approval is discussed in the freedom of information summary.

In accordance with the freedom of information provisions of 21 CFR part 20 and 514.11(e)(2)(ii), a summary of safety and effectiveness data and information submitted to support approval of this application may be seen in the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday.

The agency has determined under 21 CFR 25.33(d)(1) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under section 512(c)(2)(F)(ii) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(c)(2)(F)(ii)), this approval qualifies for 3 years of marketing exclusivity beginning March 13, 1998, because the application contains substantial evidence of the effectiveness of the drug involved or studies of target animal safety required for approval of the application and conducted or sponsored by the applicant.

List of Subjects in 21 CFR Part 522

Animal drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Center for Veterinary Medicine, 21 CFR part 522 is amended as follows:

PART 522—IMPLANTATION OR INJECTABLE DOSAGE FORM NEW ANIMAL DRUGS

1. The authority citation for 21 CFR part 522 continues to read as follows:

Authority: 21 U.S.C. 360b.

2. Section 522.1289 is added to read as follows:

§ 522.1289 Lufenuron suspension.

(a) *Specifications*. Each milliliter of sterile aqueous suspension contains 10 milligrams of lufenuron.

(b) *Sponsor*. See No. 058198 in § 510.600(c) of this chapter.

(c) [Reserved]

(d) *Conditions of use*—(1) *Cats*—(i) *Amount*. 10 milligrams per kilogram (4.5 milligrams per pound) of body weight every 6 months, subcutaneously.

(ii) *Indications for use*. For use in cats 6 weeks of age and older, for control of flea populations. Lufenuron controls flea populations by preventing the development of flea eggs and does not kill adult fleas. Concurrent use of insecticides may be necessary for adequate control of adult fleas.

(iii) *Limitations*. For subcutaneous use in cats only. The safety of this product in reproducing animals has not been established. Do not use in dogs. Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(2) [Reserved]

Dated: May 12, 1998.

Stephen F. Sundlof,

Director, Center for Veterinary Medicine.

[FR Doc. 98–14298 Filed 5–29–98; 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]

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 is publishing an amended economic impact statement, including an amended initial regulatory flexibility analysis (IRFA) that it has prepared under the Regulatory Flexibility Act (RFA), as amended by the Small Business Regulatory Enforcement and Fairness Act (SBREFA). FDA will respond to comments to this amended economic analysis statement, and publish in the **Federal Register** an amended final economic impact statement prior to the effective date of the September 30, 1997 rule.

DATES: Submit written comments by July 1, 1998 on this amended economic analysis statement.

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Comments should be identified with the docket numbers found in brackets in the heading of this document.

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

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 (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 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.

FDA, in response to a comment on the proposed latex labeling regulation (61 FR 32618, June 24, 1996) concerning the application of the rule to combination products, stated in the preamble to the final rule that it intended to require combination products (i.e., drug/device and biologic/device combinations) that contain natural rubber device components to be labeled in accordance with the final rule (62 FR 51021 at 51026).

After publication of the final rule, the agency received numerous inquiries about, and objections to the application of the natural rubber labeling requirements to combination drug/device products, and combination biologic/device products that currently are regulated under drug and biologic authorities. In the **Federal Register** of May 6, 1998 (63 FR 24934), FDA issued a notice 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, FDA had decided that further opportunity for public comment should be provided on how natural rubber labeling requirements should be applied to all products regulated as drugs and biologics. Accordingly, FDA announced that it does 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.

In the June 24, 1996 proposed rule, 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 proposed 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 manufactures 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.

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 has decided to issue an amended economic impact analysis, including an Initial Regulatory Flexibility Analysis (IRFA), and offer opportunity for further comment before the implementation of the rule. If comments received persuade the agency that the conclusions of its amended economic analysis are erroneous, 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. In any event, FDA will respond, in the **Federal Register**, to comments received in response to this amended economic impact statement.

II. Federal Rules that May Duplicate, Overlap, or Conflict with the Final Rule

FDA does not believe that the final rule duplicates, overlaps, or conflicts with any existing Federal rules. Although 21 CFR 801.5 defines adequate directions for use, and lists certain situations where directions for use may be considered inadequate, there is no regulation requiring a specific labeling statement that reduces the risks associated with natural rubber products by informing consumers about the presence natural rubber. Without the final regulation, manufacturers may provide a wide variety of information about natural rubber that may not be adequate to provide consumer protection, or may provide no information at all. FDA believes that this regulation will assure that necessary safety information is provided to the public, and that standardized information is the best method to inform the public about risks presented by natural rubber containing products.

III. Public Outreach

Each of the **Federal Register** documents concerning these products is available to small businesses on FDA's website. In addition to the publication in the **Federal Register** of the proposed rule, the final rule, and this amended economic analysis, FDA has conducted extensive outreach to a wide audience, including small businesses, on labeling requirements for products containing natural rubber.

Prior to the issuance of any proposal, FDA has discussed agency concerns about latex allergies and the need for labeling on products containing natural rubber at numerous public meetings, including several meetings of the American Society for Testing Materials (ASTM), a major consensus standards development organization in the United States. After the proposal was published, FDA continues a public dialogue on the labeling regulations at a variety of meetings, including meetings with the U.S. Pharmacopeia, the ASTM, and representatives of the Health Industry Manufacturers Association (HIMA), a trade association representing medical device manufacturers, including many that qualify as small businesses. FDA's Division of Small Manufacturers Assistance (DSMA) handled numerous telephone inquiries from businesses that were interested in obtaining information about the proposal.

At the same time the final labeling regulation was published, DSMA faxed correspondence to 100 industry organizations for further broadcast to their membership. That correspondence provided information about the labeling requirements as well as agency contacts who would handle inquiries and comments about the regulation. FDA then held further meetings concerning the rule with standards setting organizations whose membership includes small businesses as well as additional meetings with HIMA members. FDA also sponsored a national conference devoted to latex issues that reached the largest audience of any teleconference previously produced by FDA. Interested

individuals and businesses at 5,000 downlinks had an opportunity at that teleconference to exchange views with agency staff and industry experts on the subject of latex allergies and the implementation and impact of FDA's labeling requirements.

IV. Analysis of Impacts

FDA has examined the impacts of the 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 natural 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. The agency contracted with Eastern Research Group, Inc., (ERG), Lexington, MA, to conduct an economic analysis of this rule. The substantive portions of the ERG analysis are reproduced in their entirety in Appendix 1.

Based on other information referenced in this document, and on the analysis performed by the ERG, FDA has prepared an amended economic analysis statement, including an amended IRFA. 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.

The ERG analysis estimated that this rule will affect approximately 1,110 small businesses. Total annualized compliance costs for small businesses are estimated at $1.3 million, which represent 0.04 percent of revenues for small medical device manufacturers. Although this economic analysis indicates that this rule will not have a significant economic impact on a substantial number of small entities, the agency is soliciting comments on this IRFA. In the event that FDA, after receiving further comments to this amended analysis, determines that the rule does have a significant effect on a substantial number of small entities, FDA is providing the following discussion and analysis of alternatives that minimize effects on small businesses.

V. Alternatives

A. Voluntary Compliance

FDA could have issued guidance stating that FDA considered statements about the presence of natural rubber necessary to comply with existing general statutory and regulatory prohibitions against false and misleading labeling (21 U.S.C. 352(a)), and failure to provide adequate directions for use (21 U.S.C. 352(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.

B. 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. Based on the ERG report figures, the total industry cost of compliance for this rule with a 1 year implementation period is $48.7 million. The total annualized costs are calculated at $3.2 million per year. The costs for a 1 year effective date are 28 percent lower than a 6 month 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.

C. 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.

D. 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.

E. 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 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.

VI. 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*, 78:41–44, 1997.

2. Kaczmarek, R., B. Silverman, T. Gross, et al., ''Prevalence of Latex-specific IgE Antibodies in Hospital Personnel,'' *Annals of Allergy, Asthma & 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. Lhermet, 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. Fischer, et. al., ''Latex Allergy in Hospital Employees,'' *Annals of Allergy*, 72:245–249, 1994.

VII. Requests for Comments

Interested persons may, on or before July 1, 1998 submit to the Dockets management Branch (address above) written comments regarding this amended economic analysis statement on issues relating to natural rubber devices. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket numbers found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: May 26, 1998.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

BILLING CODE 4160–01–F

Appendix 1

EXECUTIVE SUMMARY

FDA issued a final rule on September 30, 1997 requiring label warnings on medical devices and medical device packaging that contains natural rubber that comes into contact with humans. The final rule is effective one year after publication (September 30, 1998). Under contract to FDA, ERG examined the cost and small business impacts of the regulation.

ERG estimated that the natural rubber warning rule will affect approximately 43 FDA-defined categories and 17,000 models of medical devices. ERG estimated the total industry cost of compliance at $48.7 million. Annualized over an infinite time horizon, the total costs are calculated at $3.2 million per year. ERG also estimated, based largely on FDA registration and listing data, that 1,111 small businesses must comply with the rule. Total annualized compliance costs for small businesses are estimated at $1.3 million, which represent 0.04 percent of revenues for small medical device manufacturers.

ERG also quantified the costs of alternative versions of the regulation in which industry is allowed a shorter (6 months) and a longer (24 months) implementation period than the base case (12 months). Under the 6-month alternative, the annualized costs of compliance are $4.1 million, an increase in costs of 27.9 percent from the base case. Under the 24-month alternative, the annualized costs are $1.9 million, a reduction of 40.4 percent from the base case. ERG also reviewed the cost implications (but did not quantify the effects) of an alternative regulatory provision under which affected businesses would not be allowed to use stickers to come into compliance. This option was judged to increase the size of inventory losses, especially for small businesses.

SECTION ONE

STUDY PURPOSE AND METHODOLOGY

The purpose of this rule is to require a warning label on medical devices and packaging containing latex. This is 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 of adverse effects related to reactions to natural latex proteins contained in medical devices, including 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.

1.1 Overview of Study Methodology

FDA published a final rule on September 30, 1997 requiring warning statements on products that have natural rubber-containing medical device components that might contact humans. The labeling must state: "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions." Similar warnings are required for products containing dry natural rubber or whose packaging has natural rubber or dry natural rubber.

ERG estimated the costs of compliance and the small business impacts of the regulation. To develop the cost estimates, ERG developed a study methodology encompassing the following topics:

- Estimating the number of labels revised per medical device
- Estimating the number of devices affected
- Modeling medical device labeling revisions

- Forecasting medical device manufacturer compliance responses and costs
- Calculating with a formal model medical device relabeling costs

1.2 Number of Labels Affected per Medical Device

The FDA-mandated warning statement is required on all device labels, including the principal display panel of the device packaging, the outside package, container, or wrapper, and the immediate device package, container, or wrapper. The warning must also appear on promotional materials. Where applicable, package inserts and Instructions for Use pamphlets must also be revised. While some labeling also includes physician operating manuals, technician or maintenance manuals, or other lengthy labeling, the natural rubber-containing devices generally do not include these items. ERG interpreted the regulation not to require a warning on shipping cartons.

FDA surveyed its medical device reviewers for the affected product categories and solicited information on the number of labels included in product shipments. FDA's reviewers estimated for most product categories that two to three device labels would be affected. Based on these inputs, and to ensure that costs are not underestimated, ERG used an estimate of 3 levels of labeling per device in developing the cost estimates.[1]

[1] The three levels of labeling should not be interpreted as three labels per medical device. Based on discussions with medical device manufacturers, ERG determined that most of the natural rubber-containing medical devices are not sold individually but rather in cases consisting of numerous units. ERG assumed that a representative case (third level packaging) has four boxes (second level packaging) each of which contains ten individually wrapped (primary packaging) units of the given medical device. Thus, the number of labels per case is 45 in the cost computations.

1.3 Number of Medical Devices Categories and Models Affected

FDA identified 43 medical device categories that are addressed by the regulation. FDA device reviewers also estimated the percentage of devices in each category that are covered by the regulation. Table 1-1 lists the device categories, the number of listed devices per category (i.e., the number of devices manufacturers are authorized to offer for sale), and the percentage share of devices within each category that contains natural rubber components that contact humans. The regulated devices include 5 categories of tracheal tubes, 4 of condoms, and 3 of catheters.

Within each of the medical device categories, it was also necessary to estimate the number of device models that are distinctly labeled. Manufacturers separately prepare and print each set of labels and therefore their labeling costs will be a multiple of the number of labels they revise. To address this point, ERG collected sales catalogues for approximately one-half of the medical device categories covered. The catalogues provided sufficient information to support estimates of the number of distinctly labeled models. ERG estimated that on average manufacturers sold 14 models of each of the listed medical devices. In developing these estimates, ERG was cognizant both of the number of different models sold (number of sizes, variety of styles), and of the possibility that numerous similar models will be packaged with the same base set of labeling. Manufacturers often use a production line labeling machine or other method to print a distinguishing model number on different models that are otherwise shipped with identical labeling. Similarly, manufacturers often prepare Instructions for Use and other labels to be applicable for multiple device models. In such cases, a manufacturer that sells ten models of a given device might only be changing one set of labeling. ERG's estimates of the number of models affected are displayed in Table 1-2.

For some medical device categories, ERG did not have adequate access to sales catalogues or other information on the number of models per FDA listing of affected devices. ERG applied the estimate of 14 models per listing to those categories where other data were unavailable.

Table 1-1
FDA Estimates of the Medical Device Categories Affected and Device Listings Per Category

Device Product Code	Product	Percent Containing Natural Rubber [a]	Levels of Labeling	Number of Registrations per Category	Number of Listings per Category [b]
BSJ	Mask, gas, anesthetic	50	1	28	28
BSK	Cuff, tracheal tube, inflatable	1	*3*	7	7
BSR	Stylet, tracheal tube	10	3	13	13
BSY	Catheters, suction, tracheobronchial	10	1	32	32
BTQ	Airway, nasopharyngeal	20	2	13	13
BTR	Tracheal tube (w/wo connector)	5	2	30	30
CAT	Cannula, nasal, oxygen	1	2	30	30
CBH	Device, fixation, tracheal tube	50	2	16	16
CBI	Tracheal/Bronchial tube	5	2	5	5
DWL	Stocking, medical support	5	1	15	15
DZB	Headgear, extraoral, orthodontic	20	2	16	16
ECI	Band, elastic, orthodontic	10	1	27	27
EMX	Balloon, epistaxis	50	3	16	16
EXJ	Condoms, urosheath type	*100*	*3*	12	*13*
EYC	Catheter, upper urinary tract	100	2	1	1
EYR	Tourniquet, gastro-urology	20	1	1	1
FCD	Kit, barium, enema, disposable	40	3	4	4
FCE	Kit, enema (for cleaning purposes)	40	3	19	19
FGD	Catheter, retention, barium enema with bag	40	3	2	2
FMC	Gloves	*100*	*3*	110	*135*
FMF	Piston syringe	95	2	77	77
FPF	Bottle, hot/cold, water	80	3	12	12
FQM	Elastic, bandage	10	1	89	89
FXX	Face, mask, surgical	100	1	56	56
GAX	Tourniquet, nonpneumatic	20	1	26	26
HDW	Diaphragm, contraceptive	80	3	3	3
HIS	Condoms	*100*	*3*	44	*48*
HOY	Ophthalmic eye shields	100	2	44	44
ILG	Stocking, elastic	5	1	7	7
INP	Tips and pads, cane, crutch, and walker	80	1	37	37
JOH	Tube, tracheostomy and tube cuff	1	*3*	9	9
JOW	Sleeve, limb, compressible	100	2	26	26
KCY	Tourniquet, pneumatic	20	1	12	12
KGO	Gloves, surgeons	*100*	*3*	54	*66*
KME	Bedding, disposable, medical	5	1	38	38
KMO	Binder, elastic	5	1	5	5
KNT	Tubes, gastrointestinal (and accessories)	5	3	40	40
KYZ	Irrigating syringe	90	2	61	61
LCG	Intestinal splinting tubes	50	3	1	1
LLJ	Condoms, organ protection	*100*	*3*	1	*1*
LTZ	Condoms, with nonoxynol-9	*100*	*3*	19	*21*
LYY	Gloves, latex	*100*	*3*	319	*392*
MBU	Condoms, intravaginal pouch	*100*	*3*	5	*5*
	Total	**NA**	**NA**	**1,382**	**1,499**
	Average	**49.37**	**2.14**	**NA**	**NA**

Source: FDA survey

[a] The numbers in italics are ERG estimates. ERG assumed that 100 percent of products included natural rubber that would contact humans in the absence of survey information on the product category.

[b] For condom and glove categories, ERG did not have complete listing data from FDA and estimated the number of listings based on the number of registered establishments.

Table 1-2
ERG Estimates of the Number of Medical Device Models Affected

Product	Number of Listings per Category [a]	Number of Models Per Listing [b]	Percent Containing Natural Rubber [c]	Total Models to be Changed, by Category
Mask, gas, anesthetic	28	5	50	70
Cuff, tracheal tube, inflatable	7	2	1	1
Stylet, tracheal tube	13	4	10	6
Catheters, suction, tracheobronchial	32	6	10	20
Airway, nasopharyngeal	13	3	20	8
Tracheal tube (w/wo connector)	30	28	5	42
Cannula, nasal, oxygen	30	1	1	1
Device, fixation, tracheal tube	16	19	50	152
Tracheal/Bronchial tube	5	28	5	7
Stocking, medical support	15	*14*	5	11
Headgear, extraoral, orthodontic	16	*14*	20	45
Band, elastic, orthodontic	27	*14*	10	38
Balloon, epistaxis	16	2	50	16
Condoms, urosheath type	*13*	*14*	*100*	182
Catheter, upper urinary tract	1	52	100	52
Tourniquet, gastro-urology	1	*14*	20	3
Kit, barium, enema, disposable	4	13	40	21
Kit, enema (for cleaning purposes)	19	4	40	31
Catheter, retention, barium enema with bag	2	2	40	2
Gloves	*135*	*14*	*100*	1890
Piston syringe	77	*14*	95	1025
Bottle, hot/cold, water	12	*14*	80	135
Elastic, bandage	89	*14*	10	125
Face, mask, surgical	56	23	100	1288
Tourniquet, nonpneumatic	26	*14*	20	73
Diaphragm, contraceptive	3	*14*	80	34
Condoms	*48*	*14*	*100*	672
Ophthalmic eye shields	44	5	100	220
Stocking, elastic	7	*14*	5	5
Tips and pads, cane, crutch, and walker	37	*14*	80	415
Tube, tracheostomy and tube cuff	9	30	1	3
Sleeve, limb, compressible	26	*14*	100	364
Tourniquet, pneumatic	12	*14*	20	34
Gloves, surgeons	*66*	*14*	*100*	924
Bedding, disposable, medical	38	*14*	5	27
Binder, elastic	5	*14*	5	4
Tubes, gastrointestinal (and accessories)	40	*14*	5	28
Irrigating syringe	61	22	90	1208
Intestinal splinting tubes	1	*14*	50	7
Condoms, organ protection	*1*	*14*	*100*	14
Condoms, with nonoxynol-9	*21*	*14*	*100*	294
Gloves, latex	*392*	*14*	*100*	5488
Condoms, intravaginal pouch	*5*	*14*	*100*	70
Total	**1,499**	**NA**	**NA**	**15,055**

Source: FDA survey, ERG estimates

[a] For condom and glove categories, ERG did not have complete listing data from FDA and estimated the number of listings based on the number of registered establishments. These estimates are presented in italics.

[b] The numbers in italics are based on the average number of models per listing, as estimated from ERG's review of medical device product catalogues.

[c] The numbers in italics are ERG estimates. ERG assumed 100% natural rubber content in the absence of survey information on the product category.

In total, ERG estimated that approximately 15,000 medical device models are affected by the regulation. The largest groups are estimated to be latex gloves (over 8,000 models over multiple glove categories) and condoms (approximately 1,000 models over several condom categories).

ERG interpreted the FDA rule also to apply to packaging materials that include natural rubber constituents. Such materials are used in cold seal packaging, which is a common method of sealing for sterile packages, such as individually wrapped elastic bandages and gauze. Based on discussions with affected manufacturers, ERG estimated that approximately 2,000 medical device models are sold in cold seal packaging. Combining the number of affected medical devices (approximately 15,000) with those sold in natural rubber-containing packaging (approximately 2,000), ERG estimated that labeling for a total of approximately 17,000 medical device models is regulated under this rule.

1.4 Modeling the Label Revision Process at Medical Device Companies

Most medical device manufacturers prepare and periodically revise numerous labels. The extensive standardization of the label preparation routine allowed ERG to forecast the costs that companies will incur to respond to the natural rubber labeling rule. The principal components of the labeling preparation process are:

- Regulatory affairs staff identify the need for a revised label. This staff typically coordinates the labeling review and revision process with other departments (including marketing, medical, and legal departments) and prepares the new labeling language.

- Graphic artists and label layout specialists prepare revised labels. This might be done by in-house or external staff. Once completed, the revised label is normally sent to outside vendors for final printing.

- The manufacturing side of the company receives and reviews the final revised labels. The manufacturing operation incurs costs to:

- Replace and discard inventory of old labels
- Incorporate the new labels into the material control and inventory systems
- Modify labeling and packaging equipment as necessary to accommodate new labels

Each of these components of the labeling revision process is modeled in the cost analysis, as described in Sections 1.6 and 1.7.

1.5 Predicting Manufacturer Compliance Responses and Associated Costs

Medical device companies will incur costs according to their selected method of achieving compliance and the circumstances in which they must prepare for labeling compliance. The compliance responses judged relevant to this rulemaking are grouped into four categories:

- Modify labels immediately
- Apply temporary additional labels, such as sticker labels, and modify labels permanently at a later date
- Incorporate this new labeling requirement in the course of other labeling revisions underway or planned
- No revisions needed, existing warning label is in compliance.

Manufacturers in the first category will develop revised labels and incorporate them into their production and packaging processes during the implementation year. The second group will also incur relabeling costs but for various reasons cannot implement new labels into their processes in time to meet the implementation deadline. Thus, these manufacturers will also need to apply temporary labels, most commonly sticker labels, to meet the FDA requirements. The third group of manufacturers is assumed not to incur any compliance costs specific to the natural rubber labeling rule because they are revising labels for other reasons in any case. Finally, the last group of manufacturers had already implemented a warning label that meets the FDA requirements based on previous discussions with the agency.

Table 1-3 presents the four options and the estimates of the frequency with which they are forecast to be used. The forecasts are based on discussions with the manufacturers contacted for this study and ERG estimates of the likely patterns of compliance. (These forecasts of manufacturer responses to the regulation are varied when alternative versions of the regulation are considered in Section 2.3.)

As the table notes, ERG judged that some manufacturers will need to change their labeling or packaging configurations to accommodate the warning statement. For example, manufacturers could find that they need to use larger labels, or that they need to increase carton size to provide needed label space. (Two of the manufacturers contacted for this study mentioned problems fitting the warning onto their labels; other manufacturers did not express concern about available labeling area or other problems with their labeling configurations). On the basis of these contacts, ERG judged that manufacturers would need to reformat or otherwise revise labeling and packaging configurations for 10 percent of the affected medical device models.

1.6 Incorporation of the Natural Rubber Warning Costs into Voluntary Relabeling Activities

Medical device manufacturers sometimes revise product labeling for reasons other than FDA regulatory requirements, such as changes in foreign labeling regulations, expectations of marketing advantages from relabeling, the desire to publicize device improvements and modifications in labeling, and expectations of greater clarity and/or reduced product liability exposure. If a medical device company is revising labels in any case, the regulatory affairs staff can also incorporate new regulatory requirements (such as the natural rubber warning language) at a negligible incremental cost. Therefore, ERG assumed that manufacturers of models that are being relabeled anyway will not incur any regulatory cost.

The number of medical devices likely to be relabeled voluntarily by medical device companies over the year's implementation time granted with this rule is significant, although no statistics are available on this subject. ERG is also aware, however, that some manufacturers

Table 1-3

Forecast of Compliance Categories by Company Size

Category	For Natural Rubber-Containing Devices Company Size Small	Medium	Large	For Devices in Natural-Rubber Containing Packaging All Companies
Category 1: Revision of principal labeling				
(a) Modify labeling with no change in labeling format	35%	40%	45%	75%
(b) Modify labeling with a major change in labeling format	10%	10%	10%	5%
Category 2: Addition of supplemental labels	30%	20%	10%	20%
Category 3: Incorporation of labeling revision into changes otherwise being made	10%	15%	20%	0%
Category 4: No necessary revisions	15%	15%	15%	0%
Total	**100%**	**100%**	**100%**	**100%**

almost never voluntarily revise their labeling. These companies might frequently introduce new versions of their devices and, therefore, are unwilling to revise labeling that will soon be superseded in any case.

In the case of the natural rubber warning statement, the timing of the rule nearly coincides with the European Union (EU) deadline of June 1998 for medical device companies to satisfy EU language and label-marking requirements. In discussing the EU deadline with medical device companies in early 1998, some confirmed that they were actively relabeling products to meet the EU requirements and were incorporating the FDA requirement as they went. Others, however, stated that they had satisfied the EU requirements well before September 1997 and, therefore, the timing of FDA's regulation did not ease their relabeling task.

The coincidental timing of the FDA natural rubber rule and the EU rule is of potential value only to those medical device companies marketing devices to Europe. Based on a survey of 223 medical device manufacturers in Medical Device and Diagnostics magazine (MD&DI), approximately 50 percent of manufacturers overall sell their devices in Europe (Bethune, 1997). An estimated 90 percent of large manufacturers sell to the EU.

ERG made the conservative judgment (as shown in Table 1-3) that, despite the potential overlap of the FDA and EU requirements, only approximately 10 to 20 percent of medical device models (for small to large companies) would be voluntarily relabeled within the implementation period of this regulation. The estimate reflects their relative participation levels for small to large companies in foreign exporting of medical devices.

ERG also considered the possibility that manufacturers are able to incorporate other labeling changes while incorporating the natural rubber warning, thereby forestalling additional relabeling in future years. For example, manufacturers could simultaneously enhance the labeling presentation of their cartons and containers, incorporate non-U.S. labeling requirements besides those originating from the EU, and incorporate the most up-to-date information into their IFU pamphlets. Nevertheless, the rapid technological obsolescence of many devices and the limited

value of labeling as a marketing tool for medical devices (especially for devices that are not sold over-the-counter) means that companies gain relatively little from such labeling enhancements. Therefore, ERG did not adjust the costs to recognize other potential benefits of the relabeling activities.

1.7 The Formal Structure of the Labeling Revision Model

The labeling revision costs per medical device model are the sum of the following cost elements:

$$TC_i = (RA)_I + (ART) + (MC)_I + (IIL)_I + (IL)_I + (TR)_I + (SL)_I + (LF)_I$$

where:

I = Size of company (small, medium, and large)

TC = Total relabeling costs per device model

RA = Costs incurred by the regulatory affairs department in modifying labeling content

ART= Artwork costs (cost for graphic art work and supplies)

MC = Costs of preparing for new printing runs and incorporating the new labeling into manufacturing operations

IIL = Irreducible inventory loss that occurs for all labeling changes due to company needs for a margin of error in labeling inventories

IL = Excess labeling inventory losses that result from the need to change labeling on a shorter cycle than originally envisioned by a company, due to regulatory implementation deadlines

TR = Cost of translating the warning statement into 12 languages

SL = Cost of purchasing and applying supplementary labels

LF = Additional cost of redesigning labeling and/or packaging when labeling space limitations will not allowing the warning statement to be included in the currently formatted labels.

ERG's estimates of the unit costs incurred at each stage of the relabeling process by small, medium, and large manufacturers are incorporated into the relabeling model. These estimates and assumptions are presented in the next section.

1.8 Medical device relabeling model assumptions

The description of model assumptions (See Table 1-4) is organized as follows:

- Regulatory affairs
- Artwork costs
- Manufacturing and printing costs
- Inventory costs
  - Irreducible inventory costs
  - Excess inventory losses
- Translation costs
- Supplementary labeling
- Major labeling format changes

1.8.1 Regulatory Affairs

This cost element addresses the labor costs needed to analyze new or revised regulatory requirements, prepare labeling changes, and obtain signoffs on the labeling changes from all relevant departments (not including manufacturing areas, such as materials control and quality control). Labor costs are those costs generated by regulatory affairs professionals and labeling department personnel (if separate), including editors and proofreaders. This category also covers professionals from other departments (including those responsible for legal affairs, medical issues, and marketing) that review and sign off on labeling revisions.

Table 1-4

Medical Device Model Assumptions and Parameters

Element	Components involved	Company Size: Small	Medium	Large
Regulatory Affairs (RA)	Labor hours per model for a minor change	6	12	24
	Regulatory affairs labor wage rate ($ per hour)	$33.66	$33.66	$33.66
	Subtract 10% from labor cost for blanket approval savings	90%	90%	90%
Artwork (ART)	Artwork and graphics costs per model	$600	$600	$600
Manufacturing (MC)	Hours per model to incorporate new label into process	4	8	20
	Production worker wage rate ($ per hour)	$18.06	$18.06	$18.06
Irreducible Minimum Inventory Loss (IIL)	All labeling and packaging losses	$500	$2,000	$5,000
Excess Inventory Loss (IL)	All labeling and packaging levels	$750	$3,000	$7,500
	Percentage of models where excess inventory losses occur (applies to models where stickers are not used)	5%	5%	5%
	Average excess inventory loss per model	$38	$150	$375
Translation (TR)	Cost of translating into 12 languages ($50 per language)	$600	$600	$600
	Percentage of companies that incur translation costs	30%	40%	60%
	Average translation cost per company	$180	$240	$360
Supplemental Labels (SLBL)	*Use of non-standard labels (stickers)*			
	6-week lease cost of pressure sensitive labeler (includes parts, labor, adjustment costs)	$5,400	$5,400	$10,800
	Number of production workers required for attaching labels	2	4	16
	Total cost of labor for manual attachment of labels assuming the process will last 6 weeks	$8,669	$17,338	$69,350
	Number of cases produced per model/yr per establishment size	6,000	20,000	60,000
	Total leasing and labor cost per model	$1,005	$1,624	$5,725
	Cost of a pressure sensitive label	$0.0200	$0.0100	$0.0050
Major Labeling Format Changes (LF)	*For all label text area changes*			
	Additional hours of regulatory affairs input per model	3	6	12
	Regulatory affairs labor wage rate ($ per hour)	$33.66	$33.66	$33.66
	Additional artwork cost per model	$600	$600	$600
	Additional manufacturing hours to revise packaging/labeling for	8	16	40
	Production worker wage rate ($ per hour)	$18.06	$18.06	$18.06

Regulatory affairs costs vary with the size of the manufacturer and the complexity and scope of the labeling change. Because the required warning in this case is so short (one sentence), with the exact language provided by FDA, regulatory affairs staff will require relatively little time to discuss the necessary warning language. Nevertheless, the regulatory affairs staff will need to (1) discuss the incorporation of the required language into other or additional warnings it provides on its products, (2) consider the exact placement of the warning statement on each label, and (3) add the warning into any advertising and promotional material that is in preparation for release after the implementation date of this rule.

On average, companies are estimated to spend 6 to 24 hours per model on this label change. Larger companies expend more hours per model due primarily to the higher number of reviews and signoffs required for a labeling change.

No separate costs are estimated for making changes to promotional materials associated with natural-rubber containing medical devices. Advertising copy is assumed to be revised frequently and, therefore, is likely to be revised and updated during the 12-month implementation period. The new warning statement would be incorporated with essentially no incremental costs during revisions. To the limited extent to which manufacturers might have advertising or promotional materials that are not frequently revised, ERG assumed that the hours estimate is adequate to address the additional changes in promotional materials.

1.8.2 Artwork Costs

Manufacturers incur costs for the labor of graphic artists, the purchasing of graphic art supplies, film supplies (to produce camera-ready copies of revised labels), new printing plates, and the printing of sample labels. In general, the variables that influence artwork costs include the complexity of the labeling revision, the potential for conflict with marketing or other labeling considerations, and the design complexity. In this case, graphic artists will need little time to add the warning statement, but will still need to access the computer graphics file for each label and fit the warning into the available area of the existing labels. Variables that influence the cost of new printing plates include the type of printing process used and the design complexity (especially the number of colors) of the original labeling.

For this regulation, artwork costs were estimated at $600 per model (across all size classes), with the costs covering all three levels of labeling. These costs were estimated to be representative artwork costs for all medical device manufacturers, whether they perform the relabeling in house or using outside vendors.

No separate artwork costs are assumed for revision of advertising copy and other promotional materials. As noted, ERG assumed that these materials are revised frequently and that the natural rubber warning statement can be incorporated at essentially no incremental cost.

1.8.3 Manufacturing and Printing Costs

Manufacturing and/or materials management personnel order printing of new labels, perform necessary quality-control reviews of the new labels when they arrive, incorporate the new label into manufacturing processes, and oversee removal of the old label from the master batch records and from the bill-of-materials that governs manufacturing operations. The manufacturing and printing cost category is defined to consist entirely of labor costs.

ERG estimated that it takes medical device manufacturers from 4 to 20 hours to incorporate a revised label into manufacturing. The large manufacturer estimate was influenced by circumstances at some large manufacturers that use exceptionally high speed and automated production processes and complicated production systems that require considerable management for each new set of labels.

1.8.4 Inventory Losses

Irreducible Inventory Losses - The irreducible minimum inventory loss represents the extra labels that manufacturers prepare to allow a margin of error in production and that are then discarded when labels are revised. These losses are defined as inevitable because manufacturers generally print enough labeling materials to ensure that sales are not constrained by a shortfall in this relatively low cost input to the production process. In this case, for example, manufacturers might try to time the introduction of new labels to ensure that all label inventories generated after a specific date have the new warning statement. Nevertheless, there are so many production, labeling, and packaging elements to coordinate that manufacturers cannot be certain of precisely eliminating old inventories. In this case, manufacturers probably will want to switch all of their labeling (primary, secondary, instructions for use, etc.) at the same time to prevent confusion among consumers. Thus, it is very likely that varying quantities of inventory will be lost for different label items.

ERG noted that for an OTC pharmaceutical labeling requirement, the National Drug Manufacturers Association had recently estimated an irreducible inventory loss of $1,000 per shelf-keeping-unit (SKU) (NDMA, 1997). The estimate for OTC products is likely to be higher than that for medical devices due to the higher speed of production on average (more production units per hour) than would generally apply to medical devices. On the other hand, ERG noted that medical device companies would sometimes be discarding inventory for more distinct labeling items per model than would OTC pharmaceutical manufacturers. Medical device manufacturers contacted for this study varied between those who said inventory losses were negligible and those

who predicted losses of many thousands of dollars. Based on these data, ERG estimated the irreducible inventory loss at $500 to $5,000 across the size classes.

Excess Inventory Losses - Excess inventory losses of labeling are defined as those, in addition to the irreducible minimum losses, that result from companies having to relabel within a shorter cycle than they envisioned when they stocked their label inventories. In developing the estimate of excess inventory losses, ERG determined that most manufacturers require no more than 6 months of regulatory lead time to deplete virtually their entire inventory of labels. Most of the companies contacted for this study stated that their inventory losses would be negligible. Many companies appear to keep no larger label inventory than that representing 3 months of production. Thus, with the one year lead-time accorded for the natural rubber labeling rule, ERG judged that there would rarely be a significant inventory loss for medical device manufacturers. In making this estimate, ERG assumed that medical device companies became aware of the rule reasonably soon after its publication.

ERG judged, nevertheless, that a small percentage (5 percent) of medical device companies would incur excess inventory losses for reasons that they could not control. The companies that face such losses are judged most likely to be those that face one or more exceptional circumstances in making labeling changes. For example, a small percentage of companies use special labeling components or materials that cannot be quickly provided by suppliers. For example, a few companies use foreign suppliers of specialized packaging and labeling materials that require 6 to 9 months to acquire. Such companies are likely to purchase relatively large inventories in order to avoid delays in production and to minimize the expense of the material acquisition process. Furthermore, in these cases the inventory that is eventually discarded is likely to be relatively costly. Other companies might have invested in relatively large label inventories for some reason, such as to ensure adequate supplies for European sales.

For companies incurring these excess inventory losses, the value of discarded inventory was estimated to vary from $750 to $7,500 per model for small to large manufacturers. The values

are approximate and will certainly vary with the manufacturer's preparedness. As noted, most companies contacted for the study indicated that no inventory losses would occur.

1.8.5 Translation Costs

A minority of medical device companies will incur translation costs to comply with the labeling rule. Non-English translations of the warning statement are a regulatory cost for companies that sell devices worldwide using a single set of labeling.[2] Thus companies will translate the warning into all of the language featured in their labeling. Translation costs are not relevant for companies that do not sell devices internationally (which applies to roughly one-half of all medical device manufacturers), or for companies that use separate labeling for international sales. With the recent expansion in language requirements for products sold in the EU, most companies that use a single set of labeling are providing 12 languages or more on their labeling.

For the cost estimates, ERG assumed a translation cost of $50 per language for each of 12 languages for the affected devices. This cost applies only once per company because all device types and models can use the same translation. Based on the relative distribution of international sales of medical devices, ERG estimated that 30 percent of small companies to 60 percent of large companies will incur translation costs.

[2]According to FDA regulation, non-English translations of labeling on devices sold in the United States must be consistent with the English language label.

1.8.6 Supplementary Labeling Costs

Medical device companies that cannot introduce new labels in time to meet the implementation deadline will resort to the use of supplementary labels, such as stickers. The use of supplementary labels will be especially common among medical device manufacturers who would otherwise face substantial label or product inventory losses. ERG estimated that 10 to 30 percent of companies will use supplementary labels.

Based on discussions with industry consultants and medical device manufacturers, ERG estimated that manufacturers choosing to apply supplementary labels will temporarily lease a pressure-sensitive labeler (automatic or semi-automatic) and hire from 2 to 16 temporary production workers. The temporary production workers are needed to operate the labelers and to manually apply those stickers that cannot be run through or handled by the labeling equipment. The lease cost of a pressure-sensitive labeler for a packaging line is estimated at approximately $1,600 per month. Companies will incur additional engineering and installation costs, estimated at $3,000 per labeler, to adapt the leased labelers to their production operations. ERG estimated that small and medium manufacturers would lease one labeler, and large companies 2 labelers. ERG estimated that the equipment and workers will be employed for a six-week period. The unit cost of a pressure sensitive supplementary label is estimated at $0.02, $0.01, and $0.005 for small, medium, and large companies, respectively. The estimated costs of all additional equipment and temporary workers were spread over all of the models manufactured per company. The total equipment leasing cost per model for supplementary labeling was estimated to vary from $1,005 for small to $5,725 for large manufacturers. Furthermore, the total cost of supplemental labels per model was estimated at $1,350 to $3,375 across company size categories.[3]

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[3]Because supplemental labels are a temporary solution, ERG assumed that they will only be applied to 3 months' production to deplete excess inventories.

1.8.7 Costs of Major Labeling Format Changes

Some medical device companies will incur additional costs to reformat their labels when their existing labels cannot accommodate the new warning statement. This problem is likely to arise most often among products sold worldwide with the same labeling because of the burden of multi-language translations and additional EU labeling specifications. ERG judged that the bulk of the costs for reformatting will be incurred in the implementation year as company staff formulate methods of achieving compliance. Thus, ERG estimated that regulatory affairs, artwork, and manufacturing changeover costs would all be incurred in the first year. ERG judged that the ongoing incremental cost of additional labeling materials, such as if physically larger labels are required, would be negligible and they have not been modeled.

SECTION TWO

COSTS OF COMPLIANCE AND REGULATORY FLEXIBILITY ANALYSIS

This section presents the unit and total industry costs of compliance. ERG then extends the analysis to small businesses in order to address the Small Business Regulatory Enforcement Fairness Act (SBREFA) requirements.

Compliance costs are distributed among business size categories using data from the Small Business Administration (SBA, 1998). For the medical device manufacturing Standard Industrial Classifications (SICs 384 and 385), SBA defines a small business as an entity employing fewer than 500 workers (SBA, 1996). For this analysis, ERG also defined medium-sized businesses as those employing between 500 and 2,499 employees and large businesses as those that employ 2,500 or more.

2.1 Unit Costs of Compliance

ERG combined the individual cost elements to derive the total unit relabeling costs per model for each compliance category (See Table 2-1). The unit costs for the simplest case of permanent labeling revisions (Category 1 (a)) are estimated at $1,404 for small and $7,089 for large companies. The total unit relabeling costs for the supplementary labeling compliance alternative (Category 2) range from $4,394 to $16,775 per model over the three size categories. The relatively large unit cost for applying stickers reflects the costs of hiring temporary labor to affix labels and leasing and operating labeling equipment. Furthermore, with stickers, the artwork (ART) and manufacturing change (MC) components of the label revision process are incurred twice (once for the sticker and once for the permanent label changes). This option will nevertheless be considered attractive for companies that wish to avoid even larger product or labeling material inventory losses.

Table 2-1

Unit Costs of Compliance, by Size Category

		Category 1		Category 2
Company Size	**Cost Element**	**Revision w/o Change in Format**	**Revision with Change in Format**	**Supplementary Labeling**
Small	Regulatory Affairs	$181.76	$282.74	$181.76
	Artwork	$600.00	$1,200.00	$1,200.00
	Manufacturing Change	$72.24	$216.72	$144.48
	Irreducible Inventory Loss	$500.00	$500.00	$500.00
	Excess Inventory Loss	$37.50	$37.50	NA
	Translation	$12.86	$12.86	$12.86
	Supplemental Labeling	NA	NA	$1,350.00
	Equipment Leasing Costs	NA	NA	$1,004.91
Total		**$1,404.37**	**$2,249.83**	**$4,394.02**
Medium	Regulatory Affairs	$363.53	$565.49	$363.53
	Artwork	$600.00	$1,200.00	$1,200.00
	Manufacturing Change	$144.48	$433.44	$288.96
	Irreducible Inventory Loss	$2,000.00	$2,000.00	$2,000.00
	Excess Inventory Loss	$150.00	$150.00	NA
	Translation	$17.15	$17.15	$17.15
	Supplemental Labeling	NA	NA	$2,250.00
	Equipment Leasing Costs	NA	NA	$1,624.11
Total		**$3,275.16**	**$4,366.08**	**$7,743.75**
Large	Regulatory Affairs	$727.06	$1,130.98	$727.06
	Artwork	$600.00	$1,200.00	$1,200.00
	Manufacturing Change	$361.20	$1,083.60	$722.40
	Irreducible Inventory Loss	$5,000.00	$5,000.00	$5,000.00
	Excess Inventory Loss	$375.00	$375.00	NA
	Translation	$25.72	$25.72	$25.72
	Supplemental Labeling	NA	NA	$3,375.00
	Equipment Leasing Costs	NA	NA	$5,725.03
Total		**$7,088.98**	**$8,815.30**	**$16,775.21**

2.2 Total Costs of Compliance

To derive total costs, it was necessary to estimate the distribution of the affected natural rubber-containing medical device models by size category. The distribution of compliance costs among business size categories will be correlated with their relative shares of models requiring relabeling. This distribution is not known, however. ERG notes from the SBA data that small firms represent slightly more than 90 percent of all firms but only approximately 25 percent of all employment. It is reasonable to assume that small firms' share of models is substantially less than their share of the population of firms but larger than their share of employment. ERG assumed for this analysis that 60 percent of models are produced by small businesses. ERG also assumed, based on their relative shares of industry employment, that 25 percent of models are produced by medium-sized businesses and 15 percent by large businesses. The final distribution of compliance costs among size categories varies from these percentages to some extent, however, because the unit compliance costs estimated for the different size categories are not exactly proportional to the distribution of models.

Table 2-2 presents the aggregate cost forecasts across company size categories for all affected medical devices. The total first-year costs for the industry are estimated at $48.7 million, and the annualized costs (using an infinite time horizon) are calculated at $3.2 million per year. Annualized compliance costs per year are calculated at $1.3 million for small businesses (40.6 percent of total costs), $0.9 million for medium businesses (28.1 percent), and $1.0 for large businesses (31.3 percent).

Table 2-2

Total Costs of Compliance, By Company Size

Cost Element	Small Companies	Medium Companies	Large Companies	All Companies
Regulatory Affairs	$1,546,796	$1,220,586	$1,382,609	$4,149,991
Artwork	$7,132,770	$2,633,250	$1,376,708	$11,142,728
Manufacturing Change	$928,374	$692,077	$915,764	$2,536,215
Irreducible Inventory Los	$3,587,375	$5,602,583	$7,839,313	$17,029,271
Excess Inventory Loss	$164,432	$302,281	$495,764	$962,477
Translation	$102,571	$53,757	$45,477	$201,805
Supplemental Labeling	$3,953,565	$1,816,688	$946,659	$6,716,912
Equipment Leasing Costs	$2,964,397	$1,384,963	$1,636,356	$5,985,716
Total Costs	**$20,380,281**	**$13,706,185**	**$14,638,649**	**$48,725,115**
Total Annualized Costs	**$1,333,289**	**$896,666**	**$957,669**	**$3,187,624**

2.3 Regulatory Flexibility Analysis

This section addresses the potential impact of the natural rubber labeling rule on small medical device manufacturers. ERG estimates the affected number of small businesses and then calculates regulatory impacts as a share of industry revenues.

2.3.1 Estimated Number of Affected Firms

The Regulatory Flexibility Act (RFA) requires agencies to determine whether a proposed rule may have a significant effect on a substantial number of small entities. As noted, SBA defines a small business in the medical device manufacturing SICs as an entity employing fewer than 500 employees.

SBA's database, which is based on U.S. Bureau of the Census data, provides a complete size distribution of establishments and businesses in SICs 384 and 385 (See Table 2-3). The SBA data shows 4,185 small businesses in SICs 384 and 385, encompassing all types of medical device manufacturers, including numerous businesses that are not affected by the natural rubber warning rule.

To restrict the estimate to affected small businesses, ERG combined the SBA data with the registration and listing data provided by FDA (see Section 1, Table 1-1). The FDA data enumerates the number of establishments registered for manufacturing of natural rubber-containing medical devices. ERG first distributed the number of registered establishments (1,382) by size according to the overall industry distribution of establishments by size provided in the SBA data. ERG noted that 83.0 percent of establishments in the SBA data are small. Using this estimate, ERG derived an estimate of 1,147 affected small establishments. Next, ERG adjusted the small establishment figure by the ratio of establishments to businesses for small establishments, as found in the SBA data (1.03 establishments per small business). In this fashion, ERG calculated the number of affected small businesses at 1,111.

Table 2-3

Distribution of Medical Device Manufacturing Firms (SIC 384 & 385) by Employment Size

SIC and Industry		Employment Size: Small 0-499 Employees	Medium 500-2499 Employees	Large 2500+ Employees	Industry Total
SIC 3841	Firms	1,150	92	38	1,280
Surgical and Medical Instruments	Establishments	1,166	201	119	1,486
and Apparatus	Employment	32,960	71,151	48,873	152,984
	Avg. Employment Per Firm	29	773	1,286	120
	Receipts ($000)	$4,540,616	$11,000,701	$7,410,287	$22,951,604
	Receipts Per Firm ($000)	$3,948	$119,573	$195,008	$17,931
SIC 3842	Firms	1,497	78	39	1,614
Orthopedic, Prosthetic, and	Establishments	1,583	185	102	1,870
Surgical Appliances and Supplies	Employment	42,559	54,080	34,436	131,075
	Avg. Employment Per Firm	28	693	883	81
	Receipts ($000)	$5,489,162	$9,785,433	$6,789,356	$22,063,951
	Receipts Per Firm ($000)	$3,667	$125,454	$174,086	$13,670
SIC 3843	Firms	633	14	6	653
Dental Equipment and Supplies	Establishments	648	31	15	694
	Employment	9,950	6,077	2,683	18,710
	Avg. Employment Per Firm	16	434	447	29
	Receipts ($000)	$1,126,612	$898,459	$424,483	$2,449,554
	Receipts Per Firm ($000)	$1,780	$64,176	$70,747	$3,751
SIC 3844	Firms	89	22	10	121
X-Ray Apparatus and Tubes and	Establishments	90	39	23	152
Related Irradiation Apparatus	Employment	2,270	11,702	7,344	21,316
	Avg. Employment Per Firm	26	532	734	176
	Receipts ($000)	$505,496	$2,990,676	$1,967,144	$5,463,316
	Receipts Per Firm ($000)	$5,680	$135,940	$196,714	$45,151
SIC 3845	Firms	308	50	22	380
Electromedical and	Establishments	312	66	31	409
Electrotherapeutic Apparatus	Employment	12,339	28,634	12,960	53,933
	Avg. Employment Per Firm	40	573	589	142
	Receipts ($000)	$2,196,916	$6,044,250	$2,607,372	$10,848,538
	Receipts Per Firm ($000)	$7,133	$120,885	$118,517	$28,549
SIC 3851	Firms	508	26	7	541
Ophthalmic Goods	Establishments	521	56	16	593
	Employment	8,619	18,674	10,235	37,528
	Avg. Employment Per Firm	17	718	1,462	69
	Receipts ($000)	$670,169	$1,969,449	$1,126,372	$3,765,990
	Receipts Per Firm ($000)	$1,319	$75,748	$160,910	$6,961
Total, All SICs	Firms	4,185	282	122	4,589
	Establishments	4,320	578	306	5,204
	Employment	108,697	190,318	116,531	415,546
	Avg. Employment Per Firm	26	675	955	91
	Receipts ($000)	$14,528,971	$32,688,968	$20,325,014	$67,542,953
	Receipts Per Firm ($000)	$3,472	$115,918	$166,598	$14,718
	Establishment:Firm Ratio	1.0323	2.0496	2.5082	1.1340
	Establishments as a Percentage of Industry Total	83.0%	11.1%	5.9%	100.0%

Source: SBA, 1998.

2.3.2 Compliance Costs as a Share of Small Medical Device Manufacturer Revenues

In order to measure the impact of the final rule on small businesses, ERG calculated the ratio of industry compliance costs to industry revenues. Based on the SBA database, the average revenues per firm ranges from $3.5 million to $166.6 million for small to large companies (see Table 2-4). The annualized compliance costs per firm are estimated at $1,200, $11,973, and $29,559 for small, medium, and large firms, respectively. Consequently, the annualized compliance costs per firm represent 0.04 percent of revenues for small medical device businesses.

2.3.3 Recordkeeping and Reporting Burden

Manufacturers are required to place a warning statement on the labeling of affected medical devices. Revising labeling is a standard procedure in medical device manufacturing that companies routinely follow. No new reporting and recordkeeping activities are required. Therefore, no additional professional skills are required.

2.3.4 Impact of Changes in Regulatory Implementation Lead Time on Costs of Compliance

The computed total cost of compliance is based on the 12-month implementation lead time and the other elements described in the published natural rubber warning regulation by the FDA. FDA also considered alternatives to the regulation, as follows:

- The same labeling requirements with an implementation period of 6 months.
- The same labeling requirements with an implementation period of 24 months.
- The implementation lead time of 12 months, but no allowance for use of stickers as a temporary labeling measure, due to concerns that stickers might become lost or dislodged during medical device distribution.

Table 2-4

Compliance Costs as a Share of Medical Device Manufacturer Revenues

	Small Companies	Medium Companies	Large Companies	All Companies
Number of Affected Establishments [a]	1,147	153	81	1,382
Number of Affected Firms [b]	1,111	75	32	1,219
Revenues per Firm	$3,471,678	$115,918,326	$166,598,475	$14,718,447
Total Annualized Compliance Costs	$1,333,289	$896,666	$957,669	$3,187,624
Annualized Compliance Costs per Firm	$1,200	$11,973	$29,559	$2,616
Annualized Compliance Costs as Percent of Revenue	0.035%	0.010%	0.018%	0.018%

Source: FDA survey, ERG estimates, and Small Business Administration 1998.

Notes:

[a] Based on the number of registered establishments.

[b] The number of affected firms is computed by dividing the number of affected firms in each size category by the establishment:firm ratio in same category

ERG quantified the impacts of the shorter and longer implementation periods, but did not estimate costs for the last alternative, which is discussed at the end of this section.

To consider shorter or longer implementation periods, ERG adjusted its cost methodology to address the impact of implementation times on (1) the magnitude of excess inventory losses incurred by manufacturers, (2) the percentage of models with excess inventory losses, and (3) the forecast of compliance options taken by manufacturers. With a 6-month lead time, ERG doubled its estimates of the average excess inventory loss per model incurred to $1,500 for small businesses, $6,000 for medium-sized businesses, and $15,000 for large businesses. ERG also judged that, with a shorter lead time, it is likely that many more manufacturers would incur excess inventory losses (see Section 1.7.4 for a discussion of the circumstances that create excess inventory losses). Thus, the percentage of medical device models for which excess inventory losses are incurred was increased from 5 to 20 percent for the 6-month implementation period alternative.

For the 24-month implementation period, ERG judged that essentially all manufacturers would avoid excess inventory losses. Extremely few manufacturers carry labeling inventories of more than 2 years. Hence, no excess inventory losses were estimated in this case.

Table 2-5 presents ERG's forecasts of the compliance options manufacturers will choose for the 6-month and 24-month regulatory implementation lead time alternatives. ERG assumed that the use of supplementary labeling would be more common with shorter lead times because more manufacturers would be (1) unable to get new labels prepared in time, and (2) would use stickers to avoid losses of label or product inventories. With a 24-month implementation period, ERG estimated that essentially no manufacturers would need to use supplementary labels.

Tables 2-6 provides a comparison of the total compliance costs under the base case (12-month implementation period) and the two alternative implementation times. With the 6 month-implementation time, annualized compliance costs are estimated to be $4.1 million,

Table 2-5

Forecast of Compliance Categories by Company Size For Regulatory Alternatives

6-Month Regulatory Implementation Period

Category	For Natural Rubber-Containing Devices Company Size: Small	Medium	Large	For Devices in Natural-Rubber Containing Packaging: All Companies
Category 1: Revision of principal labeling				
(a) Modify labeling with no change in labeling format	25%	30%	35%	55%
(b) Modify labeling with a major change in labeling format	10%	10%	10%	5%
Category 2: Addition of supplemental labels	40%	30%	20%	40%
Category 3: Incorporation of labeling revision into changes otherwise being made	10%	15%	20%	0%
Category 4: No necessary revisions	15%	15%	15%	0%
Total	**100%**	**100%**	**100%**	**100%**

24-Month Regulatory Implementation Period

Category	For Natural Rubber-Containing Devices Company Size: Small	Medium	Large	For Devices in Natural-Rubber Containing Packaging: All Companies
Category 1: Revision of principal labeling				
(a) Modify labeling with no change in labeling format	55%	50%	45%	85%
(b) Modify labeling with a major change in labeling format	10%	10%	10%	5%
Category 2: Addition of supplemental labels	0%	0%	0%	0%
Category 3: Incorporation of labeling revision into changes otherwise being made	20%	25%	30%	10%
Category 4: No necessary revisions	15%	15%	15%	0%
Total	**100%**	**100%**	**100%**	**100%**

Table 2-6

Total Costs of Compliance with Regulatory Alternatives

Lead Time	Small Companies	Medium Companies	Large Companies	All Companies
6 Months				
Total Costs	$24,668,459	$17,428,687	$20,229,273	$62,326,420
Total Annualized Costs	$1,613,824	$1,140,194	$1,323,410	$4,077,429
Percent Change in Annualized Costs from 12-Month Lead Time	21.0%	27.2%	38.2%	27.9%
12 Months				
Total Costs	$20,380,281	$13,706,185	$14,638,649	$48,725,115
Total Annualized Costs	$1,333,289	$896,666	$957,669	$3,187,624
Percent Change in Annualized Costs from 12-Month Lead Time	NA	NA	NA	NA
24 Months				
Total Costs	$10,429,015	$8,571,096	$10,061,787	$29,061,898
Total Annualized Costs	$682,272	$560,726	$658,248	$1,901,246
Percent Change in Annualized Costs from 12-Month Lead Time	-48.8%	-37.5%	-31.3%	-40.4%

approximately 28 percent higher than the base case. With the 24-month implementation period, annualized compliance costs are estimated to be $1.9 million, approximately 40 percent lower.

FDA also considered a prohibition on the use of supplementary labels (i.e., stickers) to comply with the rule due to concerns about the effectiveness of this method of labeling. ERG did not quantify the resulting compliance costs due to the difficulty of measuring the potentially very large costs incurred by certain manufacturers. A number of firms use stickers to avoid extensive repackaging of existing product inventory that will not be sold prior to the end of the regulatory implementation period or loss of expensive labeling inventories. Under this alternative, the percentage of companies incurring excess inventory losses and the size of the inventory losses would increase. At least some companies might incur fairly large inventory losses.

ERG forecast for the base case (12-month implementation scenario) that small businesses were three times more likely than large businesses to use stickers. During contacts to medical device manufacturers, ERG observed that small businesses were much more sensitive to potential losses of label inventories and more likely to benefit by organizing a temporary effort to add stickers to products.

In conclusion, the base case of a 12-month implementation period, with sticker labels allowed, alleviates the cost impacts, particularly those on small businesses. The sticker option also allows numerous companies to lessen potentially significant inventory losses and, based on contacts made during this study, allows a few companies to avoid losses that they would consider quite damaging.

Furthermore, the 12-month implementation period allows the large majority of companies sufficient time to exhaust existing label inventories and avoids the much greater cost impacts that would accompany a 6-month implementation period. ERG did not quantify the cost impacts of possible logistic difficulties that some companies, such as those that manufacture large numbers of natural-rubber containing devices, might face attempting to revise all affected labeling within a 6-month timeframe. These companies might need to delay relabeling of other products, hire and train

new labeling staff, incur overtime costs for labeling staff, and incur other exceptional costs. The 24-month implementation period, on the other hand, only eliminates excess inventory losses.

REFERENCES

Bethune, John. 1997. 1997 Business Outlook. Greater Risks, Greater Rewards. Medical Device & Diagnostics Industry. March.

Bruno, Michael. 1986. Label Industry Facts and Guidelines: Design-Printing-Application. Label Printing Industries of America.

FDA Survey 1998, Latex Products

National Drug Manufacturers Association. 1997. Comments on the Nonprescription Drug Manufacturers Association on Proposed Labeling Requirements for Over-the-Counter Human Drugs. November 4.

Small Business Administration. 1996. Table of Size Standards. March 1.

Small Business Administration. 1998. Firm Size Data Provided by the Bureau of the Census. Office of Advocacy www.sbaonline.sba.gov/ADVO/stats.

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