DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAR 12 2001

Mr. Gerry Pukach
Regulatory Affairs Manager
Cintas Corporation
7247 National Drive
Hanover, Maryland 21076

Re: Docket #00P-1657

Dear Mr. Pukach:

This is in response to your petition dated November 30, 2000, that requested a variance from the labeling regulation for natural rubber-containing medical devices, incorporated in 21 CFR 801.437.

Your petition requested that boxes of adhesive bandages, assembled by Cintas from various bandages provided by Cintas' suppliers, be labeled with the alternate statement, "...product *may* contain natural rubber latex ...," or "...*may* contain dry natural rubber." You requested these alternate statements on the grounds that maintaining two separate stocks of labeled boxes, one for latex-containing bandages and one for non-latex bandages, may cause you to make labeling errors. In addition, you have anticipated an increase in cost to the consumer.

We are denying your request for such alternate labeling because it is not consistent with the intent of the regulation. The preamble of the final rule clearly explains that the retail packages of adhesive bandages require specific information about natural rubber latex or dry natural rubber on the labels of both the outer and individual packages. (See 62 Federal Register 51021 at 51027, copy enclosed.)

We believe that the label statement on the outer bandage box provides information to the purchaser/dispenser of the product. The label on the individual bandage wrappers provides information to the user in the event the product becomes separated from the outer box, which is customary in many medical care facilities.

The latex labeling regulation serves two purposes. First it provides a cautionary statement regarding latex reactions. Second, it ensures that devices that contain natural latex or dry rubber are identified clearly. The statement that the product "may contain" latex or dry natural rubber does not fulfill the second requirement. Furthermore, your suggestion that a user should read the individual package for latex information does not meet the intent of the rule to provide this information on the product package prior to purchase or distribution.

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Finally, we wish to remind you that sterile bandages are not exempt from the Good Manufacturing Practice requirements, described in 21 CFR 820. Specifically, section 820.120 requires that manufacturers "... control labeling and packaging operations to prevent labeling mixups." The controls needed for two versions of the required labeling are minimal and can be implemented easily by your firm.

I hope this response has been helpful.

Sincerely yours,

Linda S. Kahan
Deputy Director for Regulations Policy
Center for Devices and
Radiological Health

Enclosure
62 FR 51021 for Docket No. 96N-0119

"significant regulatory action" under Executive Order 12866; (2) is not a "significant rule" under DOT Regulatory Policies and Procedures (44 FR 11034, February 26, 1979); and (3) will not have a significant economic impact, positive or negative, on a substantial number of small entities under the criteria of the Regulatory Flexibility Act. A copy of the final evaluation prepared for this action is contained in the rules docket. A copy of it may be obtained by contacting the rules docket at the location provided under the caption **ADDRESSES**.

List of Subjects in 14 CFR Part 39

Air transportation, Aircraft, Aviation safety, Incorporation by reference, Safety.

Adoption of the Amendment

Accordingly, pursuant to the authority delegated to me by the Administrator, the Federal Aviation Administration amends part 39 of the Federal Aviation Regulations (14 CFR part 39) as follows:

PART 39—AIRWORTHINESS DIRECTIVES

1. The authority citation for part 39 ontinues to read as follows:

Authority: 49 USC 106(g), 40113, 44701.

§39.13 [Amended]

2. Section 39.13 is amended by adding a new airworthiness directive (AD) to read as follows:

97-20-11 Socata—Groupe Aerospatiale: Amendment 39-10148; Docket No. 97-CE-15-AD.

Applicability: Model TBM 700 airplanes (serial numbers 1 through 109), certificated in any category, that do not have the main landing gear (MLG) inboard doors and the door locking control mechanism removed (MOD 70-065-32) in accordance with the Technical Instruction of Modification OPT70 KO59-32, dated December 1995, as referenced in Socata Service Bulletin (SB) 70-073, Amdt. 1, dated June 1996.

Note 1: This AD applies to each airplane identified in the preceding applicability provision, regardless of whether it has been modified, altered, or repaired in the area subject to the requirements of this AD. For airplanes that have been modified, altered, or repaired so that the performance of the requirements of this AD is affected, the owner/operator must request approval for an alternative method of compliance in accordance with paragraph (d) of this AD. The request should include an assessment of the effect of the modification, alteration, or repair on the unsafe condition addressed by this AD; and, if the unsafe condition has not been eliminated, the request should include specific proposed actions to address it.

Compliance: Required within the next 100 hours time-in-service after the effective date of this AD or within the next 6 calendar months after the effective date of this AD, whichever occurs first, unless already accomplished.

To prevent the MLG from failing to extend because of corroded MLG inboard locking hinges, which could result in loss of control of the airplane during landing operations, accomplish the following:

(a) Remove the MLG inboard doors and the door locking control mechanism (MOD 70-065-32) in accordance with the Technical Instruction of Modification OPT70 KO59-32, dated December 1995, as referenced in Socata SB 70-073, Amdt. 1, dated June 1996.

(b) As of the effective date of this AD, no person may undo MOD 70-065-32 on any affected airplane, by reinstalling the MLG inboard doors and the door locking control mechanism.

(c) Special flight permits may be issued in accordance with sections 21.197 and 21.199 of the Federal Aviation Regulations (14 CFR 21.197 and 21.199) to operate the airplane to a location where the requirements of this AD can be accomplished.

(d) An alternative method of compliance or adjustment of the compliance time that provides an equivalent level of safety may be approved by the Manager, Small Airplane Directorate, FAA, 1201 Walnut, suite 900, Kansas City, Missouri 64106. The request shall be forwarded through an appropriate FAA Maintenance Inspector, who may add comments and then send it to the Manager, Small Airplane Directorate.

Note 2: Information concerning the existence of approved alternative methods of compliance with this AD, if any, may be obtained from the Small Airplane Directorate.

(e) The removal required by this AD shall be done in accordance with the Technical Instruction of Modification OPT70 KO59-32, dated December 1995, as referenced in Socata Service Bulletin 70-073, Amdt. 1, dated June 1996. This incorporation by reference was approved by the Director of the Federal Register in accordance with 5 U.S.C. 552(a) and 1 CFR part 51. Copies may be obtained from Socata—Groupe Aerospatiale, Socata Product Support, Aeroport Tarbes-Ossun-Lourdes, B P 930, 65009 Tarbes Cedex, France; or the Product Support Manager Socata—Groupe Aerospatiale, North Perry Airport, 7501 Pembroke Road, Pembroke Pines, Florida 33023. Copies may be inspected at the FAA, Central Region, Office of the Regional Counsel, Room 1558, 601 E. 12th Street, Kansas City, Missouri, or at the Office of the Federal Register, 800 North Capitol Street NW., suite 700, Washington, DC.

(f) This amendment (39-10148) becomes effective on November 13, 1997.

Issued in Kansas City, Missouri, on September 24, 1997.

Henry A. Armstrong,

Acting Manager, Small Airplane Directorate, Aircraft Certification Service.

[FR Doc. 97-25832 Filed 9-29-97; 8:45 am]

BILLING CODE 4910-13-U

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96N-0119]

21 CFR Part 801

Natural Rubber-Containing Medical Devices; User Labeling

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule requiring labeling statements on medical devices, including device packaging containing natural rubber that contacts humans. The rule requires labeling of medical devices containing natural rubber latex that contacts humans to state: "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions."; labeling of medical devices containing dry natural rubber that contacts humans to state: "This Product Contains Dry Natural Rubber."; labeling of medical devices containing natural rubber latex in their packaging that contacts humans to 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 to state: "The Packaging of This Product Contains Dry Natural Rubber."; and that the claim of hypoallergenicity be removed from the labeling of medical devices that contain natural rubber. These requirements are being established in response to numerous reports of severe allergic reactions and deaths related to a wide range of medical devices containing natural rubber.

EFFECTIVE DATE: This final rule is effective September 30, 1998.

FOR FURTHER INFORMATION CONTACT: Donald E. Marlowe, Center for Devices and Radiological Health (HFZ-100), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20850, 301-443-2444, FAX 301-443-2296.

SUPPLEMENTARY INFORMATION:

I. Background

Natural latex is a milky fluid obtained in commercial quantities primarily from the *Heavea brasiliensis* (rubber) tree. There is often confusion concerning the terminology used to describe the raw agricultural materials derived from rubber-producing plants; products made from various intermediate forms of the

incorrectly implies that such device may be used safely by persons sensitive to natural latex proteins. For these reasons, FDA is requiring that the hypoallergenic claim be removed from the labeling of devices that contain natural rubber.

C. Effects of This Regulation on Premarket Submission Requirements

FDA will not require a new submission under section 510(k) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 360(k)) based upon labeling changes made to comply with this rule, provided that no other changes requiring a new 510(k) submission under 21 CFR 807.81 are made to the device. Devices subject to an approved premarket approval application, however, must submit any change to the device labeling that is required by this rule in the next interim report under 21 CFR 814.39(e). Combination products that have device and drug components but are regulated under drug premarket approval provisions shall indicate the labeling change in a supplement for changes that may be made before FDA approval, as required by 21 CFR 314.70(c). Combination products that have device and biological components, but that are regulated under the biologic premarket approval provisions, shall inform the agency of the labeling change in the manner described under 21 CFR 601.12.

III. Summary of Comments

The agency received 62 comments, all of which supported the principle of natural rubber labeling for the protection of natural rubber sensitive individuals. The comments, however, differed greatly in their specific approaches.

1. A few comments suggested using the term "crepe rubber," instead of "dry rubber," and suggested using the term "synthetic rubber" instead of "synthetic latex."

The agency agrees that "synthetic rubber" should be used to describe components of certain natural rubber products covered by this regulation and has added that term in the definition of "natural rubber" in § 801.437(b) (21 CFR 801.437(b)). Although the agency has discussed the meaning of crepe rubber in the preamble to this regulation, the agency does not agree that the term "crepe rubber" should be used in place of "dry natural rubber" in the regulation because the agency believes the term "dry natural rubber" is the term most commonly used to describe rubber manufactured by the DNR process.

2. One comment pointed out that there are other sources of natural rubber besides that identified in the preamble of the proposed rule, the *H. brasiliensis* tree.

The agency agrees and has clarified in the preamble of this regulation that there are other sources of plant-derived natural rubber used in the manufacture of devices that are subject to this rule. The preamble notes that the *H. brasiliensis* tree is the primary source of commercial natural latex, instead of the only source.

3. Several comments claimed that there is no information to suggest that dry natural rubber has caused allergic reactions in individuals sensitive to natural latex proteins; therefore, dry natural rubber should not be included in the labeling requirement.

The agency recognizes that there are lower levels of natural latex proteins in products produced by the dry natural rubber process. The agency, however, does not agree that there is no information to suggest that dry natural rubber has caused allergic reactions in individuals sensitive to natural latex proteins. To the contrary, there are numerous reports that levels of natural latex proteins found in dry rubber can cause allergic reactions (Refs. 24 through 27). Accordingly, the agency has concluded that it is in the best interest of the public health to provide labeling information that a product contains dry natural rubber, so that individuals who are sensitive to the levels of natural latex proteins found in dry natural rubber may make an informed decision regarding the use of the product.

While the agency believes that persons who may respond to the levels of natural latex proteins found in dry natural rubber need to be informed of the dry rubber content in a device, the agency does not believe that those individuals need to be informed of the health consequences associated with dry natural rubber. Because allergy is a dose-response phenomenon, persons who may react to natural latex protein levels found in dry rubber would have already experienced previous allergic reactions to the higher levels of natural latex proteins found in natural rubber latex products (see Ref. 28). Therefore, those individuals would generally be aware that dry natural rubber may cause them to suffer an allergic reaction. Accordingly, FDA is requiring that products that contain only dry rubber have labeling that informs consumers of the dry rubber content, but is not requiring that such products bear labeling that states the potential health consequences from the use of the product. Therefore, FDA is requiring in the final regulation, § 801.437(e), that devices that contain dry natural rubber bear labeling with the following statement: "This Product Contains Dry Natural Rubber."

Persons who would not react to the levels of natural latex proteins found in dry rubber, but would react to the higher levels of natural latex proteins found in natural rubber latex products, however, may never have been aware of previous allergic reactions (Ref. 28). These persons, therefore, need to be advised of the potential health consequences of natural rubber latex products. Accordingly, FDA is requiring products containing natural rubber latex to carry labeling that states the potential health consequences of such products, as well as a natural rubber latex content statement. Therefore, FDA is requiring in the final regulation, § 801.437(d), that devices containing natural rubber latex have labeling with the following statement in bold print: "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions."

This statement is also required 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 will also advise a person who is aware of his or her sensitivity to natural rubber that the product contains an ingredient that may cause a reaction.

4. Some comments claimed that the applicability of the labeling statement to devices that contain natural rubber "that may directly or indirectly contact humans" is overly broad. One comment suggested that the labeling statement be required only on devices that have an "intended use" that may lead to contact with humans. Other comments suggested the statement be limited to devices which would directly contact tissues.

The agency does not believe that the application of the labeling statement to devices that contain natural rubber "that may directly or indirectly contact humans" is overly broad. Latex proteins may elicit an allergic reaction in individuals who are sensitive to natural rubber, even if the proteins are introduced to the individual through an indirect route. The agency, however, recognizes that the term "indirect contact" may be interpreted more broadly than the agency intends. Therefore, in order to avoid confusion, the agency has modified the regulation to require the labeling statements only if the natural rubber contacts humans. The final regulation, § 801.437(b), defines the term "contacts humans" to mean that the natural rubber contained

its packaging, beyond that found in the adhesive (e.g., a device packaged in a latex sheath) is likely to contact the user or patient and must be labeled as containing natural rubber.

In order to avoid confusion and to clarify to the consumer whether it is the device itself or its packaging that contains natural rubber, however, the agency believes that a distinct labeling statement is appropriate for devices that have packaging that contains natural rubber that contacts humans. Accordingly, under § 801.437(f) and (g) of the final regulation, such devices shall have labeling with one of the following statements: "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 agency notes that if one of these packaging statements is required, it shall appear regardless of whether there is a natural rubber statement relating to the product itself. For example, a device that contains dry natural rubber that contacts humans and is also packaged in dry natural rubber that contacts humans shall be labeled with both the statements: "Caution: The Packaging of This Product Contains Dry Natural Rubber." and "This Product Contains Dry Natural Rubber."

7. Several comments suggested that the labeling statements be required only on finished medical devices, and that device components be exempt.

The agency agrees in part. The regulation applies to all finished devices and components that are intended to contact or are likely to contact the user or patient. The labeling statement does not apply to components shipped directly to a manufacturer or processor for use in the manufacture of a device because these components, during the time before distribution to consumers, would not be intended to contact, or likely to contact the user or patient. Under these circumstances, the parts or components are not accessible to health care workers or patients. If, however, a device component is sold directly to a consumer, including a patient or health care worker, and it is intended to contact or likely to contact a user or patient, it is required to be labeled under this regulation, regardless of whether it must be attached, inserted, or used in conjunction with other devices. Replacement parts marketed as accessories for medical devices that are ntended to contact or likely to contact a user or patient also require the labeling statement.

8. One comment suggested that in vitro diagnostic devices be exempt because only dry natural rubber is used, there is usually no patient contact with the natural rubber components, and space is very limited for labeling. One comment suggested that other devices that do not contact the patient be exempted, regardless of whether the natural rubber contacts the tissues of the health care worker.

The agency believes that in vitro diagnostic devices should be exempt only to the extent that the natural rubber used in vitro diagnostic devices is not intended to contact or is not likely to contact the user or the patient. FDA, however, is requiring labeling for such devices if they are intended to contact or are likely to contact health care workers or other users, as well as the patient, because all latex-sensitive persons who use the device need to be informed of the product's natural rubber content.

9. One comment requested an exemption for the labeling of natural rubber latex condoms because such condoms clearly contain latex. The comment also believed an exemption should apply to latex condoms because space for labeling is limited, a warning regarding allergic reactions may have a chilling effect on the use by individuals who are not sensitive to natural rubber, and the statement may lead to confusion in differentiating between latex and natural skin condoms because natural skin condoms also contain some natural rubber latex and would require the statement as well.

The agency disagrees and will require latex condoms to bear a labeling statement that the product contains natural rubber latex that may cause allergic reactions. Even though consumers may be aware that the product contains latex, FDA believes that the additional information that natural rubber latex may cause allergic reactions is essential information to individuals who are not aware that natural rubber latex may cause allergic reactions. The agency believes that there is sufficient room on condom packaging for the required statement.

FDA does not believe that the statement will have a chilling effect on the use of condoms by individuals who are not sensitive to natural latex proteins. The statement, however, would clearly provide important information to individuals who are sensitive to natural latex proteins.

The agency further disagrees with the suggestion that the labeling statement would be required on natural skin condoms, and thereby confuse consumers with respect to the differences between latex and natural skin condoms. Although natural skin condoms do contain a natural rubber elastic band, this band is wrapped within the natural skin sheath, and there is no evidence to indicate that the natural rubber ever contacts the user. Therefore, natural skin condoms that have a latex component that is not intended to contact or likely to contact the user do not require the labeling statement. Accordingly, the absence of any latex labeling requirement for natural skin condoms obviates the comments concern about confusion that may result from latex labeling statements on both latex and natural skin condoms.

10. Although most comments supported the requirements of standard labeling requirements, some comments suggested that the proposed labeling statements were overly prescriptive, and that manufacturers should have wide latitude in the wording of the statement provided it contain a general latex ingredient statement. Other comments stated that the labeling statements did not provide sufficient warnings, and suggested that the agency require a caution stating that use of the device may lead to chronic asthma, dermatitis, or even anaphylactic shock and death.

The agency does not agree with comments suggesting the labeling should state possible reactions with specificity. FDA believes that the statement advising consumers that a product may cause an allergic reaction is specific enough to provide adequate warning.

The agency also does not believe that the required labeling statements are overly prescriptive and that manufacturers should be given wide latitude in the wording of labeling statements. The agency has determined that requiring standardized statements for devices containing natural rubber is the best approach for providing the essential information in a clear, consistent, and accurate manner.

FDA realizes that there may be some circumstances where it may be appropriate to tailor specific information concerning a device. If a manufacturer believes use of statements that vary from those prescribed by this regulation is appropriate, § 801.437(i) of the final regulation provides that the manufacturer may petition the agency for an exemption or variance from these requirements by submitting a citizen petition under 21 CFR 10.30. Unless the agency has specifically granted an exemption or variance, the agency will consider any variation from the required statement to be noncompliant, and the device will be deemed misbranded.

11. Several comments suggested that the agency recommend the use of

amount of extractable natural latex protein that would not elicit an allergic reaction for this option to be practicable. Evidence indicates that some persons are reactive to extremely low levels of proteins (Ref. 31). The agency is unable to determine what minimum amount of natural latex proteins fails to elicit a reaction in some individuals, and, therefore, cannot exempt devices containing less than that minimum.

15. Several comments requested clarification on the level of packaging that would require a labeling statement. Some comments requested additional flexibility in the placement of the statement so that the statement may be put on the device labeling other than the label, especially where the device label may be too small to carry such a statement. Another comment recommended that the statement be required not only on the label and in other labeling, but on the device itself if the device is dispensed in bulk, as in the case with natural rubber latex examination gloves. Other comments suggested that bulk devices either remain in the original package in order to preserve the label, or that the agency require the user facility to educate and monitor the use of bulk devices containing natural rubber. Still another comment suggested that where bulk devices are removed to a separate dispensing container, the dispensing container also be required to be labeled with a natural rubber content statement.

FDA believes that the required labeling statements may be fitted on small labels. Because of the importance of the information contained in the labeling statements for individuals sensitive to natural latex proteins, the agency will require the appropriate statements concerning the natural rubber content of the products to be prominently and legibly displayed on all device labels, and other labeling, and to appear on the principal display panel of the device packaging, the outside package, container or wrapper, and the immediate device package, container, or wrapper.

This means, for example, that 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 be required to display the appropriate statement on the dispensing container, as it is the immediate device container or package.

If the packaging of a device contains natural rubber, the final regulation requires that a separate statement that specifically cautions the user that the natural rubber is contained in the packaging itself. Statements relating to the natural rubber content of the packaging do not have to appear on the same levels of labeling as the cautionary statements relating to natural rubber content in the actual product. The statements cautioning the user that the packaging contains natural rubber shall appear, instead, only on the packaging that contains the natural rubber, and the outside package, container, or wrapper. Placement of cautionary statements in these locations should warn consumers adequately of the possible risks of allergic reactions to the packaging, while avoiding the potential for confusion that the actual products contain natural rubber.

FDA believes that requiring devices to remain in their original package at the user site, requiring labeling statements on dispensers that are sold separately from the natural rubber containing devices, and requiring user facilities to provide education concerning latex products and to monitor bulk product use, is impracticable and beyond the scope of the regulation. Furthermore, because of the potential manufacturing difficulties, the agency will not require devices to be embossed, imprinted, or otherwise labeled on the individual, unwrapped device. The agency believes that the labeling requirements in this regulation will provide adequate protection to the users and patients.

16. The vast majority of comments supported the removal of the "hypoallergenic" claim from the labeling of medical devices that contain natural rubber. Those comments that expressed unease about the removal of the claim stated that the term does convey meaningful information to the user. These comments suggested that an alternative term be applied, or that the regulation allow device labeling to state that the device presents a reduced potential for sensitizing users to natural rubber, or that the device contains less than a specified limit of natural latex proteins or processing chemicals as established by the agency. One comment stated that, until the agency proves that the tests currently employed are insufficient to support the "hypoallergenic" claim, the claim should be allowed.

The agency agrees that the term "hypoallergenic" provides important information to the consumer who is sensitive to processing chemicals, but believes that the term "hypoallergenic" on products containing natural rubber will mislead consumers to conclude erroneously that the product may not cause latex protein allergic reactions.

In the past, manufacturers have labeled their products "hypoallergenic" on the basis of results of the modified (human) Draize test. While this test may be appropriate for detecting sensitivity to residual levels of processing chemicals, the test cannot detect the presence of natural latex proteins. Furthermore, current manufacturing processes cannot reduce the levels of natural latex proteins below that to which some individuals may react.

The agency disagrees that the "hypoallergenic" label should be allowed to remain on devices that contain natural rubber until the agency proves that the tests currently employed are insufficient to support the "hypoallergenic" claim, or that claims should be allowed regarding reduced levels of latex proteins. The agency has received reports of allergic reactions to natural rubber gloves labeled as hypoallergenic. Given that the modified (human) Draize Test is not designed to detect levels of natural latex proteins that would not induce allergic responses, and that the agency is not aware of any current manufacturing processes that are designed to remove latex proteins below a level that may cause adverse reactions, the agency believes that it has sufficient evidence that the tests currently employed do not support the claim "hypoallergenic" with respect to the potential for allergic reactions to natural latex proteins.

The agency does agree that alternative statements should be applied to convey information about devices with reduced residual chemical levels to consumers who are sensitive to chemicals. For this reason, the agency is developing guidance for manufacturers who want to make claims relating to latex devices that have reduced manufacturing chemical residues. FDA will announce the availability of this draft guidance document entitled "Testing for Skin Sensitization to Chemicals in Latex Products" in a future issue of the Federal Register.

17. A few comments stated that the reference to the draft guidance document entitled "Testing for Skin Sensitization to Chemicals in Latex Products" in the preamble to the June 24, 1996 proposed rule, upon which this final rule is based, was inappropriate because the document is still in draft form, while another comment suggested the agency reference the draft guidance document in the regulation itself.

The agency does not believe it is appropriate to incorporate a draft guidance document into a regulation. The agency, however, does believe that

agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

If a rule has a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. This rule primarily requires a labeling change which would not have a significant economic impact on small entities. Although this rule will require a labeling change on a substantial number of medical devices, manufacturers will be allowed up to 1 year after the effective date of this regulation to exhaust their existing supply of labeling, therefore, most manufacturers would exhaust their existing supply of labels. Moreover, the cost of reformatting the labeling, which is $1,000 to $2,000 for each different kind of device, is not significant. Accordingly, under the Regulatory Flexibility Act (5 U.S.C. 605(b)), the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

VII. References

The following references have been placed on display in the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857, and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. "Introduction to Latex Compounding and Processing," *The Vanderbilt Latex Handbook*, 3d ed., 1987.

2. Tomazic, V., T. Withrow, B. Fisher, and S. Dillard, "Short Analytical Review—Latex-Associated Allergies and Anaphylactic Reactions," *Clinical Immunology Immunopathology*, 64:89–97, 1992.

3. Slater, J., and S. Chabra, "Latex Antigens," *Journal of Allergy and Clinical Immunology*, 89:673–678, 1992.

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5. Turjanmaa, K., "Incidence of Immediate Allergy to Latex Gloves in Hospital Personnel," *Contact Dermatitis*, 17:27–275, 987.

6. Turjanmaa, K., K. Laurila, S. Makinen-Kiljunen, and T. Reunala, "Rubber Contact Urticaria-Allergenic Properties of 19 Brands of Latex Gloves," *Contact Dermatitis*, 19:362–364, 1989.

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8. FDA Medical Alert—Allergenic Reactions to Latex-Containing Medical Devices, March 29, 1991.

9. Heese, A., J. Hintzenstern, K-P Peters, H. Koch, and O. Hornstein, "Allergic and Irritant Reactions to Rubber Gloves in Medical Health Services," *Journal of the American Academy of Dermatology*, No. 5 (Part 1): 831–839, November 1991.

10. Hintzenstern, J., A. Heese, H. Koch, K-P Peters, and O. Hornstein, "Frequency, Spectrum and Occupational Relevance of Type IV Allergies to Rubber Chemicals," *Contact Dermatitis*, 24:244–252, 1991.

11. Lahti, A., and K. Turjanmaa, "Prick and Use Tests With 6 Globe Brands in Patients With Immediated Allergy to Rubber Proteins," *Contact Dermatitis*, 26:259–262, 1992.

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13. Berky, Z., J. Luciano, and W. James, "Latex Glove Allergy—A Survey of the U.S. Army Dental Corps," *Journal of the American Medical Association*, 268:2695–2697, 1992.

14. Gonzalez, E., "Latex Hypersensitivity: A New and Unexpected Problem," *Hospital Practice*, pp. 137–151, February 15, 1992.

15. Stehlin, D., "Latex Allergies: When Rubber Rubs the Wrong Way," *FDA Consumer*, pp. 16–21, September 1992.

16. ACAI (American College of Allergy & Immunology) Interim Recommendations to Health Professionals & Organizations Regarding Latex Allergy Precautions, March 1992.

17. Young, M., M. Meyers, L. McCulloch, and L. Brown, "Latex Allergy—A Guideline for Perioperative Nurses," *Association of Operating Room Nurses Journal*, 56:488–502, 1992.

18. Dias, M., I. Conchon, M. Cortes, F. Pereira, and R. Alonso, "Anaphylactic Intraoperative Reaction to Latex," *Contact Dermatitis*, 32:305–306, 1995.

19. Safadi, G. S., T. J. Safadi, G. T. Terezhalmy, J. S. Taylor, J. R. Battisto, and A. L. Melton, "Latex Hypersensitivity: Its Prevalence Among Dental Professionals," *Journal of the American Dental Association*, 127:83–88, 1996.

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List of Subjects in 21 CFR Part 801

Labeling, Medical devices, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 801 is amended as follows:

PART 801—LABELING

1. The authority citation for 21 CFR part 801 continues to read as follows:

Authority: Secs. 201, 301, 501, 502, 507, 519, 520, 701, 704 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 331, 351, 352, 357, 360i, 360j, 371, 374).

2. Section 801.437 is added to subpart H to read as follows:

§ 801.437 User labeling for devices that contain natural rubber.

(a) Data in the Medical Device Reporting System and the scientific literature indicate that some individuals are at risk of severe anaphylactic reactions to natural latex proteins. This labeling regulation is intended to minimize the risk to individuals sensitive to natural latex proteins and protect the public health.

(b) This section applies to all devices composed of or containing, or having packaging or components that are composed of, or contain, natural rubber that contacts humans. The term "natural

CC: HFZ-1 (DFeigal)
HFZ-215 (JSheehan)
HFZ-300 (CUldriks)
HFZ-300 r/f
HFZ-330 (SNiedelman)
HFA-305 (Dockets Management)
Draft: jFarnham:2/22/2001
Reviewed:Mstratmeyer:2/26/01
Edit:Culdriks:3/5/01:caf:3/6/01
F/t:cfrye:3/6/01
Cintpet.let