DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 801

[Docket No. 96N–0119]

Amended Economic Impact Analysis of Final Rule Requiring Use of Labeling on Natural Rubber Containing Devices

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; amended economic analysis statement.

SUMMARY: The Food and Drug Administration (FDA) is issuing an amended economic analysis statement relating to a final rule that published in the **Federal Register** of September 30, 1997 (62 FR 51021), requiring labeling statements concerning the presence of natural rubber latex in medical devices. This rule was issued in response to numerous reports of severe allergic reactions and deaths related to a wide range of medical devices containing natural rubber. The final rule becomes effective on September 30, 1998. In order to allow further comment on the economic impact of the September 30, 1997, final rule, FDA published in the **Federal Register** of June 1, 1998, an amended economic impact statement, including an amended initial regulatory flexibility analysis (IRFA) that it prepared under the Regulatory Flexibility Act (RFA), as amended by the Small Business Regulatory Enforcement and Fairness Act (SBREFA). After considering comments submitted in response to the June 1, 1998, amended economic analysis statement, FDA is issuing the amended final economic impact statement, including an amended final regulatory flexibility analysis.

DATES: The September 30, 1997, final rule is effective on September 30, 1998, except for products that contain natural rubber latex solely in cold-seal type packaging. The rule will not apply to these products for an additional 270 days from the September 30, 1998, effective date of the final rule. Elsewhere in this issue of the **Federal Register**, FDA is announcing a stay of the effective date of the September 30, 1997, final rule for these products.

ADDRESSES: References are available in the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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, 301–827–4777, FAX 301–827–4787.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of September 30, 1997 (62 FR 51021), FDA published a final rule (to be codified at 21 CFR 801.437), under its authority in section 505(a) and (f) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 352(a) and (f)), requiring certain labeling statements on medical devices that contain or have packaging that contains natural rubber. This rule becomes effective on September 30, 1998. The agency issued this rule because medical devices composed of natural rubber may pose a significant health risk to some consumers and health care providers who are sensitized to natural latex proteins. FDA has received numerous reports about adverse effects related to reactions to natural latex proteins contained in medical devices, including 16 deaths following barium enemas. These deaths were associated with anaphylactic reactions to the natural rubber latex cuff 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. It is estimated that 5 to 17 percent of health care workers are sensitive to latex proteins (Refs. 1 through 5.)

The September 30, 1997, final rule (hereinafter referred to as the final rule) specifically requires that devices that contain natural rubber that is intended to contact or is likely to contact the health care worker or patient 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. These statements are as follows: ''This Product Contains Dry Natural Rubber.''; ''Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.''; ''The Packaging of This Product Contains Dry Natural Rubber.''; and ''The Packaging of This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions.'' The final rule also prohibits the use of the word ''hypoallergenic'' on devices that contain natural rubber latex.

In the June 24, 1996, proposed rule (61 FR 32618), FDA stated that it did not believe that the proposed rule would be a significant regulatory action as defined by Executive Order 12866, and certified under the Regulatory Flexibility Act (5 U.S.C. 601–602) that the rule would not have a significant economic impact on a substantial number of small entities. FDA stated that it believed the rule's proposed effective date 180 days after publication would allow manufacturers to exhaust their existing labeling supplies.

FDA received comments concerning the economic impact of the proposed rule stating that the requirement would have a major impact on multinational companies, costing at least $15,000 per device for labeling. Another comment stated that the agency underestimated the impact of the rule, as each manufacturer will need to draft, review, and relabel primary and secondary packages of hundreds, if not thousands of devices.

Based on FDA's information, the agency responded that it did not agree that the regulation would require the relabeling of hundreds or thousands of devices, and that agency estimates of relabeling costs were between $1,000 to $2,000 for each type of device. The agency also noted that the extended 1 year effective date should allow most manufacturers to exhaust their current labeling stock prior to the effective date of the regulation. On this basis, the agency stated that the final rule was not a significant regulatory action under the Executive Order, and certified that although a substantial number of small entities would be affected by the rule, the estimated $1,000 to $2,000 cost of implementing the final rule would not have a significant economic impact on those entities (62 FR 51021 at 51029).

On October 7, 1997, the Office of the Chief Counsel for Advocacy of the U.S. Small Business Administration submitted a comment stating that the agency had not supplied data in the preamble to the final rule to support its cost estimates. The agency also received information from industry, subsequent to the issuance of the final rule, identifying additional products that would be subject to the final rule. On the basis of this information, FDA issued an amended economic impact analysis, including an IRFA, and offered opportunity for further comment before the implementation of the rule (63 FR 29552). FDA stated that after consideration of these comments, FDA will decide whether to issue the rule on its current effective date, to stay the effective date of the final rule, and/or repropose the rule.

II. Comments to the Amended Economic Impact Analysis Statement

FDA received three comments to the amended economic analysis. Two comments were from the Health Industry Manufacturers Association

(HIMA), and the other comment was from an in vitro diagnostic manufacturer.

The in vitro diagnostic manufacturer stated that health care professionals using in vitro products are trained in and expected to follow universal precautions for handling potential biohazards by wearing protective gloves. Accordingly, the comment maintained that health care professionals would not come into contact with latex in in vitro diagnostic products.

FDA believes that training in universal precautions will not prevent contact with the latex in in vitro diagnostic products for several reasons. Contact may occur under a variety of situations including failure to follow universal precautions, the absence of wearing protective gloves during the set up phase of testing, the retrieval of the products from storage or packing, or the disposal of products. While FDA does not believe that in vitro diagnostic products may be categorically excluded from the scope of this rule because of the universal precautions that may be undertaken, FDA believes that given the variety of product designs, there may be certain in vitro diagnostic products that may contain latex that are designed in such a manner as to preclude contact with the user. Currently, FDA is unaware of any products that are designed in such manner. If, however, there are such products, these products would not be subject to the final rule.

The in vitro diagnostic manufacturer and HIMA also commented that if in vitro diagnostic devices fell within the scope of the rule, they had not been included in the amended economic impact analysis. This omission was an oversight. FDA referred this comment and others described below to Eastern Research Group (ERG), Lexington, MA for analysis. ERG, after considering comments to the June 1, 1998, amended economic impact analysis, has issued an amended economic impact analysis which includes in vitro diagnostic products. The substantive parts of this analysis are reproduced in their entirety in Appendix 1 of this document.

HIMA submitted two comments. One comment requested an extension of the comment period to the economic impact analysis until July 31, 1998. Subsequently, HIMA submitted timely preliminary substantive comments.

FDA denied the request for an extension to the comment period. The public has now had two separate opportunities to comment on the economic impact of this rule. Interested persons had 90 days to respond to the economic impact statement in the proposed rule (61 FR 32618). FDA received only two comments related to the economic impact of the proposed rule. The amended economic impact analysis provided an additional opportunity for comment on the economic impact. FDA believes that 30 days is an adequate time to respond to the comments, particularly given the fact that this is the second opportunity for comment.

Moreover, FDA needed to notify the public whether the comments related to the costs of the rule would result in a stay of the rule, a reproposal of the rule, or whether FDA would retain the September 30, 1998, effective date. FDA needed sufficient time to analyze the comments and publish in the **Federal Register** a document notifying the public of its course of action before the September 30, 1998, effective date. FDA believes that allowing until July 31, 1998, for the submission of the second round of comments would not have allowed the agency adequate time to analyze comments and publish in the **Federal Register** a document in sufficient time before the September 30, 1998, effective date of the rule.

While HIMA's request for an extension was pending, HIMA submitted timely comments to FDA from several of its members. The fact that many HIMA members submitted responses within the comment period further demonstrates that the period of time was adequate for the submission of comments.

HIMA raised several substantive comments in its July 1, 1998, submission. These comments stated that HIMA was uncertain if the June 1, 1998, estimate included costs related to the following items or factors: New plates and film for each new label, purchasing or manufacturing new relabeled boxes and cartons, slow moving inventory or sterile products that cannot be repackaged, ''specialty'' products that are manufactured on an intermittent basis and kept in inventory for 2 to 3 years, and inability to place sticker labels on existing inventory for products that are sterile or carry several layers of packaging. HIMA also stated that one member had estimated the total cost per SKU to be $28,000.

These cost factors stated by HIMA were considered by ERG and FDA. Moreover, the figure reported to HIMA by one member for total cost per SKU does not affect the conclusions of FDA and ERG about the economic impact of this rule. The final ERG report, which is reproduced in Appendix 1, addresses these comments in further detail.

HIMA also stated that the agency did not comply with the Regulatory Flexibility Act in that it did not publish the initial regulatory flexibility analysis at the time of the publication of the proposed rulemaking. FDA does not agree. Regulatory flexibility analyses are only required if there is a significant impact on a substantial number of small entities. If an agency certifies there is no significant impact on a substantial number of small entities, the agency is not required to perform an initial or final regulatory flexibility analysis (5 U.S.C. 605(b)).

In both the proposed and final rules, FDA certified that under 5 U.S.C. 605(b) no such analysis was required (61 FR 32618, June 24, 1996; 62 FR 51021 at 51029, September 30, 1997). The first ERG analysis, as described in the **Federal Register** of June 1, 1998, and the subsequent ERG analysis, as described below, that responds to industry comments, supports FDA's conclusion that no regulatory flexibility analysis under 5 U.S.C. 603 and 604 is required. Even if such an analysis is required, FDA believes that the agency can satisfy the requirements under 5 U.S.C. 603 and 604 by issuing amended initial and final analyses after a proposed rule is issued.

III. Analysis of Impacts

During the course of reexamining the appropriateness of its certification that no regulatory flexibility analysis was required, FDA has already gathered sufficient information to perform a regulatory flexibility analysis. Accordingly, although FDA believes no regulatory flexibility analysis is required because there is no significant impact on a substantial number of small entities, FDA is providing a final regulatory flexibility analysis, as described below, in this amended economic impact analysis statement.

FDA has examined the impacts of the final rule under Executive Order 12866, the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act (2 U.S.C 1501 *et seq.*). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule has a significant impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities. Title II of the Unfunded Mandates Reform Act (21 U.S.C. 1532) requires that agencies prepare a written assessment of

anticipated costs and benefits before proposing any rule that may result in an expenditure in any 1 year by State, local, and tribal governments, in the aggregate, or by the private sector of $100 million (adjusted annually for inflation).

The agency believes that this rule is consistent with the regulatory philosophy and principles identified in Executive Order 12866 and in these two statutes. The purpose of this rule is to add labeling statements that will help ensure the safe and effective use by health care workers and patients of natural rubber devices. Potential benefits include early recognition of symptoms that could develop into severe latex allergies, and the prevention of severe allergic reactions and death that may occur if persons who are allergic to natural rubber inadvertently use natural rubber devices.

Based on other information referenced in this document, and on the analysis performed by the ERG, FDA is issuing this amended economic analysis statement. Since the rule does not impose any mandates on State, local or tribal governments, or the private sector that will result in an expenditure in any 1 year of $100 million or more, FDA is not required to perform a cost-benefit analysis according to the Unfunded Mandates Reform Act. The rule is not a significant regulatory action as defined by the Executive Order.

ERG amended its report based on comments received to the June 1, 1998, amended economic analysis statement. The final ERG analysis estimated that this rule will affect approximately 2,340 small businesses. Total annualized compliance costs for small businesses are estimated at $4.1 million, which represent 0.05 percent of revenues for small medical device manufacturers. This economic analysis indicates that this rule will not have a significant economic impact on a substantial number of small entities.

The final natural rubber latex labeling rule would require certain labeling statements on products that contain natural rubber latex. This rule would not invoke new recordkeeping and reporting requirements. Manufacturers of several types of products may include natural rubber latex and therefore be subject to this rule. Manufacturers of the products listed in Table 1–1 of the final ERG report will be subject to the final rule (63 FR 29552 at 29560).

Manufacturers of natural rubber latex devices need to employ certain professional skills to implement the new labeling requirements. Regulatory affairs staff will need to identify the need for a revised label, and coordinate the labeling review and revision processes with other departments such as marketing, medical and legal departments, and prepare the new labeling language. Graphic artists and label layout specialists will prepare the revised labels. Art work might be prepared by in-house or external staff. Once prepared, the revised label is normally sent to outside vendors who prepare new printing plates and perform final printing. The manufacturing personnel receive and review the final revised labeling, replace and discard old inventory, incorporate the new labels into the material control and inventory systems, and modify labeling and packaging equipment as necessary to accommodate new labels.

IV. Steps Taken to Minimize the Economic Impact on Small Entities and Regulatory Alternatives Examined

FDA has analyzed several alternatives and taken several steps to minimize the economic impact of this final rule on small entities. FDA did not receive any comments regarding proposed regulatory alternatives in response to the June 1, 1998, amended economic analysis statement. As discussed previously, FDA received a comment asking for clarification regarding the applicability of the final rule to in vitro diagnostic products, a request for an extension of the comment period, and several questions from HIMA relating to costs analysis issues. FDA's response to those comments is discussed in section II of this document.

A. Application of the Rule to Combination Products and Packaging

Although FDA did not receive any comments to the June 1, 1998, amended economic analysis statement proposing any regulatory alternatives, FDA did receive requests from industry, since publication of the final rule, for alternative approaches regarding the applicability of the rule. FDA considered both these alternatives, and modified the application of the rule under these requests in a manner that reduces the economic impact of the rule on industry, including small entities.

First, FDA received comments from industry requesting that the rule does not apply to combination products containing device components that had previously been regulated solely as drugs or biologics. In the **Federal Register** of May 6, 1998 (63 FR 24934), FDA issued a document stating that upon consideration of these comments and the need to provide a uniform labeling approach for all drug and biological products, including combination products, the agency did not intend to apply the final rule to combination products currently regulated as drugs or biologics, and instead intends to initiate a separate proceeding to propose rulemaking requirements for labeling statements on natural rubber-containing products regulated as drugs and biologics, including combination products, currently regulated under drug or biologic authorities.

Second, on June 5, 1998, HIMA submitted a citizen petition requesting a stay of the implementation of the final rule as it pertains to packaging (Ref. 6). As a basis for the stay, HIMA cited several grounds, including assertions that many manufacturers were confused as to the applicability of the rule to cold seal packaging, and, therefore, needed additional time to come into compliance with the new labeling requirements.

On June 19, 1998, FDA responded to this petition by stating it would stay the effective date of the latex labeling statements required by the final rule for cold-seal packaging for an additional 270 days from the September 30, 1998, effective date of the final rule. The stay of the effective date for the provisions of the September 30, 1997, final rule as they relate to cold-seal packaging is published elsewhere in this issue of the **Federal Register**. FDA is not granting a stay of the effective date for all packaging because of the evidence of serious risks latex poses for certain individuals and the need to inform those individuals of the presence of natural rubber latex in devices (Ref. 7).

B. Voluntary Compliance

FDA could have issued guidance stating FDA considered statements about the presence of natural rubber necessary to comply with existing general statutory and regulatory prohibitions against false and misleading labeling (section 505(a) of the act), and failure to provide adequate directions for use (section 505(f)). Given the significant health risks associated with natural rubber products, FDA does not believe that existing general statutory labeling authority and regulations provide adequate protection to ensure that health care workers and patients are warned about the risks associated with natural rubber.

Without the final regulation, manufacturers may not provide any information at all. The ERG report and FDA's own experience indicate that some manufacturers never voluntarily revise their labeling. Even if it could be assumed that all manufacturers would voluntarily provide some labeling information about the presence of

natural rubber, such information is likely to be presented in a variety of ways that may confuse consumers and limit the effectiveness of the natural rubber statement. FDA believes that the provision of consistent, accurate information to consumers is critical. FDA believes that this regulation, which provides accurate, consistent information in a standardized manner, will assure that the safety information is communicated effectively to the public.

C. Implementation Periods

FDA considered various implementation periods for the effective date after the issuance of the final rule. The June 24, 1996, proposed rule proposed an effective date 6 months after the publication of the final rule. The final rule has reduced the impact on small businesses by extending the effective date to 1 year after issuance of the final rule for all products, except those containing natural rubber latex solely in cold-seal type packaging. For those products the agency is providing, for the reasons stated previously, an additional 270 days to comply with the rule.

Based on the ERG report figures, the total industry cost of compliance for this rule with a 1-year implementation period is $64.1 million. This figure may be somewhat higher than actual costs because of the extension for compliance granted to cold seal packaged products, however FDA did not reduce cost estimates related to this variable. The total annualized costs are calculated at $9.1 million per year. The costs for a 6-month effective date are 26 percent greater than a 1-year effective date. Allowing a 24-month implementation date would reduce costs by 40 percent.

FDA rejected the 6-month implementation period and extended the implementation period to 1 year to allow manufacturers of products containing natural rubber latex, including small businesses, to reduce costs by depleting existing inventories and coordinating this labeling change with other planned labeling changes. Although costs could further be reduced by allowing a 24-month implementation period, FDA believes that the public need for this information about devices that pose serious risks justifies rejecting this alternative.

D. Exempting Small Businesses

FDA has considered the option of exempting small businesses from the final regulation. The ERG report estimates that approximately 83 percent of the manufacturers of natural rubber latex products are small businesses. FDA believes that given that the large majority of manufacturers of products containing natural rubber latex are small businesses, and given the risks associated with these devices, exempting small businesses from this regulation would result in a significant decrease of consumer protection. Accordingly, FDA does not believe that small businesses should be exempt from this regulation.

E. Allowance of Supplementary Labeling

FDA could have chosen a regulatory alternative that would require that all labeling be directly printed on the existing packaging and labeling. Such a regulatory provision would decrease the possibility that the required statement would become dislodged during distribution. Instead, the final rule allows the use of supplementary labeling (stickers) to provide the required labeling information. As noted in the ERG report, this will allow a number of firms, including small businesses, to reduce costs by avoiding extensive repackaging of existing product inventory that will not be sold prior to the end of the regulatory implementation period. FDA decided to include this option in the final rule.

F. Requiring a Labeling Statement on Only One Level of Labeling

Under the provisions of the final rule, FDA estimates that most devices covered under the final rule will bear the required natural rubber statement on two or three levels of labeling. FDA considered requiring labeling statements on only one level of labeling. This alternative was rejected because of the importance of the information contained in the required labeling statements. Users may not have the necessary opportunity to read the statement if it is included only on some levels of labeling. For some products, especially those with multiple users, some labeling may be discarded prior to use by subsequent consumers. The inclusion of the statement on each level of labeling increases the likelihood that consumers will be aware of the risks posed by the natural rubber in the product.

V. References

The following references have been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Kibby, T., and M. Akl, ''Prevalence of Latex Sensitization in a Hospital Employee Population,'' *Annals of Allergy, Asthma and Immunology*, 78:41–44, 1997.

2. Kaczmarek, R. G., B. G. Silverman, T. P. Gross, et al., ''Prevalence of Latex-specific IgE Antibodies in Hospital Personnel,'' *Annals of Allergy, Asthma and Immunology*, 76:51–56, 1996.

3. Arellano, R., J. Bradley, and G. Sussman, ''Prevalence of Latex Sensitization Among Hospital Employees Occupationally Exposed to Latex Gloves,'' *Anesthesiology*, 77:905–908, 1992.

4. Lagier, F., D. Vervloet, I. Lhernet, et al., ''Prevalence of Latex Allergy in Operating Room Nurses,'' *Journal of Allergy and Clinical Immunology*, 90:319–322, 1992.

5. Yassin, M., M. Lierl, T. Fisher, et al., ''Latex Allergy in Hospital Employees,'' *Annals of Allergy*, 72:245–249, 1994.

6. June 5, 1998, HIMA citizen petition requesting a stay of the implementation of the final rule as it pertains to packaging.

7. June 19, 1998, FDA response to HIMA citizen petition requesting stay of the implementation of the final rule as it pertains to packaging.

VI. Public Outreach

FDA has conducted extensive public outreach relating to the final rule to small businesses. Interactions with the public on issues relating to this rule are discussed in detail in the amended economic analysis statement published in the **Federal Register** of June 1, 1998 (63 FR 29552, at 29553 and 29554).

Dated: August 13, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 98–23304 Filed 8–28–98; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 801

[Docket No. 96N–0119]

Natural Rubber-Containing Medical Devices; User Labeling; Cold Seal Adhesives Partial Stay

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The final rule for user labeling requirements for natural rubber-containing medical devices, 21 CFR 801.437, was published on September 30, 1997, and becomes effective on September 30, 1998. The Food and Drug Administration (FDA) is adding a note to that rule to stay, for 270 days from the effective date, paragraphs (f) and (g) as those final rule requirements relate to device packaging that uses ''cold seal'' adhesives. Labeling changes required by other paragraphs of this final rule must be incorporated in the labeling of devices