generally accepted opinion that when vaginal contraceptives are used as the primary method of birth control, douching should be delayed for at least 6 hours after coitus (45 FR 82014 at 82030). The agency concurs.

Reference

1. Silverman, E. M. and A. G. Silverman, ''Persistence of Spermatozoa in the Lower Genital Tracts of Women,'' *Journal of the American Medical Association*, 240:1875–1877, 1978.

20. One comment suggested that the labeling of OTC vaginal contraceptive drug products include a warning specifying possible adverse allergic reactions such as itching and burning in the vaginal area and in the penile area. The comment also recommended that the warning advise consumers to discontinue use if these symptoms occur.

The agency agrees with the comment that consumers should be warned about possible allergic reactions such as burning and itching that may occur when using vaginal contraceptive drug products. The agency also agrees that the warning should advise consumers to discontinue use if these symptoms should occur. Furthermore, if the irritation persists after use has been discontinued, it could indicate a problem other than an allergic reaction to the product, so that a physician should be contacted. The agency believes the following warning is appropriate for inclusion in the labeling of OTC vaginal contraceptive drug products: ''If you or your partner develops irritation, such as burning or itching in the genital area, stop using this product. If irritation continues, contact your physician.''

21. One comment stated that the Category II labeling claims recommended by the Panel (45 FR 82014 at 82040) are not proper subject matter for the OTC drug review and should not be classified. The comment argued that these claims are not indications for use, but rather are statements of fact which are unrelated to the safety or effectiveness of a vaginal contraceptive drug. The comment added that the claims cannot legally be prohibited if truthful and should not be placed in Category II without a finding that they are inherently false or misleading.

The OTC drug review program establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded. One aspect of the program is to develop standards for certain parts of the labeling of OTC drug products. Because of time, resources, and other considerations, FDA has not set standards for all labeling found in OTC drug products. Accordingly, OTC drug monographs address only those labeling items that are related in a significant way to the safe and effective use of covered products by lay persons. These labeling items are the product statement of identity; names of active ingredients; indications for use; directions for use; warnings against unsafe use, side effects, and adverse reactions; and claims concerning mechanism of drug action.

Based on the discussion above, the agency tentatively concludes that the Panel's entire list of Category II labeling claims as well as certain descriptive terms included in the Panel's recommended list of other allowable statements (recommended § 351.56(c)), i.e., safe, effective, powerful, highly) would be outside the scope of a monograph, if one were being established. Because all OTC vaginal contraceptive drug products will require an approved application for marketing, such claims can be evaluated, during the approval process, on a product-by-product basis for compliance with section 502 of the act (21 U.S.C. 352) relating to labeling that is false or misleading.

22. After reviewing the Panel's recommended labeling, the agency has tentatively determined that the following additional changes in the Panel's recommendations are warranted. Although the Panel recommended ''spermicide'' as an indication, the agency believes that it would be more appropriate as an optional statement of identity. In addition, although the Panel recommended a number of indications statements, the agency believes that the indication ''For the prevention of pregnancy'' is sufficient to convey to consumers the intended use of the product. The agency has also tentatively determined that the statement ''If your physician has told you that you should not become pregnant, ask your physician if you can use this product for contraception,'' should be a warning instead of a direction statement.

D. Comments on Combinations

23. One comment objected to the Panel's statement at 45 FR 82014 at 82026 that if two or more Category I vaginal contraceptive active ingredients are combined, the specific ingredients as well as the combination product must be subjected to laboratory and clinical testing according to the recommended testing guidelines. The comment argued that no useful purpose is served or information gained by clinical testing of single Category I ingredients and that such testing is not required under FDA's OTC combination policy.

As discussed in section I. D., comment 25 of this document, testing guidelines for conditions that industry wishes to upgrade to monograph status will not be included. However, criteria for establishing combinations of OTC drugs as generally recognized as safe and effective are provided in 21 CFR 330.10(a)(4)(iv). Guidance on OTC combination drug products has also been provided in the agency's General Guidelines for OTC Drug Combination Products (Ref. 1). Thus, two or more safe and effective OTC vaginal contraceptive active ingredients may be combined provided the final formulation of the product meets the combination policy in all respects. The Panel did not include any contraceptive combinations in its monograph because the data were insufficient for any of the combinations that were reviewed to be generally recognized as safe and effective. The agency concurs with the Panel's decision. Furthermore, as noted in section I. A., comment 3 of this document, the agency is proposing to require that all combination or single-ingredient OTC vaginal contraceptive drug products be subject to approved applications prior to marketing.

Reference

1. Food and Drug Administration, ''General Guidelines for OTC Drug Combination Products, September 1978,'' Docket No. 78D–0322, Dockets Management Branch.

24. One comment stated that the data on which the Panel based its Category II classification of the combinations: (1) Phenylmercuric acetate and boric acid; (2) phenylmercuric acetate, boric acid, and nonoxynol 9; and (3) phenylmercuric acetate, octoxynol 9, and sodium borate show that these combinations were so classified because of ''hazards'' associated with the use of phenylmercuric acetate rather than with the use of boric acid or sodium borate (Refs. 1 through 6). The comment added that it appears that the use of borates in vaginal contraceptives is for ''pH control.'' The comment also noted that boron compounds were listed as inactive ingredients in the Panel's report (45 FR 82014 at 82042) and were not placed in Category II, as were mercury-containing compounds.

The agency agrees that boron compounds should not have been included as active ingredients in the listing of Category II combinations. The submissions of data on OTC vaginal contraceptive drug products containing boron compounds (Refs. 1 through 6) indicate that the boron compounds are included in these products as