

contact your physician.” At the November 22, 1996, NDAC meeting (Ref. 1), the committee also noted that penile irritation could occur. The agency is aware that the labeling of most OTC marketed vaginal spermicides containing nonoxynol 9 bears a warning to stop use and ask a doctor if irritation of the vagina or penis occurs or continues. In this document, the agency is proposing a similar warning. The agency is not aware of any data that suggest increased penile irritation from frequent use of nonoxynol 9 may increase the risk of getting STDs from infected female partners. However, the agency encourages more research and studies to evaluate this potential safety concern.

## II. The Agency's Proposal

The agency is proposing to amend part 201 (21 CFR part 201) by adding § 201.325 entitled “Over-the-counter drugs for vaginal contraceptive use containing nonoxynol 9 as the active ingredient; required warnings.” This section would require new warnings for all OTC vaginal contraceptive drug products containing nonoxynol 9 as the active ingredient, whether marketed under an NDA or the ongoing OTC drug review. The agency is proposing to require the following warnings be added to the labeling of all marketed OTC vaginal contraceptives containing nonoxynol 9: “Sexually transmitted diseases (STDs) alert [heading in bold type]: This product does not [this word highlighted in bold type] protect against the AIDS virus (HIV) or other sexually transmitted diseases (STDs).”

Based on the studies, the agency is also proposing a warning to inform users of OTC vaginal spermicides containing nonoxynol 9 that frequent use can increase vaginal irritation and may increase the risk of getting the AIDS virus (HIV) or other STDs from infected partners. The statements would also quantify the definition of “frequent use” by adding “(more than once a day)”. The proposed warning states:

Ask a doctor before use if you have [heading in bold type] a new sex partner, multiple sex partners, or unprotected sex. Frequent use (more than once a day) of this product can increase vaginal irritation, which may increase the risk of becoming infected with the AIDS virus (HIV) or other STDs from infected partners. Ask a doctor or other health professional for your best birth control method.

The agency is also proposing a warning to stop use and ask a doctor if irritation of the vagina or penis occurs. The agency recommended a similar warning in the NPRM (60 FR 6892 at 6901): “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.” The agency is revising that warning in this document to state: “Stop use and ask a doctor if [heading in bold type] you or your partner get burning, itching, a rash, or other irritation of the vagina or penis.” Further, the warning that reads “For vaginal use only” needs to be included in accordance with the requirements in § 201.66(c)(5)(i).

Because of the public health concerns regarding the transmission of STDs and the AIDS virus (HIV), the agency believes that manufacturers should inform consumers as soon as possible that nonoxynol 9 does not protect against the AIDS virus (HIV) and that frequent use of nonoxynol 9 can increase vaginal irritation. FDA encourages manufacturers of all OTC vaginal contraceptive drug products containing nonoxynol 9 to implement the agency's proposed labeling warnings voluntarily as soon as possible, subject to the possibility that FDA may change the wording of the statements, as a result of comments submitted in response to this proposal. The agency considers these warnings important to the safe use of OTC vaginal contraceptive drug products containing nonoxynol 9.

Because there is no final monograph for these products at present, manufacturers of OTC vaginal contraceptive drug products containing nonoxynol 9 are required to follow the labeling requirements in § 201.66 as of the first major labeling revision after May 16, 2002. The agency intends to consider the labeling revisions in this proposal, when finalized, to be the first major labeling revision after May 16, 2002, for products that have not already converted to the “Drug Facts” labeling format, and to require those products to conform to § 201.66 at that time. For products that have already converted to the “Drug Facts” format, the agency will require the labeling revisions in this proposal to be implemented by the effective date of the final rule.

In addition, the agency is proposing to require additional labeling information which would convey to consumers that studies have raised safety concerns that increased vaginal irritation (i.e., irritation or damage to the cell lining of the vagina that may or may not produce symptoms) caused by frequent use of nonoxynol 9 may make one more susceptible to the risk of getting the AIDS virus (HIV) or other STDs from infected partners and that consumers who use these products frequently should seek further advice from a doctor or other health professional for their best birth control method. In the interest

of public health, the information would also include a statement to encourage the use of a latex condom with every sexual act to help to reduce the risk of getting the AIDS virus (HIV) and other STDs. The agency is proposing that this labeling be included either on the outside container or wrapper of the retail package under the “Other information” section of the “Drug Facts” labeling in accordance with § 201.66 or in a package insert. Many of the marketed OTC vaginal contraceptive drug products already have a package insert that contains information on how to use the product and this new information could readily be incorporated in that package insert. The agency is proposing the following labeling:

- Studies have raised safety concerns that frequent use (more than once a day) of products containing nonoxynol 9 can increase vaginal irritation, which may increase the risk of getting the AIDS virus (HIV) or other STDs from infected partners. Vaginal irritation may include symptoms such as burning, itching, or a rash, or you may not notice any symptoms at all. If you use these products frequently and/or have a new sex partner, multiple sex partners, or unprotected sex, see a doctor or other health professional for your best birth control and methods to prevent STDs.
- Correct use of a latex condom with every sexual act will help reduce the risk of getting the AIDS virus (HIV) and other STDs.

The studies suggest a possible correlation between increased vaginal irritation from frequent use and the risk of transmission of the AIDS virus (HIV) and other STDs. Because of this significant safety concern, the agency is asking for comments on how to best present this information in the product labeling.

## III. Questions to be Addressed

The agency is concerned with how well consumers understand the language in the proposed warnings and whether the proposed warnings convey the safety concerns for nonoxynol 9 adequately. The agency invites public comments on the following questions:

1. Do the proposed warnings under the headings “Sexually transmitted diseases alert,” “Ask a doctor before use if you have,” and “Stop use and ask a doctor if” adequately convey the safety concerns to consumers? What revisions, if any, would be useful?
2. Are there other data to support, expand, or refute the proposed warnings?
3. Are there additional data to further clarify or specifically quantify the term “frequent use” in the proposed warning that states: “Frequent use (more than once a day) of this product can increase