representative payee without a face-to-face interview.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 884

[Docket No. FDA–2004–N–0511] (formerly Docket No. 2004N–0556)

RIN 0910–AF21

Obstetrical and Gynecological Devices; Designation of Special Controls for Male Condoms Made of Natural Rubber Latex

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the classification regulation for condoms to designate a special control for male condoms made of natural rubber latex (latex). The special control for the device is the guidance document entitled ''Class II Special Controls Guidance Document: Labeling for Natural Rubber Latex Condoms Classified Under 21 CFR 884.5300.'' The FDA will publish a notice in the **Federal Register** announcing the availability of the special control guidance document no later than the effective date of this final rule.

DATES: *Effective Date*: This rule is effective January 9, 2009.

Compliance Dates: Premarket notification submissions (510(k)s) for latex condoms filed on or after the effective date of this rule are expected to comply with the requirement of special controls at the time that the 510(k) is submitted. Latex condoms cleared for marketing on or after the effective date of the rule but submitted in 510(k)s filed before the effective date of the rule are expected to comply with the requirement of special controls on or before March 10, 2009. Latex condoms legally marketed before the effective date of this rule are expected to comply with the requirement of special controls December 10, 2009. Specific information on how the rule will be implemented can be found in section II.B of this document.

FOR FURTHER INFORMATION CONTACT: Colin M. Pollard, Center for Devices and Radiological Health (HFZ–470), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–1180.

SUPPLEMENTARY INFORMATION:

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I. Background

In the **Federal Register** of November 14, 2005 (70 FR 69102), FDA proposed to amend existing classification regulations to designate a labeling guidance document as the special control for condoms made of natural rubber latex (latex condoms), classified under 21 CFR 884.5300, and latex condoms with spermicidal lubricant containing nonoxynol-9 (N–9), classified under § 884.5310 (21 CFR 884.5310). As proposed, the final rule amends § 884.5300 (21 CFR 884.5300) and designates a guidance document containing labeling recommendations as the special control for latex condoms. However, FDA continues to review the comments it received in response to its general and specific requests for comment on latex condoms with spermicidal lubricant and to evaluate the controls appropriate for condoms with spermicidal lubricant (§ 884.5310). Therefore, FDA is not issuing a final rule on that device at this time.[1]

In the following sections of this preamble, FDA addresses the statutory framework, regulatory history, and scientific information related to latex condoms; summarizes the final rule; and responds to the comments on FDA's designation of special controls for the latex condom.

A. Statutory Framework

The Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 301 *et seq.*), as amended, including the Medical Device Amendments of 1976 (the 1976

[1] On December 19, 2007, FDA published a final rule, codified at 21 CFR 201.66(c)(5)(ii)(H) and 21 CFR 201.325, that requires that labeling of OTC vaginal contraceptive/spermicidal drug products containing N–9 bear the following warnings:

- For vaginal use only
- Not for rectal (anal) use
- Sexually transmitted diseases (STDs) alert: This product does not protect against HIV/AIDS or other STDs and may increase the risk of getting HIV from an infected partner
- Do not use if you or your sex partner has HIV/AIDS. If you do not know if you or your sex partner is infected, choose another form of birth control.
- When using this product you may get vaginal irritation (burning, itching, or a rash)
- Stop use and ask a doctor if you or your partner get burning, itching, a rash or other irritation of the vagina or penis

Other information in the new labeling includes:

- When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate the risk of catching or spreading HIV, the virus that causes AIDS.
- Studies have raised safety concerns that products containing the spermicide nonoxynol 9 can irritate the vagina and rectum. Sometimes this irritation has no symptoms. This irritation may increase the risk of getting HIV/AIDS from an infected partner.
- You can use nonoxynol 9 for birth control with or without a diaphragm or condom if you have sex with only one partner who is not infected with HIV and who has no other sexual partners or HIV risk factors
- Use a latex condom without nonoxynol 9 if you or your sex partner has HIV/AIDS, multiple sex partners, or other HIV risk factors
- Ask a health professional if you have questions about your best birth control and STD prevention methods.

amendments) (Public Law 94–295) and the Safe Medical Devices Act of 1990 (SMDA) (Public Law 101–629), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

FDA refers to devices that were in commercial distribution before May 28, 1976 (the date of enactment of the 1976 amendments), as preamendments devices. Under section 513 of the act, FDA classifies these devices after the agency takes the following steps: (1) receives a recommendation from a device classification panel (an FDA advisory committee); (2) publishes the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) publishes a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

FDA refers to devices that were not in commercial distribution before May 28, 1976, as postamendments devices. Postamendments devices are classified automatically by statute (section 513(f) of the act) into class III without any FDA rulemaking process. These devices remain in class III unless FDA does one of the following: (1) reclassifies the device into class I or II; (2) issues an order classifying the device into class I or II in accordance with section 513(f)(2) of the act; or (3) issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the act, to a legally marketed device that has been classified into class I or class II or to a preamendments device of a type that has yet to be initially classified in accordance with section 513(b). The agency determines whether new devices are substantially equivalent to predicate devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and regulations at part 807 (21 CFR part 807).

Under the 1976 amendments, class II devices were defined as devices for which there was insufficient information to show that general controls themselves would provide reasonable assurance of safety and effectiveness, but for which there was sufficient information to establish performance standards to provide such assurance. SMDA broadened the definition of class II devices to mean those devices for which the general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness, but for which there is sufficient information to establish special controls to provide such assurance, including performance standards, postmarket surveillance, patient registries, development and dissemination of guidelines, recommendations, and any other appropriate actions the agency deems necessary (section 513(a)(1)(B) of the act).

B. Regulatory History of Latex Condoms [2]

Prior to enactment of the 1976 amendments, latex condoms were marketed in the United States for both contraception and prophylaxis, i.e., reducing the risk of sexually transmitted infections (STIs).[3] As a preamendments device, the latex condom was classified along with hundreds of other devices during FDA's original classification proceedings. Based primarily on the recommendations of experts on the Obstetrics and Gynecology Device Classification Panel, FDA classified latex condoms into class II by regulation published in the **Federal Register** of February 26, 1980 (45 FR 12710). Condoms were identified as ''* * * a sheath which completely covers the penis with a closely fitting membrane. The condom is used for contraceptive and for prophylactic purposes (preventing transmission of venereal disease) * * *'' (§ 884.5300). This classification regulation does not include condoms with spermicidal lubricant, which are postamendments devices classified under § 884.5300.

At the time that latex condoms were classified into class II, the statutory definition of that class contemplated the establishment of mandatory performance standards for all class II devices, in accordance with section 514(b) of the act (21 U.S.C. 360d(b)). Because of the complex process associated with issuing mandatory performance standards, the agency did not establish a performance standard for condoms or virtually any other class II device before the SMDA in 1990 provided additional options for special controls for class II devices. This rulemaking will for the first time establish a special control for latex condoms.

Latex condoms are also subject to the requirement of premarket notification, a general control requiring a determination of substantial equivalence before they may be marketed, and other general controls, including good manufacturing practices (quality system regulation), registration and listing, adverse event reporting, and the prohibitions on adulteration and misbranding. This device is also subject to labeling requirements applicable to all devices, including a statement of principal intended action(s) and adequate directions for use as described in part 801 (21 CFR part 801).

In addition to the general labeling requirements, latex condoms are subject to specific labeling requirements addressing expiration dating and latex sensitivity (21 CFR 801.435 and 801.437). FDA established expiration dating requirements in response to shelf life studies showing that important latex condom properties can change over time. The expiration dating regulation addresses the risk of latex condom deterioration due to product aging and helps ensure that consumers have information regarding the safe use of latex condoms (62 FR 50501, September 26, 1997). The latex sensitivity labeling requirements were added in response to numerous reports of severe allergic reactions and deaths related to a wide range of medical devices containing natural rubber (62 FR 51021 at 51029, September 30, 1997).

In addition to the history of action regarding latex condoms undertaken under the act, on December 21, 2000, Congress enacted Public Law 106–554, which required that FDA ''reexamine existing condom labels'' and ''determine whether the labels are medically accurate regarding the overall effectiveness or lack of effectiveness of condoms in preventing sexually transmitted diseases, including [human papillomavirus].'' In this review, FDA considered the following:

- Physical properties of condoms
- Condom slippage and breakage during actual use
- Plausibility for STI-risk reduction attributable to condoms
- Evaluations of condom effectiveness against STIs by other Federal agencies, and
- Clinical studies of condoms' protection against STIs published in peer-reviewed journals.

[2] As discussed in the 2005 proposed rule (70 FR 69102 at 69112), the proposal was limited to latex condoms, which represent the vast majority of condoms marketed in the United States. As discussed in the proposal, FDA intends to address condoms made from other materials (natural membrane (skin) or synthetic materials) at a future date.

[3] With the exception of a reference to the 2005 proposed replacement of ''venereal disease'' with ''sexually transmitted disease,'' FDA is using ''sexually transmitted infection'' or ''STI'' instead of ''sexually transmitted disease'' or ''STD'' in the final rule and special controls guidance document. This is discussed in more detail at section III.

As a result of this review of scientific information and of existing latex condom labeling, FDA concluded that existing latex condom labeling was medically accurate in presenting the conclusion that, as an overall matter, condoms are effective in reducing the risk of STIs. To help consumers make appropriate choices for their particular needs, and therefore to ensure the safe and effective use of condoms, FDA proposed to establish a labeling special control to address some additional, more nuanced information about condoms and STIs, as well as to provide information about contraception, and about appropriate directions and precautions for use of latex condoms. The present rulemaking grew out of that initiative.

C. Overview of Proposed Rule

In the **Federal Register** of November 14, 2005 (70 FR 69102), FDA issued a proposed rule to amend the classification regulations for condoms (§§ 884.5300 and 884.5310). The proposed regulatory changes were intended to help ensure that latex condoms were used safely and effectively by providing labeling conveying a concise, accurate message that neither exaggerated the degree of protection provided by latex condoms, nor undervalued overall STI-risk reduction provided by latex condom use.

FDA proposed to amend the identification section of the regulations to change the wording ''venereal disease'' to ''sexually transmitted diseases.'' FDA also proposed to add classification sections to each of the regulations, segregating the subset of condoms in each classification that were made of latex. Finally, FDA proposed to designate as a special control a guidance document with labeling recommendations for latex condoms, because the agency believed that this control, together with general controls, could reasonably assure the safety and effectiveness of these devices. The draft special controls guidance recommended labeling to inform consumers about the extent of protection provided by latex condoms against unintended pregnancy and against STIs, including labeling that informed consumers that STIs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact. The draft guidance recommended that labeling explain that latex condoms can reduce the risk of STIs, such as gonorrhea and chlamydia, that are spread to or from the penis by direct contact with the vagina and genital fluids. It further recommended labeling that indicated that some STIs, such as genital herpes and human papillomavirus (HPV), may also be transmitted by contact with infectious skin or mucosa not covered by the latex condom, and that latex condoms provide less protection against these STIs.

FDA proposed to establish the labeling guidance as a special control, by rulemaking, because it meant that manufacturers would be required to address the issues identified in the guidance. Unlike a regular guidance, which imposes no requirements, where a guidance document has been designated as a special control by a rule, manufacturers must address the issues identified in the guidance, either by following the recommendations in the guidance or by some other means that provides equivalent assurances of safety and effectiveness. At the same time, establishing a guidance document as a special control affords greater flexibility than a rule mandating specific labeling language and can facilitate updating labeling as new scientific information becomes available because the special control permits manufacturers to use any labeling that affords equivalent assurances of safety and effectiveness for latex condoms.

In response to FDA's requests for comment, more than one hundred commenters submitted information and comments to the two dockets (one docket for the proposed rule and one docket for the draft special controls guidance document). Comments were submitted by consumers, health professionals, industry, academia, state and Federal government agencies, as well as professional societies and organizations. The comments included different points of interest and concern. Many comments discussed issues involving latex condoms with spermicidal lubricant containing nonoxynol-9, and as discussed earlier, FDA continues to review those comments. In some cases, commenters filed comments to the dockets for both the rule and for the guidance; in other cases, comments were filed in only one docket. Because of the intertwined nature of the proposed rule and guidance and because of the significant overlap in comments, FDA considered all comments in preparing both the final rule and the intended final special control guidance document.[4]

[4] The term ''intended final special control guidance document'' refers to the version of the guidance that is currently available for reference only at *http://www.fda.gov/cdrh/comp/guidance/1548ref.html*, pending approval under the Paperwork Reduction Act (the PRA). (See Section VII.)

D. Additional Scientific Information Developed After the Completion of the Proposed Rule and Draft Special Control Guidance

1. FDA Update of Epidemiology

In developing the 2005 proposed rule and draft guidance, to assess the overall effectiveness of latex condoms in preventing transmission of STIs, FDA evaluated a variety of scientific evidence and information about condoms and STIs. In particular, FDA considered the physical properties of a condom, which make it capable of acting as a barrier to the pathogens that cause STIs; evidence regarding condom slippage and breakage during actual use; plausibility for STI-risk reduction attributable to condoms, which draws on information about the different routes of transmission of different STIs; and evidence from good quality epidemiological studies published in peer-reviewed journals evaluating condoms and STI-risk reduction, including evaluations of condom effectiveness against STIs by other Federal agencies.

FDA's evaluation divided common STIs into two groups in relation to their usual routes of sexual transmission. FDA identified as Group I those STIs that are sexually transmitted solely either to or from the head of the penis, an area that is covered when a latex condom is used. Group I STIs include HIV/Acquired Immune Deficiency Syndrome (AIDS), gonorrhea, chlamydia, trichomoniasis,[5] and hepatitis B virus (HBV). FDA identified as Group II those STIs that can be transmitted not only through contact with the head of the penis, but also through contact with infected skin outside the area that is covered when a latex condom is used. Group II STIs include HPV, herpes simplex virus (HSV), syphilis, and chancroid. Considering the means of transmission of STIs and the extensive information on the physical characteristics and performance of condoms, as well as the specific clinical data available, FDA concluded that there was strong support for the conclusion that latex condoms reduce the overall risk of transmission

[5] FDA's 2005 proposed rule identified trichomoniasis as a group I STI based on its route of transmission but did not consider any significant new information regarding trichomoniasis because none existed at that time. Neither the prior labeling recommendations nor the draft special control guidance recommended making specific claims for condom effectiveness against trichomoniasis. In formulating this final rule and special control guidance document, FDA also has found no new information about condom effectiveness against this specific pathogen, and does not include specific recommendations for labeling to address it.

of STIs. FDA also concluded that the degree of risk reduction for different types of STIs varies with their routes of transmission.

As discussed in section III.C, FDA's scientific conclusions were generally supported by the public comments. In preparing this final rule, moreover, FDA ensured that its scientific basis remains sound. Using the same approach as in 2005, analyzing systematic reviews[6] and, when those were not available, analyzing individual clinical studies for STIs, FDA reviewed more recent epidemiological studies and analyses published in peer-reviewed publications from December 2004, the cut-off date for studies considered in developing the proposed rule, through April 30, 2008. Consistent with its findings in 2005, FDA confirmed that latex condoms provide effective protection against all STIs evaluated. FDA findings from its updated review are described in more detail next.

Group I STIs

In the 2005 proposal, FDA concluded that latex condoms, when used correctly and consistently, are effective in reducing the risk of transmission of Group I STIs (70 FR 69102 at 69108). No new data undermine this conclusion and some new studies of particular Group I STIs provide additional support for it. Therefore, FDA's conclusion related to the Group I STIs continues to be that latex condoms when used correctly and consistently are effective in reducing the risk of transmission of group I STIs.

HIV

Well-designed studies evaluated prior to the proposed rule show the effect of consistent condom use on reducing the risk of HIV infection (70 FR 69102 at 69107 to 69108). One well-designed study conducted a meta-analysis (where results of all studies selected are pooled and analyzed) of studies of HIV-discordant subjects (where HIV status is known at the outset of the study, and an uninfected partner has sex with an infected partner) and found that condoms were 90 to 95 percent effective in reducing the incidence of new infections when used consistently. Another study was a systematic review of longitudinal studies and found that consistent use of condoms results in at least an 80 percent reduction in HIV incidence.

No new systematic reviews of condom effectiveness in reducing the risk of HIV infection have been published since the cut-off for studies considered in formulating FDA's proposed rule. On the basis described in the proposed rule, FDA's conclusion remains that consistent and correct use of latex condoms is highly effective in reducing the risk of HIV infection.

Gonorrhea and Chlamydia

Consistent with the FDA conclusions presented in 2005 (70 FR 69102 at 69108), one systematic review presented in 2006 demonstrated that consistent and correct use of condoms reduces risk of both gonorrhea and chlamydia in men and women (Ref. 9).

Hepatitis B Virus (HBV)

As was the case when FDA published its proposed rule, FDA is aware of no systematic reviews of condom effectiveness against HBV infection. Nor were any new epidemiological studies of condom use and HBV infection published during the period of FDA's review for preparation of this final rule. As discussed in the 2005 proposal (70 FR 69102 at 69108), one cross-sectional study showed that correct and consistent condom use was significantly associated with lower prevalence of HBV.

Group II STIs

In the 2005 proposal, FDA concluded that latex condoms, when used correctly and consistently, are effective in reducing the risk of transmission of group II STIs. Studies published since December 2004 support, and in the case of HPV, provide additional evidence for, this conclusion, as discussed below.

HPV

No new systematic reviews of condoms and HPV infection have been published since December 2004. At the time of the 2005 proposed rule, the clinical data regarding the effect of condom use on reducing the risk of infection with HPV was limited, but two systematic reviews supported the conclusion that correct and consistent use of latex condoms can reduce the rates of genital warts and cervical cancer, the main diseases associated with HPV infection (70 FR 69102 at 69108).

Since December 2004, several individual studies have addressed condom use and HPV infection, not only the incidence of HPV-related disease. Of particular note, a longitudinal study of the association of condom use and risk of genital HPV infection found that women who reported consistent condom use for the eight months prior to HPV testing were less likely to acquire a first-time infection of HPV and that women who reported 100 percent condom use in the prior eight months had no cervical squamous intraepithelial lesions detected on their Pap tests (Ref. 10) (hereinafter referred to as ''2006 Winer et al. study''). Another study published since the cut-off for the 2005 proposed rule found a higher prevalence of HPV in women who did not use condoms (Ref. 4). Yet another study published since the 2005 proposed rule demonstrated an association between prolonged HPV infection and less consistent condom use (Ref. 7). These newer studies now support the conclusion that condom use not only reduces the risk of genital warts and cervical cancer, it also reduces the risk of HPV infection itself.

Genital Herpes Simplex Virus (HSV)

No new systematic reviews of condoms and HSV infection have been published since December 2004. FDA's 2005 conclusions about latex condom effectiveness were based on the 2002 systematic review showing that condom use reduced the risk of HSV–2 infection for women (70 FR 69102 at 69108). A more recent prospective study showed effectiveness of condom use in reducing the risk of HSV infection in men and replicated effectiveness in women (Ref. 8), supporting the findings of the 2002 systematic review and FDA's 2005 conclusions.

Syphilis

As was the case when FDA published its proposed rule, FDA is not aware of any systematic reviews of condom effectiveness against syphilis infection. FDA's 2005 conclusions about latex condom effectiveness were based primarily on the data from two prospective studies, discussed in the preamble to the proposed rule (70 FR 69102 at 69108), that showed condom use provided significant protection against syphilis. More recently, one study evaluated risks of STIs, including syphilis, in female sex workers and found that failure to use a condom was associated with an increased risk of syphilis (Ref. 6). This information continues to support the conclusion made in the 2005 proposal that correct and consistent latex condom use reduces the risk of syphilis.

Chancroid

Chancroid infection is extremely rare in the United States. In 2006, only 33

[6] As stated in the proposed rule (70 FR 69102 at 69107), a systematic review means a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research and to collect and analyze data from studies that are included with the review.

new cases were reported in the United States. (Ref. 1). As in 2005, when FDA published its proposed rule, FDA knows of no systematic review of condom effectiveness against this STI. No new epidemiological studies of condom use and chancroid infection have been identified. Therefore, FDA's conclusions about latex condom effectiveness toward chancroid remain based on the study discussed in the 2005 proposal that reported that condom use was associated with a significantly reduced risk of genital ulcer disease (presumed to be chancroid) among prostitutes in Kenya (70 FR 69102 at 69108).

In summary, FDA believes that conclusions from the additional studies published in peer-reviewed publications from December 2004 through April 30, 2008, are consistent with FDA's 2005 conclusions about latex condom effectiveness. Newer evidence, such as the systematic review of the effect of condom use on transmission of gonorrhea and chlamydia infections (Ref. 9) and the recent epidemiological studies showing that condom use reduced HPV infection (Refs. 7 and 10), replicate or strengthen the basis for these conclusions.

2. Latex Condom Label Comprehension Study

As described in more detail below, many commenters expressed concern that FDA's proposed language for latex condom labeling was confusing, especially in its efforts to describe two tiers of protection afforded by condoms against STIs. These comments expressed serious concerns that FDA's latex condom labeling proposal was overly complex and would ultimately be misunderstood by the consumer. Many argued that this same confusion and misunderstanding would lead to unmerited negative impressions of latex condoms and—ultimately—to an unfounded decrease in latex condom use. One commenter also submitted a study it had conducted of consumer comprehension of the labeling proposed in the draft guidance, the results of which supported the comments that this labeling was not well understood. (This comment and study are discussed in section III of this document, where FDA discusses and responds to comments in detail.)

In light of these important comments on the labeling recommendations it had proposed, to inform its final rulemaking, FDA conducted a study to see whether typical consumers understand latex condom labeling, testing both the current labeling and the labeling proposed in the 2005 draft guidance document.

FDA Study Objectives

FDA contracted for a latex condom label comprehension study. Conducted in November and December 2007, the study was designed to measure and compare consumer understanding of the labeling recommended for latex condoms under FDA's 1998 guidance document, ''Latex Condoms for Men, Information for 510(k) Premarket Notifications: Use of Consensus Standards for Abbreviated Submissions,'' which is found on currently marketed latex condoms, and the latex condom labeling proposed in the 2005 draft special controls guidance. The study specifically focused on FDA's proposal to include more detailed information in the labeling about the relative degree of protection that condoms provide against different STIs.[7]

Study Design

Participants were recruited from six shopping malls, four retail pharmacies, and three literacy centers in 11 communities throughout the United States. Eight hundred and forty-four (844) participants between the ages of 18 and 54 were divided almost evenly to review either the current or proposed latex condom labeling. Each participant was asked to respond to a set of questions intended to measure his or her understanding of the labeling. When responding to the questions, participants were allowed to look at the labeling provided.

Quotas were established to attain an equal distribution by sex and pre-specified proportions of respondents by age and reading ability. The Rapid Estimate of Adult Literacy in Medicine (REALM) test (Ref. 3) was used to assess reading level, and a threshold score was chosen, which divided the group into normal-literacy (ninth grade reading level and above) and low-literacy (eighth grade reading level and below). Of the 844 subjects, 430 were classified as normal-literate, 405 as low-literate, and nine had no REALM score.

FDA Study Results

Poorer readers and those with less education (two variables not highly correlated) had lower comprehension scores than those with a higher reading level. However, there were no differences based on age, race, ethnicity, income, or the type of neighborhoods where the respondents resided.

Participants understood the basic message in both the current and proposed labeling that latex condoms help protect against transmission of sexually transmitted infections (>80 percent correct responses). When comparing equivalent questions between the current and proposed latex condom labeling, for every comparison with a significant difference in rates of comprehension, the difference favored the current latex condom labeling over the proposed latex condom labeling. Study participants did not understand the more complex messages about the relative degree of protection provided by condoms against different STIs (<30 percent correct responses).

The study was not designed to determine the reasons for the differences in consumer comprehension of the two labeling versions. However, FDA's proposed labeling was unarguably lengthier, with considerably more information than current labeling. Study analysis suggests that shorter and simpler labeling will more likely result in better consumer comprehension.

II. Summary of the Final Rule

A. Overview of the Final Rule

In developing this final rule, FDA considered all of the comments, as well as its updated review of scientific evidence and results of the latex condom label comprehension study. FDA concludes that the scientific evidence today continues to fully support the overall effectiveness of latex condoms in reducing the risk of transmission of common STIs. That evidence supports the conclusions that correct and consistent use of latex condoms reduces the risk of transmission of HIV/AIDS and other STIs such as gonorrhea that are sexually transmitted solely by contact with the head of the penis (via genital fluids). Also, the evidence available today provides even more support than was available at the time of publication of the proposed rule for the conclusion that latex condoms are effective in reducing the risk of transmission of other STIs, such as genital herpes and HPV, that can be transmitted not only by contact with the head of the penis, the area covered by a latex condom, but also by contact with infected skin outside the area covered by the latex condom.

In developing the final rule and intended final special control guidance document, FDA not only affirmed the underlying scientific conclusions, but

[7] The study also focused on the new warnings proposed for condoms with nonoxynol-9 (N–9) in the lubricant; as described in the introductory paragraph of section I of this preamble, FDA's proposal to designate a labeling guidance as a special control for those devices remains open, as FDA is still considering the comments and other data, including these study results, that are relevant to that proposal.

also considered whether the labeling statements recommended in the draft special control guidance document, in particular the statements addressing the effectiveness of latex condoms against the two groups of STIs, were adequately clear. Based on comments that criticized the labeling contained in the draft guidance as, among other things, ''misleading,'' ''overly complex,'' ''difficult to understand,'' and ''negative possibly discouraging use,'' as discussed in section I, FDA sponsored a latex condom label comprehension study. This study supported commenters who maintained that the labeling contained in the draft guidance was too confusing for consumers, and did not effectively and adequately communicate the effectiveness of latex condoms against these two groups of STIs.

Taking account of the comments and other information described in this preamble, FDA's final rule and intended final special control guidance remain consistent with the proposal but incorporate some changes. The final rule, like the proposal, amends the identification section of § 884.5300 to change the terminology used. As proposed, the final rule also creates new classification sections distinguishing condoms made of natural rubber latex from condoms made of other materials, including natural membrane and synthetic materials. Finally, as proposed, the final rule designates a guidance document containing labeling recommendations as the special control for the subset of condoms made of natural rubber latex, to address issues of safety and effectiveness discussed below and to convey the basic scientific conclusions already described. In response to comments and in consideration of the other information described previously, FDA has simplified the labeling recommended for latex condoms, including the labeling statements regarding the degree of protection afforded by latex condoms against the two groups of STIs. FDA has also updated the recommended directions for use and precautions to help ensure consistent and correct use of latex condoms. Finally, FDA has assigned a new title to the final guidance document designated as a special control by this rule in order to avoid confusion with the draft guidance made available in November 2005, which remains available as the proposed special control for latex condoms with spermicidal lubricant in association with the pending proposal to amend § 884.5310. (See Section I.)

B. Implementation Strategy

FDA intends to implement this final rule as described in the following paragraphs. The general approach remains consistent with what was set forth in the 2005 proposed rule, but certain time frames have been extended. Specifically, this final rule will be effective 60 days after its date of publication, rather than the 30 days anticipated in the proposed rule. The implementation strategy takes account of the changed effective date of the final rule, while remaining generally consistent with the implementation strategy outlined in the proposed rule.

The proposed rule anticipated that latex condoms legally marketed prior to the effective date of a final rule would have 11 months after the effective date, or a total of 12 months from publication of the final rule, to meet the requirements of special controls. That proposed rule also anticipated that latex condoms that were the subject of pending 510(k) applications on the effective date of any final rule but cleared subsequently would be expected to comply with the requirement of special controls for latex condoms no more than 60 days after the effective date of the final rule.

For the final rule, FDA intends the following implementation strategy. Latex condoms that are the subject of premarket notification submissions (510(k)s) filed on or after the effective date of this rule are expected to comply with the requirement of special controls immediately upon the rule taking effect. Therefore, a firm submitting a 510(k) for a latex condom on or after the effective date of this rule must show that its device meets the recommendations of the special control guidance (as made available after PRA approval) or in some other way provides equivalent assurances of safety and effectiveness.

Latex condoms that are the subject of a 510(k) that is pending on the effective date of this final rule but are subsequently cleared are expected to comply with the requirement of special controls by following the recommendations in the special control guidance (as made available after PRA approval) or providing equivalent assurances of safety and effectiveness on or before 120 days after the date of publication of this final rule.

Latex condoms that were legally marketed prior to the effective date of this final rule are expected to comply with the requirement of special controls by following the recommendations in the special control guidance (as made available after PRA approval) or providing equivalent assurances of safety and effectiveness no more than 13 months after the date of publication of this final rule. As in the proposal, this gives firms marketing these latex condoms 11 months from the effective date of the final rule to achieve compliance, and a total period of 13 months from the date of publication of the final rule, rather than the 12 months from publication defined under the proposal. FDA believes that this period will allow for the production of new labeling to meet the requirement of special controls without leading to product shortages, while promoting the regulatory purpose of ensuring that this new labeling is available to consumers in a timely fashion.

C. Issues Requiring Special Controls

In the 2005 proposed rule, FDA identified several issues associated with the use of latex condoms that required special controls to help provide a reasonable assurance of safety and effectiveness. The issues included the risks of unintended pregnancy and of STI transmission, and the issue of incorrect or inconsistent use, which undermines the effectiveness of the latex condom in protecting against unintended pregnancy and STI transmission.

In the final rule, FDA is designating a guidance document with labeling recommendations as the required special control for latex condoms to address the issues of safety and effectiveness associated with these devices—the risks of unintended pregnancy and of STIs, and the issue of incorrect or inconsistent use.

1. Unintended Pregnancy

One of the principal intended actions of latex condoms is contraception. Latex condoms can greatly reduce the risk of unintended pregnancy, but cannot eliminate it. The special controls guidance recommends that the labeling indicate that latex condoms are intended to prevent pregnancy. Labeling should also indicate that latex condoms do not completely eliminate the risk of pregnancy. The guidance also recommends that the package insert contain contraceptive effectiveness information comparing pregnancy rates for latex condoms to rates for other contraceptive options available in the United States including drugs, devices, and methods of permanent sterilization, as well as a statement that consumers who have questions about contraceptive options, particularly because of health reasons for avoiding pregnancy, should contact a health care provider.

2. Transmission of Sexually Transmitted Infections (STIs)

The other principal intended action of latex condoms is protection against the transmission of STIs. The intended final special controls guidance recommends that labeling state that latex condoms are intended to prevent HIV infection (AIDS) and other STIs. In addition, the labeling should include a statement that condoms do not completely eliminate the risk of STIs. Labeling should indicate that latex condoms reduce the risk of STIs by providing a barrier against the source of infection. Labeling should indicate that latex condoms are most effective at reducing transmission of STIs such as HIV infection (AIDS) and gonorrhea that are spread by contact with the head of the penis, an area covered when the condom is used. Labeling should also indicate that condoms are less effective against STIs such as HPV and herpes that can also be spread by contact with infected skin that is not covered by the latex condom.

The intended final guidance also recommends labeling that indicates that a health care provider should be contacted if a consumer believes they may have an STI. The intended final special controls guidance further recommends that labeling indicate that for more information on latex condoms or STIs, a health care provider or public health agency should be contacted.

3. Incorrect or Inconsistent Use

In order to get the most protection from a latex condom, latex condoms must be used correctly every time a consumer has sex. To promote correct use, the intended final special controls guidance recommends that labeling include directions for use and precautions against incorrect use. To promote consistent use, the intended final special controls guidance recommends that labeling state that to get the most protection from a latex condom, a condom be used correctly every time the consumer has sex.

III. Comments and FDA's Responses

More than 100 commenters submitted information and comments to the two dockets for the proposed rule and draft special controls guidance document. The commenters included consumers, health professionals, industry, academia, State and Federal agencies, professional societies, and organizations. Because of the intertwined nature of the documents and the significant duplication of comments between the dockets for the proposed rule and draft special controls guidance document, FDA is summarizing and responding to the comments to both dockets in this preamble.

In general, the comments stated that FDA had properly described the science regarding latex condom effectiveness, on which FDA based its proposed special control labeling recommendations. None of the comments questioned the importance of accurate latex condom labels. Many comments indicated that consumers deserve to understand how and why condoms work. However, as previously noted, a substantial number of comments stated that the specific labeling recommendations in the draft guidance document were too complex to be effective in conveying this important information to consumers, and could inadvertently lead to misimpression regarding the safety and effectiveness of condoms, particularly for use in reducing the risk of STIs.

In issuing the final rule designating the revised guidance document as a special control, FDA is affirming the safety and effectiveness of condoms for contraception, as well as for reducing the risk of transmission of STIs, including those most common in the United States. In response to comments, and in light of the consumer comprehension studies provided in those comments and described previously, FDA has revised the recommended labeling messages contained in the intended final special control guidance document to simplify them and better communicate the essential information they contain. Following is a summary of the specific comments and the agency's responses.

A. Identification Section of the Classification Regulation

(Comment 1) One comment stated that FDA should substitute ''sexually transmitted infections'' wherever it was using ''sexually transmitted diseases.'' This comment pointed out that the purpose of the latex condom is to prevent the infection; the diseases are the clinical sequellae of the infection.

(Response) FDA agrees with this comment, and notes that the term ''sexually transmitted infection'' has gained currency in the clinical community. Accordingly, FDA have revised the language in § 884.5300 and the labeling recommendations in the special controls guidance document to use ''sexually transmitted infection'' or ''STI.''

B. Establishment of a Guidance Document as a Special Control

(Comment 2) One commenter disagreed with the decision by FDA to issue labeling guidelines under special controls guidance rather than mandating through regulation specific new language on all condom labeling to address the concerns FDA has identified. The commenter did not agree with giving flexibility to manufacturers on the wording used.

(Response) FDA believes a special control guidance will provide an appropriate level of control over labeling. Unlike a regular guidance, which imposes no requirements, where a guidance document has been designated as a special control by a rule, manufacturers must address the issues identified in the guidance, either by following the recommendations in the guidance or by some other means that provides equivalent assurances of safety and effectiveness. If a manufacturer proposes to use a means other than the labeling recommendations set forth in the intended final special control guidance, the manufacturer will need to establish equivalent assurance of safety and effectiveness of the alternative.

C. FDA's Review of Scientific Information

The 2005 proposed rule included a summary of FDA's review of the medical accuracy of latex condom labeling, which included an extensive review of the scientific information related to condoms. As discussed in the proposal, FDA considered the physical properties of condoms, condom slippage and breakage during actual use, the plausibility for STI-reduction attributable to condoms, evaluations of condom protection against STIs by other Federal agencies, and clinical data regarding condom protection against STIs. The follow sections discuss the comments and FDA's responses related to this review.

1. General Comments

(Comment 3) Many of the comments commended the proposed rule and draft special controls guidance document as well grounded in the scientific and medical evidence and consistent with the findings from clinical studies in the available literature.

(Response) FDA agrees. In addition to the studies on which the 2005 proposal was based, as described previously, peer-reviewed epidemiological studies published subsequently have also supported the conclusion that latex condom use reduces the risk of STIs.

2. Slippage and Breakage

(Comment 4) One comment challenged FDA's estimate of the rates of condom slippage and breakage in actual use and expressed concerns that

some ''key points'' were missing, including the experience of the user. More specifically, the commenter ''would have preferred that most slippage and breakage fall within the 2–4% range with experienced users toward the 2% and lower range and inexperienced users at the higher 4% range and above.'' This comment also disagreed with FDA's statement that condom slippage and breakage data support the conclusion that condoms reduce the risk of STI transmission and stated ''[s]lippage and breakage data does not support the conclusion that condoms help, rather the opposite.'' The commenter stated that the labeling recommendations should reflect that even with perfect use, an individual can become infected when slippage and breakage occurs.

(Response) FDA disagrees that the slippage and breakage data do not support the conclusion that condoms reduce the risk of STI transmission. FDA notes that rates of slippage and breakage during use have been measured for many different commercially available latex condoms, typically ranging between 0.5–2% (70 FR 69102 at 69105). FDA believes that these low rates of condom slippage and breakage, when taken together with studies of condom properties discussed in the proposed rule (see 70 FR 69102 at 69104 to 69105), support the conclusion that latex condoms, when used consistently and correctly, provide a reliable barrier to STI pathogens. FDA concurs with the commenter's point that even with correct and consistent use, slippage and breakage can occur. FDA does not believe, however, that additional wording is necessary to underscore this point regarding perfect use. FDA believes that the labeling recommendations as crafted accurately reflect the overall conclusion that when used correctly and consistently, latex condoms reduce the risk of STI transmission but do not completely eliminate it.

3. Risk Reduction

(Comment 5) One comment suggested that FDA's analysis overlooked infectivity. This comment recommended changes to the FDA conclusion about condom effectiveness to reflect this.

(Response) FDA does not believe that discussion of infectivity would benefit consumers in making safe and effective use of latex condoms. While the infectivity of the pathogen is among the factors that affect the baseline risk of acquiring a specific STI, even the most infective STI pathogen cannot penetrate an intact latex condom. Infectivity of the pathogen thus only impacts the net risk of infection despite condom use where the latex condom does not present a barrier to interrupt the potential path of transmission—either because the infected skin is outside the area covered by the condom, or because the condom has failed (a rare event with correct use). In its intended final labeling recommendations, FDA has already described that condoms derive their effectiveness from providing a barrier to the source of infection and that condoms are less effective against STIs that are transmitted by contact with infected skin outside the area covered by the condom (as well as by contact with the head of the penis). Recommended labeling also emphasizes the importance of correct and consistent use to maximize the protection provided by a latex condom, but acknowledges that use of condoms does not completely eliminate the risk of STI transmission. As labeling does not quantify the amount of risk reduction for specific STIs, FDA does not believe that addition of discussion of infectivity would provide useful information beyond the expression of limits and of conditions to optimize benefit already provided.

(Comment 6) One comment challenged FDA's conclusions regarding the degree of risk reduction afforded by latex condoms when the population evaluated in epidemiologic studies from which data were obtained consisted of commercial sex workers (CSWs). This comment stated that ''One must use caution when generalizing prostitute studies to the general population.''

(Response) The commenter did not provide additional details or support for his statement, but referenced an epidemiologic study (70 FR 69102 at 69117, reference 31, Kjaer, S.K., E.I. Svare, A.M. Worm, et al.). The authors of that study noted that CSWs are likely to have become sexually active at a younger age compared to other populations, and speculated that early and multiple STIs in this population might lead to a more robust immunologic response among chronically infected compared to other populations. Importantly, however, the authors noted that this latter theory is unproven.

Conducting studies outside the United States, in places and populations where the disease prevalence is high, makes it possible to obtain valid outcomes data from studies that are reasonably sized and would likely be impossible to conduct in lower risk populations in the United States. Despite differences between the study populations and typical U.S. users, FDA believes conclusions from such studies are relevant, because the following fundamental elements that the studies address are identical in the study population and in the expected U.S. user population: (1) Primary study endpoint (presence of infection); (2) pathogen (individual STI); (3) route of transmission (sexual); and (4) prophylaxis (latex condom).

4. Evaluation of Latex Condom Effectiveness

(Comment 7) One comment strongly criticized the June 2000 Workshop convened by the National Institutes of Health (NIH) with other Federal public health agencies and outside experts (70 FR 69102 at 69106), its deliberative process, and the conclusions that were issued afterwards. This comment stated that available evidence today actually supports a stronger statement regarding latex condom effectiveness for STI prevention, especially those STIs transmitted by contact with genital fluids.

(Response) FDA agrees that there is more evidence today on the effectiveness of latex condoms against acquisition of various STIs than was available when the June 2000 workshop was held. This includes additional data that further support the longstanding public health message that latex condoms are highly effective against HIV/AIDS. As described previously in section I, it also encompasses new data now showing that condoms protect against HPV infection as well as the clinical sequellae of HPV infection, genital warts and cervical cancer.

(Comment 8) One comment stated that FDA's labeling proposal was misleading regarding condom use lowering the risk of HPV infection and disease. It cited a 1999 letter from Dr. Richard Klausner, then director of the National Cancer Institute, to the U.S. House of Representatives Commerce Committee stating ''the conclusion that condoms are ineffective against HPV infection is based on the results of several long term studies that have failed to show that barrier contraceptives prevent cervical HPV infection, dysplasia or cancer,'' as well as the summary report of the June 2000 Workshop on condom effectiveness.

(Response) As discussed in section I, many studies described in the published literature since 2000, including two systematic reviews (discussed in the 2005 proposed rule, 70 FR 69102 at 69108), support the conclusion that correct and consistent latex condom use can reduce the rates of cervical dysplasia and genital warts, diseases associated with HPV infection.

Moreover, as discussed in section I.D.1, since December 2004, several individual studies have addressed condom use and HPV infection and demonstrated that use of latex condoms reduces the risk of HPV infection itself. The letter from Dr. Klausner and the HPV conclusions of the June 2000 Workshop report have been superseded by the evidence.

(Comment 9) Another comment stated that FDA's summary of the evidence is misleading where it states ''[The Centers for Disease Control and Prevention's] report cited three studies (not included in the June 2000 Workshop report) that showed a statistically significant reduction in risk of HPV infection attributable to condoms, but noted that most studies did not show this effect'' (70 FR 69102 at 69107). This comment stated that only one of the three reports identified demonstrated true risk reduction; the other two were not statistically significant because their confidence interval touched on 1.0.

(Response) As noted by the comment, two of the three studies regarding the effect of condom use on HPV infection that were cited had a confidence value with an upper bound of 1.0. FDA's 2005 draft guidance reflected the limited evidence then available regarding the effect of condom use on HPV infection itself, by recommending statements based on the evidence regarding the effect of latex condom use on clinical consequences of HPV infection, cervical cancer and genital warts, which came from studies other than those addressed by the comment. As described in section I.D. of this document, moreover, subsequent to publication of the proposed rule, additional studies of HPV infection have published that have shown statistically significant reduction in HPV infection.

The best-designed study to date evaluating whether latex condoms reduce the risk of HPV infection is the 2006 Winer et al. study published after the 2005 proposed rule was issued (Ref. 10). Compared to previous studies on condoms and HPV infection, the 2006 Winer et al. study had a prospective, longitudinal design which provided critical information on the temporal relationship between condom use and HPV infection. Another asset in this study design is that study subjects provided information on condom use every 2 weeks in order to improve the precision of reported condom use. Also, data were collected using electronic diaries, a method that may yield more truthful reporting on condom use behavior than through ace-to-face interviews. Study inclusion criteria limited participation to women who first had intercourse with a male partner within two weeks before enrollment or during the study. This ensured that HPV infections detected during the study were truly ''incident,'' that is, truly occurred during the course of the study in a previously uninfected woman. Incident HPV infection, or lack of infection, was then evaluated as it related to 100 percent, 50 to 99 percent, 5 to 49 percent or <5 percent condom use. The adjusted hazard ratio for incident HPV for women whose partners had used condoms 100 percent of the time over the 8 months of the study compared to women whose partners used condoms <5 percent of the time was 0.3, 95 percent confidence interval 0.1 to 0.6 with p-value 0.003. This result is statistically significant. The conclusion of the study was that ''among newly sexually active women, consistent condom use by their partners appears to reduce the risk of cervical and vulvovaginal HPV infection.''

FDA believes that the results of the 2006 Winer et al. support the conclusion that consistent latex condom use reduces the risk of cervical and vulvovaginal HPV infection, which is stronger than the conclusion in the 2004 CDC Report to Congress that ''condoms may provide some protection in preventing transmission of HPV infections but that protection is partial at best.''

D. Labeling Recommendations

As discussed earlier, in the 2005 proposed rule, FDA identified several issues associated with the use of latex condoms that required special controls to help provide a reasonable assurance of safety and effectiveness. The issues included the risks of unintended pregnancy and of STI transmission, and the issue of incorrect or inconsistent use. FDA proposed to designate a guidance document with labeling recommendations as the required special control for latex condoms, to address the issues of safety and effectiveness associated with these devices. The following sections discuss the comments and FDA's responses related to the labeling recommendations of the special controls guidance document.

1. General

(Comment 10) Many comments expressed concerns that FDA had allowed ''politics'' to influence FDA policy. For example, one comment stated that the proposed rule appeared to ''bring politics and morality into what should be a science based process.'' Many commenters shared a concern that the proposed labeling would ''discourage'' the use of condoms and undermine the public's confidence in condoms.

(Response) As discussed in the 2005 proposal, FDA's efforts to improve latex condom labeling and thereby help ensure the safety and effectiveness of condoms grew out of a statutorily mandated review of existing latex condom labeling to determine whether it was medically accurate with respect to the overall effectiveness or lack of effectiveness of condoms in preventing transmission of STIs, including HPV. FDA concluded that latex condoms help protect against all STIs, but better against some than others. More accurate information about the effectiveness of latex condom use with respect to STI transmission can lead to better choices by individuals who seek to protect themselves against these infections and potentially to reduced transfer of STIs. The final rule and intended final special control guidance are based on FDA's scientific evaluation of all available evidence.

2. Comprehension

(Comment 11) Many comments stated that, although consistent with the evidence, the FDA proposal for latex condom labeling was overly complex and confusing, especially in regards to STIs transmitted through skin to skin contact. Some comments were concerned that the labeling might discourage condom use due to confusion or misunderstanding.

Other comments stated that latex condom labeling needs to be clear and positive. Many comments strongly encouraged FDA to re evaluate its labeling proposal with the objectives of keeping it simple, clear, correct, and specific.

(Response) The labeling recommendations of the draft guidance reflected an attempt to strike a balance between providing more information for the consumer and creating a complex message that might be misunderstood. These and other comments about label comprehension prompted FDA to sponsor a label comprehension study of both current labeling and the labeling recommendations included in the draft guidance. The results of the FDA-sponsored label comprehension study were discussed in section I and contributed to FDA's simplification of the labeling recommended in the intended final special control guidance.

(Comment 12) One commenter submitted the results from its own label comprehension study, conducted in January 2006, to evaluate how well the general public understood FDA's proposed latex condom labeling. This study, using a paper-and-pencil

questionnaire, surveyed a convenience sample of 247 men and women between 18 and 30 years of age in Austin, Texas. The study concluded that it is important for condom labeling to provide clear and specific information to users on risk reduction provided by condoms for pregnancy and various sexually transmitted diseases. In general, survey respondents preferred statements that are easy to understand and provide detailed and specific information.

(Response) FDA acknowledges the value of this label comprehension study. However, the use of a small convenience sample, drawn from a highly educated university town, may have limited validity and may also be difficult to generalize because it lacks geographic and educational diversity. These limitations contributed to FDA's decision to conduct its own study. As described previously, in consideration of this study and the numerous comments regarding the complexity and potential for misunderstanding of labeling, as well as FDA's own labeling study, the intended final special controls guidance document contains substantially simplified labeling recommendations.

(Comment 13) Many comments shared the view that FDA would be ''misleading and misinforming millions of Americans if the label is changed * * *.'' One commenter expressed concern that ''the addition of extensive labels to condom packaging may constitute 'red flags' to consumers intending to have sex, and that those flags may increase sex without the protection of condoms.''

(Response) FDA's labeling initiative should in no way be construed to mean that condoms do not work. As explained in the preamble to the proposed rule and updated and reaffirmed here, scientific evidence supports the conclusion that latex condoms are effective in reducing the risk of pregnancy and the overall risk of STI transmission, although latex condoms are more effective with regard to some STIs than others. In fact, as described earlier, the data supporting overall latex condom effectiveness in reducing STI transmission are stronger today than ever. In light of comments and consumer comprehension data, FDA has made revisions to the labeling to clarify the wording and reflect this overall conclusion.

(Comment 14) Many comments stated that the FDA proposal lacked balance, with far more emphasis than necessary on what a condom cannot do and not enough emphasis on the benefits of condom use. One comment stated that ''[g]iven that many persons prefer sex without condoms and the new labeling clarifying that condoms may not be as effective as desired or imagined, many people may chose [sic] to simply have sex, forego the condom, and take their risks.'' In contrast, two comments stated that the FDA condom labeling proposal overstated condom effectiveness, and lacked sufficient balance with too little scientific detail. These two comments stated that the proposal alternates between complexity that makes it difficult to understand and scientific imprecision.

(Response) After consideration of the many comments on this and related risk messaging principles, and based on the results of its label comprehension study, FDA concluded that the labeling in its draft special controls guidance document created an unacceptable level of confusion and misunderstanding. FDA also concluded, consistent with findings from its label comprehension study, that putting more scientific words and phrases into the limited space available for latex condom labeling would only lead to more consumer confusion. The latex condom labeling now recommended in the intended final special control guidance document has focused the message of latex condom intended use and simplified the message on differential effectiveness.

(Comment 15) Some comments acknowledged a need for a two tier message regarding the degree of protection afforded by condoms for different STIs, but stated that the message needed to remain simple. Some comments stated the key message is that although condoms provide less protection against STDs such as genital herpes and human papillomavirus, they do provide some protection.

(Response) FDA acknowledges the challenge of crafting a latex condom message that ensures that consumers not only understand the significant overall clinical benefits of latex condom use, but also understand the differing levels of protection against the various STIs. FDA continues to believe that it is important for condom labeling to provide information about differential effectiveness against STIs. Clearer information about differential risks and benefits of condom use can lead to better choices by individuals who seek to protect themselves by using condoms. In its intended final special controls guidance, FDA has refined the latex condom effectiveness message to convey this information more clearly.

3. Pregnancy

(Comment 16) One comment stated that the FDA proposed labeling for intended use was incomplete because it did not address protection against pregnancy.

(Response) FDA agrees with this comment and the intended final special controls guidance includes pregnancy protection in the primary statement of intended action.

(Comment 17) Several comments commended FDA for recommending inclusion of a table in the labeling with comparative efficacy rates for different barrier contraceptive options. Many comments suggested updating the table and presenting efficacy data on all contraceptive options. Other comments suggested including rates for both 'typical use' and 'perfect use' so consumers could see the beneficial effect of correct and consistent latex condom use. A few comments suggested that effectiveness be presented as success rates, not failure rates. One comment stated that FDA should not require such a table because it is not useful, would be confusing, and would tend to discourage condom use.

(Response) FDA agrees with the many comments in favor of including information on comparative contraceptive effectiveness. The intended final guidance recommends inclusion of up-to-date contraceptive effectiveness information comparing the percentage of women experiencing unintended pregnancy during 1 year of use of latex condoms with rates experienced during 1 year of use of other contraceptive options available in the United States including drugs, devices, and methods of permanent sterilization. The guidance recommends at minimum inclusion of typical use rates, but this does not preclude inclusion of perfect use rates. To permit manufacturers flexibility to fit contraceptive effectiveness information in their labeling and accommodate new data as it becomes available, the guidance no longer provides a specific recommended table format.

Regarding whether contraceptive effectiveness information should be expressed as ''success'' or ''failure,'' FDA notes that contraceptive studies evaluate pregnancy as the primary outcome measure. The statistical hypothesis and analysis is built around the pregnancy rate, and this is not easily transposed to a ''success'' rate. Therefore, FDA continues to recommend that these data be presented as pregnancy rates associated with the use of condoms or other methods, but does not mandate that the term ''failure'' be used in labeling.

The agency believes that providing contraceptive effectiveness information will not confuse consumers or

discourage condom use. Rather, FDA believes that this information will help consumers to determine whether latex condoms, available without a prescription, will sufficiently address their contraceptive needs, or whether they should seek other options, including those that may require consulting a health care provider. In keeping with this purpose, the intended final guidance also recommends that contraceptive effectiveness information be accompanied by a statement advising consumers to consult a health care provider if they have any questions about contraception, particularly because of health reasons for avoiding pregnancy.

4. STIs

(Comment 18) One comment stated that the labeling in the draft guidance that described the differential effectiveness of condoms against Group I and Group II STIs should include a complete list of the STIs in each group.

(Response) FDA declines to recommend that labeling addressing the degree of STI protection contain a complete list of STIs falling within each group. Based on the results from FDA's label comprehension study, which indicated that the message on this point in the draft guidance was not well understood, the agency is concerned that including such a list might be more confusing than helpful. FDA's intended final special controls guidance recommends a simplified message on this point, which includes examples of each type of STI, and also directs consumers to consult a health care provider or public health agency for more information on condoms or STIs.

(Comment 19) Several commenters expressed concern that latex condom labeling should not lose sight of the primary message that condoms are highly effective against HIV infection, the most serious of all STIs. Some of these comments also emphasized the importance of distinguishing between condom attributes and user behavior, i.e., to emphasize the protective benefit if used properly.

(Response) None of the new studies reviewed by FDA since publication of the 2005 proposed rule uncovered any new information to detract from FDA's earlier finding that condoms are effective against HIV/AIDS, arguably the most serious STI because of its devastating consequences. Consistent with this evidence, FDA's intended final special controls guidance recommends labeling that specifically reflects the conclusion that condoms are effective against HIV/AIDS. Recommended labeling also indicates that to get the most protection from latex condoms, consumers should use them correctly every time they have sex.

5. Correct and Consistent Use

(Comment 20) One comment emphasized that user behavior concepts such as correct use and consistent use are true for almost all devices and drugs but do not belong in the statement of intended action. This comment went on to state that precautions to ensure correct and consistent use are important considerations for optimizing effectiveness and should be placed elsewhere on the labeling. This comment also noted that stating that condoms do not *eliminate* risk is redundant with the statement that condoms *help to reduce* risk and is therefore unnecessary.

(Response) FDA agrees with this comment in part. FDA's intended final guidance recommends a simple statement of intended action, that latex condoms are intended to prevent pregnancy, HIV/AIDS, and other STIs. Because information about optimal use conditions and their effect on risk reduction also deserves labeling prominence, the intended final special control guidance recommends that a statement emphasizing the importance of correct and consistent use be included in a section on the retail package entitled ''Important Information.'' In addition, the guidance recommends specific directions and precautions to help ensure such use. With regard to the question of redundancy, FDA believes that it is useful and appropriate that condom labeling explicitly reflect the results of scientific studies, which indicate that risk reduction from condoms is not 100 percent, and therefore continues to recommend a specific statement that condoms do not completely eliminate the risk of pregnancy and STIs.

(Comment 21) One commenter stated that FDA's recommended language for the rear panel of the condom retail package was not accurate because it did not contain the statement that condoms must be used consistently and correctly to provide benefit. This commenter recommended that a new section be included in condom labeling titled ''Consequences of Incorrect and Inconsistent Condom Use,'' which would include the statement ''With the exception of genital herpes and HIV, we have no clinical studies that show any risk reduction from inconsistent condom use * * *.'' Elsewhere the same commenter noted that none of the studies in HIV sero-discordant couples asked about correct use. Another commenter made a related point, stating ''Although 'correct and consistent use' appears almost 15 times [in the preamble to the proposed rule] almost all condom use studies with an STI outcome actually only measured consistent condom use. The word 'correct' should be struck from the [rulemaking] document when it occurs in this context.''

(Response) These comments do not disagree with FDA's view that condom labeling should communicate that correct and consistent use are important to obtain the maximum benefit from a latex condom. FDA agrees that the correctness of condom use is more difficult to evaluate in an epidemiologic study than whether or not the condom was used for every act of intercourse. Nevertheless, FDA believes that condom effectiveness is in part a function of correct use, and therefore that labeling should communicate the importance of correct use to achieve best results.

In the intended final special control guidance, both correct and consistent use are addressed in the section called ''Important Information'' on the rear panel of the recommended labeling, with a recommended statement which reads: ''To get the most protection from a latex condom, use one correctly every time you have sex.'' In addition, the recommended labeling contains directions for use and precautions to help ensure correct and consistent use, including the reminder to use a new condom for each act of sex. The intended final special control guidance also recommends labeling addressing the degree of STI protection afforded by condoms, which describes that the reduction in risk of STIs afforded by latex condoms results from their ability to provide a barrier against the source of infection, and elaborates on the difference in effectiveness against STIs that are spread by contact with the head of the penis (an area that a condom covers) and those also spread by contact with infected skin not covered by the condom. FDA believes it is understood in this discussion of how condoms achieve their effect that the condom must in fact be used to be effective. FDA believes that the recommended labeling appropriately and accurately communicates the importance of using latex condoms correctly and consistently to obtain their benefits.

6. Risk Reduction

(Comment 22) One comment stated that FDA should substitute ''risk reduction'' for words such as ''prevent/prevention'' and ''protect/protection'' to avoid the perception that risk reduction is total (i.e., 100 percent).

(Response) In the intended final special control guidance, FDA recommends an initial statement of the intended action of condoms, which includes an example stating that ''Latex condoms are intended to prevent pregnancy, HIV/AIDS, and other sexually transmitted infections.'' The agency believes that this is an example of an appropriate, plain language statement of the intended action of a latex condom. FDA agrees, however, that it is important that consumers appreciate that risk reduction offered by condoms is not complete. In language recommended for inclusion on the rear panel of the retail package in a box entitled ''Important Information,'' the intended final guidance recommends a statement, ''Latex condoms do not completely eliminate the risks of pregnancy and sexually transmitted infections.'' The guidance also recommends the ''Important Information'' include a statement characterizing latex condoms as reducing the risk of STI transmission. Although the recommended wording is not identical to the language suggested by the commenter, FDA believes that the recommended labeling clearly conveys that use of a latex condom does not guarantee complete elimination of risks of pregnancy or STIs. Consistent with these statements on the outer package, the recommended package insert also contains a section called ''Degree of STI Protection'' which describes the relative risk reduction that can be expected for STIs that differ in the way that they are transmitted.

(Comment 23) One comment stated that FDA should recommend latex condom labeling to include a data table showing the amount of risk reduction afforded by condoms for the common STIs. This comment indicated that the table should include estimates for ''perfect use'' and ''typical use,'' further suggesting that ''typical use'' is a synonym for ''inconsistent use.'' Another comment recommended that latex condom labeling should give information on differential effectiveness in quantitative terms. That is, labeling should present the amount of risk reduction provided by latex condom use, numerically for each STI.

(Response) FDA disagrees with these comments because the data are not sufficiently developed to provide meaningful numbers to consumers.

(Comment 24) One comment recommended the statement ''For STIs however such as gonorrhea/chlamydia, which are much more infectious [than HIV], incorrect or inconsistent condom use can very quickly lead to an infection'' be included in a new section called ''Consequences of Incorrect and Inconsistent Condom Use.''

(Response) FDA does not agree the previous statement should be included in condom labeling because we are not aware of scientific studies supporting the conclusion that ''incorrect or inconsistent condom use can very quickly lead to an infection'' for certain STIs. The temporal relationship between incorrect or inconsistent condom use and infection has not been measured systematically (with the exception of the 2006 Winer et al. study who evaluated ''always,'' ''inconsistent,'' and ''almost never'' condom use and incident HPV infection). We agree with the commenter's implicit premise that, to get the most protection from a latex condom, one should use a condom correctly every time one has sex and the recommended labeling reflects this accordingly.

(Comment 25) Two comments stated that latex condom labeling should discuss the difference between the degree of risk reduction afforded by a latex condom when used correctly during a single act of penile-vaginal intercourse compared with degree of risk reduction accumulated during typical use over time during many acts of penile-vaginal intercourse. The comments stated that the degree of risk reduction is higher during a single act compared to cumulative risk reduction over many acts of intercourse.

(Response) Although FDA agrees in principle with the concept that risk is lower during a single event compared to overall risk from multiple possible exposures, it is important to note that all of the studies evaluated by FDA looked at cumulative risk over many possible exposures. None of the studies FDA reviewed evaluated latex condom effectiveness against STIs during a single act of intercourse between an uninfected person and an infected partner. FDA does not believe that adding a discussion of hypothetical risk reduction during a single use would improve the latex condom label.

(Comment 26) Several comments stated that the latex condom labeling recommendations in the draft guidance document focused on penile-vaginal sex and do not specifically address oral sex or anal sex. Some commenters suggested that labeling should be revised to specifically indicate that condoms help prevent transmission of STIs between the penis and mouth or rectum. Other comments stated that FDA's draft guidance generically refers to sexual contact without stating that scientific data are only available on risk reduction provided by a condom during penile-vaginal intercourse. One comment suggested that the rule and guidance document need to be ''clear * * * that we are talking about the use of the male latex condom as used in vaginal intercourse.'' Another indicated that FDA should view condom use ''for everything but penile-vaginal sex [as] 'off-label'.''

(Response) Like the draft guidance, the labeling recommendations in the final guidance document do not specifically address oral or anal sex. This is not a change from the current labeling of condoms and is reflective of the lack of premarket clearance or approval submissions requesting an indication for use specifically for oral or anal sex. Although most of the reliable epidemiological data about latex condoms and STIs come from studies conducted in populations who engage in penile-vaginal intercourse, a meta-analysis evaluated a number of studies that tested behavioral interventions designed to increase condom use during all forms of sexual contact and concluded that there was an overall decrease in STIs from increased condom use (Ref. 2). Other scientific information about the basis of latex condom effectiveness against STIs—which indicates that latex condoms reduce the transmission of STIs to which they provide a physical barrier—is applicable to sexual contact between the penis and mouth or rectum. FDA believes the labeling recommendations reflect the information available.

7. Directions for Use and Precautions

(Comment 27) One comment stated that the directions for use in the FDA proposal are outdated and include steps for which there is no underlying reason, e.g., squeeze air out of condom tip. This comment pointed to a simplified set of five steps for correct condom use, developed by the Information and Knowledge for Optimal Health (INFO) Project, Johns Hopkins Bloomberg School of Public Health (Ref. 5).

(Response) FDA reviewed the five-step directions for use of condoms recommended by the INFO Project, and some of its approach was adopted in the intended final special control guidance. FDA also included some of its own general recommendations for developing medical device patient labeling, such as recommendations for the use of diagrams.

(Comment 28) One comment suggested modification of the storage precaution, from ''Store condoms in a cool, dry place'' to ''Avoid condom exposure to direct sunlight or storage for prolonged periods at temperatures above 100 F.''

(Response) FDA agrees in principle with this comment and has adopted it in the following slightly revised format in the intended final special controls guidance: ''Avoid exposure of the condom to direct sunlight. Store latex condoms in a cool, dry place (below 100° F).'' FDA notes that the model language in the guidance may be varied so long as it provides appropriate directions for use and precautions that contribute to ensuring safety and effectiveness of the specific condom in question.

(Comment 29) One comment requested that the directions for use in the labeling be in boldface font.

(Response) FDA does not agree with this comment. Highlighting techniques, such as bold, are used to emphasize important words or phrases, or for headings. Bolding all the directions for use would overdo this highlighting technique, and could decrease the impact of the directions.

(Comment 30) Another comment stated that the directions for use should include another bullet explaining how to properly dispose of a latex condom.

(Response) FDA agrees with this comment and has added a recommendation in the intended final special controls guidance to include in the directions for use a direction on how to properly dispose of a latex condom.

8. Additional Information

(Comment 31) One comment stated that latex condom labeling should include a recommendation that sexually active persons seek advice from a health care professional and that sexually active persons be vaccinated against HBV and HPV.

(Response) FDA's intended final special controls guidance recommends that latex condom labeling include advice to consumers to contact a health care provider if the consumer believes that he/she may have an STI, as well as directing consumers to contact a health care provider or public health agency for more information on latex condoms or STIs. FDA believes this labeling, which is similar to the first element suggested by the comment, is appropriate in light of the recognition that condoms reduce, but do not eliminate, the risk of STIs. Consumers who believe they are infected with an STI and are using condoms to reduce the risk that they will transmit that STI to their partner should also seek advice from a health care practitioner, because treatment options may be available that will not only benefit the infected person, but will also help to further reduce (or eliminate) the risk of STI transmission. Advising consumers who may already be infected with an STI to complement condom use with seeking advice from a health care practitioner thus helps to ensure the safe and effective use of condoms for STI prevention. Similarly, FDA's recommendation that labeling alert consumers to contact a health care provider or public health agency for more information on latex condoms or STIs complements the labeling recommendations regarding the degree of protection against different types of STIs. This labeling will help ensure safe and effective use of condoms by alerting consumers to additional resources that can expand on the basic information regarding STI transmission provided by the labeling and also help the consumer evaluate their individual circumstances.

However, FDA believes that it would be inappropriate for latex condom labeling to advise all sexually active persons to be vaccinated against HPV and HBV in part because these vaccines are not universally indicated for ''all sexually active individuals.'' For example, the currently available HPV vaccine is not approved for use in men. The HBV vaccine is indicated only for populations at risk for HBV. A recommendation to be vaccinated against HPV and/or HBV should be offered by a health care professional after consultation with the individual.

(Comment 32) One comment recommended that FDA should work with NIH, CDC, and other research colleagues to monitor the impact of the new labeling and to learn how to better reduce the adverse consequences of sex.

(Response) This comment did not address the substance of the rulemaking or labeling recommendations. If important new evidence becomes available, FDA may reconsider its approach in light of that evidence.

(Comment 33) A few comments commended FDA for its labeling proposal but warned that it should avoid additional educational information about social behaviors or public health programs. These comments stated that this kind of information is not appropriate for latex condom labeling. Another comment asked that references to pregnancy and HIV programs be placed in the labeling.

(Response) FDA believes that the purpose of latex condom labeling is to adequately identify the product and its intended action, with information about the product, including adequate directions for use and any other necessary cautions or warnings, to ensure safe and effective use. As discussed earlier, FDA is including as recommended labeling a statement that consumers should consult a health care practitioner or public health authorities for more information about condoms or STIs. This labeling complements the recommended labeling regarding the degree of protection against different types of STIs, which FDA's label comprehension study and numerous comments indicated needed to be kept simple in order to be well understood. By alerting consumers to additional resources that can expand on the basic information regarding STI transmission provided by the labeling, and also help the consumer evaluate their individual circumstances, the recommended labeling regarding contacting a health care practitioner or public health agency will help to ensure the safe and effective use of latex condoms.

E. Comments in Response to FDA's Specific Requests

FDA's 2005 proposed rule included specific requests for comments. Several of the specific requests related to latex condoms with spermicidal lubricant containing N–9. As discussed in the introductory paragraph of section I, FDA continues to review the comments it received related to that device. FDA also specifically requested comments on whether its labeling recommendations should include more detailed information on the prevention of genital HPV infection and information on different approaches for prevention of cervical cancer (FDA responded to one comment related to this request in section III.D.8). Finally, FDA specifically requested comment on potential special controls for nonlatex condoms without N–9. FDA received the following comments in response to FDA's requests.

1. Human Papillomavirus (HPV)

(Comment 34) In response to FDA's specific request related to HPV, one commenter stated that ''[c]ondoms can reduce the transmission of seminal fluid carrying the human papillomavirus. Therefore, decreasing the direct effect of these fluids on the cervix may be helpful in decreasing the risk of cervical dysplasia and neoplasia. It would be appropriate for labels to indicate that HPV still can be acquired through direct skin contact in areas not protected by the condom.''

(Response) FDA's labeling recommendations in the intended final special controls guidance document are consistent with this comment. FDA's labeling recommendation is that the package insert indicate that latex condoms reduce the risk of transmitting STIs by providing a barrier against the source of infection but also include statements that ''Latex condoms are less

effective against STIs, such as Human Papillomavirus (HPV) and herpes. These STIs can also be spread by contact with infected skin that is not covered by the condom.''

2. Nonlatex Condoms Without Nonoxynol-9

(Comment 35) One comment indicated that consumers should be aware that latex condoms might cause an allergic reaction and the use of a nonlatex condom might reduce this risk. The comment noted that ''special controls beyond evidence-based labeling do not appear to be warranted.'' Another comment recommended that FDA require that packaging between latex condoms, latex condoms with N–9, natural membrane condoms, and novelty condoms look ''clearly different.''

(Response) FDA appreciates the information submitted and intends to consider these comments when FDA evaluates the regulatory approach to these devices.

F. Implementation

(Comment 36) One comment stated that the 1-year period proposed for implementing new condom labeling for latex condoms legally marketed before the effective date of this final rule is unrealistically short. This comment said it will take approximately 24 months, not 12 months, to implement all the required changes because the draft labeling may necessitate changes to packaging with its requisite capital equipment changes.

(Response) In the final guidance, FDA has shortened the statement of intended action to be placed on the individual foil packet (primary package). As a result of this change, a different size foil package for the individual condom should not be needed. FDA has also shortened the recommended statements to be included in the package insert and made more clear the flexibility permitted to manufacturers to determine how to present certain elements, such as contraceptive effectiveness information. Therefore, FDA does not believe that capital equipment changes will be needed to implement this special control. In addition, as discussed in section II, latex condoms legally marketed before the effective date of this final rule will be expected to comply with the requirement of special controls within 11 months after the effective date, as was proposed. However, the effective date of this final rule will be 60 days after publication, not 30 days as anticipated, so manufacturers will have a total of 13 months after publication to comply with the requirement of special controls.

IV. Environmental Impact

The agency has determined under 21 CFR 25.34(b) 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.

V. Analysis of Impacts

FDA has examined the impacts of the final rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is not an economically significant regulatory action under the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. FDA does not believe that the final rule will have a significant economic impact on a substantial number of small entities, but recognizes the uncertainty of its estimates. In the proposed rule the agency solicited but did not receive specific comments on its estimates and methodology of analysis of the impact of the rule on small businesses.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing ''any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any one year.'' The current threshold after adjustment for inflation is $130 million, using the most current (2007) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

A. Background

The purpose of this final rule is to amend the classification regulation for condoms to designate a labeling guidance as a special control for latex condoms. As discussed earlier in this preamble, latex condoms are currently classified into class II in accordance with section 513 of the act. The special controls guidance identifies particular issues associated with these devices and recommends labeling to address those issues. The benefit of this final rule is that establishing the labeling guidance as a special control ensures that manufacturers will provide consumers with the information they need to make an informed decision regarding the use of latex condoms and to use them safely and effectively. The labeling guidance helps ensure that information provided to consumers does not undervalue the overall STI-risk reduction provided by latex condom use, but does not exaggerate the effectiveness of latex condoms against certain types of STIs. More specific information about the effectiveness of latex condoms with respect to pregnancy and STI transmission, as well as clearer directions for use and precautions about how to obtain the maximum benefit from latex condoms, can lead to better choices by individuals who seek to protect themselves against unintended pregnancy and STIs. Establishing a rule designating as a special control a guidance document that contains labeling recommendations, rather than establishing a labeling regulation, provides both the agency and manufacturers greater flexibility and will result in providing consumers with any new or enhanced information more quickly. The agency believes this special control will, together with the general controls, provide reasonable assurance of the safety and effectiveness of these devices.

B. Affected Entities and Scope of Effect

The final rule will affect persons responsible for the labeling of latex condoms, which, in most cases, will be manufacturers of condoms, including repackagers. Manufacturers of latex condoms, including repackagers, will need to address the issues identified in the special controls guidance document. A firm need only show that its device meets the recommendations of the guidance document or in some other way provides equivalent assurances of safety and effectiveness. To meet the recommendations of the special controls guidance document, wording on the retail package, including the principal display panel, the primary condom package (individual foil), and package insert will most likely need changes to conform to the guidance document.

Agency records show there are approximately 35 entities that manufacture or repackage latex condoms affected by this final rule. FDA does not track the number of different product and package combinations (stockkeeping units (SKUs)) on the market. Based on data FDA received from industry, FDA estimates that currently there are between 500 and 1,000 SKUs on the market that will need labeling changes. If the products are sold with a retail package, the wording on each of these SKUs will need to be changed. Because manufacturers can often use the same individual foil and package inserts across their product lines, the number of versions of foil and insert labeling that require changes will be less than the number of SKUs.

Based on the agency's experience with the industry and anecdotal information from manufacturer and retail Web sites, FDA estimates that there will be a total of 802 to 1,605 labeling changes to retail packages, individual foils, and package inserts. FDA assumed that 95 percent of the SKUs (475 to 950) are marketed with 3 levels of labeling (a retail package, individual foil, and package insert), and the remaining 5 percent have 2 levels (a foil and package insert). For the SKUs with three levels of labeling, FDA further assumed that for every 3 retail package redesigns there would be 1 foil label redesign, and for every 4 retail package redesigns, there would be 1 package insert redesign. FDA based these assumptions on FDA's knowledge that a single condom type is often sold in several retail packages containing different numbers of condoms, in which case retail packages would be different for each SKU but package inserts and foil labels would be shared by multiple SKUs. The distribution of the different labeling that would need to be redesigned is listed in Table 1 of this document and includes 475 to 950 retail packages, 183 to 367 foils, and 144 to 288 inserts. (Sample calculation: (500 x 0.95 / 3) + (500 x 0.05) foils and (500 x 0.95 / 4) + (500 x 0.05) inserts.)

C. Costs of Implementation

Frequent package changes or redesigns are standard business practice in the consumer healthcare products market. Manufacturers with products intended for retail sales will have established routines for product relabeling and employees with the technical expertise to implement labeling changes. The cost to relabel a product can be broken into three basic components: regulatory, graphics, and manufacturing. The regulatory component includes determining what changes are necessary, drafting the wording for the new labeling, and coordinating the review and revisions. The graphics component includes preparing the layouts, proofs, and printing. Finally, the manufacturing component includes incorporating the new labeling into the manufacturing system, discarding old labeling inventory, and making any changes to the packaging line to accommodate the new labeling, if necessary.

The final rule designates a special controls guidance document that recommends changes to wording and some additional text. Many of the labeling recommendations are similar to statements in existing condom labeling, but are being updated to reflect current information. These changes should not require major changes in the design or layout of existing labeling and FDA believes that the changes can be incorporated without having to increase the dimensions of any of the labeling. As discussed elsewhere in the preamble, FDA received one comment that suggested that manufacturers might need to increase package size to accommodate the proposed wording. After conducting a label comprehension study and considering other comments and information, FDA shortened and reworded the recommended labeling. In addition, the intended final special controls guidance does not specify a particular format for the contraceptive effectiveness information. The agency believes that with the changes to the wording and increased flexibility in presentation, we have addressed these concerns.

The itemized cost estimates used in this analysis were derived from a study performed for FDA by Eastern Research Group, Inc. (ERG), an economic consulting firm, to estimate the economic impact of the 1999 Over-the-Counter Human Drug Labeling Requirements final rule (64 FR 13254, March 17, 1999).[8] Because the packaging requirements for latex condoms are similar to those of many over-the-counter (OTC) drugs, the cost to redesign and print the labeling for OTC drugs is an appropriate proxy for the estimated costs to redesign and print condom labeling. For this analysis, cost estimates were adjusted to account for inflation using the producer price index (PPI) for finished consumer goods, and current wage rates specific to the medical device industry were substituted for the wages used by ERG in the original OTC drug labeling impact study.[9]

FDA estimates that the regulatory component of each labeling redesign would require between 8 to 16 hours per SKU. Using a wage rate of $44.17, the incremental cost of the one-time regulatory component cost to redesign would be $353 to $707 per labeling redesign (8 to 16 hours x $44.17/hour).[10] The one-time cost of the graphic component was estimated to be $640 per labeling redesign.[11] The one-time cost of the manufacturing component, which included the incorporation of the new labeling into the manufacturing system and discarding the remaining inventory of the old labeling, was estimated to require between 3 and 5 hours per label. Using the wage rate of $21.84 for a production employee, this cost would range from about $66 to $109 per label (3 (to 5) hours x 21.84/hour).[12] The value of the old labeling inventory would vary greatly depending on the type and complexity of the labeling, the average sales per SKU, and the length of the implementation period granted. Based on the ERG study, with a 13-month implementation period FDA estimates that the one-time inventory loss would range from $478 to $1,913 per foil or package insert and from $1,435 to $5,738 per carton.[13]

FDA believes that by providing manufacturers with a 13-month period to achieve compliance for those latex condoms that are legally marketed before the rule is effective, there will be

[8] Eastern Research Group, Inc., Cost Impacts of the Over-the-Counter Pharmaceutical Labeling Rule (March 1999). Contract number 223–94–8031, Docket No. 96N–0420, OTC Volume 28 FR, Division of Dockets Management.

[9] The ERG cost estimates were based on estimates made in 1998. The annual PPI for finished consumer goods rose by 27.5 percent between 1998 and 2007 (from 130.7 to 166.6, *http://www.bls.gov*). Wage estimates are from the Bureau of Labor Statistics, May 2007 National Industry-Specific Occupational Employment and Wage Estimates, NAICS 339100—Medical Equipment and Supplies Manufacturing (*http://www.bls.gov*).

[10] Mean hourly wage for a compliance officer, SOC 13–1041, in NAICS 339100 is $31.55, which was increased by 40 percent to account for employee benefits and equals $44.17 (*http://www.bls.gov*).

[11] ERG estimated the cost at $500 per redesign. Adjusting for inflation, the cost would be $638 ($500 x 1.275) and was rounded to $640. (See footnotes 7 and 8).

[12] Mean hourly wage for the average production worker is $13.75, SOC 51–0000, in NAICS 339100, which was increased by 40 percent to account for employee benefits and equals $19.25 (*http://www.bls.gov*).

[13] ERG estimated that when there was no implementation period granted, the average inventory loss for OTC drug container labels ranged from $1,500 to $6,000 for small to medium sized OTC drug firms. With a 14-month implementation period that loss decreased by 3/4. The value of carton inventory was estimated to be about 3 times greater than container labels. Allowing for inflation (see footnote 6) the 0-month estimates are approximately $1,913 and $7,650, respectively (e.g., $1,500 x 1.275).

enough time for them to sell their existing product inventory and have enough newly labeled inventory on hand to meet demand without a disruption in supply. The total estimated incremental one-time costs to the industry for each component of a labeling redesign was calculated by multiplying the cost per label by the number of labels affected and are presented in table 2 of this document. Because of the uncertainty of the estimates, only the lowest and highest estimated costs are presented rather than reporting the intermediate values that would be obtained using other pairings of high with low values in the ranges estimated. The total one-time incremental cost to the industry was estimated to be between $1.7 million and $9.0 million. The cost to individual firms to comply with this rule would vary greatly depending on the number of products they produced, how the products were packaged, and the sales volume. As stated earlier in this document, frequent labeling changes are a cost of doing business in the consumer healthcare products market and firms would have the skills necessary to comply with this rule. Because the steps followed for a firm-initiated change are the same as for regulatory change, the labeling recommendations could be incorporated at the time a firm is implementing a firm-initiated labeling change for little additional cost, and thus, the economic impact will be mitigated by the number of firm-initiated labeling changes made during the implementation period. In addition, because most labeling equipment can handle different labeling sizes and types and because there are a large number of companies available that can provide contract labeling services, FDA does not believe that any manufacturer would incur major costs such as the need to purchase new labeling or packaging equipment as a result of this rule.

D. Regulatory Flexibility Analysis

There are about 12 domestic entities that manufacture or repackage condoms. The Small Business Administration (SBA) has established criteria to identify small entities in given industries using the North American Industry Classification System Code (NAICS). The NAICS for manufacturing latex condoms is 326299 (All Other Rubber Product Manufacturing). Firms in this industry are considered small if they have fewer than 500 employees. Ten of the 12 domestic entities affected by this rule are small as defined by SBA.

The one-time cost to relabel, including the inventory loss, will range from about $3,000 to $9,000 per unique product SKU. When the SKUs differ only by the quantity per carton the one-time cost per SKU are even less, ranging from about $2,100 to $6,400 because the foil and insert labels are the same.

As discussed earlier in this document, while the cost to the industry to revise latex condom labeling is small, FDA lacks sufficient specific information on the distribution of costs and characterization of the industry to certify that this rule would not have a significant economic impact on a substantial number of small entities. Thus, while FDA does not believe that this final rule will have a significant effect on a substantial number of small entities, FDA recognizes the uncertainty of the estimates.

TABLE 1.—ESTIMATED NUMBER OF LABEL DESIGNS THAT MAY NEED TO BE MODIFIED

Component	Low-End Estimate	High-End Estimate
Cartons	475	950
Foils	183	367
Inserts	144	288
Total	802	1,605

TABLE 2.—ESTIMATED RANGE OF COMPLIANCE COSTS BY FUNCTION

Component	Range	Hours	Wage/Hour	Cost/Label	Number of Labels	Total	
						Low	High
Regulatory	Low	8	$44.17		802	$283,395	
	High	16			1,605		$1,134,286
Graphic	Low			$640	802	$513,280	
	High				1,605		$1,027,200
Manufacturing	Low	3	$21.84		802	$52,547	
	High	5			1,605		$175,266
Inventory—foil & insert	Low			$478	327	$156,306	
	High			$1,913	655		$1,253,015
Inventory—carton	Low			$1,435	475	$681,625	
	High			$5,738	950		$5,451,100
Total Costs						$1,687,153	$9,040,867

VI. Federalism

FDA has analyzed this final rule in accordance with the principles set forth in Executive Order 13132. Section 4(a) of the Executive order requires agencies to ''construe * * * a Federal statute to preempt State law only where the statute contains an express preemption provision or there is some other clear evidence that the Congress intended preemption of State law, or where the exercise of State authority conflicts with the exercise of Federal authority under the Federal statute.'' Federal law includes an express preemption provision that preempts certain state requirements ''different or in addition to'' certain federal requirements applicable to devices. 21 U.S.C. 360k; *Medtronic* v. *Lohr*, 518 U.S. 470 (1996); *Riegel* v. *Medtronic*, 128 S.Ct. 999 (2008). In this rulemaking, FDA has determined that general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of the device, and that there is sufficient information to establish special controls to provide such assurance. FDA has therefore imposed a special control to address the risks of unintended pregnancy, transmission of sexually transmitted infections, and incorrect or inconsistent use. This special control creates ''requirements'' for specific medical devices under 21 U.S.C. 360k, even though product sponsors have some flexibility in how they meet those requirements. *Papike* v. *Tambrands, Inc.*, 107 F.3d 737, 740–42 (9th Cir. 1997).

In addition, as with any Federal requirement, if a State law requirement makes compliance with both Federal law and State law impossible, or would frustrate Federal objectives, the State requirement would be preempted. See *Geier* v. *American Honda Co.*, 529 U.S. 861 (2000); *English* v. *General Electric Co.*, 496 U.S. 72, 79 (1990); *Florida Lime & Avocado Growers, Inc.*, 373 U.S. 132, 142–43 (1963); *Hines* v. *Davidowitz*, 312 U.S. 52, 67 (1941).

The preemptive effects are the result of existing law set forth in the statute as interpreted in decisions of the United States Supreme Court. FDA therefore has not sought separate comment on the preemptive effect of this action because it is not seeking independently to preempt state law beyond the effects of 21 U.S.C. 360k or existing case law.

VII. Paperwork Reduction Act of 1995

This final rule contains no collections of information, but designates as a special control a guidance document that contains collections of information that are subject to review by the Office of Management and Budget (OMB) under the PRA (44 U.S.C. 3501–3520). Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice announcing the submission to OMB of the proposed information collection provisions of that guidance document, Class II Special Controls Guidance Document: Labeling for Natural Rubber Latex Condoms Classified Under 21 CFR 884.5300, which contains further information about the paperwork burden for that guidance. Prior to the effective date of this final rule, FDA will publish a notice in the **Federal Register** announcing OMB's decision to approve, modify, or disapprove the information collection provisions in the guidance designated as a special control by this final rule and announcing the availability of the final guidance as approved. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

VIII. References

The following references have been placed on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday. (FDA has verified the Web site addresses, but FDA is not responsible for subsequent changes to the Web sites after this document publishes in the **Federal Register**.)

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10. Winer, R.L., J.P. Hughes, Q. Feng, S. O'Reilly, N.B. Kiviat, K.K. Holmes, L.A. Koutsky, ''Condom Use and the Risk of Genital Human Papillomavirus Infection in Young Women,'' *The New England Journal of Medicine*, 2006 June 22;354(25):2645–54.

List of Subjects in 21 CFR Part 884

Medical devices.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 884 is amended as follows:

PART 884—OBSTETRICAL AND GYNECOLOGICAL DEVICES

■ 1. The authority citation for 21 CFR part 884 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

■ 2. Section 884.5300 is revised to read as follows:

§ 884.5300 Condom.

(a) *Identification.* A condom is a sheath which completely covers the penis with a closely fitting membrane. The condom is used for contraceptive and for prophylactic purposes (preventing transmission of sexually transmitted infections). The device may also be used to collect semen to aid in the diagnosis of infertility.

(b) *Classification.* (1) Class II (special controls) for condoms made of materials

other than natural rubber latex, including natural membrane (skin) or synthetic.

(2) Class II (special controls) for natural rubber latex condoms. The guidance document entitled ''Class II Special Controls Guidance Document: Labeling for Natural Rubber Latex Condoms Classified Under 21 CFR 884.5300'' will serve as the special control. See § 884.1(e) for the availability of this guidance document.

Dated: October 28, 2008.

Jeffrey Shuren,

Associate Commissioner for Policy and Planning.

[FR Doc. E8–26825 Filed 11–7–08; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[TD 9430]

RIN 1545–BH99

Information Reporting for Discharges of Indebtedness

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Final and temporary regulations.

SUMMARY: This document contains final and temporary regulations relating to information returns for cancellation of indebtedness by certain entities. The temporary regulations will avoid premature information reporting from certain businesses that are currently required to report and will reduce the number of information returns required to be filed. The temporary regulations will impact certain lenders who are currently required to file information returns under the existing regulations. The text of these temporary regulations also serves as the text of the proposed regulations as set forth in the Proposed Rules section in this issue of the **Federal Register**.

DATES: *Effective Date:* These regulations are effective on November 10, 2008.

Applicability Date: For dates of applicability, see § 1.6050P–1T(h).

FOR FURTHER INFORMATION CONTACT: Barbara Pettoni at (202) 622–4910 (not a toll-free number).

SUPPLEMENTARY INFORMATION:

Background

This document contains amendments to the Income Tax Regulations (26 CFR part 1) under section 6050P relating to information reporting for cancellation of indebtedness by certain entities. The amendments will reduce the number of information reports required to be filed under section 6050P.

In general, section 6050P requires certain entities to file information returns with the IRS, and to furnish information statements to debtors, reporting discharges of indebtedness of $600 or more. As originally enacted by the Omnibus Budget Reconciliation Act of 1993, Public Law 103–66 (107 Stat. 312, 531–532 (1993)), section 6050P applied solely to ''applicable financial entities,'' which was then defined to include only financial institutions, credit unions, and Federal executive agencies.

In 1996, final regulations were published implementing section 6050P. See TD 8654, 61 FR 262 (January 4, 1996) (the 1996 regulations). The 1996 regulations required applicable financial entities, as then defined, to issue Forms 1099–C, ''Cancellation of Debt,'' upon the occurrence of one of several ''identifiable events'' as provided in § 1.6050P–1(b)(2)(i)(A) through (H). One of these identifiable events requiring the issuance of a Form 1099–C was the expiration of a ''non-payment testing period'' pursuant to § 1.6050P–1(b)(2)(i)(H). The 1996 regulations created a rebuttable presumption (the ''36-month rule'') under § 1.6050P–1(b)(2)(iv) that this period expired if a creditor had not received a payment for 36 months. Section 1.6050P–1(b)(2)(iv) provides that the presumption that an identifiable event occurred can be rebutted by a creditor if the creditor had engaged in significant, bona fide collection activity.

After the issuance of the 1996 regulations, the Debt Collection Improvement Act of 1996, Public Law 104–134 (110 Stat. 1321, 368–369 (1996)) (the 1996 Act), expanded section 6050P to cover any executive, judicial, or legislative agency (as defined in 31 U.S.C. 3701(a)(4)) as well as any applicable financial entity. The 1996 Act was effective April 26, 1996. The Ticket to Work and Work Incentives Improvement Act of 1999, Public Law 106–170 (113 Stat. 1860, 1931 (1999)) (the 1999 Act), further expanded section 6050P by expanding the definition of ''applicable financial entity'' to include any organization ''a significant trade or business of which is the lending of money.'' The 1999 Act was effective for discharges of indebtedness occurring after December 31, 1999.

In 2002, the IRS and the Treasury Department published proposed regulations to reflect the changes to section 6050P. See REG–107524–00, 67 FR 40629 (June 13, 2002). The IRS received written (including electronic) comments on the proposed regulations and a public hearing was held on October 8, 2002. After consideration of the comments received, the IRS adopted the proposed regulations with amendments. See TD 9160, 69 FR 62181 (October 25, 2004) (the 2004 regulations). Section 1.6050P–2 of the 2004 regulations describes the circumstances in which an organization has a significant trade or business of lending money, thereby triggering an information reporting requirement when it cancels debt.

Reasons for Change

The 36-month rule of § 1.6050P–1(b)(2)(iv) was drafted at a time when section 6050P applied only to financial institutions, credit unions, and Federal executive agencies and did not extend to any executive, judicial, or legislative agency or any organization ''a significant trade or business of which is the lending of money.'' Since the publication of the 2004 regulations, commenters have raised the concern that the application of the 36-month rule to entities with a significant trade or business of lending money might trigger a reporting requirement even when the entity has not legally or practically discharged the debt. The IRS and the Treasury Department agree that it is appropriate to limit the application of the 36-month rule to the entities for which it was originally intended in order to avoid premature information reporting of cancellation of indebtedness income. Doing so will reduce the information reporting burden on entities that were not originally within the scope of the 36-month rule and will protect debtors from receiving information returns that prematurely report cancellation of indebtedness income from such entities.

The Treasury Department and IRS are still considering other comments received since the publication of the 2004 regulations, including a request to clarify the meaning of ''stated principal'' in § 1.6050P–1(c) and (d)(3) when it is applied to those who acquire a loan from a person other than the debtor. Section 1.6050P–1(c) provides that ''indebtedness'' for purposes of section 6050P means any amount owed to an applicable entity, including stated principal, fees, stated interest, penalties, administrative costs, and fines. Section 1.6050P–1(d)(3) further provides that, in the case of a lending transaction, the discharge of an amount other than stated principal is not required to be reported under section 6050P. Commenters have stated that it is