraceptive drug products contain a list of all active ingredients, arguing that consumers have a right to an informed choice when buying such products.

As discussed in section I.A., comment 6 of this document, listing of active ingredients is required for all drug products under section 502(e)(1) of the act (21 U.S.C. 352(e)(1)).

B. Comments on OTC Vaginal Contraceptive Active Ingredients

8. Three comments supported the Panel's Category I classification of menfegol and disagreed with the agency's conclusion that menfegol is a new drug because it is a new molecular entity, never before marketed as a drug in the United States. The comments stated that a lack of United States' marketing experience does not preclude a drug from being considered generally recognized as safe and effective nor require a drug to be considered a new drug. One comment argued that data on the marketing of vaginal contraceptive drug products in foreign countries can be equated to marketing in this country because the mode of action of these products is based on the spermicidal activity of an ingredient in the vagina and not on the medical problems, diets, customs, and environments of other countries. The comment urged FDA to reconsider its decision to refuse to recognize data on the marketing of a product outside the United States regardless of the ingredient, type of product, or its mode of action. Another comment added that the act defines a new drug as any drug not generally recognized as safe and effective among experts, whereas menfegol was so recognized by a panel of experts.

The Panel's Category I classification of menfegol was based on its review of safety and effectiveness data. The Panel's recommendation did not address the issue whether menfegol meets the statutory requirement concerning use of a drug. Menfegol was determined to be a new drug within the meaning of section 201(p)(2) of the act (21 U.S.C. 321(p)(2)), which defines a new drug as: * * * ''any drug * * * that * * * has become so recognized, but which has not * * * been used to a material extent or for a material time under such conditions.'' The agency's longstanding interpretation of section 201(p)(2) of the act has been that marketing outside the United States cannot fulfill this independent statutory requirement of use to a ''material extent'' and for a ''material time.'' Currently, based on several petitions to another OTC drug review rulemaking (Refs. 1, 2, and 3), the agency is reevaluating this interpretation of the act. (See section II.C., comment 34 of this document, in the tentative final