method of administration, of the potential hazard of mercury to offspring when the drug is systemically absorbed by the mother. Therefore, because of the possibility that mercury-containing compounds which can be metabolized to inorganic mercury may pose a risk to fetuses and nursing infants, the agency concurs with the Panel that such compounds are unsafe for use in vaginal contraceptive drug products.

## References

1. Al-Jobori, I. M., "Mercury Levels in Females Exposed to Phenylmercuric Acetate," Master Thesis, University of Baghdad, pp. 10–110, 1975, in OTC Vol. 110058.

2. Fukuchi, H. et al., "The Absorption of Organomercurial Compounds from the Vaginal Route of the Rabbits. I. Comparative Study on the Effect of Suppository Vehicles on the Absorption of *Omega*– Ethylmercurithio-*n*-undecanoic Acid, Phenylmercuric Acetate and Ethylmercuric Chloride after Single Dose Administration," *Chemical and Pharmaceutical Bulletin*, 12:540–548, 1964.

3. Fukuchi, H. et al., "The Absorption of Organomercurial Compounds from the Vaginal Route of the Rabbits. II. Distribution and Excretion of Omega-Ethylmercurithio-*n*undecanoic Acid and Phenylmercuric Acetate," *Chemical and Pharmaceutical Bulletin*, 12:548–557, 1964.

4. Murkami, U., Y. Kameyama, and T. Kato, "Effects of a Vaginally Applied Contraceptive with Phenylmercuric Acetate Upon Developing Embryos and Their Mother Animals," Annual Report of the Research Institute of Environmental Medicine, Nagoya University, pp. 88–99, 1955.

## C. Comments on Labeling of OTC Vaginal Contraceptive Drug Products

Although the proposed rule included in this document does not include monograph conditions, the responses to the following comments should be considered as FDA's tentative position on the labeling of OTC vaginal contraceptive drug products. FDA has considered the Panel's labeling recommendations and the following comments in developing the agency's position on labeling for OTC vaginal contraceptive drug products. This document will serve as the basis for the development of guidelines for the content and format of the labeling of OTC vaginal contraceptive drug products similar to those currently available for oral contraceptive drug products. (See 54 FR 22585 and 22624, May 25, 1989.) The agency intends to complete these guidelines for OTC vaginal contraceptive drug products after the comments to this proposal are evaluated.

11. One comment noted its continuing position that FDA lacks statutory authority to prescribe exclusive lists of terms from which indications for use for OTC drug products must be drawn and to prohibit labeling terminology which is truthful, accurate, not misleading, and intelligible to the consumer. A second comment stated that it would be inappropriate to restrict manufacturers to the specific wording recommended by the Panel for package insert statements.

In the **Federal Register** of May 1, 1986 (51 FR 16258), the agency published a final rule changing its labeling policy for stating the indications for use of OTC drug products. Under 21 CFR 330.1(c)(2), the label and labeling of OTC drug products are required to contain in a prominent and conspicuous location, either: (1) The specific wording on indications for use established under an OTC drug monograph, which may appear within a boxed area designated "APPROVED USES''; (2) other wording describing such indications for use that meets the statutory prohibitions against false or misleading labeling, which shall neither appear within a boxed area nor be designated "APPROVED USES"; or (3) the approved monograph language on indications, which may appear within a boxed area designated "APPROVED USES," plus alternative language describing indications for use that is not false or misleading, which shall appear elsewhere in the labeling. All other OTC drug labeling required by a monograph or other regulation (e.g., statement of identity, warnings, and directions) must appear in the specific wording established under the OTC drug monograph or other regulation where exact language has been established and identified by quotation marks, e.g., 21 CFR 201.63 or 330.1(g). There will be no monograph for OTC vaginal contraceptive drug products, and all labeling for these products will be approved via applications. Therefore, the comments are moot with respect to this current rulemaking.

12. Several comments agreed with the Panel that quantitative claims of effectiveness should not be required in the labeling of OTC vaginal contraceptive drug products because of the difficulty in conducting the studies that would be necessary to substantiate such claims. The size of the sample that would be needed, the variations in subject motivation, varying methods of product use, and the lack of an adequate representative population of American women were specifically cited in the comments as factors that would make such studies difficult to conduct. The comments also pointed out that the consensus of the participants in the symposium on vaginal contraception,

held by the Panel on April 28 and 29, 1978, was that quantitative effectiveness claims should not be required.

A number of comments indicated that quantitative effectiveness claims should not be required, but that manufacturers should be permitted to use these claims at their own discretion. Several of these comments also objected to the Panel's recommendation that such claims be permitted in labeling only after prior approval by FDA through the new drug procedures.

Two comments questioned whether the quantitative effectiveness claims could be written in a manner that would be understood by consumers. Providing consumers with actual numbers relevant to method effectiveness, use effectiveness, and extended-use effectiveness was specifically cited as a potential source of confusion.

One comment pointed out that the patient labeling of oral contraceptives is required to contain a discussion comparing the effectiveness of different contraceptive methods and, therefore, it would be inconsistent for FDA to conclude that there are insufficient data available to support the validity of comparative effectiveness claims in the labeling of OTC vaginal contraceptive drug products.

The agency believes that consumers should be provided with the most informative labeling available when choosing a contraceptive drug product. After reviewing the complete administrative record for this rulemaking, including the record of the Panel's symposium on vaginal contraception and the comments submitted to the Panel's report on this issue, the agency concludes that the most informative labeling for users of vaginal contraceptive drug products is information on the relative effectiveness of the various methods of contraception. The agency is currently working to create a consistent and understandable presentation of this important information to include in the labeling of all marketed contraceptive products, drugs, and devices.

13. Two comments objected to the Panel's labeling recommendations for the outer and primary containers of OTC vaginal contraceptive drug products (45 FR 82014 at 82031). The comments questioned the propriety of the Panel in specifying the order of appearance and location of the various required statements. The comments also objected to the number of required labeling statements. One comment stated that listing of all the recommended labeling statements would require the use of small illegible typeface. The second comment noted that if space were