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The Honorable Tom A. Coburn, M.D.
Ranking Member
Subcommittee on Federal Financial Management,
Government Information, Federal Services,
and International Security
Committee on Homeland Security and
Governmental Affairs
United States Senate

Subject: *Food and Drug Administration: Agency Complied with Statutory Requirement to Reexamine Condom Labels*

Dear Senator Coburn:

Sexually transmitted diseases (STDs) affect men and women of all backgrounds and economic levels and remain a major public health challenge in the United States.¹ While substantial progress has been made in preventing, diagnosing, and treating certain STDs, an estimated 19 million new infections occur annually.² According to the Centers for Disease Control and Prevention (CDC), correct and consistent use of a male latex condom can reduce, but not eliminate, the risk of STD transmission.

Although male latex condoms have been proven to be highly effective in preventing HIV/AIDS, concerns have been raised over the past decade that condom labels do not include accurate information about condoms' effectiveness in preventing other STDs, including the human papillomavirus (HPV). A provision enacted as part of the Consolidated Appropriations Act, 2001, required the Secretary of Health and Human Services (HHS) to reexamine existing condom labels³ to determine whether they are medically accurate regarding the effectiveness of condoms in preventing STDs.⁴ You asked us to address issues related to condom labels. In this report, we discuss the scope of this statutory requirement and assess the extent to which the Food and Drug Administration (FDA)—the agency within HHS responsible for the regulation of medical devices, including condoms—complied with the requirement.

¹Included among STDs are HIV/AIDS, the human papillomavirus, gonorrhea, syphilis, and chlamydia.

²Centers for Disease Control and Prevention, *Trends in Reportable Sexually Transmitted Diseases in the United States 2004, National Surveillance Data for Chlamydia, Gonorrhea, and Syphilis* (November 2005).

³The term "label" generally refers to the written or printed matter on the immediate container of a device, while "labeling" refers to all labels and other printed materials on or accompanying a device. 21 U.S.C. §§ 321(k), (m).

⁴Pub. L. No. 106-554, app. A, § 516(b), 114 Stat. 2763, 2763A-73 (2000). Throughout this report, we refer to this provision as section 516(b).

To perform our work, we reviewed laws, regulations, and guidance related to condom labeling and the legislative history of section 516(b). We focused on male latex condoms (rather than female condoms or condoms made of other materials) because, according to FDA, they represent over 97 percent of condoms sold in this country and were the focus of its review.⁵ We also interviewed FDA officials about the agency's efforts to comply with this statutory requirement. Through our interviews with FDA officials and our examination of documents, we determined that the data we used were sufficiently reliable for purposes of this report. We did not independently evaluate the evidence relied upon by FDA and summarized in FDA documents. We conducted our work from September 2007 through March 2008 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Results in Brief

FDA reviewed studies on the relationship between use of male latex condoms and STDs and determined that existing condom labeling did not provide complete information about the effectiveness of condoms in preventing the transmission of certain STDs. Section 516(b) required that the agency reexamine existing condom labels for medical accuracy with respect to STDs; it did not require FDA to take specific regulatory action. Thus, FDA's actions complied with the statutory requirement. FDA reviewed available scientific information related to condom effectiveness, including its own evaluations and those conducted by other federal agencies. These studies addressed the effectiveness of condoms in preventing a range of STDs, including HPV. Among other things, FDA noted that condoms provide less protection against HPV, which can have multiple routes of transmission, than against certain other STDs. However, FDA found that condoms, when used correctly and consistently, can be effective in reducing the risk of transmission. Based on its review, FDA found limitations in existing condom labeling and identified several areas in which improved labeling would help provide reasonable assurance of condoms' safety and effectiveness. As a result, FDA initiated regulatory action under the Federal Food, Drug, and Cosmetic Act to improve condom labeling with regard to STDs.

In commenting on a draft of this report, HHS did not comment on our findings. HHS did provide technical comments, which we incorporated as appropriate.

Background

FDA assigns medical devices to one of three classes based on the level of risk posed and the controls necessary to reasonably ensure their safety and effectiveness:

- **Class I devices** are generally those with the lowest risk and include such items as elastic bandages and tongue depressors. They are subject to "general controls," such as good manufacturing practices and requirements for manufacturers to register their devices and report adverse events.⁶

⁵Female condoms comprise less than 1 percent of the condom market.

⁶Good manufacturing practice requirements address general aspects of the device manufacturing process, including design, packaging, labeling, and storage. They are intended to ensure that devices are safe and effective and otherwise comply with the Federal Food, Drug, and Cosmetic Act. 21 C.F.R. pt. 820 (2007).

- **Class II devices**, including syringes and hearing aids, are of higher risk and are often subject to “special controls” in addition to general controls. Special controls may include guidance documents or performance standards, which are designed to help provide reasonable assurance of safety and effectiveness.⁷ Male latex condoms are Class II devices.⁸
- **Class III devices**, such as pacemakers, typically pose the highest risk and support or sustain human life, are of substantial importance in preventing impairment of human health, or present a potential unreasonable risk of illness or injury.⁹ Because general and special controls are insufficient to ensure safety and effectiveness, Class III devices are also subject to a pre-market approval process.

In addition, marketed devices in all three classes are subject to various statutory and regulatory requirements, including those related to labeling. For example, labeling must not be false or misleading and must include adequate directions for use.¹⁰ Some specific devices, including condoms, are subject to additional labeling requirements. For example, in 1997, the FDA required that condom labeling include information on expiration dates and latex sensitivity.¹¹

Condom labeling has been the subject of specific FDA actions besides regulations. For example, in 1987, FDA sent a letter to condom manufacturers with recommendations for labeling after the U.S. Surgeon General recommended the use of condoms to protect against the spread of HIV and AIDS. In addition, FDA issued voluntary guidance in 1998, which included suggested language for condom labeling—that is, the primary retail package, package insert, and the foil wrapper for individual condoms—to address the protection provided against STDs.¹² Following this guidance, a retail package would include the statement: “If used properly, latex condoms will help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases.”

Since FDA issued the 1998 guidance, however, concerns have been raised that condoms may not provide the same degree of protection against all STDs. These concerns were supported by reviews of medical research. For example, in 2000, a multi-agency workshop panel comprised of FDA and other federal agencies, including the CDC, reviewed medical literature

⁷Manufacturers of medical devices are required to address the issues identified in special control guidance documents, but are not bound to comply with the precise terms of recommendations they contain. According to FDA, most manufacturers follow the recommendations because doing so is typically the least burdensome way to ensure that a product will meet the standards of safety and effectiveness. 70 Fed. Reg. 69102, 69113 (Nov. 14, 2005).

⁸21 C.F.R. §§ 884.5300(b), 884.5310(b) (2007).

⁹Female condoms are Class III devices. 21 C.F.R. 884.5330(b) (2007).

¹⁰21 U.S.C. §§ 352(a), (f)(1).

¹¹21 C.F.R. §§ 801.435, 801.437 (2007). The regulation on expiration dating, which is specific to condoms, addresses the risk of condom deterioration due to product aging while the regulation on latex sensitivity labeling, which applies to all devices that contain natural rubber, responded to reports of severe allergic reactions and deaths related to medical devices containing natural rubber.

¹²Food and Drug Administration, *Guidance for Industry: Latex Condoms for Men: Information for 510(k) Premarket Notifications: Use of Consensus Standards for Abbreviated Submissions* (July 23, 1998).

related to the effectiveness of condoms in preventing HIV/AIDS and other STDs.¹³ The panel concluded that consistent condom use decreased the rate of HIV/AIDS transmission by approximately 85 percent and that there was insufficient information to determine the association between condom use and HPV infection or disease.¹⁴ The panel also concluded that STD transmission was dependent on a number of factors, such as a person's sexual behavior. It noted that because much of the reviewed research described in the literature had been inadequately designed, it could not provide a definitive assessment of the effectiveness of condoms in preventing STD transmission.

Subsequently, section 516(b) required HHS to reexamine existing condom labels authorized under the Federal Food, Drug, and Cosmetic Act to determine whether they are medically accurate regarding the overall effectiveness or lack of effectiveness of condoms in preventing STDs, including HPV.¹⁵

Statute Required Only an Examination of Condom Labels

The courts have long held that the language of a statute is the primary vehicle for determining congressional intent¹⁶ and, based on its language, section 516(b) required FDA to reexamine—that is, to inspect or investigate¹⁷—whether condom labels present accurate information about the effectiveness of condoms in preventing STDs. Therefore, by its own terms, section 516(b) did not require condom manufacturers to change the labeling of their products, nor did it require FDA to take action to achieve such a change. However, the Federal Food, Drug, and Cosmetic Act authorizes FDA to take regulatory action to improve the accuracy of condom labels based on the reexamination required by section 516(b).¹⁸

Section 516(b) differs significantly from earlier proposed requirements on condom labeling and HPV. Legislation introduced in 1999 would have amended the Federal Food, Drug, and Cosmetic Act to require that condom labels and labeling “bear information providing that condoms do not effectively prevent the transmission of the human papillomavirus and that such virus can cause cervical cancer.”¹⁹ This language was included in the Breast and Cervical Cancer Prevention and Treatment Act of 2000 when it was passed by the House of

¹³FDA, the U.S. Agency for International Development, CDC, and National Institutes of Health (NIH), cosponsored the workshop. During the workshop, a panel comprised of agency representatives and outside experts reviewed and discussed about 140 peer-reviewed publications to evaluate evidence related to the effectiveness of male latex condoms in preventing HIV/AIDS and other STDs.

¹⁴National Institute of Allergy and Infectious Diseases, National Institutes of Health, and Department of Health and Human Services; *Workshop Summary: Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease (STD) Prevention* (July 20, 2001).

¹⁵Section 516(b) did not include a deadline for FDA to comply with the statutory requirement.

¹⁶*See, e.g., Hartford Underwriters Insurance Co. v. Union Planters Bank, N.A.* 530 U.S. 1 (2000); *Aldridge v. Williams*, 44 U.S. (3 How.) 9 (1845).

¹⁷*See* Philip B. Gove, editor, *Webster's Third New International Dictionary of the English Language* (1966).

¹⁸21 U.S.C. § 371 (authorizing FDA to promulgate regulations for the efficient enforcement of the Federal Food, Drug, and Cosmetic Act). *See also* 21 U.S.C. § 360c(a)(1)(B) (authorizing FDA to take appropriate action, including the issuance of guidelines and recommendations as special controls, to provide reasonable assurance that class II devices are safe and effective); 21 U.S.C. § 352(a) (providing that a device with labeling that is false or misleading is considered misbranded under the Federal Food, Drug, and Cosmetic Act, and therefore, not marketable).

¹⁹*See* H.R. 3248, 106th Cong. § 3 (1999).

Representatives in May 2000.²⁰ Subsequently, the Senate passed an amended version of the bill, which did not contain a provision on condom labeling. When the House of Representatives took up the Senate-passed version of the legislation in October 2000, it again considered a condom labeling provision. This provision would have required a reexamination of condom labels, rather than a change in labeling.²¹ However, this provision was not enacted as part of the Breast and Cervical Cancer Prevention and Treatment Act of 2000. Nevertheless, a similar provision—section 516(b)—was included in the Consolidated Appropriations Act, 2001, enacted several months later. In short, the language of section 516(b) evolved from a provision that would have required changes to condom labeling to a provision that did not by itself require such changes.

FDA Complied with the Statutory Requirement and Also Initiated Regulatory Action

By reviewing available studies on the relationship between condom use and STDs and identifying limitations in condom labeling prepared under existing guidance, FDA complied with the statutory requirement to reexamine existing condom labels.²² In a 2005 notice of proposed rulemaking concerning male latex condoms, FDA summarized its extensive review of available scientific information, including its own evaluations and those conducted by the National Institutes of Health (NIH) and CDC, on the effectiveness of condoms in preventing a range of STDs, including HPV.²³ FDA considered whether a reduction in STDs could be attributed to condom use and reviewed clinical data specifically addressing condom effectiveness against various types of STDs. FDA noted that condoms can limit the contact necessary for transmission of STDs and, accordingly, may reduce the risk of transmission. However, FDA also noted that because the risk of disease varies by type of STD and route of transmission, the utility of condoms in protecting against individual STDs may vary as well.²⁴ Because of its precise mode of transmission, FDA concluded that condoms, when used correctly and consistently, provide less protection against HPV than against certain other STDs.

²⁰See 146 Cong. Rec. H2687-H2698 (daily ed. May 9, 2000) (regarding consideration of H.R. 4386, Breast and Cervical Cancer Prevention and Treatment Act of 2000).

²¹See 146 Cong. Rec. H9843-H9852 (daily ed. Oct. 12, 2000) (regarding consideration of H.R. 4386, Breast and Cervical Cancer Prevention and Treatment Act of 2000, as passed by the Senate); see also See H. R. Rep. No. 106-975, at 3 (2000) (providing for House consideration of H.R. 4386, as amended by the Senate, and adding at the end of the Senate amendment additional provisions, including the following: “The Secretary of Health and Human Services shall reexamine existing condom labels that are authorized pursuant to the Federal Food, Drug, and Cosmetic Act to ensure that the labels are medically accurate and not misleading regarding the overall effectiveness and lack of effectiveness of condoms in preventing sexually transmitted diseases, including HIV infection and infection with the human papillomavirus.”)

²²In response to section 516(b), FDA assessed the medical accuracy of condom labeling, considering the material accompanying condoms, including packaging, as well as the foil wrapper in which individual condoms are contained.

²³70 Fed. Reg. 69102 (Nov. 14, 2005). This notice of proposed rulemaking also summarized FDA’s conclusions regarding the effectiveness of male latex condoms in other respects, such as in pregnancy prevention, which were beyond the scope of our report.

²⁴With respect to male latex condoms treated with nonoxynol-9 (N-9), FDA concluded that the lubricant does not protect against HIV/AIDS or other sexually transmitted diseases and that use can cause irritation, which may increase the risk of HIV transmission with infected partners.

Based on its review of scientific and medical research, FDA identified limitations in existing labeling guidance. Most notably, FDA found that labeling consistent with existing guidance would not provide specific information about the reduced level of protection provided by condoms against the transmission of certain STDs, such as HPV, “that can be transmitted through contact with infected skin outside the area covered by the condom.”²⁵ Further, the agency identified several areas in which improved labeling would help provide reasonable assurance of condoms’ safety and effectiveness.

As a result of its reexamination of condom labeling, FDA initiated regulatory action to improve condom labeling with regard to STDs. Specifically, in the 2005 notice of proposed rulemaking, FDA proposed to amend its regulations to designate labeling guidance, including recommendations addressing the effectiveness of male latex condoms in preventing STDs, as a “special control.” Separately, FDA also issued draft labeling guidance and invited comments on this guidance.²⁶ Specifically, with respect to the transmission of STDs, FDA recommended that labeling explain that condoms can greatly reduce, but not eliminate, the risk of acquiring or transmitting HIV. It also recommended that labeling explain that condoms can reduce the risk of transmitting or acquiring certain STDs and that labeling identify others, such as HPV, against which condoms provide less protection. Table 1 compares the language regarding STDs recommended by existing labeling guidance and recommended language contained in the draft labeling guidance issued in 2005.

²⁵FDA also found that existing labeling does not provide specific information about the potential risks of N-9 lubricated condoms.

²⁶*Draft Guidance for Industry and FDA Staff, Class II Special Controls Guidance Document: Labeling for Male Condoms Made of Natural Rubber Latex*; 70 Fed. Reg. 69156 (Nov. 14, 2005).

Table 1: Selected FDA Existing and Proposed Condom Labeling Language Related to STDs

	Existing	Proposed
Retail package	If used properly, latex condoms will help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases.	<i>Front Panel:</i> When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. <i>Back Panel:</i> Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. A latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on STD protection, please read the enclosed insert.
Package insert	If used properly, latex condoms will help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases, including chlamydia infections, genital herpes, genital warts, gonorrhea, hepatitis B, and syphilis.	Important Information: When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. Latex condoms can also reduce the risk of other sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to or from the penis by direct contact with the vagina and genital fluids. Condoms provide less protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer. For more information on STDs, consult your health care provider or information provided by government public health agencies.
Individual condom package	If used properly, latex condoms will help to reduce the risk of transmission of HIV infection (AIDS) and many other sexually transmitted diseases.	When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS.

Source: FDA; GAO presentation of FDA guidance.

Notes: In the November 14, 2005 draft guidance, FDA also proposed labeling changes related to condom effectiveness in pregnancy prevention.

The table does not include the existing or proposed labeling guidance related to STDs that FDA developed for condoms with non-oxynol 9 spermicidal lubricant.

FDA received over 400 comments in response to the notice of proposed rulemaking and draft guidance, about half of which suggested that the recommended labeling language was confusing. Based on these concerns, FDA initiated a two-stage condom label comprehension study to evaluate public understanding of the proposed labeling recommendations and help shape a final rule and accompanying labeling guidance.²⁷ The first stage was designed to test consumers' understanding of both current condom labeling and the proposed labeling, and FDA officials told us this stage was completed in December 2007. As of March 2008, FDA officials said that the agency was analyzing the results of the first stage. Agency officials were

²⁷See 72 Fed. Reg. 33232 (June 15, 2007).

unsure when this analysis would be completed and whether a second stage would be undertaken.

Agency Comments

We provided a draft of this report to HHS for comment. The department provided technical comments, which we incorporated as appropriate.

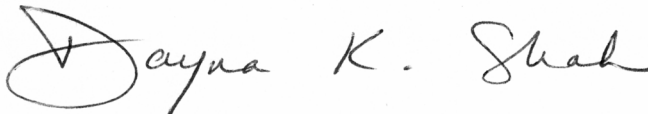
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Sincerely yours,



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Director, Health Care



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