

economic impact. Therefore, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities. No further analysis is required under the Regulatory Flexibility Act (5 U.S.C. 605(b)).

The agency invites public comment regarding any substantial or significant economic impact that this proposed rule would have on companies marketing OTC vaginal contraceptive drug products containing nonoxynol 9. Types of impact may include, but are not limited to, costs associated with relabeling or repackaging. Comments regarding the impact of this proposed rule should be accompanied by appropriate documentation. The agency is providing a period of 90 days from the date of publication of this proposed rule in the **Federal Register** for comments on this subject to be developed and submitted. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this proposed rule in the preamble to the final rule.

V. Paperwork Reduction Act of 1995

FDA tentatively concludes that the labeling requirements proposed in this document are not subject to review by the Office of Management and Budget because they do not constitute a "collection of information" under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the proposed labeling statements are a "public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

VI. Environmental Impact

The agency has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency tentatively concludes that the

proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

VIII. Request for Comments

Interested persons may submit written or electronic comments on the proposed rule, the agency's specific questions in section III of this document, and the agency's economic impact determination to the Dockets Management Branch (see **ADDRESSES**) by April 16, 2003. Three copies of all written comments are to be submitted. Individuals submitting written comments or anyone submitting electronic comments may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

IX. Proposed Effective Date

Because of the importance of the proposed warnings to the safe use of OTC vaginal contraceptive drug products containing nonoxynol 9, the agency is proposing that any final rule that may publish based on this proposal become effective 6 months after its date of publication in the **Federal Register**.

X. References

The following references are on display in the Dockets Management Branch (see **ADDRESSES**), under Docket No. 80N-0280, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. FDA, Transcript of Joint Meeting of the Nonprescription Drugs, Reproductive Health Drugs, Anti-Infective Drugs and Antiviral Drugs Advisory Committees, in OTC vol. 11ATFM3, November 22, 1996.
2. Letter from D. L. Bowen, FDA, to R. W. Soller, Nonprescription Drug Manufacturers Association, coded LET 6.
3. Letter from D. L. Bowen, FDA, to R. W. Soller, Nonprescription Drug Manufacturers Association, coded LET 7.
4. Jim Shelton's Pearls for July 2000, "Spermicides and Protection Against STDs," Johns Hopkins Center for Communication Programs, in OTC vol. 11ATFM3, 2000.
5. Jim Shelton's Pearls for September 2000, "Nonoxynol-9 and HIV Transmission," Johns Hopkins Center for Communication Programs, in OTC vol. 11ATFM3, 2000.
6. University of Florida, "HIV/AIDS Information/Resources."
7. Drugs.com (Drug Information Online), "Spermicides Vaginal," in OTC vol. 11ATFM3.
8. Van Damme, L., "Advances in Topical Microbicides," presented at the XIII

International AIDS Conference, Durban, South Africa, July 9-14, 2000.

9. Letter from H. D. Gayle, National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention, in OTC vol. 11ATFM3, August 4, 2000.

10. Van Damme, L. et al., "Effectiveness of COL-1492, a Nonoxynol-9 Vaginal Gel, on HIV-1 Transmission in Female Sex Workers: A Randomised Controlled Trial," *The Lancet*, 360:974-977, 2002.

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15. Amaral, E. et al., "Study of the Vaginal Tolerance to Acidform, an Acid Buffering Gel," *Contraception*, 60(6):361-366, 1999.

16. Stafford, M. K. et al., "Safety Study of Nonoxynol-9 as a Vaginal Microbicide; Evidence of Adverse Effects," *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 17:327-331, 1998.

17. Rosenstein, I. J. et al., "Effect on Normal Vaginal Flora of Three Intravaginal Microbical Agents Potentially Active Against Human Immunodeficiency Virus Type 1," *The Journal of Infectious Diseases*, 177:1386-1390, 1998.

18. Poindexter III, A. N. et al., "Comparison of Spermicides on Vulvar, Vaginal, and Cervical Mucosa," *Contraception*, 53:147-153, 1996.

19. Coggins, C. et al., "Safety of Three Formulations of Nonoxynol-9 Containing Vaginal Spermicides," *International Journal of Gynecology and Obstetrics*, 68:267-268, 1999.

20. Watts, H. et al., "The Effects of Three Nonoxynol-9 Preparations on Vaginal Flora and Epithelium," *The Journal of Infectious Diseases*, 180:426-437, 1999.

21. Niruthisard, S., R. E. Roddy, and S. Chutivongse, "The Effects of Frequent Nonoxynol-9 Use on the Vaginal and Cervical Mucosa," *Journal of the American Venereal Disease Association*, 18:176-179, 1991.

22. Roddy, R. E. et al., "A Dosing Study of Nonoxynol-9 and Genital Irritation," *International Journal of STD and AIDS*, 4:165-170, 1993.

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