Contains Nonbinding Recommendations

Guidance for Industry

User Labeling for Devices that Contain Natural Rubber (21 CFR 801.437); Small Entity Compliance Guide; Guidance for Industry

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance

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Preface

Public Comment

Comments and suggestions may be submitted at any time for Agency consideration to Dockets Management Branch, Division of Management Systems and Policy, Office of Human Resources and Management Services, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD, 20852. When submitting comments, please refer to the exact title of this guidance document. Comments may not be acted upon by the Agency until the document is next revised or updated.

For questions regarding the use or interpretation of this guidance contact John J. Farnham, Office of Compliance, Center for Devices and Radiological Health (HFZ-332), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301-594-4616.

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This guidance represents 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.

Introduction

This guidance is intended to help manufacturers of medical products that contain natural rubber latex, the majority of whom are small businesses. This guidance addresses specific federal regulations for labeling medical products that contain natural rubber latex. This guidance does not apply to products made from synthetic latex or synthetic rubber that do not include natural rubber in their formulations.

FDA has noted an increase in the number of deaths reported to the agency that are associated with an apparent sensitivity to natural latex proteins contained in medical devices. FDA's initial focus involved deaths following barium enema procedures that were associated with anaphylactic reactions to the natural rubber latex cuff used on the tip of barium enema catheters. Scientific studies and case reports have documented sensitivity to natural latex proteins found in a wide range of medical devices. In order to protect the public health and minimize the risks associated with the use of natural latex protein sensitivity, FDA has developed a labeling regulation that provides important information to individuals who are sensitive to natural latex proteins. This rule was published in the Federal Register of September 30, 1997 (62 FR 51029). This rule was codified in Title 21 of the Code of Federal Regulations (21 CFR 801.437) and became effective on September 30, 1998.

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.

The Least Burdensome Approach

The issues identified in this guidance document represent those that we believe need to be addressed before your device can be marketed. In developing the guidance, we carefully considered the relevant statutory criteria for Agency decision-making. We also considered the burden that may be incurred in your attempt to comply with the guidance and address the issues we have identified. We believe that we have considered the least burdensome approach to resolving the issues presented in the guidance document. If, however, you believe that there is a less burdensome way to address the issues, you should follow the procedures outlined in the "A Suggested Approach to Resolving Least Burdensome Issues" document. It is available on our Center web page at: http://www.fda.gov/cdrh/modact/leastburdensome.html

Summary of the Regulation

The final rule identifies specific labeling statements for use on medical devices and device packaging when they contain natural rubber that contacts humans. The kind of latex and use of the latex, either for a device or for packaging, is associated with specific labeling information, as follows:

- labeling of medical devices containing natural rubber latex that contacts humans should state: "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.";
- labeling of medical devices containing dry natural rubber that contacts humans should state: "This Product Contains Dry Natural Rubber.";
- labeling of medical devices containing natural rubber latex in their packaging that contacts humans should state: "Caution: The Packaging of This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.";
- labeling of medical devices containing dry natural rubber in their packaging that contacts humans should state: "The Packaging of This Product Contains Dry Natural Rubber.";
- and the claim of hypoallergenicity should be removed from the labeling of medical devices that contain natural rubber.

Questions and Answers on the Rule

1. To which devices does this rule apply?

The rule applies to all medical devices composed of or containing, or having packaging or components that are composed of, or contain, natural rubber that contacts humans. The term "natural rubber" includes natural rubber latex, dry natural rubber, and synthetic latex or synthetic rubber that contains natural rubber in its formulation.

2. What is natural latex?

"Natural latex," for the purposes of this rule, is defined as a milky fluid that consists of extremely small particles of rubber obtained from plants, principally from the H. *brasiliensis* (rubber) tree, dispersed in an aqueous medium. It contains a variety of naturally occurring substances, including cis-1,4-polyisoprene in a colloidal suspension and plant proteins, which are believed to be the primary allergen.

3. What is natural rubber?

"Natural rubber," for the purposes of this rule, includes all materials made from or containing natural latex. Products that contain natural rubber are made using two commonly employed manufacturing processes, the natural rubber latex (NRL) process, and the dry natural rubber (DNR) process**.**

4. What is the NRL manufacturing process?

The NRL manufacturing process involves the use of natural latex in a concentrated colloidal suspension. Products are formed from natural rubber latex by dipping, extruding, or coating, and are typically referred to as containing or made of "natural rubber latex." Examples of products that may contain natural rubber latex include medical gloves, catheters, tracheostomy tubes, and condoms.

5. What is the DNR manufacturing process?

The DNR manufacturing process involves the use of coagulated natural latex in the form of dried or milled sheets. Products are formed from dry natural rubber by compression molding, extrusion, or by converting the sheets into a solution for dipping. These products are typically referred to as containing or made of dry natural rubber or ``crepe'' rubber. Examples of

products that may contain dry natural rubber include syringe plungers, vial stoppers, and injection ports on intravascular tubing.

6. What does the phrase "contains natural rubber" mean in this rule?

A device "contains natural rubber," for the purposes of this rule, when the device is composed of natural rubber or the device contains components formulate from natural rubber. The phrase, "contains natural rubber," as used herein, also includes products described as made of "synthetic latex" or "synthetic rubber" that include natural rubber in their formulations. Synthetic latex or synthetic rubber that does not include natural rubber in its formulation is not subject to this rule.

7. What does the phrase "contacts humans" mean for the purpose of this rule?

"Contacts humans," for the purposes of this rule, means that the natural rubber contained in a medical device is intended to contact or is likely to contact the user or patient. This includes contact when the natural rubber containing device is connected to the patient by a liquid path or an enclosed gas path; or the natural rubber containing device is powdered, and the powder may carry natural latex proteins that may contaminate the environment of the user or patient.

8. What labeling statements does the rule specify?

The device may bear one or more of four labeling statements depending on the type of natural rubber in the device and depending on whether the natural rubber is in the device itself or in its packaging.

(a) Medical devices containing rubber produced by the NRL process that contacts humans should bear labeling with the following statement in bold print:

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

Representative examples of devices that contain NRL include: Cuffed enema/enterolysis catheters, latex condoms (with or without spermicidal lubricant), wound drains, cuffed airways, latex surgical gloves, and latex examination gloves.

(b) Medical devices containing rubber produced by the DNR process that contacts humans should include the following statement in bold print in their labeling:

"This Product Contains Dry Natural Rubber."

Representative examples of devices that contain DNR include: Anesthesia masks, electrode pads, contraceptive diaphragms, crutch pads and tips, wheelchair tires, elastic components of bandages, face masks, syringe plungers, parenteral drug vial stoppers, and intravenous injection ports.

(c) Medical devices having packaging that contains natural rubber that contacts humans should bear labeling with one of the following statements as appropriate in bold print:

> **"Caution: The Packaging of This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions."**

OR

> **"The Packaging of This Product Contains Dry Natural Rubber**."

The purpose of such statements is to inform individuals who are sensitive to natural rubber about the presence of natural rubber in the packaging of devices that may be, by themselves, natural rubber-free.

(d) Medical devices containing natural rubber latex should be labeled with the following statement in bold print:

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

This statement is also identified for use if a device contains both natural rubber latex and dry natural rubber that may contact humans. In this instance, the single statement will serve to advise a person who may not be aware that natural rubber may cause reactions and provide notice to a person who is aware of his or her sensitivity to natural rubber contained in the product.

9. Is there a labeling statement that may not be acceptable under this rule?

Devices containing natural rubber that contact humans should not contain the term "hypoallergenic"' on their labeling. FDA has determined that the term "hypoallergenic" on products containing natural rubber would likely mislead consumers to conclude erroneously that the product may not cause latex protein allergic reactions.

10. How should this information be displayed in the labeling?

Because of the importance of the labeling information for those individuals sensitive to natural latex proteins, the inclusion of the latex labeling information on each level of labeling increases the likelihood that consumers will be aware of the risks posed by the natural rubber in the product. This means that the latex labeling information should be prominently and legibly displayed on all device labeling; the principal display panel of the device packaging; the outside package; the container or wrapper; the immediate device package; the container or wrapper; and the device label.

For example, the labeling statement for adhesive bandages that are individually wrapped and sold in a box would appear on each individually wrapped bandage, on the box, and on any individual pieces of labeling, such as an "instructions for use" sheet included in the box. Devices packaged and sold in bulk dispensing containers would display the appropriate statement on the dispensing container, as it is the immediate device container or package.

11. May I request an exemption or variance from this rule?

Any affected person may request an exemption or variance from the requirements of this section by submitting a citizen petition in accordance with federal regulations that explain the citizen petition procedures in Title 21 CFR Sec. 10.30 of this chapter.

12. Who may I contact for further information on this rule?

You may contact John J. Farnham, Center for Devices and Radiological Health (HFZ-332), Food and Drug Administration, 2098 Gaither Rd., Rockville, MD 20850, 301-594-4616.