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## **Draft Guidance for Industry and FDA Staff**

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### **Class II Special Controls Guidance Document: Labeling for Male Condoms Made of Natural Rubber Latex**

*This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.*

#### **I. Introduction**

The Food and Drug Administration (FDA) has developed this draft guidance as a special controls guidance for male condoms made from natural rubber latex (latex condoms). This draft guidance will be issued in conjunction with a Federal Register notice announcing the proposal to amend the two existing classifications for condoms from class II (performance standards) to class II (special controls). The amended classifications would designate this labeling guidance document a special control for latex condoms, with or without spermicidal lubricant. This guidance is issued for comment purposes only. If a final rule to amend the classification for condoms is not issued, the final guidance document will not be issued.

This guidance document describes a means by which latex condoms may comply with the requirement of special controls for class II devices. FDA believes that adherence to the labeling recommendations described in this guidance document, in addition to the general controls, will provide reasonable assurance of the safety and effectiveness of latex condoms and, therefore, is proposing to designate this guidance as the special control for those devices. Following the implementation of a final rule amending the classification regulations for these devices, labeling on latex condoms

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with or without spermicidal lubricant will need to address the issues requiring special controls identified in this guidance document unless the device manufacturer in some other way provides equivalent assurances of safety and effectiveness.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

## **II. Background**

FDA believes that special controls, when combined with the general controls, will be sufficient to provide a reasonable assurance of the safety and effectiveness of latex condoms, with or without spermicidal lubricant. Thus, a manufacturer who intends to market a device of this type should (1) conform to the general controls of the Federal Food, Drug, and Cosmetic Act (the Act), including the 510(k) requirements described in 21 CFR 807 Subpart E and the Quality Systems Regulation (21 CFR Part 820), and (2) address in user labeling the specific issues requiring special controls associated with these devices as identified in this draft guidance.

This draft special controls guidance document provides the classification and product codes for latex condoms (refer to Section IV). In addition, other sections of this draft guidance document list the issues requiring special controls identified by FDA and describe labeling measures that, if followed by manufacturers, will generally address the issues requiring special controls associated with these devices.

The labeling recommendations in this draft guidance document reflect an extensive review on the part of the Agency, in consultation with the National Institutes for Health (NIH) and the Centers for Disease Control and Prevention (CDC), of the available medical literature on the safety and effectiveness of condoms intended to prevent pregnancy and provide protection against sexually transmitted diseases (STDs). In addition, the Agency considered other relevant information related to the barrier properties of latex condoms and the various routes of transmission of STDs. A summary of FDA's review method and conclusions is described in the notice of proposed rulemaking for condoms and condoms with spermicidal lubricant that will publish in the same Federal Register that announces the availability of this draft guidance document. References are also provided in Section VIII of this guidance.

This draft guidance document also identifies issues requiring special controls related to nonoxynol-9 (N-9), used as a spermicide in the lubricant of some latex condoms, and provides labeling recommendations intended to help address these issues. These recommendations are based on the Agency's review of the literature related to N-9,

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including an extensive review by FDA's Center for Drug Evaluation and Research (CDER) of the possible health effects of N-9 on users of vaginal contraceptives. (Relevant references are provided in Section VIII of this guidance.)

### **III. Existing Labeling Requirements**

While this draft guidance document describes labeling *recommendations* regarding ways of meeting the proposed special control for latex condoms, there are also other specific labeling *requirements* for latex condoms contained in the following two regulations:

- User labeling for latex condoms (21 CFR 801.435)
- User labeling for devices that contain natural rubber (21 CFR 801.437)

Additionally, condom manufacturers must ensure that their devices meet the general labeling requirements for medical devices described in 21 CFR Part 801.

Existing labeling requirements for latex condoms include the following:

#### **A. Expiration date (21 CFR Section 801.435)**

The retail and primary condom package (individual foil) must include an expiration date that is no later than five years from the date of product packaging. This expiration date must be supported by shelf life data developed by the condom manufacturer. For details, please see 21 CFR 801.435, "*User labeling for latex condoms*," effective March 25, 1998. This regulation addresses the risk of condom deterioration due to product aging.

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**B. Caution regarding natural rubber latex and allergic reactions (21 CFR Section 801.437)**

Latex condoms, and all other devices composed of, or containing, natural rubber latex that contacts humans, are required to bear the following statement in bold print:

**Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.**

This statement must appear on all device labels, and other labeling, and must also appear on the principal display panel of the device packaging, the outside package, container or wrapper, and the immediate device package, container, or wrapper. For details, please see 21 CFR 801.437, "*User labeling for devices that contain natural rubber.*" This final rule became effective on September 30, 1998. This labeling requirement is necessary because devices composed of, or containing, natural rubber latex, pose a significant health risk to some individuals.

**C. General labeling requirements**

All devices, including condoms, are subject to the general labeling provisions described in 21 CFR part 801, Subpart A. Additionally, condoms are over-the-counter (OTC) devices, and are therefore subject to the requirements for OTC devices described in 21 CFR Part 801, Subpart C. You should familiarize yourself with these labeling requirements. This draft special controls guidance is consistent with these requirements and, in fact, some of the labeling terminology used in this draft guidance is described by these regulations.

Latex condoms must also include adequate directions for use to avoid being misbranded (section 502(f) of the Act, 21 U.S.C. 352(f); 21 CFR section 801.5). Adequate directions for use help ensure that the condom will be used correctly. The following set of statements is an example of acceptable directions for use for latex condoms:

- Put the condom on after the penis is fully erect and before intimate contact. Lesions, pre-ejaculate secretions, semen, vaginal secretions, saliva, urine, and feces can all transmit disease organisms.
- Place the condom on the head of the penis and unroll or pull it all the way to the base.
- If the condom doesn't unroll, the wrong side was placed against the penis. Do not flip over. Throw it away and start over with a new condom.

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- Leave an empty space at the end of the condom to collect semen. Remove any air remaining in the tip of the condom by gently pressing the air out toward the base of the penis.
- After ejaculation and while the penis is still erect, hold onto the rim of the condom so that the condom does not slip off as the penis is carefully withdrawn.



For additional information on general labeling requirements, manufacturers are encouraged to consult with FDA's manual "Labeling: Regulatory Requirements for Medical Devices," (HHS Publication FDA 89-4203). This is available at the FDA website at <http://www.fda.gov/cdrh/dsma/470.pdf>. FDA has also included examples of labeling that incorporate the requirements of the Act and regulations and the recommendations made in this draft special controls guidance document in Section VII, below.

#### **IV. Scope**

The scope of this special controls guidance document is limited to labeling for male condoms made from natural rubber latex. Such condoms are described in the two following classification regulations:

- Condom, 21 CFR 884.5300, Panel 85, product code HIS,
- Condom with Spermicidal Lubricant, 21 CFR 884.5310, Panel 85, product code LTZ.

This guidance is not intended to be a special control for male condoms made of natural membrane (skin) or synthetic materials. Because natural membrane and synthetic condoms differ in some respects from latex condoms, the present guidance document does not address all the labeling issues for these products. Until FDA provides further specific guidance for these products, manufacturers of synthetic condoms may consult Part C of FDA's guidance document, "Testing Guidance for Male Condoms made from New Material (June 29, 1995)," <http://www.fda.gov/cdrh/ode/oderp455.html>, and manufacturers of natural membrane condoms may consult the guidance document "Guidance for Industry -- Uniform Contraceptive Labeling (July 23, 1998)," <http://www.fda.gov/cdrh/ode/contrlab.html><sup>1</sup>



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<sup>1</sup> These existing guidance documents for non-latex condoms do not currently address issues arising from the presence of nonoxynol-9 (N-9) in the spermicidal lubricant of some condoms made of these materials. FDA believes that the recommendations contained in this guidance regarding labeling to address N-9 in the spermicidal lubricant of latex condoms are also generally applicable to non-latex condoms containing N-9 in

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Subject: Note

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Wrap the used condom in a tissue and throw it in trash where others cannot handle it. Because condoms may cause problems in sewers, don't flush them down the toilet. Afterwards wash your hands with soap and water. (FDA revised July 2005. condom factsheet. [www.fda.gov/oashi/aids/condom.html](http://www.fda.gov/oashi/aids/condom.html). Accessed 11/17/05)

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Sequence number: 2

Author: pthickstun

Subject: Note

Date: 11/18/2005 10:13:33 AM

This guidance also is not intended to be a special control for male condoms made of natural rubber latex used for anal intercourse.

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## **V. Issues Requiring Special Controls**

FDA has identified the following issues requiring special controls associated with the use of latex condoms that can be mitigated by the labeling recommended in the draft special controls guidance. The recommended mitigation measures (labeling) are intended to provide information to users about the extent of protection provided by condoms to prevent pregnancy and prevent the spread of various types of STDs, as well as information about possible risks associated with certain uses of condoms with spermicidal lubricants containing nonoxynol-9 (N-9). The labeling provides important decision-making information for condom users to assist them in determining whether latex condoms are appropriate for their needs.

Table 1 includes risks associated with sexual intercourse, i.e., unintended pregnancy and STD transmission, that all latex condoms are intended to help prevent. This draft special controls guidance document addresses how manufacturers can label their condoms to help assure that they will be safe and effective for these intended uses, which are of significant personal and public health concern. Labeling for latex condoms with and without spermicidal lubricant should follow the mitigation measures suggested in Table 1. Table 2 identifies special issues associated with the spermicide, N-9. Labeling for latex condoms with N-9 in the lubricant should follow the recommended mitigation measures identified in Table 2, as well as Table 1. All the labeling recommendations are discussed in more detail in section VI.

### **A. Issues Requiring Special Controls and Recommended Mitigation Measures for Latex Condoms**

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the spermicidal lubricant, and encourages manufacturers of non-latex condoms containing N-9 to follow that aspect of this labeling guidance (see footnotes 2 and 3).

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Author: pthickstun

Subject: Note

Date: 11/18/2005 10:19:09 AM

about the effectiveness of condoms for reducing the risk of pregnancy and STIs.

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**Table 1. Identified Issues and Recommended Mitigation Measures**

Identified issues <sup>A</sup>	Recommended mitigation measures
<p>1. Risk of unintended pregnancy</p>	<p>1. Labeling should indicate that condoms can reduce, but do not eliminate, the risk of pregnancy.</p> <p>Labeling should also include a table comparing pregnancy rates resulting from condom use to those resulting from other barrier contraceptive methods.</p>
<p>2. Risk of Transmission of Sexually Transmitted Diseases (STDs)</p> <p>2a. Human Immunodeficiency Virus (HIV/AIDS)</p> <p>2b. <del>STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact.</del></p> <p>2c. STDs, such as chlamydia and gonorrhea, that are transmitted to or from the penis by contact with the vagina and genital fluids.</p> <p>2d. STDs, such as genital herpes and human papillomavirus (HPV) infection, that can be transmitted by contact with skin outside the area covered by a condom, as well as by contact with the penis.</p>	<p>2a. Labeling should indicate that latex condoms can greatly reduce, but do not eliminate, the risk of HIV transmission.</p> <p>2b. Labeling should indicate that latex condoms help reduce the risk of STD transmission to or from the penis, but that some STDs can also be transmitted by other types of sexual contact.</p> <p>2c. Labeling should indicate that latex condoms can reduce the risk of STDs transmitted to or from the penis by contact with the vagina or genital fluids, such as chlamydia and gonorrhea.</p> <p>2d. Labeling should indicate that latex condoms provide less protection for those STDs that can also be transmitted by contact with skin outside the area covered by a condom, such as genital herpes and HPV. Labeling should clarify that consistent use of condoms may provide some benefit for these STDs, such as reduced risk of herpes infection or reduced risk of developing HPV-related diseases.</p>

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Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:24:30 AM  
when used correctly and consistently

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Sequence number: 2  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:26:00 AM  
and hormonal

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Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:29:00 AM  
STIs during vaginal sex

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Author: pthickstun  
Subject: Note  
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when used correctly and consistently,

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Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:27:47 AM



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Sequence number: 6  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:40:04 AM  
at present, there is only evidence for condom effectiveness in reducing the risk of some STIs during vaginal intercourse.

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Sequence number: 7  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:35:14 AM  
STIs can be transmitted through oral, vaginal, and anal sex as well as through mutual masturbation.

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Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:34:56 AM



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Sequence number: 9  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:40:49 AM



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Sequence number: 10  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:35:00 AM



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Sequence number: 11  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:40:53 AM

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**Table 1. Identified Issues and Recommended Mitigation Measures**

Identified issues <sup>A</sup>	Recommended mitigation measures
<p>1. Risk of unintended pregnancy</p>	<p>1. Labeling should indicate that condoms can reduce, but do not eliminate, the risk of pregnancy.</p> <p>Labeling should also include a table comparing pregnancy rates resulting from condom use to those resulting from other barrier contraceptive methods.</p>
<p>2. Risk of Transmission of Sexually Transmitted Diseases (STDs)</p> <p>2a. Human Immunodeficiency Virus (HIV/AIDS)</p> <p>2b. <del>STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact.</del></p> <p>2c. STDs, such as chlamydia and gonorrhea, that are transmitted to or from the penis by contact with the vagina and genital fluids.</p> <p>2d. STDs, such as genital herpes and human papillomavirus (HPV) infection, that can be transmitted by contact with skin outside the area covered by a condom, as well as by contact with the penis.</p>	<p>2a. Labeling should indicate that latex condoms can greatly reduce, but do not eliminate, the risk of HIV transmission.</p> <p>2b. Labeling should indicate that latex condoms can reduce the risk of STD transmission to or from the penis, but that some STDs can also be transmitted by other types of sexual contact.</p> <p>2c. Labeling should indicate that latex condoms can reduce the risk of STDs transmitted to or from the penis by contact with the vagina or genital fluids, such as chlamydia and gonorrhea.</p> <p>2d. Labeling should indicate that latex condoms provide less protection for those STDs that can also be transmitted by contact with skin outside the area covered by a condom, such as genital herpes and HPV. Labeling should clarify that consistent use of condoms may provide some benefit for these STDs, such as reduced risk of herpes infection or reduced risk of developing HPV-related diseases.</p>



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Sequence number: 12  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:32:38 AM



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Sequence number: 13  
Author: pthickstun  
Subject: Pencil  
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Author: pthickstun  
Subject: Pencil  
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Sequence number: 15  
Author: pthickstun  
Subject: Pencil  
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Author: pthickstun  
Subject: Pencil  
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Sequence number: 17  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:42:05 AM  
when used correctly and consistently

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Sequence number: 18  
Author: pthickstun  
Subject: Note  
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STIs such as gonorrhea and chlamydia that are

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Author: pthickstun  
Subject: Note  
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partially

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Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:43:17 AM



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Author: pthickstun  
Subject: Note  
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Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:48:47 AM  
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**Table 1. Identified Issues and Recommended Mitigation Measures**

Identified issues <sup>A</sup>	Recommended mitigation measures
<p>1. Risk of unintended pregnancy</p>	<p>1. Labeling should indicate that condoms can reduce, but do not eliminate, the risk of pregnancy.</p> <p>Labeling should also include a table comparing pregnancy rates resulting from condom use to those resulting from other barrier contraceptive methods.</p>
<p>2. Risk of Transmission of Sexually Transmitted Diseases (STDs)</p> <p>2a. Human Immunodeficiency Virus (HIV/AIDS)</p> <p>2b. <del>STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact.</del></p> <p>2c. STDs, such as chlamydia and gonorrhea, that are transmitted to or from the penis by contact with the vagina and genital fluids.</p> <p>2d. STDs, such as genital herpes and human papillomavirus (HPV) infection, that can be transmitted by contact with skin outside the area covered by a condom, as well as by contact with the penis.</p>	<p>2a. Labeling should indicate that latex condoms can greatly reduce, but do not eliminate, the risk of HIV transmission.</p> <p>2b. Labeling should indicate that <del>latex condoms can help reduce the risk of STD transmission to or from the penis, but that some STDs can also be transmitted by other types of sexual contact.</del></p> <p>2c. Labeling should indicate that latex condoms can reduce the risk of STDs transmitted to or from the penis by contact with the vagina or genital fluids, <del>such as chlamydia and gonorrhea.</del></p> <p>2d. Labeling should indicate that latex condoms provide less protection for those STDs that can also be transmitted by contact with skin outside the area covered by a condom, such as genital herpes and HPV. Labeling should clarify that consistent use of condoms may provide some benefit for these STDs, such as reduced risk of herpes infection or reduced risk of developing HPV-related diseases.</p>

Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 10:43:23 AM



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Sequence number: 24  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 10:56:10 AM  
even

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Sequence number: 25  
Author: pthickstun  
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Date: 11/18/2005 11:05:39 AM

Labeling should also include a table indicating condom effectiveness for each of the most common STIs, including HIV, as published in peer-reviewed literature.

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<p>3. Incorrect or inconsistent use diminishing the effectiveness of condoms against the risks of unintended pregnancy and STD transmission.</p> <p>2</p>	<p>3. Labeling should include adequate precautions.</p> <p>1</p>
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<sup>A</sup> Additional risks of (1) product deterioration due to aging and (2) allergic reactions to latex have been specifically addressed in labeling regulations that are discussed in Section III of this guidance.

**B. Issues Requiring Special Controls and Recommended Mitigation Measures Related to the Use of Nonoxynol-9 (N-9) in the Spermicidal Lubricant of Latex Condoms**

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Sequence number: 1

Author: pthickstun

Subject: Note

Date: 11/18/2005 11:39:18 AM

- 3. Labeling should instruct the user to follow all the steps for correct condom use.
- 4. Labeling should instruct the user to use condoms during each sexual act.

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Sequence number: 2

Author: pthickstun

Subject: Note

Date: 11/18/2005 11:38:27 AM

- 3. There are no data to suggest that any risk reduction is afforded by incorrect use.
  - 4. Studies show no risk reduction with inconsistent use for most STIs; inconsistent use may provide some risk reduction for herpes and HIV.
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**Table 2. Identified Issues and Recommended Mitigation Measures Related to N-9<sup>2</sup>**

Identified Issues	Recommended Mitigation Measures
<p>1. <del>Actual</del><sup>1</sup> benefits of N-9 may be less than the benefits perceived by some users.<sup>2</sup></p> <p>1a. Limited contraceptive benefits of N-9 contained in spermicidal lubricant.<sup>3</sup></p> <p><sup>9</sup></p> <p>1b. N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2. Risks associated with N-9 may outweigh benefits for some users.</p> <p>2a. N-9 can irritate<sup>10</sup> vagina. This may increase the risk of getting HIV/AIDS from an infected partner.<sup>11</sup></p> <p>2b. <del>Latex</del><sup>12</sup> condoms without N-9 should be used by those at risk of acquiring or transmitting (catching or spreading) HIV/AIDS.</p> <p>2c. N-9 can irritate the rectum. This may increase the risk of HIV transmission when used for anal sex.</p>	<p>1a. Labeling should include a statement that lubricant on the condom contains the spermicide nonoxynol-9 (N-9), <del>which kills sperm, but that the extent of pregnancy protection contributed by the N-9 has not been determined.</del><sup>4, 5, 6, 7, 8</sup></p> <p>1b. Labeling should include a statement that N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2a. Labeling should inform users that use of N-9 can irritate the vagina<sup>11</sup> and that this may increase the risk of getting HIV/AIDS from an infected partner.</p> <p>2b. Labeling should inform users that <del>if they or their partner have HIV/AIDS, or if their infection status is unknown, they should choose a latex condom without N-9.</del><sup>12</sup></p> <p>2c. Labeling should inform users that condoms with N-9 should not be used for anal sex because N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.</p>

<sup>2</sup> FDA believes that the issues raised by the use of the spermicide N-9 in the lubricant of male condoms made of natural membrane or synthetic materials are very similar to the issues associated with N-9 used on latex condoms. Therefore, FDA recommends that manufacturers of synthetic condoms using N-9 implement all the identified mitigation measures related to N-9, and that manufacturers of natural membrane condoms with N-9 implement all the identified mitigation measures with the exception of item 2c of Table 2. Item 2c is not recommended for membrane condoms and could cause confusion because these condoms are only labeled for contraceptive use and include a specific statement that they do not provide protection against STDs (see "Guidance for Industry -- Uniform Contraceptive Labeling (July 23, 1998)," <http://www.fda.gov/cdrh/ode/contrlab.html>).

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Sequence number: 1  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:40:47 AM



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Sequence number: 2  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:48:24 AM  
1. Risk of unintended pregnancy

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Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:48:44 AM  
1a. Typical pregnancy rates for condoms with spermicidal lubricant have not been determined. (see Barrier Birth Control Methods in this Guidance document).

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Sequence number: 4  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:50:31 AM  
How effective a condom with N-9 is for pregnancy prevention is unknown.

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Sequence number: 5  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:21:24 PM



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Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:47:24 AM



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Sequence number: 7  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:49:31 AM



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Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:47:30 AM



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Sequence number: 9  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:57:31 AM  
2. Risk of STIs

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Sequence number: 10  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:58:00 AM  
of one partner infecting the other with HIV/AIDS.

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Sequence number: 11

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**Table 2. Identified Issues and Recommended Mitigation Measures Related to N-9<sup>2</sup>**

Identified Issues	Recommended Mitigation Measures
<p>1. Actual benefits of N-9 may be less than the benefits perceived by some users. </p> <p>1a. Limited contraceptive benefits of N-9 contained in spermicidal lubricant. </p> <p></p> <p>1b. N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2. Risks associated with N-9 may outweigh benefits for some users.</p> <p>2a. N-9 can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.   </p> <p>2b.  condoms without N-9 should be used by those at risk of acquiring or transmitting (catching or spreading) HIV/AIDS. </p> <p>2c. N-9 can irritate the rectum. This may increase the risk of HIV transmission when used for anal sex.</p>	<p>1a. Labeling should include a statement that lubricant on the condom contains the spermicide nonoxynol-9 (N-9), which kills sperm, but that the extent of pregnancy protection contributed by the N-9 has not been determined. </p> <p>1b. Labeling should include a statement that N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2a. Labeling should inform users that use of N-9 can irritate the vagina and that this may increase the risk of getting HIV/AIDS from an infected partner.   </p> <p>2b. Labeling should inform users that they or their partner have HIV/AIDS, or if their infection status is unknown, they should choose a latex condom without N-9.   </p> <p>2c. Labeling should inform users that condoms with N-9 should not be used for anal sex because N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.</p>

<sup>2</sup> FDA believes that the issues raised by the use of the spermicide N-9 in the lubricant of male condoms made of natural membrane or synthetic materials are very similar to the issues associated with N-9 used on latex condoms. Therefore, FDA recommends that manufacturers of synthetic condoms using N-9 implement all the identified mitigation measures related to N-9, and that manufacturers of natural membrane condoms with N-9 implement all the identified mitigation measures with the exception of item 2c of Table 2. Item 2c is not recommended for membrane condoms and could cause confusion because these condoms are only labeled for contraceptive use and include a specific statement that they do not provide protection against STDs (see "Guidance for Industry -- Uniform Contraceptive Labeling (July 23, 1998)," <http://www.fda.gov/cdrh/ode/contrlab.html>).

Author: pthickstun  
Subject: Note  
Date: 11/18/2005 11:59:44 AM  
of one partner infecting the other with HIV/AIDS.

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Sequence number: 12  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:04:51 PM

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Sequence number: 13  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:58:08 AM

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Sequence number: 14  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:59:31 AM

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Sequence number: 15  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:58:13 AM

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Sequence number: 16  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 11:59:35 AM

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Sequence number: 17  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:01:12 PM  
Latex condoms with N-9 should not be used by those at risk of acquiring or transmitting HIV/AIDS.

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Sequence number: 18  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:04:46 PM  
condoms with N-9 should not be used by anyone if there is any possibility that they or their partner might have HIV/AIDS.

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Sequence number: 19  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:01:23 PM

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Sequence number: 20  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:02:43 PM

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Sequence number: 21  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:03:31 PM

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Sequence number: 22  
Author: pthickstun  
Subject: Pencil

Comments from page 12 continued on next page

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**Table 2. Identified Issues and Recommended Mitigation Measures Related to N-9<sup>2</sup>**

Identified Issues	Recommended Mitigation Measures
<p>1. Actual benefits of N-9 may be less than the benefits perceived by some users.</p> <p>1a. Limited contraceptive benefits of N-9 contained in spermicidal lubricant.</p> <p>1b. N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2. Risks associated with N-9 may outweigh benefits for some users.</p> <p>2a. N-9 can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.</p> <p>2b. <del>Latex condoms without N-9 should be used by those at risk of acquiring or transmitting (catching or spreading) HIV/AIDS.</del></p> <p>2c. N-9 can irritate the rectum. This may increase the risk of HIV transmission when used for anal sex.</p>	<p>1a. Labeling should include a statement that lubricant on the condom contains the spermicide nonoxynol-9 (N-9), which kills sperm, but that the extent of pregnancy protection contributed by the N-9 has not been determined.</p> <p>1b. Labeling should include a statement that N-9 in the lubricant of the condom does not protect against HIV/AIDS or other STDs.</p> <p>2a. Labeling should inform users that use of N-9 can irritate the vagina and that this may increase the risk of getting HIV/AIDS from an infected partner.</p> <p>2b. Labeling should inform users that if they or their partner have HIV/AIDS, or if their infection status is unknown, they should choose latex condom without N-9.</p> <p>2c. Labeling should inform users that condoms with N-9 should not be used for anal sex because N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.</p>

<sup>2</sup> FDA believes that the issues raised by the use of the spermicide N-9 in the lubricant of male condoms made of natural membrane or synthetic materials are very similar to the issues associated with N-9 used on latex condoms. Therefore, FDA recommends that manufacturers of synthetic condoms using N-9 implement all the identified mitigation measures related to N-9, and that manufacturers of natural membrane condoms with N-9 implement all the identified mitigation measures with the exception of item 2c of Table 2. Item 2c is not recommended for membrane condoms and could cause confusion because these condoms are only labeled for contraceptive use and include a specific statement that they do not provide protection against STDs (see "Guidance for Industry -- Uniform Contraceptive Labeling (July 23, 1998)," <http://www.fda.gov/cdrh/ode/contrlab.html>).

Date: 11/18/2005 12:02:48 PM



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Sequence number: 23  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:01:27 PM



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Sequence number: 24  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:03:00 PM



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Sequence number: 25  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:01:29 PM



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Sequence number: 26  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:03:04 PM



## VI. Labeling Recommendations

This section provides guidance on the labeling of latex condoms grouped according to the issues identified in Tables 1 and 2 of Section V of this document. Generally, there are three different levels of packaging for condoms:

- the retail package, including the principal display panel
- the primary condom package (individual foil)
- the package insert.

The recommendations in this section indicate the level(s) of packaging where the labeling should appear and provide examples of labeling statements that adequately address the issues identified in Tables 1 and 2.

### A. Labeling Recommendations for Latex Condoms

#### 1. Pregnancy

Both the principal display panel of the retail package and the primary condom package (individual foil) should identify contraception as one of the principal intended actions of the latex condom. The following is an example of an acceptable statement:

*“When used correctly every time you have sex, latex condoms <sup>1</sup> greatly reduce, but do not eliminate, the risk of pregnancy.”*

The package insert for latex condoms should include a similar statement under a heading identifying this as “Important information.”

The package insert should also contain a contraceptive effectiveness table comparing pregnancy rates associated with condom use with pregnancy rates for other barrier contraceptive methods. This information is intended to enable contraceptive users to compare alternatives and make appropriate choices. The following table [based on a table previously published in “Guidance for Industry – Uniform Contraceptive Labeling (July 23, 1998),” <http://www.fda.gov/cdrh/ode/contrlab.html>] is recommended for the package insert of latex condoms:

# Page: 13

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Sequence number: 1  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:08:55 PM



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Sequence number: 2  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:08:40 PM  
and hormonal

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**Pregnancy Rates for Barrier Birth Control Methods**

*(For One Year of Use)*

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

*“Typical Use” rates mean that the method either was not always used correctly or was not used with every act of sexual intercourse or was used correctly but failed anyway.*

<b>Method</b>	<b>Typical Use Rate of Pregnancy</b>
<b>No Method:</b>	85%
<b>Barrier Methods:</b>	
Male Latex Condom Without Spermicide <sup>1</sup>	2% 
Diaphragm <sup>2</sup>	17% 
Cervical Cap (no previous births) <sup>2</sup>	17% 
Cervical Cap (previous births) <sup>2</sup>	30%
Female Condom	21%

<sup>1</sup> Typical pregnancy rates for a condom with spermicidal lubricant have not been determined.  
<sup>2</sup> Used with spermicide.

**2. Sexually Transmitted Diseases (STDs)**

**2a. Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS)**

The principal display panel, the package insert,  the primary condom package (individual foil) should identify  protection from  HIV/AIDS as one of the principal intended actions of the latex condom. The following is an example of an acceptable statement:

*“When used correctly every time you have sex,  latex condoms  reduce,  but do not eliminate, the risk of catching or spreading HIV, the virus that causes AIDS.”*

Since the available evidence indicates that latex condoms can  effectively reduce

## Page: 14

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Sequence number: 1  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:12:57 PM  
15% (Hatcher, 2004)

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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:12:37 PM



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Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:13:21 PM  
16%

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Sequence number: 4  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:13:44 PM  
16%

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Sequence number: 5  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:14:26 PM  
risk reduction for

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Sequence number: 6  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:14:00 PM



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Sequence number: 7  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:14:35 PM



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Sequence number: 8  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:16:57 PM  
(by about 85%)

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Sequence number: 9  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:15:54 PM  
vaginal

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Sequence number: 10  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:15:14 PM



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Sequence number: 11  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:17:26 PM

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Comments from page 14 continued on next page

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**Pregnancy Rates for Barrier Birth Control Methods**

(For One Year of Use)

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

**“Typical Use”** rates mean that the method either was not always used correctly or was not used with every act of sexual intercourse or was used correctly but failed anyway.

<b>Method</b>	<b>Typical Use Rate of Pregnancy</b>
<b>No Method:</b>	85%
<b>Barrier Methods:</b>	
Male Latex Condom Without Spermicide <sup>1</sup>	12% 
Diaphragm <sup>2</sup>	17% 
Cervical Cap (no previous births) <sup>2</sup>	17% 
Cervical Cap (previous births) <sup>2</sup>	30%
Female Condom	21%

<sup>1</sup> Typical pregnancy rates for a condom with spermicidal lubricant have not been determined.

<sup>2</sup> Used with spermicide.

## 2. Sexually Transmitted Diseases (STDs)

### 2a. Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS)

The principal display panel, the package insert,  the primary condom package (individual foil) should identify protection from HIV/AIDS as one of the principal intended actions of the latex condom. The following is an example of an acceptable statement:

*“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.”*

Since the available evidence indicates that latex condoms can effectively reduce



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transmission of HIV/AIDS as well as <sup>2</sup>prevent <sup>1</sup>pregnancy, these two principal intended uses may be combined into one statement such as:

*"When used correctly every time you have sex, latex condoms <sup>3</sup>greatly reduce <sup>4</sup>but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS."*

If a combined statement is used, this statement should appear on the principal display panel, on the primary condom package (individual foil), and in the package insert under a heading identifying this as "Important information."

2b. STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact

The retail package of condoms should indicate that there are many types of STDs and that latex condoms can help prevent the transmission of STDs that are spread to or from the penis. The labeling should also explain that some STDs may also be spread by other types of sexual contact. The following is an example of an acceptable statement:

*"Important information: There are many types of sexually transmitted diseases (STDs) <sup>6</sup>and different ways of catching or spreading infection. <sup>7</sup>Latex condom can reduce the risk of STD transmission to or from the penis. <sup>8</sup>However, some STDs can also be spread by other types of sexual contact. <sup>9</sup>For additional information on <sup>10</sup>protection, please read the enclosed insert."*

This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel.

2c. STDs transmitted to or from the penis by contact with the vagina and genital fluids

The package insert should include a statement explaining that latex condoms can help prevent the transmission of STDs that are spread to or from the penis by contact with the vagina and genital fluids. This statement should include specific examples of diseases that are spread in this manner, such as chlamydia and gonorrhea. The statement should appear in the package insert under a heading identifying this as "Important information." This statement should also refer the user to additional sources of information on STDs such as a health care provider or other information provided by government public health agencies. The following is an example of an acceptable statement:

*"Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to*

## Page: 15

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Sequence number: 1  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:19:15 PM  
the risk of

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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:19:22 PM

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Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:18:21 PM  
vaginal

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Sequence number: 4  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:18:34 PM  
(by about 85%)

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Sequence number: 5  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:18:41 PM

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Sequence number: 6  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:21:29 PM  
STIs. These infections can be spread through oral, vaginal, or anal sex as well as through mutual masturbation.

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Sequence number: 7  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:23:36 PM  
Correct and consistent use of a male latex condom during vaginal sex can partially reduce the risk of spreading many common STIs.

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Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:21:40 PM

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Sequence number: 9  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:23:30 PM

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Sequence number: 10  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:23:49 PM

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Sequence number: 11  
Author: pthickstun  
Subject: Note

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Comments from page 15 continued on next page

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transmission of HIV/AIDS as well as prevent pregnancy, these two principal intended uses may be combined into one statement such as:

*"When used correctly every time you have sex, latex condoms greatly reduce but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS."*

If a combined statement is used, this statement should appear on the principal display panel, on the primary condom package (individual foil), and in the package insert under a heading identifying this as "Important information."

2b. STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact

The retail package of condoms should indicate that there are many types of STDs and that latex condoms can help prevent the transmission of STDs that are spread to or from the penis. The labeling should also explain that some STDs may also be spread by other types of sexual contact. The following is an example of an acceptable statement:

*"Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. Latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on protection, please read the enclosed insert."*

This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel.

2c. STDs transmitted to or from the penis by contact with the vagina and genital  
herpes

The package insert should include a statement explaining that latex condoms can help prevent transmission of STDs that are spread to or from the penis by contact with the vagina and genital herpes. This statement should include specific examples of diseases that are spread in this manner, such as chlamydia and gonorrhea. The statement should appear in the package insert under a heading identifying this as "Important information." This statement should also refer the user to additional sources of information on STDs such as a health care provider or other information provided by government public health agencies. The following is an example of an acceptable statement:

*"Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to*

Date: 11/18/2005 12:24:47 PM  
particular STIs, see table in package insert.

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Sequence number: 12  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:24:56 PM



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Sequence number: 13  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:24:59 PM



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Sequence number: 14  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:28:38 PM  
STIs

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Sequence number: 15  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:28:59 PM  
STIs

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Sequence number: 16  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:26:17 PM  
during vaginal sex

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Sequence number: 17  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:26:28 PM



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Sequence number: 18  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:26:32 PM



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Sequence number: 19  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:33:39 PM  
reduce the risk of

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Sequence number: 20  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:29:14 PM  
during vaginal sex

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Sequence number: 21  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:31:40 PM



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Sequence number: 22  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:34:04 PM



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Sequence number: 23

Comments from page 15 continued on next page

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transmission of HIV/AIDS as well as prevent pregnancy, these two principal intended uses may be combined into one statement such as:

*"When used correctly every time you have sex, latex condoms greatly reduce but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS."*

If a combined statement is used, this statement should appear on the principal display panel, on the primary condom package (individual foil), and in the package insert under a heading identifying this as "Important information."

2b. STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact

The retail package of condoms should indicate that there are many types of STDs and that latex condoms can help prevent the transmission of STDs that are spread to or from the penis. The labeling should also explain that some STDs may also be spread by other types of sexual contact. The following is an example of an acceptable statement:

*"Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. Latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on protection, please read the enclosed insert."*

This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel.

2c. STDs transmitted to or from the penis by contact with the vagina and genital fluids

The package insert should include a statement explaining that latex condoms can help prevent the transmission of STDs that are spread to or from the penis by contact with the vagina and genital fluids. This statement should include specific examples of diseases that are spread in this manner, such as chlamydia and gonorrhea. The statement should appear in the package insert under a heading identifying this as "Important information." This statement should also refer the user to additional sources of information on STDs such as a health care provider or other information provided by government public health agencies. The following is an example of an acceptable statement:

*"Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to*

Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:33:52 PM



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Sequence number: 24  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:33:22 PM



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Sequence number: 25  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:30:53 PM  
STIs

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Sequence number: 26  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:37:52 PM  
only

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Sequence number: 27  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:33:58 PM



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Sequence number: 28  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:31:45 PM



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Sequence number: 29  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:39:03 PM  
for which data are available

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Sequence number: 30  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:38:13 PM



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Sequence number: 31  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:38:29 PM



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Sequence number: 32  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:40:52 PM  
partially

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Sequence number: 33  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:40:33 PM  
When used correctly every time you have vaginal sex

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Sequence number: 34  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:41:07 PM

Comments from page 15 continued on next page

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transmission of HIV/AIDS as well as ~~prevent~~ pregnancy, these two principal intended uses may be combined into one statement such as:

*"When used correctly every time you have sex, latex condoms greatly reduce but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS."*

If a combined statement is used, this statement should appear on the principal display panel, on the primary condom package (individual foil), and in the package insert under a heading identifying this as "Important information."

2b. STDs can be transmitted in various ways, including transmission to or from the penis and transmission by other types of sexual contact

The retail package of condoms should indicate that there are many types of STDs and that latex condoms can help prevent the transmission of STDs that are spread to or from the penis. The labeling should also explain that some STDs may also be spread by other types of sexual contact. The following is an example of an acceptable statement:

*"Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. Latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on protection, please read the enclosed insert."*

This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel.

2c. STDs transmitted to or from the penis by contact with the vagina and genital fluids

The package insert should include a statement explaining that latex condoms can help prevent the transmission of STDs that are spread to or from the penis by contact with the vagina and genital fluids. This statement should include specific examples of diseases that are spread in this manner, such as chlamydia and gonorrhea. The statement should appear in the package insert under a heading identifying this as "Important information." This statement should also refer the user to additional sources of information on STDs such as a health care provider or other information provided by government public health agencies. The following is an example of an acceptable statement:

*"Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea that are spread to*

(50%)

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Sequence number: 35  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:41:35 PM



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~~[1] from the penis by direct contact with the vagina and genital fluids. For more information on STDs, consult your health care provider or information provided by government public health agencies.~~

2d. STDs transmissible by contact outside the area covered by a condom

The package insert should indicate that condoms provide less protection for certain STDs, including genital herpes [2] human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against [4] these STDs [3] when they are spread in this way. [5] latex condoms every time you have sex may [7] [8] give some benefits against these STDs. For example, using a condom may lower the risk of catching or spreading genital herpes. Using a condom also may [9] lower the risk of developing HPV-related diseases, such as genital warts and cervical cancer. The statement should appear in the package insert under a heading identifying this as "Important information." The statement should also refer the user to additional sources of information on STDs such as a health care provider and/or other information provided by government public health agencies.

The following is an example of an acceptable statement:

*"Important information: Condoms provide [10] protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that [11] also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer. For more information, consult your health care provider or information provided by government public health agencies."*

The statements recommended for the package insert in 2a, 2c, and 2d above could be combined into one package insert statement that would address all the applicable identified risks of pregnancy and STDs, such as:

*"Important information:*

*When used correctly every time you have [12] latex condoms greatly reduce [13]*

# Page: 16

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Sequence number: 1  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:41:52 PM



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Sequence number: 2  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:42:44 PM  
syphilis,

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Sequence number: 3  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:44:12 PM



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Sequence number: 4  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:44:20 PM



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Sequence number: 5  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:44:50 PM  
Correctly

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Sequence number: 6  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:44:55 PM



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Sequence number: 7  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:43:30 PM



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Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:43:54 PM



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Sequence number: 9  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:45:01 PM



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Sequence number: 10  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:45:22 PM  
far

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Sequence number: 11  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:46:01 PM

Comments from page 16 continued on next page

**Contains Nonbinding Recommendations**  
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*or from the penis by direct contact with the vagina and genital fluids. For more information on STDs, consult your health care provider or information provided by government public health agencies."*

2d. STDs transmissible by contact outside the area covered by a condom

The package insert should indicate that condoms provide less protection for certain STDs, including genital herpes <sup>11</sup> human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. <sup>12</sup> Using latex condoms every time you have sex may still give some benefits against these STDs. For example, using a condom may lower the risk of catching or spreading genital herpes. Using a condom also may lower the risk of developing HPV-related diseases, such as genital warts and cervical cancer. The statement should appear in the package insert under a heading identifying this as "Important information." The statement should also refer the user to additional sources of information on STDs such as a health care provider and/or other information provided by government public health agencies.

The following is an example of an acceptable statement:

*"Important information: Condoms provide <sup>11</sup> protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, <sup>12</sup> that <sup>13</sup> also be spread by contact with infected skin outside the area covered by the condom. <sup>13</sup> Condoms cannot protect against these STDs when they are spread in this way. <sup>14</sup> Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer. For more information, consult your health care provider or information provided by government public health agencies."*

The statements recommended for the package insert in 2a, 2c, and 2d above could be combined into one package insert statement that would address all the applicable identified risks of pregnancy and STDs, such as:

*"Important information:*

*When used correctly every time you have <sup>16</sup> latex condoms <sup>17</sup> they reduce <sup>15</sup>*

these STIs

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Sequence number: 12  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:45:47 PM



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Sequence number: 13  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:46:35 PM



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Sequence number: 14  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:46:20 PM



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Sequence number: 15  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:47:36 PM  
(85%)

---

Sequence number: 16  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:47:12 PM  
vaginal

---

Sequence number: 17  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:47:15 PM



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**Draft - Not for Implementation**

but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. Latex condoms can <sup>1</sup> also <sup>2</sup> reduce the risk <sup>3</sup> of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea <sup>4</sup> that <sup>5</sup> are spread to or from the penis by direct contact with the <sup>6</sup> vagina and genital fluids. <sup>7</sup>

Condoms provide less <sup>8</sup> protection <sup>9</sup> for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that <sup>10</sup> also <sup>11</sup> be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. <sup>12</sup> Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer.

For more information on STDs, consult your health care provider or information provided by government public health agencies."

### **3. Incorrect or Inconsistent Use**

The package insert should include appropriate precautions. The following set of statements is an example of acceptable precautions regarding condom use:

- Use a new condom every time you have <sup>13</sup> ~~sexual~~ intercourse or other acts between partners that involve contact with the penis.
- Do not reuse condoms.
- Store condoms in a cool, dry place.
- If the rubber material is sticky or brittle or obviously damaged, do not use the condom.
- If a lubricant is wanted, use water-based lubricants such as [name of product]. **DO NOT USE OIL-BASED LUBRICANTS**, such as those made with petroleum jelly (e.g., Vaseline<sup>®</sup>), mineral oil, vegetable oil, or cold cream, as these may damage the condom.

Manufacturers <sup>14</sup> have additional precautions or other information that they believe is necessary for proper use of their products. Such additional information is acceptable as long as it does not conflict with or detract from the statements recommended in this guidance (or equivalent statements) or any other applicable requirements (see Section III).

## Page: 17

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Sequence number: 1  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:48:28 PM  
reduce

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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:48:20 PM

---

Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:51:47 PM  
of spreading

---

Sequence number: 4  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:52:12 PM

---

Sequence number: 5  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:49:22 PM  
during vaginal sex

---

Sequence number: 6  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:50:46 PM  
(50%)

---

Sequence number: 7  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:48:44 PM

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Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:48:49 PM

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Sequence number: 9  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:52:54 PM  
such as

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Sequence number: 10  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:52:53 PM

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Sequence number: 11  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:52:39 PM

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Comments from page 17 continued on next page

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but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. Latex condoms can also <sup>14</sup> reduce the risk <sup>15</sup> of other sexually transmitted diseases (STDs), such as chlamydia and gonorrhea <sup>16</sup> are spread to or from the penis by direct contact with the vagina and genital fluids.

Condoms provide less <sup>12</sup> protection for certain STDs, <sup>13</sup> including genital herpes and human papillomavirus (HPV) infection, that <sup>14</sup> can be spread by contact with infected skin outside the area covered by the condom. <sup>15</sup> Condoms cannot protect against these STDs when they are spread in this way <sup>16</sup> using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes <sup>17</sup> using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer.

For more information on STDs, consult your health care provider or information provided by government public health agencies.”

**3. Incorrect <sup>19</sup> Inconsistent Use**

The package insert should include appropriate precautions. The following set of statements is an example of acceptable precautions regarding condom use:

- Use a new condom every time you have <sup>20</sup> intercourse <sup>21</sup> other acts between partners that involve contact with the penis.
- Do not reuse condoms.
- Store condoms in a cool, dry place.
- If the rubber material is sticky or brittle or obviously damaged, do not use the condom.
- If a lubricant is wanted, use water-based lubricants such as [name of product]. DO NOT USE OIL-BASED LUBRICANTS, such as those made with petroleum jelly (e.g., Vaseline<sup>®</sup>), mineral oil, vegetable oil, or cold cream, as these may damage the condom.

Manufacturers <sup>23</sup> have additional precautions or other information that they believe is necessary for proper use of their products. Such additional information is acceptable as long as it does not conflict with or detract from the statements recommended in this guidance (or equivalent statements) or any other applicable requirements (see Section III).

risk reduction

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Sequence number: 12  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:52:28 PM



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Sequence number: 13  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:52:48 PM



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Sequence number: 14  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:52:20 PM



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Sequence number: 15  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:53:58 PM  
are sometimes

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Sequence number: 16  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:53:46 PM



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Sequence number: 17  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:50:15 PM



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Sequence number: 18  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:55:06 PM  
(25%)

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Sequence number: 19  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:56:31 PM



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Sequence number: 20  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:55:53 PM  
vaginal

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Sequence number: 21  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:56:03 PM



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Sequence number: 22  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:55:44 PM



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Sequence number: 23

Comments from page 17 continued on next page

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but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. Latex condoms can also ~~prevent~~ the risk ~~of~~ other sexually transmitted diseases (STDs), such as chlamydia and gonorrhea ~~are spread to or from the penis by direct contact with the vagina and genital fluids.~~

Condoms provide less ~~protection~~ for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that ~~can~~ also be spread by contact with infected skin outside the area covered by the condom. ~~Condoms cannot protect against these STDs when they are spread in this way.~~ Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes ~~and~~ using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer.

For more information on STDs, consult your health care provider or information provided by government public health agencies.”

### 3. Incorrect or Inconsistent Use

The package insert should include appropriate precautions. The following set of statements is an example of acceptable precautions regarding condom use:

- Use a new condom every time you have ~~sexual~~ intercourse or other acts between partners that involve contact with the penis.
- Do not reuse condoms.
- Store condoms in a cool, dry place.
- If the rubber material is sticky or brittle or obviously damaged, do not use the condom.
- If a lubricant is wanted, use water-based lubricants such as [name of product]. DO NOT USE OIL-BASED LUBRICANTS, such as those made with petroleum jelly (e.g., Vaseline®), mineral oil, vegetable oil, or cold cream, as these may damage the condom.

Manufacturers ~~may~~ have additional precautions or other information that they believe is necessary for proper use of their products. Such additional information is acceptable as long as it does not conflict with or detract from the statements recommended in this guidance (or equivalent statements) or any other applicable requirements (see Section III).

Author: pthickstun  
Subject: Note  
Date: 11/18/2005 12:57:39 PM  
+ all the bullets for correct use

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Sequence number: 24  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 12:58:01 PM

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**B. Labeling Recommendations Related to the Use of N-9 in Condoms with Spermicidal Lubricant**

As already noted, latex condoms are classified under one of two classification regulations, depending upon whether or not they contain a spermicidal lubricant. The following discussion and special control labeling recommendations apply only to latex condoms classified under 21 CFR 884.5310 and containing a lubricant with N-9.<sup>3</sup>

Since 1982, condoms with N-9 have been required to bear a contraceptive effectiveness statement to be classified under 21 CFR 884.5310. This contraceptive effectiveness statement was part of the reclassification order for a condom with spermicidal lubricant (see 47 FR 49201, Oct. 29, 1982). Subsequently, new information has been developed regarding the potential for N-9 to contribute to adverse health consequences in some circumstances (see References in Section VIII, below). This new information demonstrates that there are risks associated with N-9 that may outweigh its benefit as a spermicide for some users.

Through this special control, FDA is providing important decision-making information and cautions, based upon this new information, that will permit users to determine whether a latex condom containing N-9 is appropriate for their needs. This special control, which addresses the new information developed since the 1982 reclassification of condoms with spermicidal lubricant into class II, together with the general controls, should reasonably assure the safety and effectiveness of such condoms. FDA's current thinking on appropriate cautionary statements for latex condoms containing N-9 follows. When this guidance becomes final and effective as a special control, it will supersede the contraceptive effectiveness statement described in the reclassification order and in the October 29, 1982, Federal Register notice.<sup>4</sup>

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<sup>3</sup> Although this guidance document is not designated as a special control for condoms made of materials other than latex, FDA recommends (for the reasons described above in footnote 2) that manufacturers of synthetic condoms using N-9 follow all the labeling suggestions related to N-9, and that manufacturers of natural membrane condoms with N-9 follow all the N-9 labeling suggestions with the exception of the recommended anal use warning. The anal use warning is not recommended for membrane condoms and could be confusing because these condoms are labeled only for contraceptive use and include a specific statement that they do not provide protection against STDs (see "Guidance for Industry -- Uniform Contraceptive Labeling (July 23, 1998)," <http://www.fda.gov/cdrh/ode/contrlab.html>).

<sup>4</sup> When final, this draft special controls guidance document will also supersede FDA recommendations in the FDA letter to "All U.S. Condom Manufacturers, Importers, and Repackagers" (April 7, 1987) and the FDA letter to "Manufacturers, Importers, and Repackagers of Condoms for Contraception or Sexually-Transmitted Disease Prevention" (February 13, 1989).

Sequence number: 1

Author: pthickstun

Subject: Note

Date: 11/18/2005 1:03:59 PM

There are no data to suggest that condoms with N-9 are effective for contraception. Moreover there are data to suggest that use of N-9 may increase risk of HIV transmission. Therefore the general and special controls cannot assure the safety and effectiveness of such condoms.

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**1a. Limited benefits of N-9**

The retail package of latex condoms with N-9 should include a statement indicating that the lubricant on the condom contains N-9, which kills sperm, but that the extent of pregnancy protection contributed by the N-9 has not been measured. This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel. The following is an example of an acceptable statement:

*“The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however, the amount of additional pregnancy protection provided by the N-9 has not been measured.”*

Note: The abbreviation “N-9” may be used to save space on labeling but the first reference to “nonoxnyol-9” on each package panel should be spelled out.

A similar statement should also appear on the primary condom package (individual foil) as well as in the package insert.

**1b. N-9 does not protect against HIV/AIDS or other Sexually Transmitted Diseases**

The retail package of latex condoms with N-9 should include a statement that the N-9 in the product does not provide protection from HIV/AIDS or other sexually transmitted diseases. This statement should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel. The following is an example of an acceptable statement:

*“The nonoxynol-9 (N-9) lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.”*

A similar statement should also appear  ~~in the primary condom package (individual foil) as well as in the package insert.~~

**2a. Risks of N-9 irritation and transmission of HIV/AIDS**

A risk statement addressing vaginal irritation and HIV/AIDS transmission should appear on the retail package. This risk statement should be prefaced by the words “Nonoxynol-9 Warning” and should inform users of the risk of vaginal irritation and possible increased risk of transmission of HIV/AIDS from an infected partner. The following is an example of an acceptable statement:

# Page: 19

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Sequence number: 1  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:12:20 PM



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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:12:24 PM



**Contains Nonbinding Recommendations**  
*Draft - Not for Implementation*

*“Nonoxynol-9 Warning: The spermicide nonoxynol-9 (N-9) can irritate the vagina. This may increase the risk of <sup>1</sup> HIV/AIDS from an infected partner.”*

A similar statement should appear in the package insert.

2b. Users at risk of catching or spreading HIV/AIDS should <sup>3</sup> choose latex condoms without <sup>4</sup> N-9

The retail package of latex condoms containing N-9 should include a statement informing users that if they or their partner have HIV/AIDS, or if their infection status is unknown, they should choose a latex condom without N-9. This statement should be prefaced by the words “Nonoxynol-9 Warning.” The following is an example of an acceptable statement:

*Nonoxynol-9 Warning: If you or your partner has HIV/AIDS, or if you do not know if you or your partner is infected, you should choose a latex condom without nonoxynol-9 (N-9).*

A similar statement should appear in the package insert.

2c. Risks of anal use of condoms with N-9

6

The retail package of latex condoms containing N-9 should include a statement informing users that N-9 can irritate the rectum and they should not use condoms with N-9 for anal sex. This statement should be prefaced by the words “Nonoxynol-9 Warning,” and should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel. The following is an example of an acceptable statement:

*“Nonoxynol-9 Warning: <sup>7</sup> should not use condoms with nonoxynol-9 (N-9) <sup>9</sup> for anal sex. N-9 can irritate the rectum and may increase the risk of <sup>10</sup> ~~HIV/AIDS from an infected partner.~~”*

A similar statement should appear in the package insert.

Where package space permits, the agency encourages a combined N-9 statement such as:

## Page: 20

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Sequence number: 1  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:14:23 PM  
one partner infecting the other with HIV/AIDS

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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:13:29 PM



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Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:15:30 PM  
not use

---

Sequence number: 4  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:15:13 PM



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Sequence number: 5  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:15:42 PM



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Sequence number: 6  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:16:52 PM



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Sequence number: 7  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:19:10 PM  
Do no use these condoms if there is any chance that either you or your partner might have HIV/AIDS.

---

Sequence number: 8  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:18:15 PM



---

Sequence number: 9  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:18:21 PM



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Sequence number: 10  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:16:40 PM



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Sequence number: 11  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:17:42 PM

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Comments from page 20 continued on next page

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**Draft - Not for Implementation**

*“Nonoxynol-9 Warning: The spermicide nonoxynol-9 (N-9) can irritate the vagina. This may increase the risk of  catching HIV/AIDS from an infected partner.”*

A similar statement should appear in the package insert.

2b. Users at risk of catching or spreading HIV/AIDS should  choose latex condoms without N-9

The retail package of latex condoms containing N-9 should include a statement informing users that if they or their partner have HIV/AIDS, or if their infection status is unknown, they should choose a latex condom without N-9. This statement should be prefaced by the words “Nonoxynol-9 Warning.” The following is an example of an acceptable statement:

*Nonoxynol-9 Warning: If you or your partner has HIV/AIDS, or if you do not know if you or your partner is infected, you should choose a latex condom without nonoxynol-9 (N-9).*

A similar statement should appear in the package insert.

2c. Risks of anal use of condoms with N-9

The retail package of latex condoms containing N-9 should include a statement informing users that N-9 can irritate the rectum and they should not use condoms with N-9 for anal sex. This statement should be prefaced by the words “Nonoxynol-9 Warning,” and should be prominently displayed on the retail package, but may appear on a panel other than the principal display panel. The following is an example of an acceptable statement:

*“Nonoxynol-9 Warning:  ~~should not use condoms with nonoxynol-9 (N-9) for anal sex. N-9 can irritate the rectum and may increase the risk of getting~~  ~~HIV/AIDS from an infected partner.”~~ *

A similar statement should appear in the package insert.

Where package space permits, the agency encourages a combined N-9 statement such as:

one partner infecting the other with HIV/AIDS

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Sequence number: 12  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:16:45 PM



**Contains Nonbinding Recommendations**  
*Draft - Not for Implementation*

~~"The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), <sup>1</sup>which kills sperm; <sup>2</sup>however, the amount of additional pregnancy protection provided by the N-9 has not been measured.~~ <sup>3</sup>

~~<sup>5</sup>The N-9 lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.~~

<sup>6</sup>

**N-9 Warning:**

- ~~N-9 can irritate the vagina. <sup>7</sup>This may increase the risk of getting <sup>8</sup>HIV/AIDS from an infected partner.~~
- ~~If you or your partner has HIV/AIDS, or if you do not know if you or your partner is infected, you should choose a latex condom without N-9.~~
- ~~You should not use condoms with N-9 for anal sex. <sup>9</sup>N-9 can irritate the <sup>10</sup>rectum and may increase the risk of getting HIV/AIDS from an infected partner.~~

The agency recognizes that there may not be sufficient space on the primary condom package (individual foil) to include the recommended warning statements for N-9 outlined in 2a, 2b, and 2c and therefore recommends that the primary condom package include a statement referring the user to the package or package insert for more information on N-9 such as:

*"For more important information on N-9, please read the box or package insert."*

Where possible, this statement should appear directly after the labeling on the individual condom package that addresses the 1a and 1b issues.

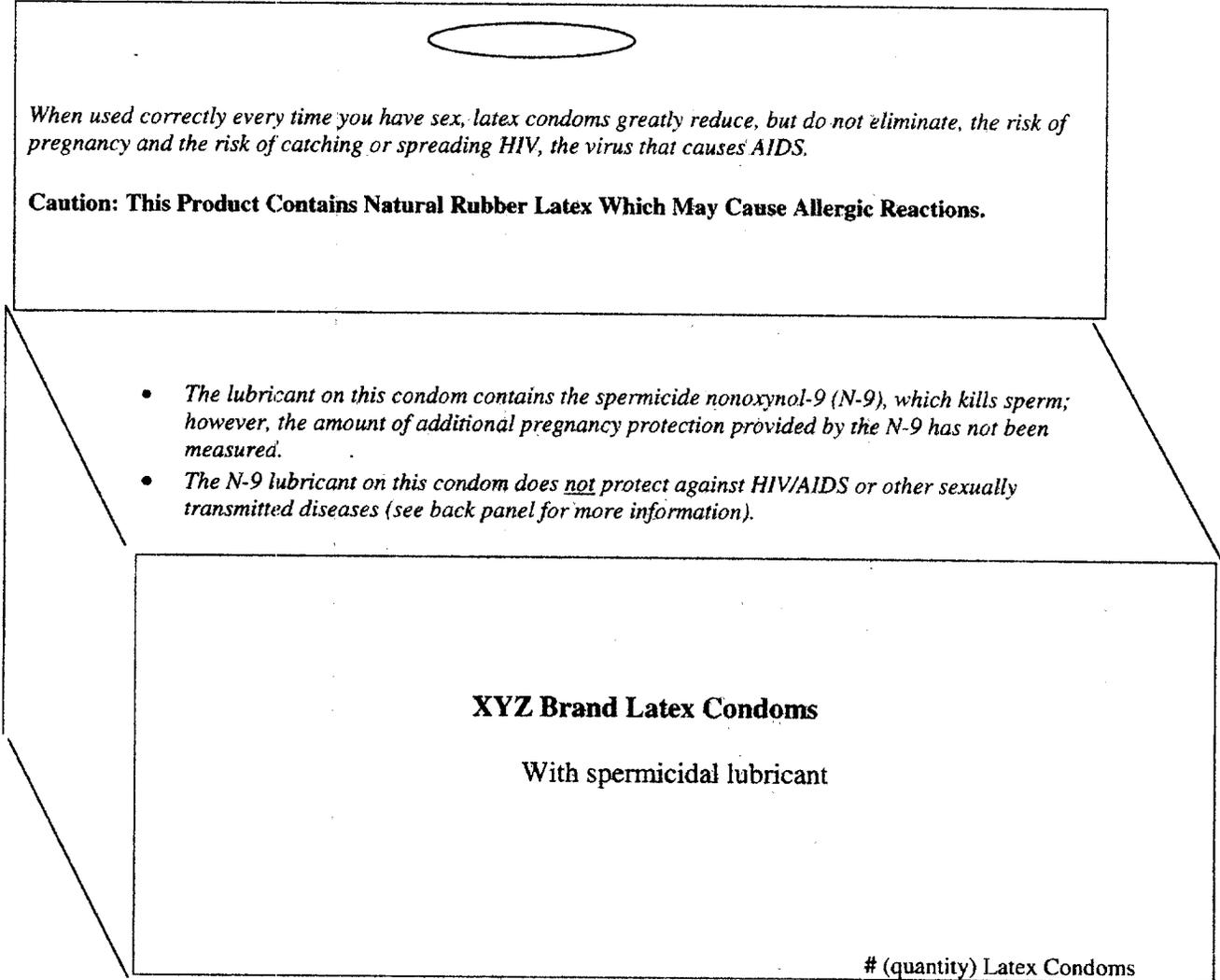
## **VII. Examples of Condom Labeling that Follow the Recommendations in the Draft Guidance**

The examples in this section are for a condom with nonoxynol-9 in order to show all of the labeling potentially applicable to a latex condom.

This page contains no comments

*Contains Nonbinding Recommendations  
Draft - Not for Implementation*

**Front panels of condom retail package:**



*When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS.*

**Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.**

- *The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however, the amount of additional pregnancy protection provided by the N-9 has not been measured.*
- *The N-9 lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases (see back panel for more information).*

**XYZ Brand Latex Condoms**

With spermicidal lubricant

# (quantity) Latex Condoms

This page contains no comments

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**Rear panel of condom retail package**

*Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. A latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on STD protection, please read the enclosed insert.*

***Nonoxynol-9 Warning:***

- The spermicide nonoxynol-9 (N-9) can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.*
- If you or your partner has HIV/AIDS, or if you do not know if you or your partner is infected, you should choose a latex condom without N-9.*
- You should not use condoms with N-9 for anal sex. N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.*

*Distributed by ABC Corporation  
Rockville, Maryland*

*EXP. Date: Jan 20XX*

This page contains no comments

**Contains Nonbinding Recommendations**  
*Draft - Not for Implementation*

**Primary condom package (individual foil):**

**Front of packet**

**One XYZ Brand  
Latex Condom with spermicidal  
lubricant**

*When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS.*

**Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.**

**Back of packet**

*The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however, the amount of additional pregnancy protection provided by the N-9 has not been measured. The N-9 lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.*

*For more important information on N-9, please read the box or package insert.*

Distributed by ABC Corporation  
Rockville, Maryland

EXP Date: Jan 20XX

**Package Insert:**

*Directions for use:*

- *Put the condom on after the penis is fully erect and before intimate contact. <sup>1</sup>resions, <sup>2</sup>pre-ejaculate secretions, semen, vaginal secretions, saliva, urine, and feces can all transmit disease organisms. <sup>3</sup>*
- *Place the condom on the head of the penis and unroll or pull it all the way to the base.*
- *If the condom doesn't unroll, the wrong side was placed against the penis. Do not flip the condom over. Throw it away and start over with a new condom.*
- *Leave an empty space at the end of the condom to collect semen. Remove any air remaining in the tip of the condom by gently pressing the air out toward the base of the penis.*
- *After ejaculation and while the penis is still erect, hold onto the rim of the condom so that the condom does not slip off as the penis is carefully withdrawn.*

# Page: 25

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Sequence number: 1  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:32:11 PM



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Sequence number: 2  
Author: pthickstun  
Subject: Pencil  
Date: 11/18/2005 1:32:36 PM



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Sequence number: 3  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:33:02 PM  
This is not a direction

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**Contains Nonbinding Recommendations**  
**Draft - Not for Implementation**

**Package insert (cont.)**

*Precautions:*

- Use a new condom every time you have sexual intercourse or other acts between partners that involve contact with the penis.
- Do not reuse condoms.
- Store condoms in a cool, dry place.
- If the rubber material is sticky or brittle or obviously damaged, do not use the condom.
- If a lubricant is wanted, use water-based lubricants such as [name of product]. **DO NOT USE OIL-BASED LUBRICANTS**, such as those made with petroleum jelly (e.g., Vaseline®), mineral oil, vegetable oil, or cold cream, as these may damage the condom.

*Important information:*

When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS. Latex condoms can also reduce the risk of other sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to or from the penis by direct contact with the vagina and genital fluids.

Condoms provide less protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer.

For more information on STDs, consult your health care provider or information provided by government public health agencies.

*Nonoxynol-9*

The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however, the amount of additional pregnancy protection provided by the N-9 has not been measured.

The N-9 lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.

*N-9 Warning:*

- N-9 can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.
- If you or your partner has HIV/AIDS, or if you do not know if you or your partner is infected, you should choose a latex condom without N-9.
- You should not use condoms with N-9 for anal sex. N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.

Sequence number: 1  
Author: pthickstun  
Subject: Note  
Date: 11/18/2005 1:31:41 PM  
Inconsistent use statement

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**Contains Nonbinding Recommendations**  
**Draft - Not for Implementation**

**Package insert (cont)**

**Pregnancy Rates for Barrier Birth Control Methods**

**(For One Year of Use)**

The following table provides estimates of the percent of women likely to become pregnant while using a particular contraceptive method for one year. These estimates are based on a variety of studies.

“**Typical Use**” rates mean that the method either was not always used correctly or was not used with every act of sexual intercourse or was used correctly but failed anyway.

<b>Method</b>	<b>Typical Use Rate of Pregnancy</b>
<b>No Method:</b>	85%
<b>Barrier Methods:</b>	
Male Latex Condom Without Spermicide <sup>1</sup>	12%
Diaphragm <sup>2</sup>	17%
Cervical Cap (no previous births) <sup>2</sup>	17%
Cervical Cap (previous births) <sup>2</sup>	30%
Female Condom	21%

<sup>1</sup> Typical pregnancy rates for a condom with spermicidal lubricant have not been determined.

<sup>2</sup> Used with spermicide.

## VIII. References

### Condom protection against STDs

1. NIH/CDC/FDA workshop on condom effectiveness (held June 2000, summary available June 2001) <http://www.niaid.nih.gov/dmid/stds/condomreport.pdf>

This page contains no comments

*Contains Nonbinding Recommendations*  
*Draft - Not for Implementation*

2. CDC STD Treatment Guidelines 2002,  
<http://www.cdc.gov/std/treatment/default.htm>
3. FDA review of currently available literature related to condom effectiveness. A bibliography is provided in the notice of proposed rulemaking for condoms and condoms with spermicidal lubricant that will publish in the same Federal Register that announces the availability of this draft guidance document.

Nonoxynol-9

4. FDA monograph on nonoxynol-9
5. WHO/CONRAD Technical Consultation on Nonoxynol-9 (June 25, 2002)  
[http://www.who.int/reproductive-health/publications/rhr\\_03\\_8/Nonoxynol\\_9.pdf](http://www.who.int/reproductive-health/publications/rhr_03_8/Nonoxynol_9.pdf)
6. OTC Vaginal Contraceptive Drug Products containing Nonoxynol-9; Required Labeling, Proposed Rule. Federal Register, Vol 68, No. 11, January 16, 2003, pp 2254-2262.  
[http://www.fda.gov/cder/otcmonographs/Vaginal\\_Contraceptive/vaginal\\_contraceptive\\_N9\\_PR\\_20030116.htm](http://www.fda.gov/cder/otcmonographs/Vaginal_Contraceptive/vaginal_contraceptive_N9_PR_20030116.htm)
7. Phillips D. Nonoxynol-9 enhances rectal infection by herpes simplex virus in mice. *Contraception* 1998; 57: 341-348.
8. Tabet SR, Surawicz C, Horton S et al. Safety and toxicity of Nonoxynol-9 gel as a rectal microbicide. *Sexually Transmitted Diseases* 1999; 26: 10: 564-571.
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**Condom Label Comprehension Study**

The Medical Institute for Sexual Health, Austin, Texas

Protocol #: MI2005CON-001

## Evaluation of comprehension of new condom labels proposed by the Food and Drug Administration

### Introduction

A medical device, as defined in the Food Drug & Cosmetic Act is "...an instrument, apparatus, implement, ...intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease..."<sup>1</sup> Although several over-the-counter and household products are recommended for preventing infections associated with sexual activity, only some are classified as medical devices and are regulated by the Food and Drug Administration (FDA). FDA-regulated devices have "approved" uses. Uses that are not approved are often referred to as "off-label." The FDA regulatory classifications of medical devices – Class I, Class II, and Class III – are assigned as a function of the risk the medical device presents to the patient and the level of regulatory control the FDA determines is necessary to legally market the device. As the classification level increases, both the risk to the patient and FDA regulatory control increases.

Since condoms are medical devices that were marketed before the passage of the Medical Device Amendments of 1976, they were placed into Class II as part of the initial classification of all existing devices. The 1976 statute anticipated the establishment of mandatory performance standards to govern each Class II device type. However, this proved to be a daunting task for FDA, and, in 1990, Congress changed the definition for Class II devices (Safe Medical Devices Act of 1990 (P.L. 101-629) to make them subject to special controls. FDA has not yet identified special controls for all devices (including condoms) that were classified into Class II prior to the 1990 statutory change.

With the increased availability of drugs and devices over the counter, it has become important to make the consumer aware of the methods and precautions associated with use of these drugs and devices. In the absence of a healthcare provider, consumers rely on labels to learn about safe and effective use of a product. The Food and Drug Administration (FDA) issues specific guidelines on the information that should be made available to users through labels when using a device such as a condom.<sup>2</sup>

Condoms are Class II medical devices and condom labeling must follow not only general device labeling regulations (21 CFR part 801), but also two specific labeling regulations, one on condom expiration dating (21 CFR 801.435) and another on user warnings about allergic reactions to natural rubber latex (21 CFR 801.437). Since 1987 the FDA has issued a series of guidance documents that address specific elements of condom labeling. According to the 1998 FDA guidance document on condoms<sup>3</sup> "The condom is used for contraception and for prophylactic purposes (to help prevent pregnancy and the transmission of sexually transmitted diseases.)" The FDA guidance is meant for penile-vaginal sex and does not specifically address the use of condoms for other types of sex such as oral sex or anal intercourse.

Few studies have looked at label comprehension of non-prescription products in the past<sup>4 5</sup> and most of these are sponsored by manufacturers of the products that are being evaluated.<sup>6</sup> Condom manufacturers are required to print instructions on condom use on the outside of the condom box, in the package insert, and on the individual foil condom package. In 1988, a study on readability of condom instructions found that of the 14 different sets of instructions included in 25 brands of condoms, 8 required at least a reading level of a high school graduate.<sup>7</sup> None required less than a 10<sup>th</sup> grade level.<sup>8, 9</sup> For optimal comprehension and compliance, health-related materials for the public should be written at a 6<sup>th</sup> grade or lower reading level, and this should hold true for condom labels as well.<sup>10</sup>

### **Study objective**

The FDA issued new proposed guidance for condom labeling in 2005.<sup>11</sup> The Medical Institute for Sexual Health conducted a study to evaluate how well the general public understands label instructions proposed by the FDA and how often users read such instructions for condoms.

### **Methodology**

The study was conducted after necessary IRB (Institutional Review Board) approval.<sup>12</sup> The research design consisted of a survey of a convenience sample of 18- to 30-year-olds in Austin, Texas. Participants were recruited at public places during January 2006. A paper-and-pencil questionnaire was filled in by those who qualified the following criteria:

- Were aged between 18 and 30 years
- Were able to read and understand English
- Had ever bought, used or seen an unused individual condom foil or package

247 people participated in the study. A copy of the questionnaire is attached as Appendix A. The statements used in the questionnaire were extracted from proposed guidelines by the FDA for condom labeling. These statements were also analyzed for ease of readability using the Flesch Reading Ease score and the Flesch-Kincaid Grade level score.<sup>13</sup>

### **Data analysis**

The data obtained from the surveys was entered into a database and analyzed using SPSS 13.0. Independent t-tests, analysis of variance (ANOVA), and chi-square tests were used to look for statistical differences and associations among different variables.

### **Results**

Of 600 people requested, 247 completed the questionnaire. There were no incomplete questionnaires. The sample had the following characteristics:

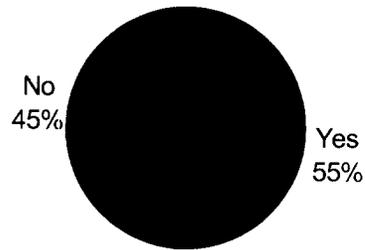
- mean age: 22 years
- Males 56%; Females 44%
- Ethnic distribution: white 57%; blacks 9%; Hispanic 17%; Native American or Alaskan 5%; Asian and others 8%
- Mean years of education: 15 (range: 4 - 22 years)

**Table 1. Responses of survey participants**

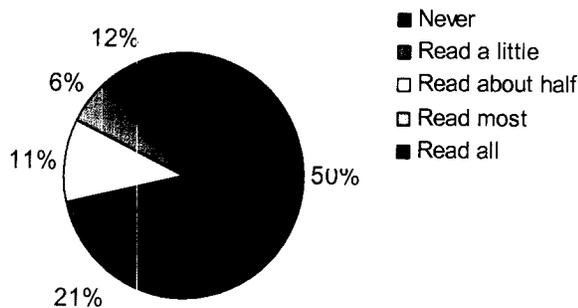
	Male N (%)	Female N (%)	All N (%)
Number of participants	138 (56)	109 (44)	247
Ethnic background			
White	89 (65)	51 (47)	140 (57)
Black	11 (8)	11 (10)	22 (9)
Hispanic	16 (12)	26 (24)	42 (17)
Native American or Alaskan	5 (4)	8 (7)	13 (5)
Asian	12 (9)	8 (7)	20 (8)
Other	4 (2)	5 (5)	1 (4)
Educational Level			
High school or less	31 (23)	16 (15)	47 (19)
Some college	79 (59)	80 (75)	159 (64)
Some post graduate	20 (15)	10 (9)	30 (12)
Beyond post graduate work	3 (1)	1 (1)	4 (2)
Ever had penile-vaginal sex			
Yes	112 (81)	91 (83)	203 (82)
No	26 (19)	18 (17)	44 (18)
Median % condom use in those who have had sex	70	70	75
Ever read all or part of the instructions and cautions on the outside of the box			
Yes	83 (60)	53 (49)	136 (55)
No	55 (40)	56 (51)	111 (45)
Ever read any part of the condom package insert			
No	62 (45)	61 (56)	123 (50)
Yes, a little	30 (22)	23 (21)	53 (22)
Yes, about half	18 (13)	9 (8)	27 (11)
Yes, most	8 (6)	7 (7)	15 (6)
Yes, all	20 (14)	9 (8)	29 (12)
Ever read all or part of the instructions and cautions on the individual foil condom package			
Yes	59 (43)	43 (39)	102 (41)
No	79 (57)	66 (61)	145 (59)
Ever checked expiration date			
Always (100% of the times)	37 (27)	25 (23)	62 (25)
Usually (70-90% of the times)	26 (19)	23 (21)	49 (20)
Sometimes (30-60% of the times)	20 (15)	12 (11)	32 (13)
Rarely (10-20% of the times)	21 (15)	17 (16)	38 (15)
Never (0% of the times)	33 (24)	32 (29)	65 (27)
Usefulness of condom label information			
Not at all useful	2 (2)	2 (2)	4 (2)
Not very useful	7 (6)	13 (12)	21 (9)
Not sure	14 (13)	9 (8)	25 (10)
Somewhat useful	50 (45)	44 (40)	104 (42)
Very useful	37 (33)	41 (38)	91 (37)
Named "genital fluids" when asked	111 (80)	78 (72)	189 (76)
Perceived risk reduction for pregnancy with N-9 condoms			
Less than with a regular condom	63 (46)	41 (38)	104 (42)
Same as with a regular condom	39 (28)	39 (36)	78 (32)
Greater than with a regular condom	36 (26)	29 (26)	65 (26)

About 82% of the respondents had ever had sex and their reported condom use was between 0-100% (average 60%, median 75%). Slightly over half had ever read all or part of the instructions and cautions on the outside of the condom box (Fig. 1). Half of the respondents had never read any of the information in the condom package insert, and only about 12% had read all of it (Fig. 2). Approximately 60% of the participants had not read all or part of the instructions on the individual foil condom package (Fig. 3). A little more than a fourth of the participants stated that they never checked the expiration date on the condom package (Fig. 4).

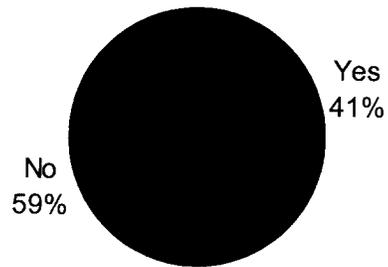
**Figure 1. Ever read instructions or cautions on the outside of the box**



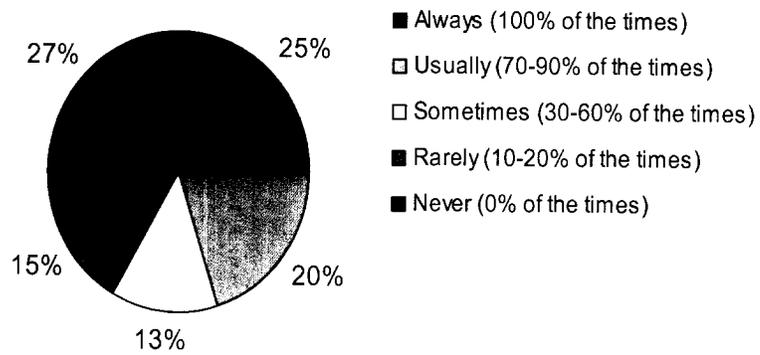
**Figure 2. Ever read any of the condom package insert (instructions inside the box)**



**Figure 3. Ever read all or part of the instructions and cautions on the individual foil condom package**



**Figure 4. How often expiration date on condom package is checked**



**Table 2. Median perceived risk reduction for pregnancy and various STIs when condoms are used every time the respondent has sex**

	All (%)	Males (%)	Females (%)
Pregnancy	86	87	85
HIV	85	95	85
Chlamydia	85	85	82
Genital herpes	70	65	70

### **Readability**

As part of the study, the proposed statements for condom labeling by the FDA were analyzed for readability using the Flesch Reading Ease score and the Flesch-Kincaid Grade Level score using Microsoft Word. The readability score of each statement and the median perceived risk reduction after reading the statements is given in table 3. As seen from the table, most statements required a 12<sup>th</sup> grade level education.

### **Statement on risk reduction**

About 80% (195) of the participants found the following label statement useful :  
 "Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. A latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on STD protection, please read the enclosed insert." 10% (25) of the participants were not sure and 10% (25) did not find this information useful.

### **Comprehension of "genital fluids"**

The term "genital fluids" was used in the proposed FDA statements for condom labeling. To evaluate what the general public comprehends from this term, study participants were asked to list the genital fluids they knew of. About 25% could not provide any response. More than 60% of those who responded mentioned terms such as semen (or sperm/seminal fluid) and about 20% mentioned vaginal fluids and synonymous terms. Other fluids mentioned included urine, menstrual blood, blood, sweat, and pre-ejaculate as shown in table 4.

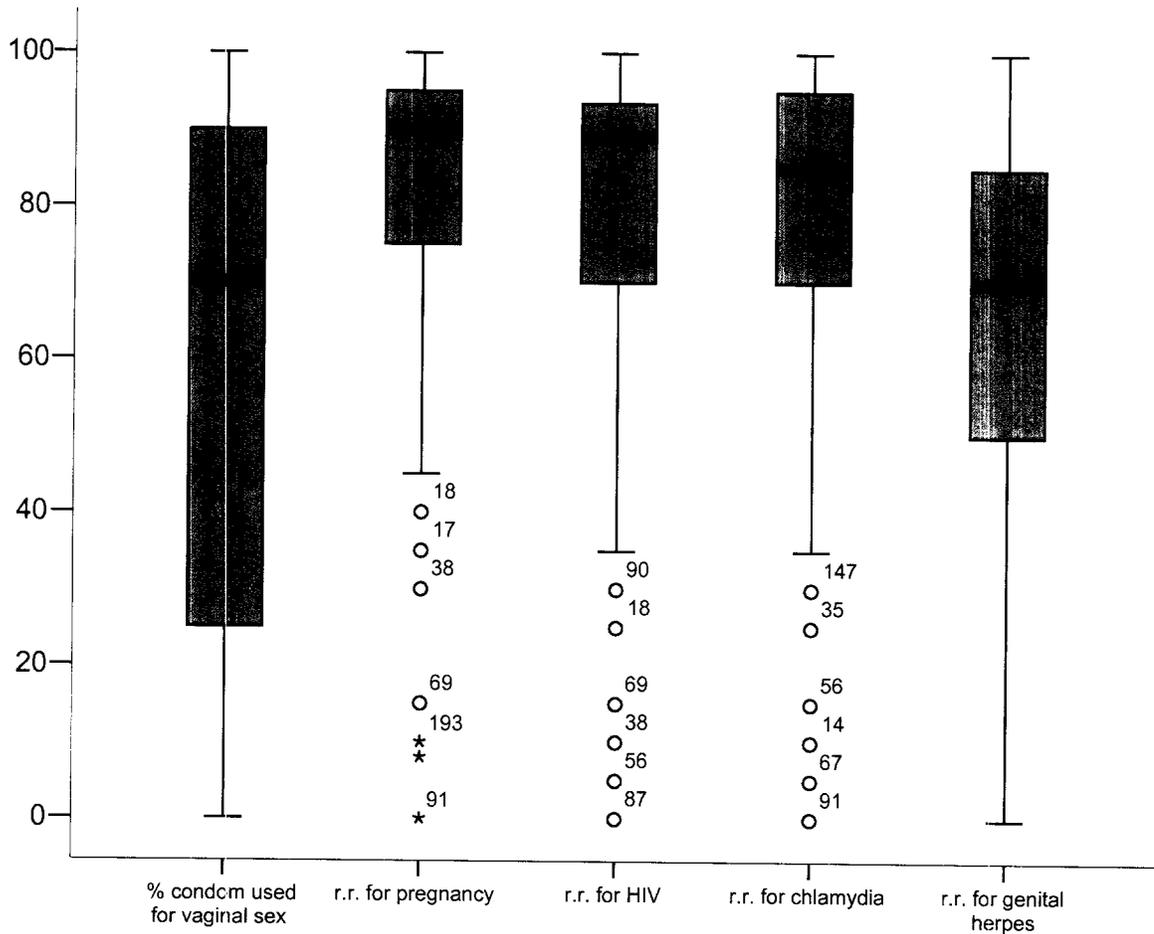
**Table 3. FDA proposed statements, their readability, and perceived risk reduction for pregnancy and STIs after reading the statements**

<b>Statement and perceived risk reduction</b>	<b>Flesch Reading ease score</b>	<b>Flesch-Kincaid Grade Level score</b>	<b>Median response</b>
When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS.	40.4	12	
Perceived risk reduction for pregnancy			86.5%
Perceived risk reduction for HIV infection			85%
Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to or from the penis, by direct contact with the vagina and genital fluids. For more information on STDs, consult your healthcare provider or information provided by government public health agencies.	18.7	12	
Perceived risk reduction for chlamydia infection			85%
Important information: Condoms provide less protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer. For more information, consult your healthcare provider or information provided by government public health agencies.	31.7	12	
Perceived risk reduction for genital herpes			70%
Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. A latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on STD protection, please read the enclosed insert.	37	11.7	
The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however the amount of additional pregnancy protection provided by N-9 has not been measured.	29.4	12	

### Condom use and perception of risk reduction

Reported condom use and perception of risk reduction by condoms among participants who had ever had vaginal sex (N=203) are shown in figure 5. In each plot, the middle 50% or inter-quartile range of the responses falls within the box (between 25<sup>th</sup> and 75<sup>th</sup> quartiles). The ends of the vertical lines or "whiskers" indicate the minimum and maximum data values, but do not extend beyond 1.5 times the inter-quartile range. Points which lie beyond the whiskers are called outliers. Outliers represent extreme values and suggest there may be errors in collecting or reporting data.

Figure 5. Box plots depicting condom use and perception of risk reduction (r.r.) for 100% consistent condom use by pregnancy and STI



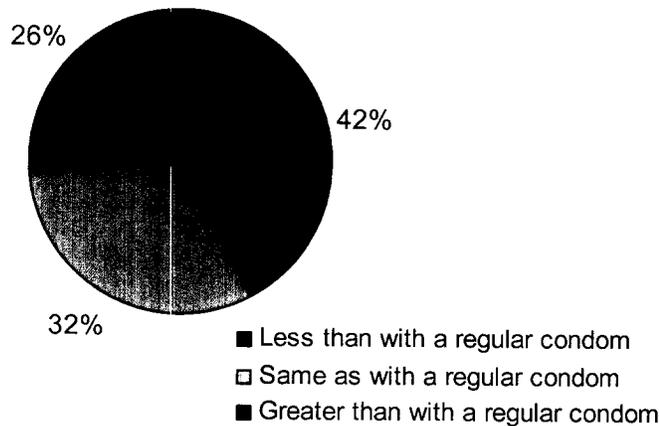
**Table 4. What do people understand by the term "genital fluids"?**

<b>Genital fluid mentioned</b>	<b>Synonyms mentioned</b>	<b>Number of times mentioned</b>
Semen	sperm, seminal fluid, cum, jizz, penial, pre-cum, spugey, monkey potion, love juice, skeet	216
vaginal fluids	vaginal secretion, vaginal juice, girl cum, vaginal fluid, vaginal lube, vaginal discharge, cowpers gland fluid, female secretions, vaginal discharge, vaginal "semen", women's secretion when vagina is excited, woman's natural lubrication, clear vaginal fluid, female ejaculate, female ejaculatory fluid	79
blood	menstrual blood, menstrual products, menstrual fluid	64
urine	piss, pee-pee, pee	62
lubrication/ secretions	discharge, ejaculate, ejaculant, pre-ejaculate	22
pus	puss, "that drippy green stuff when you have gonorrhea"	6
sweat		7
saliva		4
smegma		2
eggs		1
kidney stone		1
anal		1
placenta		1
yeast		1
breast milk		1

#### **Nonoxynol-9 effectiveness**

Study participants were asked to read FDA's proposed statement about risk reduction for pregnancy offered by condoms with N-9 (nonoxynol-9). As shown in figure 6, 42% respondents felt that their risk of pregnancy with consistent use of condoms with N-9 was less than that with consistent use of regular condoms; 32% felt the risk was the same.

**Figure 6. Risk of pregnancy when condoms with N-9 are used**



### **Warning statement**

The survey respondents were asked that if there was space for only one warning statement on the condom foil package, which of the five given statements should appear on the package. Table 5 shows the readability score of each statement and the percentage of respondents that chose the statement. Of the following, statements 1, 3, 4 and 5 are ones proposed by the FDA and statement 2 was proposed by the Medical Institute study team.

### **Effect of education level**

There was no significant association between the education level of the respondents and whether they had ever read all or part of the instructions on the outside of the condom box, those in the package insert, and on the individual foil condom package. There was no significant association between the education level of the respondents and how often they checked the expiration date on the individual foil condom package.

### **Effect of ethnicity**

Ethnic background was significantly associated with ever having had sex ( $p < 0.01$ ), reading instructions and cautions on the outside of the box ( $p < 0.01$ ), and responding to the question on genital fluids ( $p < 0.05$ ); sex of the participants was not significantly associated to these. There were no significant differences in perception of percentage risk reduction after reading the proposed statements according to sex, and ethnicity.

### **Condom expiration date**

Checking the expiration date on the individual foil condom box was associated with whether the respondent had ever had sex ( $p < 0.001$ ). About a third (34%) of the participants that never checked the expiration date on the condom package had also never had penile-vaginal sex. About 38% of those who had ever had sex stated that they rarely or never checked the expiration date on the condom package.

**Table 5. Suggested statements, their readability, and percentage response**

Suggested Statement	Flesch Reading Ease score*	Flesch Kincaid Grade Level score**	Percentage response
1. The nonoxynol-9 (N-9) lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.	28.7	12	39%
2. This condom has nonoxynol-9 (N-9). N-9 can increase the risk of HIV transmission. Do not use this condom if either you or your partner could possibly have HIV. Do not ever use for anal sex.***	65	6.3	35%
3. The spermicide nonoxynol-9 (N-9) can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.	47.1	9.2	6%
4. If you or your partner has HIV/AIDS or if you do not know if you or your partner is infected, you should choose a latex condom without nonoxynol-9 (N-9).	60.7	12	10%
5. You should not use condoms with nonoxynol-9 (N-9) for anal sex. N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.	57.9	8.7	10%

\* **Flesch Reading Ease Score** rates text on a 100-point scale; the higher the score, the easier it is to understand the document. For most standard documents, the aim is for a score of approximately 60 to 70.

The formula for the Flesch Reading Ease score is:  $206.835 - (1.015 \times \text{ASL}) - (84.6 \times \text{ASW})$

where: ASL = average sentence length (the number of words divided by the number of sentences)

ASW = average number of syllables per word (the number of syllables divided by the number of words)

\*\***Flesch-Kincaid Grade Level Score** rates text on a U.S. school grade level. For example, a score of 8.0 means that an eighth grader can understand the document. For most documents, the aim is for a score of approximately 7.0 to 8.0. The formula for the Flesch-Kincaid Grade Level score is:  $(.39 \times \text{ASL}) + (11.8 \times \text{ASW}) - 15.59$

where: ASL = average sentence length (the number of words divided by the number of sentences)

ASW = average number of syllables per word (the number of syllables divided by the number of words)

\*\*\* proposed by MI study team

### **Perceived risk reduction for STIs**

There was a significant positive correlation between percentage condom use and perceived risk reduction for genital herpes ( $p < 0.05$ ). Those participants who used condoms more regularly also thought their risk reduction for getting genital herpes was higher. The perceived risk reduction provided for pregnancy was positively correlated with perceived risk reduction for HIV ( $p < 0.001$ ), chlamydia ( $p < 0.001$ ), and genital herpes ( $p < 0.001$ ). Survey participants who thought their risk reduction provided by condoms for pregnancy was higher also thought they had higher risk reduction for infections like HIV, chlamydia and genital herpes.

Positive correlations were also seen between perceived risk reductions by condoms for HIV and chlamydia ( $p < 0.001$ ), and genital herpes ( $p < 0.001$ ). Participants that thought they had increased HIV risk reduction on condom use also thought condoms had higher risk reduction for chlamydia and genital herpes. There was a positive correlation between perceived risk reduction provided by condoms for chlamydia and for genital herpes ( $p < 0.001$ ).

**Table 6. Correlations in condom use and perceived risk reduction for pregnancy and various STIs**

Correlations	Pearson's r	Sig. (2-sided)
Correlations in those who have previously had penile-vaginal sex:		
% condom use * perceived risk reduction for pregnancy	0.02	NS
% condom use * perceived risk reduction for HIV	0.12	NS
% condom use * perceived risk reduction for chlamydia	0.09	NS
% condom use * perceived risk reduction for genital herpes	0.28*	$p < 0.01$
Correlations for all participants in perceived risk reductions		
pregnancy * HIV	0.66**	$p < 0.001$
pregnancy * chlamydia	0.61**	$p < 0.001$
pregnancy * genital herpes	0.27**	$p < 0.001$
HIV * chlamydia	0.66**	$p < 0.001$
HIV * genital herpes	0.42**	$p < 0.001$
chlamydia and genital herpes	0.56**	$p < 0.001$

\* Significant at 0.01 level

\*\* Significant at 0.001 level

NS= Not significant

## Discussion

Some of the general comments of the survey respondents included calling the label statements "retarded" or "hilarious." For the statements proposed for condoms with N-9, participants felt that the statements that mention anal sex provided better information, and that use of terms such as "greatly reduce", "reduce" and "less protection" did not provide an accurate picture of risk reduction by condoms. In general, survey respondents preferred statements that were easy to understand, detailed, and specific.

The participant's perception of risk reduction after reading the proposed condom label statements were 86% for pregnancy, 85% for HIV, 85% for chlamydia, and 70% for genital herpes (medians reported). These estimates are in most cases (except for HIV) much higher than the reported condom effectiveness in literature.<sup>14</sup> The statements on pregnancy and STI risk reduction were also found to be very difficult to read, and at a minimum of 11<sup>th</sup> grade level comprehension.

The label statements proposed for condoms with N-9 were also difficult to read and between 9-11<sup>th</sup> grade level comprehension. After reading the statements, 74% of the participants stated that they thought risk of pregnancy on using condoms with N-9 was less than or same as with a regular condom. Of the five statements put forward, a

majority of participants chose the FDA proposed statement "The nonoxynol-9 (N-9) lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases." According to the Flesch Reading Ease score, this statement was difficult to understand and to be clearly understood, it would require a 12<sup>th</sup> grade education level according to the Flesch-Kincaid Grade Level scale. The next most popular statement according to the participants was the MI proposed "This condom has nonoxynol-9 (N-9). N-9 can increase the risk of HIV transmission. Do not use this condom if either you or your partner could possibly have HIV. Do not ever use for anal sex." This statement had a score of 65 on the Flesch Reading Ease score (desirable score 60-70), and had a Flesch-Kincaid Grade Level score of 6.3, and could be understood by a person with 6<sup>th</sup> grade education. One reason for the participants' choice was the specific information provided by the statement.

The study was limited due to time considerations with respect to sample size and inadequate ethnic and socioeconomic representation of the national population of 18- to 30-year-olds. The purpose, however, was to get an idea of the comprehension of condom labeling as proposed by FDA by the general public.

### Conclusion

It is important that the condom labels provide clear and specific information to users on risk reduction provided by condoms for pregnancy and various sexually transmitted infections. As condoms are available for purchase over the counter, it is important that condom labels are simple and easy to read.

### References:

- <sup>1</sup> Federal Food, Drug, and Cosmetic Act, as amended through December 31, 2004. US Food and Drug Administration Web site. Available at <http://www.fda.gov/opacom/laws/fdact/fdctoc.htm>. Accessed September 29, 2005.
- <sup>2</sup> US department of health and human services, Food and Drug Administration. Draft guidance for industry and FDA staff: Class II special controls guidance document: Labeling for male condoms made of natural rubber latex, 2005. Available at <http://www.fda.gov/cdrh/comp/guidance/1548.pdf>. Accessed on February 9, 2006.
- <sup>3</sup> US Food and Drug Administration. *Guidance for Industry: Latex Condoms for Men. Information for 510(k) Premarket Notifications: Use of Consensus Standards for Abbreviated Submissions*. July 23, 1998. Available at [http://www.fda.gov/cdrh/ode/92\\_html](http://www.fda.gov/cdrh/ode/92_html).
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- <sup>5</sup> Friedman CP, Romeo D, Hinton SS. Healthcare decisions and product labeling: Results of a consumer comprehension study of prototype labeling for proposed over-the-counter cholestyramine. *Am J Med* 1997; 102: 50-6.
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- <sup>7</sup> The readability of printed materials is measured using scales that are based on sentence length, word count, and polysyllabic word count. The Centers for Disease Control and Prevention (CDC) recommend the SMOG Readability Formula for assessing the readability of health-related materials. Flesch-Kincaid Grade Level Index is another commonly used scale that can be used for single sentences or small paragraphs with less than 10 sentences.

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<sup>8</sup> Most health care materials are written at 10<sup>th</sup> grade level even though most adults read between 8<sup>th</sup> and 9<sup>th</sup> grade level. Richwald GA, Wamsley MA, Coulson AH, Morisky DE. Are Condom instructions readable? Results of a readability study. *Public Health Rep.* 1988 Jul-Aug; 103 (4): 355-9.

<sup>9</sup> Kirsch I, Jungeblut A, Jenkins L, Kolstad A. Adult Literacy in America: a first look at the findings of the national adult literacy survey. Washington, D.C.: National Center for Education statistics, U.S. Department of Education, 1993.

<sup>10</sup> Safer RS, Keenan J. Health Literacy: The gap between physicians and patients. *Am Fam Physician*, 2005 Aug; 72 (3): 463-8.

<sup>11</sup> US Department of Health and Human Services. Food and Drug Administration. Draft guidance for industry and FDA staff: Class II special controls guidance document: Labeling for male condoms made of natural rubber latex, 2005.

<sup>12</sup> IRB ID # 2159

<sup>13</sup> The Flesch Reading Ease Score rates text on a 100-point scale; the higher the score, the easier it is to understand the document. For most standard documents, the aim is for a score of approximately 60 to 70. The Flesch-Kincaid Grade Level Score rates text on a U.S. school grade level. For example, a score of 8.0 means that an eighth grader can understand the document. For most documents, the aim is for a score of approximately 7.0 to 8.0.

<sup>14</sup> National Institutes of Health. Workshop Summary: Scientific Evidence on Condom Effectiveness for Sexually Transmitted Disease Prevention. 2001, July 20. Available at: <http://www.niaid.nih.gov/dmid/stds/condomreport.pdf>. Accessed January 25, 2006.

## APPENDIX A

The Food & Drug Administration (FDA) has proposed new labeling language for condoms. We would like to know what you think these statements mean.

The following survey is entirely voluntary and you can withdraw participation at any time. The survey responses will remain anonymous and completely confidential and the information provided will only be used for research purposes. For participation you will be given a gift certificate worth \$ 7.00.

The **purpose** of this study is to evaluate how easy it is for young adults to understand new condom labels that are being proposed by the FDA.

**If you agree to participate in this study you will be asked to:**

- Complete a survey about the proposed new condom labels; the survey will include questions about age, sex and ethnic background.

**It should take you about 10 minutes to complete the survey.**

**Risks of participation include:**

- Embarrassment due to the sensitive nature of the questions

**Benefits of participation include:**

- The information provided by you and other young adults will be used to help FDA to make a decision on their new condom labels
- Increased awareness on how much risk reduction is provided by condoms for sexually transmitted diseases (STDs) and pregnancy

**Incentive:**

You will receive a \$7 gift certificate for completing the survey.

**Confidentiality:**

The information provided by you will not be linked to your names or other identifying information. The records of this study will be kept confidential and will be used only for research purposes. The information obtained from you will not be accessible to anyone other than the researchers at the Medical Institute, Austin, TX. Any publications will exclude any information that will make it possible to identify you as a participant.

**Contacts and questions:**

Please feel free to ask for more information at any time by getting in touch with us. You can reach us at:

Sheetal Malhotra  
Epidemiologist  
The Medical Institute,  
1101 S Capital of Texas Hwy, B100  
Austin TX 78746  
Ph. 512-328-6268 ext. 206  
E-mail: [smalhotra@medinstitute.org](mailto:smalhotra@medinstitute.org)

**Screening questions:**

A. Are you between the ages of 18 and 30?

- Yes (Go to next question)
- No (Thank and terminate)

B. This survey asks opinions on the information on condom labels. Have you seen an unused condom in its individual foil package or box?

- Yes (Go to survey questions on the next page)
- No (Thank and terminate)

**Statement of Consent**

**I have read the above information and have sufficient information to make a decision about participating in this study. By proceeding to the next question, I consent to participate in the study.**

Please tell us a little about yourself:

1. Age \_\_\_\_\_
2. Sex \_\_\_\_\_
3. Race/ethnicity:
  - White
  - Black
  - Hispanic
  - Native American or Alaskan
  - Asian
  - Other, please specify \_\_\_\_\_
4. How many years of education have you completed? \_\_\_\_\_

Please answer the following questions. The questions are of a personal nature and all responses will be kept confidential.

5. Have you ever had penile-vaginal sex?
  - Yes
  - No
6. Approximately what percentage of times have you used a condom while having penile-vaginal sex? \_\_\_\_\_
7. Did you *ever* read all or part of the instructions and cautions on the **outside of the condom box**?
  - Yes
  - No
8. Did you ever read any of the condom package insert (instructions **inside the box**)?
  - No
  - Yes, I read a little of it
  - Yes, I read about half of it
  - Yes, I read most of it
  - Yes, I read all of it
9. Did you ever read all or part of the instructions and cautions on the **individual foil condom package**?
  - Yes
  - No

10. How often have you checked the expiration date on an individual foil condom package?

- Always (100% of the times)
- Usually (70-90% of the times)
- Sometimes (30-60% of the times)
- Rarely (10-20% of the times)
- Never (0% of the times)

The following sentences are the statements that the FDA proposes to put on the outside of the box.

*Q. # 11 and 12 refer to the following statement*

“When used correctly every time you have sex, latex condoms greatly reduce, but do not eliminate, the risk of pregnancy and the risk of catching or spreading HIV, the virus that causes AIDS.”

11. Based on this statement, if you used condoms every time you had sex, compared to not using condoms at all, how much would it reduce your and your partner’s risk of pregnancy? ((Mark **X** on the following scale, which ranges from 0% (not a tall) to 100% (completely) at the point that indicates your answer)

0.....10.....20.....30.....40.....50.....60.....70.....80.....90.....100%

12. Based on this statement, if you used condoms every time you had sex, compared to not using condoms at all, how much would it reduce your risk of getting HIV? ((Mark **X** on the following scale, which ranges from 0% (not a tall) to 100% (completely) at the point that indicates your answer)

0.....10.....20.....30.....40.....50.....60.....70.....80.....90.....100%

*Q. # 13 refers to the following statement*

“Important information: There are many types of sexually transmitted diseases (STDs) and different ways of catching or spreading infection. A latex condom can reduce the risk of STD transmission to or from the penis. However, some STDs can also be spread by other types of sexual contact. For additional information on STD protection, please read the enclosed insert.”

13. How useful do you find this information about STDs?

- Not at all useful
- Not very useful
- Not sure

- Somewhat useful
- Very useful

*Q. # 14 and 15 refer to the following statement*

“Important information: Latex condoms can reduce the risk of sexually transmitted diseases (STDs), such as chlamydia and gonorrhea, that are spread to or from the penis, by direct contact with the vagina and genital fluids. For more information on STDs, consult your healthcare provider or information provided by government public health agencies.”

14. Based on this statement, if you used condoms every time you had sex, compared to not using condoms at all, about how much would it reduce your risk of getting chlamydia? (Mark **X** on the following scale, which ranges from 0% (not a tall) to 100% (completely) at the point that indicates your answer)

0.....10.....20.....30.....40.....50.....60.....70.....80.....90.....100%

15. List all the genital fluids that you know

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*Q. # 16 refers to the following statement*

“Important information: Condoms provide less protection for certain STDs, including genital herpes and human papillomavirus (HPV) infection, that can also be spread by contact with infected skin outside the area covered by the condom. Condoms cannot protect against these STDs when they are spread in this way. Using latex condoms every time you have sex may still give you some benefits against these STDs. For example, using a condom may lower your risk of catching or spreading genital herpes. Using a condom also may lower your risk of developing HPV-related diseases, such as genital warts and cervical cancer. For more information, consult your healthcare provider or information provided by government public health agencies.”

16. Based on this statement, if you used condoms every time you had sex, compared to not using condoms at all, about how much would it reduce your risk of getting genital herpes? (Mark **X** on the following scale, which ranges from 0% (not a tall) to 100% (completely) at the point that indicates your answer )

0.....10.....20.....30.....40.....50.....60.....70.....80.....90.....100%

*Q. # 17 refers to the following statement*

“The lubricant on this condom contains the spermicide nonoxynol-9 (N-9), which kills sperm; however the amount of additional pregnancy protection provided by N-9 has not been measured.”

17. Based on this statement, if you used condoms with N-9 every time you had sex, your and your partner's risk of getting pregnant is (circle one answer)
- Less than with a regular condom (without N-9)
  - Same as with a regular condom (without N-9)
  - Greater than with a regular condom (without N-9)

18. There is only space for one warning statement on the condom foil package. Please place an **X** next to the one statement that you think should go on the package

\_\_\_\_\_ The nonoxynol-9 (N-9) lubricant on this condom does not protect against HIV/AIDS or other sexually transmitted diseases.

\_\_\_\_\_ This condom has nonoxynol-9 (N-9). N-9 can increase the risk of HIV transmission. Do not use this condom if either you or your partner could possibly have HIV. Do not ever use for anal sex.

\_\_\_\_\_ The spermicide nonoxynol-9 (N-9) can irritate the vagina. This may increase the risk of getting HIV/AIDS from an infected partner.

\_\_\_\_\_ If you or your partner has HIV/AIDS or if you do not know if you or your partner is infected, you should choose a latex condom without nonoxynol-9 (N-9).

\_\_\_\_\_ You should not use condoms with nonoxynol-9 (N-9) for anal sex. N-9 can irritate the rectum and may increase the risk of getting HIV/AIDS from an infected partner.

## **Nonoxynol-9 & STDs, Including HIV**

The Medical Institute for Sexual Health, Austin, Texas

MISH/MCHB/TP – 20050613  
Hendricks, Kate & Malhotra, Sheetal  
13 June 2005, Rev 17-Nov-05

Hendricks, K Malhotra S. Nonoxynol-9 & STDs, including HIV. Austin, TX: Medical Institute of Sexual Health; June 13, 2005. Technical Paper MISH/MCHB/TP-20050613

## Nonoxynol-9 & STDs, Including HIV

In March 2005 the United States Government Accountability Office (GAO) published a report entitled: *HHS Efforts to Research and Inform the Public about Nonoxynol-9 and HIV*.<sup>1</sup> This document reviews both the evaluative and informational efforts of federal agencies concerning the safety and efficacy of nonoxynol-9 (N-9) for reducing the risk of HIV transmission. Unless otherwise referenced, noneditorial statements in our paper are drawn from this GAO report. Since the GAO report stated that "concern about the safety of N-9 in preventing HIV began to surface about 1990," in this paper we also review and summarize randomized controlled trials (RCTs) since that year.

Three federal agencies share responsibility for medical and public health research and drug and device safety and efficacy. These are the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Food and Drug Administration (FDA). The CDC evaluates, funds, and conducts research, and disseminates information to protect and enhance public health. The NIH funds and performs basic and applied research intended to advance both the fields of medicine and public health. The FDA regulates the manufacture and sale, as well as the labeling, of drugs and devices.

By early 1988 approximately 56,000 cases of AIDS had been reported in the United States; more than 31,000 of these resulted in death.<sup>2</sup> That same year, in response to the rising epidemic, the Surgeon General collaborated with the CDC to produce and mail to the American public 107 million brochures about AIDS transmission, risk avoidance, and risk reduction. Included in the brochure section "What Is All The Talk About Condoms?" were the statements "A condom with a spermicide may provide additional protection. Spermicides have been shown in laboratory tests to kill the virus."<sup>3</sup> The *only* spermicide ever sold in the US is N-9.

So what exactly is N-9, how does it work, how is it regulated, why did the Surgeon General think it could help in the AIDS epidemic, and what have we found out about its safety and efficacy since 1988?

N-9 was initially developed as a spermicidal contraceptive and has been sold in the United States for more than half a century in a variety of preparations for vaginal use (creams, gels, foams). Condoms with N-9 have been available since the early 1980s.

N-9 is a detergent that induces motility defects in the spermatozoa.<sup>4</sup> N-9 by itself is classified as an over-the-counter drug; combined with a condom, it is considered a device. Over-the-counter drugs and devices are regulated by two different parts of the FDA and by two different mechanisms. Drugs sold over-the-counter before 1975 were reviewed through a "monograph process" – known within the FDA as an "over-the-counter drug review" (see the GAO report). The process has three steps: (1) an advisory panel reviews data on active ingredients and *provisionally* classifies them as either "safe and effective," "not safe and effective," or "more data needed"; (2) the FDA publishes a draft monograph in the *Federal Register* and reviews comments; and (3) the FDA publishes a final monograph in the *Federal Register*.

In 1980 an advisory panel to the FDA *provisionally* classified N-9 as "safe and effective." In 1995 the FDA called for additional research. Currently, the FDA is reviewing a large National Institute of Child Health and Development-funded study of N-9.<sup>5</sup> The trial was intended to evaluate both the safety and efficacy of N-9 as a contraceptive. Just over 1,500 18- to 40-year-old women were randomly assigned to use either (a) one of three gels (~50, 100, or 150 mg of N-9); (b) a film (100 mg of N-9); or (c) a suppository (100 mg of N-9). From 10% - 22% of women became pregnant within six months of typical use of the various formulations. Over a seven-month period, 11% to 14% had urinary tract infections; 8% to 12% had bacterial vaginosis; 13% to 17% had candidal infections; and 19% to 26% complained of vulvar or vaginal irritation without concurrent infection. The incidence of STIs such as chlamydia or gonorrhea were not assessed as part of the study. The authors of the study concluded that N-9 was safe - but less effective than other "modern" contraceptives. The FDA has yet to make and publish a final ruling on the safety and efficacy of N-9 as a vaginal contraceptive.

Condoms are regulated as devices. The term "device" covers everything from simple tongue depressors to implanted devices such as pacemakers. Devices fall into three Classes - I, II, or III. Very low risk devices such as bandages are categorized as Class I and require only simple measures - general controls - such as registration, quality controls for manufacturing, truthful branding, and reporting of adverse events. Condoms are Class II devices. In addition to general controls, Class II devices *may* require "special controls" such as performance standards, surveillance, or clinical studies. At present, condoms, along with many other Class II devices marketed prior to 1976, have no special controls. They are, however, subject to three specific labeling requirements: (1) The "principal [*sic*] display panel" must include a statement about intended action(s); (2) an expiration date must appear; and (3) the label must carry a warning about allergic reactions to natural rubber latex.<sup>6</sup> As previously mentioned, condoms *with* N-9 are also classified as devices, and are thus subject to looser regulations than N-9 alone.

So why did the federal government think that N-9 might be useful in the fight against AIDS? It is difficult to say *exactly* why health officials in the federal government held this view, but they may have been influenced by a few clinical studies published during the late 1980s that suggested efficacy against gonorrhea and chlamydia<sup>7</sup> and one *in vivo* study that looked at N-9 and HIV.<sup>8</sup> In 1988 researchers in Denver - in recognition that prudence called for skepticism of condoms as a sole means of STI prevention - published a laboratory-based evaluation of condoms with and without N-9 as physical and chemical barriers to a variety of STIs, including HIV. HIV was inactivated during simulated "intercourse" in 20 separate runs with (N = 10) and without (N = 10) purposeful "rupture" of condoms.

Table 1 summarizes the information provided to the public and health professionals by the CDC and the FDA from 1990 through 2004. From 1993 through 1998, CDC's statements intended for the public or health professionals were, at best, ambiguous.

**Table 1. Selected Events and Publications Related to N-9's Potential Use as a Microbicide: 1990 - 2004<sup>9</sup>**

Year	CDC	FDA
1990		brochure <sup>10</sup> states "Some experts believe nonoxynol-9 may kill the AIDS virus during intercourse, too. So you might want to use a spermicide along with a latex condom as an added precaution..."
		magazine article <sup>11</sup> states "Although it has not been scientifically proven, it is possible that nonoxynol-9 may reduce the risk of transmission of the AIDS virus during intercourse..."
1993	MMWR <sup>12</sup> states "No reports indicate that nonoxynol-9 used alone without condoms is effective for preventing sexual transmission of HIV...No data exist to indicate that condoms lubricated with spermicides are more effective than other lubricated condoms in protecting against the transmission of HIV infection.... Therefore, latex condoms with or without spermicides are recommended."	
	STD treatment guidelines <sup>13</sup> state that "protection of women against HIV infection should not be assumed from the use of vaginal spermicides, vaginal sponges, or diaphragms."	
1997	publication <sup>14</sup> states "CDC does not recommend using spermicide alone to prevent HIV infection."	
1998	STD treatment guidelines <sup>15</sup> state that "vaginal spermicides offer no protection against HIV infection, and spermicides are not recommended for HIV prevention . . . the consistent use of condoms, with or without spermicidal lubricant or vaginal application of permicide is recommended."	
		magazine article <sup>16</sup> state "The spermicide nonoxynol-9, used in some condoms, has been shown to be effective as a contraceptive, and may reduce the risk of transmitting certain STDs. But the spermicide has not been proven to prevent sexual transmission of HIV."
		magazine article <sup>17</sup> states "... spermicides alone... do not give adequate protection against HIV and other STDs."
1999		website <sup>18</sup> states "Some experts believe nonoxynol-9 may kill the AIDS virus during intercourse, too. So you might want to use a spermicide along with a latex condom as an added precaution..."
2000	halts' all studies actively pursuing N-9's use as a microbicide	
	letter <sup>19</sup> issued to health care providers and public health personnel states that because N-9 has been shown to be ineffective against HIV and may increase HIV risk among certain user groups, N-9 should not be recommended for HIV prevention	
2002	report in MMWR <sup>20</sup> states "Sexually active women should consider their individual HIV/STD infection risk when choosing a method of contraception. Providers of family planning services should inform women at risk for HIV/STDs that N-9 contraceptives do not protect against these infections."	
	STD treatment guidelines <sup>21</sup> state "Recent evidence has indicated that vaginal spermicides containing nonoxynol-9 (N-9) are not effective in preventing...HIV infection. Thus, spermicides alone are not recommended for STD/HIV prevention. Frequent use of spermicides containing N-9... may be associated with an increased risk of HIV	

Year	CDC	FDA
	<i>transmission...Purchase of any additional condoms lubricated with the spermicide N-9 is not recommended...</i>	
2003		removed 1999 statement from website
2004		proposed warning labels <sup>22</sup> state that vaginal contraceptive products with N-9 do not protect against HIV or other STDs and that frequent use of N-9 can increase vaginal irritation, which may increase the risk of contracting HIV or other STDs. The warnings also indicated that the labeled products were for vaginal use only.

### \* NIH and CDC

#### Source:

- 1 HHS: *Efforts to Research and Inform the Public about Nonoxynol-9 and HIV*. GAO Report [serial online]. March 2005.
- 2 Food and Drug Administration. *Condoms and STDs...Especially AIDS* [brochure online].
- 3 Latex condoms lessen risks of STDs. *FDA Consumer* [serial online]. 1990.
- 4 Update: barrier protection against HIV infection and other sexually transmitted diseases. *MMWR* [serial online].
- 5 1993 Sexually transmitted diseases treatment guidelines. *MMWR* [serial online]. 1993.
- 6 What we know about nonoxynol-9 for HIV and STD prevention. *CDC Update*. April 1997.
- 7 1998 guidelines for treatment of sexually transmitted diseases. *MMWR* [serial online]. 1998.
- 8 Condoms: barriers to bad news. *FDA Consumer* [serial online]. 1998.
- 9 On the teen scene: preventing STDs. *FDA Consumer* [serial online]. 1993.
- 10 *Condoms and STDs...Especially AIDS* [brochure online].
- 11 *Dear Colleague Letter*. August 4, 2000 [online].
12. Nonoxynol-9 spermicide contraception use - United States, 1999. *MMWR* [serial online]. 2002.
- 13 Centers for Disease Control and Prevention. Sexually transmitted disease treatment guidelines 2002. *MMWR* [serial online]. 2002.
- 14 *FDA Proposes New Warnings for Over-the-Counter Contraceptive Drugs Containing Nonoxynol-9*. January 16, 2003. Talk Paper

Even though some statements in 1993 and 1998 clearly stated that there was no evidence that N-9 reduced the risk for HIV, spermicide use (ie, N-9) was still recommended (ie, "...condoms with or without spermicides are recommended [1993]" and "...the consistent use of condoms, with or without spermicidal lubricant or vaginal application of spermicide is recommended [1998]"). It was not until 2000 that CDC warned healthcare professionals that N-9 might actually increase HIV risk. FDA statements to the public throughout the 1990s and up through 2003 appear to have been based solely on the thoughts or feelings of "some experts" who suggested that N-9 might kill the AIDS virus and provide other added benefits to the user. It wasn't until 2003 that the FDA warned the public that N-9 could increase HIV risk.

Because the GAO report states that "concern about the safety of N-9 in preventing HIV began to surface about 1990," we reviewed and summarize randomized controlled trials (RCTs) published since that year (Table 2). In this table, we indicate by a "+" sign that N-9 had a significant beneficial effect on the outcomes of interest; by a "-" sign that N-9 had a significant harmful effect; or by a "0" sign, that it had no effect. After excluding meta-analyses, we were able to identify 12 randomized controlled trials of N-9 that (1) were published since 1990; and (2) evaluated either STIs, including HIV, or macroscopic or microscopic vaginal lesions. Eleven of the trials compared N-9 to a placebo - usually a vaginal moisturizer - and women were generally encouraged to use, or to continue to use, condoms; one trial compared condoms with N-9 to plain condoms. Most of the female participants were prostitutes.

Of the eight studies that separately evaluated chlamydia and gonorrhea, no effect on either STI was observed in seven and no effect on chlamydial infections and an increased risk for gonorrhea was observed in the eighth study. One study out of Thailand looked at cervical infections – defined as chlamydia *or* gonorrhea; no significant effect was observed. Two to four studies evaluated whether N-9 affected syphilis, bacterial vaginosis, or candidiasis; no effect was observed in any. All six studies that evaluated trichomoniasis showed no effect. Nine studies evaluated epithelial disruption, visible lesions, or both. Although most showed no effect, two showed significantly more epithelial disruption in the N-9 group, and one of these two also showed significantly more lesions. Seven studies evaluated HIV infection. Although the first five found no effect, HIV risk was actually increased in N-9 users in the last two that were performed.<sup>33,34</sup> This increased risk was particularly apparent in the women who used N-9 (52.5 mg gel) more than 3.5 times per day.

**Table 2. Randomized Controlled Trials of N-9 for STI prevention, 1990 – 2004**

Study (Year)	HIV	Chlam	GC	GC or Chlam	Syph	Trich	Vaginosis	Candida	Epith Disrupt	Visible Lesion
Niruthisard (1992) <sup>23</sup>				0						
Kreiss (1992) <sup>24</sup>	0	0	0			0			-	
Martin (1997) <sup>25</sup>									0	0
Van Damme (1998) <sup>26</sup>									0	
Roddy (1998) <sup>27</sup>		0	0			0		0		
Roddy (1998) <sup>28</sup>	0	0	0						0	
Rustomjee (1999) <sup>29</sup>	0	0	0		0	0			0	0
Van Damme (2000) <sup>30</sup>									0	0
Richardson (2001) <sup>31</sup>	0	0	-		0	0	0	0		0
Roddy (2002) <sup>32</sup>	0	0	0							
Van Damme (2002) <sup>33</sup>	-	0	0		0	0		0	0	0
Hoffman (2004) <sup>34</sup>	-	0	0		0	0	0	0	-	-

0 = outcome was included in study, but no significant effect observed for N-9 vs. placebo

- = outcome was included in study, and N-9 appeared to be harmful

+ = outcome was included in study, and N-9 appeared to be beneficial

We were unable to find any epidemiological studies that evaluated N-9 as either a protective or risk factor for HIV acquisition when used during anal intercourse. There are, however, publications suggesting that, as late as 2003, many men who have sex with

men (MSM) "believed" that N-9 was of some benefit for this activity and were still using it as a lubricant.<sup>35</sup> Given that some studies *have shown* an increase in vaginal lesions, and that use during anal intercourse was always "off label," it would seem prudent to advise against any use during anal intercourse. And indeed - recent reports by the CDC, the World Health Organization (WHO), and the Contraceptive Research and Development Program - suggested that N-9 not be used at all during anal intercourse.<sup>20</sup>

In conclusion, **with frequent use, N-9 appears to increase rather than decrease the risk of HIV infection.** In our opinion, N-9 should not be used at all, for contraceptive or any other purpose, by *anyone* who is at risk for HIV infection. This would include *anyone* with multiple partners.

It is understandable when government officials in the early throes of a deadly outbreak (such as anthrax, SARS, or AIDS in humans or hoof and mouth disease or bovine spongiform encephalopathy in animals) make *interim recommendations* that lack a sound basis in evidence. Officials are, after all, expected to *do something* to protect the public's health. And when new diseases first emerge, there isn't much evidence on which to base recommendations. It is, however, unacceptable for these heat-of-the-moment recommendations to be perpetuated *ad infinitum* without a basis in evidence. In the case of N-9, multiple studies in the 1990s failed to show a beneficial effect. Data from these negative studies should have triggered officials to drop all suggestions that the public use a spermicide (N-9) for HIV prevention.

## References

<sup>1</sup> US General Accountability Office. *HHS: Efforts to Research and Inform the Public about Nonoxynol-9 and HIV*. GAO Report [serial online]. March 2005. Publication GAO-05-399. Available at: <http://www.gao.gov/new.items/d05399.pdf>. Accessed May 30, 2005.

<sup>2</sup> Maikhuri JP, Dwivedi AK, Dhar JD, Setty BS, Gupta G. Mechanism of action of some acrylophenones, quinolines and dithiocarbamate as potent, non-detergent spermicidal agents. *Contraception*. 2003;67:403-408.

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