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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 801, 878, and 880

[Docket No. 98N-0313]

RIN 0910-AB74

Surgeon's and Patient Examination Gloves; Reclassification

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing regulations to reclassify all surgeon's and patient examination gloves as class II medical devices because it believes that general controls are insufficient to provide a reasonable assurance of safety and effectiveness. The reclassified gloves, including those made of natural rubber latex (NRL) or synthetic material, will be regulated in four categories: Powdered surgeon's gloves, powder-free surgeon's gloves, powdered patient examination gloves, and powder-free patient examination gloves. The proposed special controls are in the form of a proposed guidance document entitled "Medical Glove Guidance Manual," which includes recommended protein and glove powder limits, and new label caution statements including protein and powder labeling requirements. FDA is also proposing to require expiration dating. This proposed rule is intended to reduce the adverse health effects from allergic and foreign body reactions caused by the natural latex (NL) protein allergens and glove powder found on surgeon's and patient examination gloves and to reduce the adverse health effects from defects in the barrier integrity and quality of surgeon's and patient examination gloves.

DATES: Written comments by (*insert date 90 days after date of publication in the Federal Register*). Written comments on the information collection requirements should be submitted by (*insert date 30 days after date of publication in the Federal Register*).

ADDRESSES: Submit written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit written comments on the information collection requirements to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn.: Wendy Taylor, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: Donald E. Marlowe, Center for Devices and Radiological Health (HFZ-100), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-4777.

SUPPLEMENTARY INFORMATION:

I. Background

Surgeon's and patient examination gloves are intended to provide an effective barrier against potentially infectious materials and other contaminants. However, the use of surgeon's and patient examination gloves has been associated with a number of adverse health effects in patients and users, including allergic reactions, foreign body reactions, and irritation.

NL is a milky fluid that consists of extremely small particles of rubber obtained from plants, principally from the *Heavea brasiliensis* (rubber) tree, dispersed in an aqueous medium. NL contains a variety of naturally occurring substances, including plant proteins, which are believed to be the primary allergens associated with NL allergy. NL is employed in the natural rubber latex manufacturing process. Products made by the natural rubber latex manufacturing process, such as medical gloves, are referred to as containing or made of NRL. For a more complete description of the NRL manufacturing process and further definition of related terms, see the final rule entitled "Natural Rubber-Containing Medical Devices; User Labeling," published on September 30, 1997 (62 FR 51021), and codified in part 801 (21 CFR part 801) at § 801.437.

Glove powder is defined as the total particulate matter on a finished glove, including donning and dusting powder, as well as former-release (or mold-release) compounds and manufacturing debris. The main component of donning and dusting powder is most commonly cornstarch.

Health care workers, comprised of physicians, dentists, pharmacists, nurses, technologists, technicians, and phlebotomists, use millions of NRL gloves during procedures involving millions of patients; this makes NRL gloves a significant source of exposure to NL allergens (Ref. 1).

Studies of health care workers, blood donors, and ambulatory surgical patients have demonstrated an appreciable prevalence of NL sensitivity (Refs. 2 to 8). FDA has received 330 reports of adverse events attributed to NL allergy occurring in patients and health care workers, which suggests that allergic reaction to NRL products in health care settings manifests itself in a variety of symptoms ranging from dermatitis to anaphylaxis (Ref. 9). The general population is directly exposed to NRL from a variety of sources, including consumer products such as industrial gloves and NRL balloons, as well as medical devices such as barrier contraceptives and NRL gloves.

FDA has significant concerns about the role of glove powder as a carrier of airborne allergens, because NL allergens have been shown to bind to cornstarch. A number of published clinical and experimental studies support this conclusion (Refs. 10 to 14). In addition to the role of glove powder as a carrier of airborne allergens, FDA is also aware that glove powder contributes to a number of other adverse health effects. As particulate matter, it can cause foreign body reactions, resulting in inflammation, granulomas and adhesions of peritoneal tissues after surgery (Refs. 15 to 19). Glove powder may serve as an absorbent or adsorbent for unbound chemicals that may be irritants or chemical contact sensitizers. In addition, glove powder from nonsterile patient examination gloves may also support microbial growth and act as a carrier for endotoxins (Ref. 20). These multiple concerns of adverse health effects associated with particulate matter from the surface of medical gloves constitute compelling reasons for FDA to reduce the amount of powder on all gloves, as well as to ensure that both powdered gloves and powder-free alternatives are

clearly labeled so users and consumers may make informed choices. Although data is not currently available to quantify a maximum allowable level of glove powder, decreased exposure to glove powder will decrease the prevalence of adverse health effects. Therefore, FDA is recommending a powder level it believes is achievable by industry.

In June 1997, the National Institute of Occupational Safety and Health (NIOSH) issued a safety alert recommending the use of powder-free, reduced protein content NRL or synthetic gloves as a means to reduce exposure to NL allergens, specifically via the airborne route of exposure (Ref. 21). While FDA agrees with the goal of reducing exposure to airborne allergens, FDA is concerned that efforts to produce powder-free gloves with satisfactory donning properties may require additional manufacturing processes that, if not appropriately controlled, have deleterious effects on physical properties, performance, and shelf-life of the gloves (Refs. 22 and 23).

II. Statutory Authority

The Federal Food, Drug, and Cosmetic Act (the act), as amended by the Medical Device Amendments of 1976 (the 1976 amendments) (Public Law 94–295), the Safe Medical Devices Act of 1990 (SMDA) (Public Law 101–629), and the Food and Drug Administration Modernization Act of 1997 (FDAMA) (Public Law 105–115), established a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the act (21 U.S.C. 360c) established three categories (classes) of devices, depending on the regulatory controls needed to provide a reasonable assurance of their safety and effectiveness.

The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval). The effect of classifying a device into class I is to require that the device meet only the general controls that are applicable to all devices. The effect of classifying a device into class II is to require the device to meet special controls as well as general controls, which together provide reasonable assurance of the safety and effectiveness of the device. Class II devices are devices which cannot be classified in class I because general controls by themselves are insufficient to provide reasonable assurance of safety and effectiveness and for which there

is sufficient information to establish special controls to provide such assurance, including the issuance of performance standards, postmarket surveillance, patient registries, and guidelines (see section 513(a)(1)(B) of the act). The effect of classifying a device into class III is to require each manufacturer of the device to submit to FDA a premarket approval application (PMA) that includes information concerning safety and effectiveness of the device.

Under section 513 of the act, devices that were in commercial distribution before May 28, 1976 (the date of enactment of the amendments), generally referred to as preamendments devices, are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

A device that is first offered in commercial distribution after May 28, 1976, generally referred to as a postamendments device, and which FDA determines to be substantially equivalent to a device classified under this scheme, is classified into the same class as the device to which it is substantially equivalent. The agency determines whether new devices are substantially equivalent to previously offered devices by means of premarket notification procedures in section 510(k) of the act (21 U.S.C. 360(k)) and part 807 of the regulations (21 CFR part 807). A device that was not in commercial distribution prior to May 28, 1976, and that has not been found by FDA to be substantially equivalent to a legally marketed device, is classified automatically by statute (section 513(f) of the act) into class III, without any FDA rulemaking proceeding.

Reclassification of classified preamendments devices is governed by section 513(e) of the act (21 U.S.C. 360c(e)). This section provides that FDA may, by rulemaking, reclassify a device (in a proceeding that parallels the initial classification proceeding) based upon "new information." The reclassification can be initiated by FDA or by the petition of an interested person. The term "new information," as used in section 513(e) of the act, includes information developed as a result of the reevaluation of the data before the agency when the device was originally classified,

as well as information not presented, not available, or not developed at that time. (See, e.g., *Holland Rantos v. United States Department of Health, Education, and Welfare*, 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn v. Finch*, 422 F.2d 944 (6th Cir. 1970); *Bell v. Goddard*, 366 F.2d 177 (7th Cir. 1966).)

Reevaluation of the data previously before the agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of changes in “medical science.” (See *Upjohn v. Finch*, supra, 422 F.2d at 951.) However, regardless of whether data before the agency are past or new data, the “new information” on which any reclassification is based is required to consist of “valid scientific evidence,” as defined in section 513(a)(3) of the act (21 U.S.C. 360c(a)(3)) and 21 CFR 860.7(c)(2). FDA relies upon “valid scientific evidence” in the classification process to determine the level of regulation for devices. For the purpose of reclassification, the valid scientific evidence upon which the agency relies must be publicly available. Publicly available information excludes trade secret and/or confidential commercial information.

On November 21, 1997, the President signed into law FDAMA. Section 206 of FDAMA added a new section 510(m) (21 U.S.C. 360(m)) to the act. Section 510(m)(2) of the act provides that FDA may, on its own initiative or upon petition of an interested person, exempt a class II device from the requirement of premarket notification in section 510(k) of the act, if FDA determines that a 510(k) submission is not necessary to provide reasonable assurance of the safety and effectiveness of the device. Such an exemption would permit manufacturers to introduce the generic type of device into commercial distribution without first submitting a premarket notification to FDA.

Section 701(a) of the act (21 U.S.C. 371(a)) authorizes FDA to issue substantive binding regulations for the efficient enforcement of the act. (*Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973); see also *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U.S. 645, 653 (1973); *National Ass'n of Pharmaceutical Manufacturers v. FDA*, 637 F.2d 877 (2d Cir. 1981);

National Confectioners Ass'n v. Califano, 569 F.2d 690 (D.C. Cir. 1978); *National Nutritional Foods Ass'n v. Weinberger*, 512 F.2d 688 (2d Cir.), cert. denied, 423 U.S. 825 (1975).)

Section 502(a) of the act (21 U.S.C. 352(a)) provides that a device is misbranded “[I]f its labeling is false or misleading in any particular.” Section 201(n) of the act (21 U.S.C. 321 (n)) provides that, in determining whether labeling of a regulated article (such as a device) is misleading

* * * there shall be taken into account * * * not only representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling * * * fails to reveal facts material in light of such representations * * * with respect to consequences which may result from the use of the article to which the labeling * * * relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual.

The courts have upheld FDA’s authority to prevent false or misleading labeling by issuing regulations requiring label warnings and other affirmative disclosures (See, e.g., *Cosmetic, Toiletry, and Fragrance Association v. Schmidt*, 409 F. Supp. 57 (D.D.C. 1976), aff’d without opinion, Civil No. 75–1715 (D.C. Cir. August 19, 1977), even in the absence of a proven cause-and-effect relationship between product usage and harm (*Council for Responsible Nutrition v. Goyan*, Civil No. 80–1124 (D. D. C. August 1, 1980)).

FDA may impose testing requirements in a labeling regulation issued under its general rulemaking authority. (See, e.g., *American Frozen Food Inst. v. Mathews*, 413 F. Supp. 548 (D.D.C. 1976), aff’d per curiam sub nom. *American Frozen Food Inst. v. Califano*, 555 F.2d 1059 (D.C. Cir. 1977); see also *National Nutritional Foods Ass'n v. Weinberger*, supra.) Thus, FDA may require that all manufacturers use the same conditions to test aging to ensure that the expiration date reflects the period of time a product can be used safely. Similar requirements are imposed in § 801.430(f) for absorbency testing for menstrual tampons, and in § 801.420(c)(4) on hearing aid manufacturers and distributors who must determine and state technical data values for hearing aid labeling in accordance with specified test procedures. The hearing aid regulation has been upheld. (*American Speech and Hearing Ass'n v. Califano*, Medical Devices Report (CCH) No.

77–1327 §§ 15004, 15007 (D.D.C. August 23, 1977) aff'd No. 77–1327 (D.C. Cir. Dec. 19, 1977).)

Food regulations issued under section 701(a) of the act also impose many such specific testing requirements (see e.g., 21 CFR 113.40 (tests for low-acid canned foods); 21 CFR 155.190(b)(2)(i) (test for determining drained weight of canned tomatoes); 21 CFR 161.190 (method for determining color designation of tuna)).

III. Powder and Protein Concerns

Although FDA has been concerned about airborne NL allergens associated with the use of powdered medical gloves and has undertaken continued efforts to address these concerns, recent heightened awareness within the health care community and State and Federal Government agencies of adverse health effects has prompted this proposed action.

Over the past 3 years, FDA has received requests to ban the use of all glove powders. These requests have been based on a number of clinical and experimental studies reporting that cornstarch on surgical gloves can reduce tissue resistance to infection, enhance the development of infection, cause formation of granulomas and adhesions, act as a carrier of NL protein from NRL products, and serve as a potential source of occupational asthma. Although a ban of all powdered medical gloves has been requested by petitioners and would reduce the problem of airborne powder, it would not completely address the problem of NL allergy and would potentially leave a significant and important need for high quality barrier products unmet.

One of the concerns regarding glove powder, in general, is its capability, as particulate material, to cause foreign body reaction, resulting in inflammation, granulomas and adhesions of peritoneal tissues after surgery (Refs. 15 to 19). Although cornstarch was considered to be absorbable by United States Pharmacopeia (USP), changes in the sterilization processes have reduced absorbability significantly (Ref. 15). Cornstarch represents a growth source for bacteria, and it is also a carrier of endotoxin, which can play a role in enhancing both delayed and immediate hypersensitivity (Ref. 20). Clinical experience suggests that powder on NRL gloves, in addition to its role in Type I allergy, may also be a contributing factor in the development of irritant

dermatitis and Type IV allergy. Irritant skin reactions have been observed in association with frequent exposure to glove powder. Compromised skin barrier properties resulting from such reactions may permit penetration of allergens and other substances into the skin, thereby increasing chances for the development of both Type I and Type IV allergy (Ref. 24).

In addition, a significant concern, specific to NL gloves, exists regarding the role of glove powder as a carrier of airborne NL allergens. A number of respiratory problems and episodes of bronchial spasms in hospital employees and patients, reported since the mid 1980's, were ascribed to inhalation of airborne NL allergens in settings with heavy use of powdered gloves (Refs. 25 to 30). The implication of glove powder in the previous clinical reports was based on medical histories of individuals presenting with symptoms, on positive skin tests, positive tests for the presence of antibodies to NL allergens in blood and, in some cases, on positive inhalation challenge tests. A number of published clinical and experimental studies support this conclusion.

Binding of NL proteins to cornstarch was demonstrated in recent laboratory studies, which support a causal relationship between asthmatic reactions in individuals with NL allergy and the exposure to airborne particles from NL products (Refs. 10 and 11). The level of exposure and the severity of the reactions depend on both the amount of powder and the amount of NL protein allergens on the finished products. Measurements of airborne particle levels in environments where NL gloves were used frequently demonstrated that the level of airborne allergen is directly related to the frequency of powdered NL glove usage in particular areas and to the level of allergen and/or powder on the gloves used (Refs. 12 and 14).

Direct evidence that NL protein allergens, bound to the glove powder particles, provoke respiratory allergic reactions and asthma-like attacks has been documented by the bronchial provocation tests with powders on NL gloves. The bronchial provocation tests were performed by having allergic individuals inhale the extracts from powder-free surgeon's gloves, from powdered surgeon's gloves, and from cornstarch powder not exposed to NL. The studies indicated that cornstarch powder not exposed to NL did not cause any reaction in sensitized subjects, while

nebulized powdered NL surgeon's glove extract, and to some extent, nebulized powder-free glove extract induced bronchoconstriction in tested subjects (Ref. 31).

However, the scientific data to define the quantitative relationship between respiratory allergic reactions and powder level on NL gloves are not available at this time. Such data and the specific dose-response relationship would be difficult to establish, because allergenicity of the airborne glove powder depends on the amount of powder and also on the amount of powder-bound allergenic proteins. Standardized methods for measuring the amount of powder-bound proteins or allergens and the amount of inhaled powder are not available.

NL protein has been widely reported as a cause of Type I sensitivity in individuals who have been exposed to NL devices (Refs. 2 to 8). Repeated exposure to NL protein is considered to increase the probability that an individual will become sensitized. Total water-extractable protein on the finished NL product is considered an indirect measure of the potential allergenicity. Because several NL proteins have already been identified as allergenic and others may be identified in the future, exclusion of any proteins from the evaluation may result in an inaccurate determination of potential allergenicity. The total water-extractable protein level measured using the standard American Society for Testing and Materials (ASTM) D 5712 method was found to correlate well with currently used allergen measurement methods. Most importantly, a total water-extractable protein level correlates also with the skin prick test, which is a direct measure of allergic response in sensitized individuals (Ref. 32). Since May 1991, FDA has advised manufacturers of NL devices to reduce the water-extractable protein on their NL devices. This reduction is now addressed in the Quality System (QS) Regulation at 21 CFR 820.3(p) and 820.70(h).

Initially, a labeling claim for a protein level was not accepted in a 510(k) submission because a standard test method for measuring water-extractable protein in NL did not exist. In 1995, with the help of industry and FDA, ASTM published the "ASTM Standard Test Method for Analysis of Protein in Natural Rubber and its Products, D 5712-95." FDA subsequently issued a document entitled "Interim Guidance On Protein Content Labeling Claim For Latex Medical Gloves," which

is based on this test method. Manufacturers were allowed to use this guidance to submit a 510(k) submission for NL gloves identifying the level of water-extractable protein for the device. FDA is now proposing that a recommended limit on water-extractable protein per glove and the actual protein level appear on the label.

The amount of powder required for satisfactory donning of gloves has not been quantified, and the level of glove powder used varies greatly. Limited laboratory data from measurements of a number of surgeon's and patient examination gloves demonstrated that powder levels ranged from 70 to 375 milligrams (mg) per glove for surgeon's gloves and from 50 to 426 mg per glove for patient examination gloves (Ref. 31). Because of the multiple concerns regarding adverse health effects associated with particulate matter from the surface of surgeon's and patient examination gloves, FDA is now proposing that a recommended limit on glove powder and the actual level of glove powder appear on the label. FDA recognizes there is a correlation between powder level and ease of glove donning and that powder level is correlated with adverse health effects. For this reason, FDA is encouraging industry to find the balance between donning requirements and reducing the risks of adverse health effects.

Lowering the powder level and the amount of protein on surgeon's and patient examination gloves will reduce exposure to NL allergens and benefit both allergic individuals and those at risk to develop allergy. In addition, the reduction of glove powder levels will help reduce exposure to particulate materials responsible for foreign body reactions. However, the reduction of powder and protein levels must be accomplished by methods that do not compromise the availability of or barrier properties of surgeon's and patient examination gloves.

IV. Barrier and Other Quality Issues

In the **Federal Register** of October 21, 1980 (45 FR 69723), FDA issued a final rule classifying the patient examination glove into class I and exempting manufacturers of the device from compliance with premarket notification procedures under section 510(k) of the act and certain requirements of the current good manufacturing practice (CGMP) regulation. FDA granted the

exemptions in the 1980 regulation because, at that time, no adverse experiences had been related to patient examination gloves. Furthermore, the role of the gloves as a protective barrier against human immunodeficiency virus (HIV) transmission was not recognized and the concomitant risks associated with glove failure were not well understood.

In the **Federal Register** of January 19, 1982 (47 FR 2810 at 2852), FDA proposed that the surgeon's glove be classified into class II because of concerns about tissue compatibility and the risk of infection if the devices were not properly sterilized. Comments offered in response to the proposed classification stated that those problems could be addressed through general controls, including labeling and CGMP adherence, and recommended that the device be classified into class I because of the history of its safe and effective use. In the **Federal Register** of June 24, 1988 (53 FR 23856), FDA issued a final rule classifying the surgeon's glove into class I without exemptions. Manufacturers and importers of surgeon's gloves have been required to comply with the premarket notification and CGMP regulations since the initial classification of the device.

Over the years, many issues regarding surgeon's and patient examination gloves have been brought to the attention of FDA. The acquired immune deficiency syndrome (AIDS) epidemic resulted in an elevated reliance on medical gloves as a barrier against blood-borne viral transmission. The increased demand for gloves soon outstripped the domestic supply. Foreign glove manufacturers began to meet the demand for additional gloves. Many manufacturers with little or no medical glove manufacturing experience began operations, resulting in large quantities of gloves of uncertain quality entering the U.S. market.

Following the advent of AIDS as a major public health concern and recommendations from the Centers for Disease Control and Prevention (CDC) that health care workers use appropriate barrier precautions to prevent exposure to the HIV virus, FDA recognized the need for greater assurance that cross-contamination between patients and health care workers be prevented. Accordingly, in the **Federal Register** of January 13, 1989 (54 FR 1602), FDA revoked the exemption for patient examination gloves from certain CGMP requirements in order to assure that

manufacturers provide an acceptable manufacturing quality level. FDA similarly revoked the exemption from premarket notification requirements for patient examination gloves. On December 12, 1990 (55 FR 51254), FDA published regulations describing certain circumstances under which surgeon's and patient examination gloves would be considered adulterated, and establishing the sampling plans and test methods the agency would use to determine whether gloves were adulterated (§ 800.20 (21 CFR 800.20)). Subsequently, FDA initiated inspections of glove manufacturers to assure conformance with the acceptable quality levels (AQL) identified in that regulation.

FDA has sought to address many concerns regarding the quality and barrier integrity of medical gloves. Certain processes or conditions can often contribute to degradation of the barrier. NL degrades if it is not correctly formulated and processed. Proper formulation includes the use of stabilizers, antiozonants, and antioxidants to reduce degradation. Improper curing can also cause thin spots on the glove surface, which may lead to early barrier failure.

Gloves composed of synthetic polymer, such as nitrile, are produced by essentially the same processes as NL. The same accelerators, antioxidants, and stabilizers are used to reduce degradation. Thus, improper formulation and processing may also lead to rapid degradation of synthetic gloves.

Storage conditions can also cause degradation of the polymers, whether natural or synthetic. These storage conditions include the temperature at which the material is held, the humidity of their environment, and any radiation (for example, sunlight or fluorescent lights) to which the material may be exposed.

Additionally, chlorination is widely used to reduce the tackiness of NL gloves and thus eliminate the need for donning powder. Chlorination works by degrading the surface of the gloves. Therefore, chlorination must be carefully controlled in order to prevent destruction of the glove barrier. Improperly chlorinated gloves rapidly degrade, and breaks in the latex film may occur in a matter of months.

Another concern has been the presence of minute defects known as pinholes, which directly affect the barrier integrity of the gloves. FDA studies of micro-photographs of defective NL devices have shown that dust, dirt, rust, paint chips, charred starch, insect parts, and other debris may cause pinholes. Therefore, appropriate environmental and processing controls, as required by the QS regulation, are needed. Manufacturers also need to control other causes of pinholes such as former vibration, air bubbles in the dipping tanks, dirty formers, incorrect formulation, and excessive curing temperatures.

If gloves have pinholes, breaks or tears, viruses can potentially penetrate the glove wall, eliminating or reducing the gloves' effectiveness as a barrier. On April 6 and 7, 1989, the University of Maryland, in conjunction with FDA, held a conference entitled "Latex as a Barrier Material," which reiterated the value of NL as a barrier film and generated continued support towards more research in this area by industry and FDA.

Although manufacturers have data to show that their gloves meet their company AQL for defects when the gloves are shipped, for some manufacturers, the same gloves which passed the manufacturer's tests are sometimes rejected at the port of entry in the United States because the gloves fail the FDA water leak test at that point. This test result disparity, whether due to degradation or for other reasons, is a primary reason why, upon importation, the gloves of some manufacturers have been detained without physical examination. Manufacturers should assure, by means of stability testing, that their surgeon's and patient examination gloves will continue to meet the manufacturers' specifications over the expected life of the gloves.

FDA is aware that microbial growth on gloves also can be a problem. The QS regulation requires manufacturers to control processing, shipping and storage environment, and contamination when these can adversely affect the product. Therefore, processing controls should include: Using only cornstarch with an acceptable bioburden, properly storing the cornstarch until it is used, applying cornstarch by established procedures, cooling the cornstarch slurry and/or using an antimicrobial in the cornstarch slurry tanks, checking finished gloves on a sampling basis to assure

that excessive cornstarch is not applied, keeping the finished gloves clean, establishing and meeting a dryness specification for finished gloves, and protecting finished gloves from adverse environmental conditions.

Although synthetic materials have improved in recent years, NL gloves may be superior to some synthetic gloves in regard to barrier properties (Ref. 34). Both NL and synthetic surgeon's and patient examination gloves provide protection against microorganisms; however, it has been demonstrated that compared to vinyl, NL has more effective and durable barrier qualities (Refs. 35 and 36).

There are other safety and performance issues related to gloves and other barrier devices that are currently being considered by industry and FDA. These issues include puncture resistance, tear resistance, reliability, and biocidal claims.

V. The Proposed Rule

Based upon new information that was not presented, not available, or not developed when FDA originally classified surgeon's and patient examination gloves, FDA has reevaluated its classification in light of changes in the medical science discussed in sections III and IV of this document. The new, publicly available, valid scientific evidence demonstrates that these gloves should not remain as class I devices because of: (1) Barrier integrity concerns; (2) degradation of quality during storage; (3) contamination concerns; and (4) concerns about exposure to NL allergens and the role of glove powder as a carrier of airborne NL allergens, and the inability of general controls to address these concerns. The agency believes that general controls are no longer sufficient to provide reasonable assurance of the gloves' safety and effectiveness and, therefore, FDA is proposing that these gloves be reclassified into class II.

Surgeon's and patient examination gloves are intended for use as an effective barrier against potentially infectious materials and other contaminants. Risk to the user or patient may result from lack of barrier integrity from degradation, pinholes, breaks, tears, or loss of quality during storage, potentially causing penetration of the glove wall by viruses or other infectious materials. When

glove powder comes into contact with compromised human tissue, risk to the user or patient may result from foreign body reactions caused by NL allergens bound to the glove powder. Allergic reactions may also be caused by inhalation of NL allergens bound to the glove powder. Reducing the degree of risk to acceptable levels depends on effective maintenance of the barrier properties of the gloves and on reducing exposure to NL allergens, particularly exposure to airborne NL allergens. The highest risk products are those with large amounts of glove powder and NL protein and those products with poor barrier properties.

In order to enable users to distinguish between powdered and powder-free gloves and to choose the glove type appropriate for their needs, FDA proposes to reclassify surgeon's gloves into two separate classifications, based on powder level: Powdered surgeon's gloves, and powder-free surgeon's gloves. FDA similarly proposes to reclassify patient examination gloves into two categories: Powdered patient examination gloves, and powder-free patient examination gloves.

FDA is proposing that these gloves be subject to two special controls: A guidance document entitled, "Medical Glove Guidance Manual," and new user labeling requirements. FDA believes that the proposed guidance document and user labeling requirements are necessary to provide reasonable assurance of the safe and effective use of the devices. The guidance is currently being issued in draft as a Level 1 guidance consistent with the good guidance practices (GGP's) FDA adopted for the development, issuance, and use of guidance documents (62 FR 8961, February 27, 1997). Elsewhere in this issue of the **Federal Register**, FDA is announcing the availability of the guidance in draft form, to provide an opportunity for comment.

The proposed guidance document recommends that manufacturers of powdered surgeon's and patient examination gloves limit the amount of powder to no more than 120 mg of powder per glove, regardless of glove size. In order to limit total exposure to the user, a "per glove" measurement (mg per glove) is used instead of the "per unit" dose (mg per gram (g) of glove material). Under the proposed labeling requirements, manufacturers of all powdered gloves would be required to include the actual level of glove powder on the label. FDA believes that the

recommended limit should be sufficient for proper donning of gloves, but would reduce exposure to airborne glove powder particles. In addition to the role of glove powder as a carrier of airborne allergens, FDA is also aware that glove powder contributes to a number of other adverse health effects. As particulate matter, it can cause foreign body reactions, resulting in inflammation, granulomas and adhesions of peritoneal tissues after surgery (Refs. 15 to 19). Glove powder may serve as an absorbent or adsorbent for unbound chemicals that may be irritants or chemical contact sensitizers.

The proposed guidance document further recommends that manufacturers of powder-free surgeon's and patient examination gloves limit the amount of total trace (residual) powder to no more than 2-mg particulate weight (based on the ASTM test standard D 6124-97) per glove, regardless of glove size. Previously, this limit was recommended to manufacturers who wanted to market gloves with a powder-free labeling claim. A number of premarket notification submissions based on this claim already have been cleared for market.

The proposed guidance document also recommends that manufacturers of NL surgeon's and patient examination gloves limit the amount of water-extractable protein on the gloves to no more than 1,200 micrograms (μg) of protein per glove, regardless of glove size. In order to limit total exposure to the user, a "per glove measurement" (mg per glove) is used instead of a "per unit" dose (mg per g of glove material). Under the proposed labeling requirements, labeling on all NL gloves would be required to include the level of water-extractable protein measured, as recommended in the guidance, by the currently recognized ASTM D 5712 modified Lowry method. The lowest acceptable amount of water-extractable protein that may be stated in the labeling will be limited by the sensitivity of the current ASTM D 5712 test method to 50 μg of protein per g of natural rubber product (which translates to 300 μg per glove for a 6 g glove, i.e., $6 \times 50 = 300$). FDA believes that without a more sensitive standard method, lower claims would be misleading.

The proposed labeling requirements are a special control intended to provide guidance to users of surgeon's and patient examination gloves. They would require manufacturers to provide new caution statements, which would include both the FDA recommended limit for glove powder and protein levels, as well as the actual glove powder and protein levels present in the manufacturer's gloves. The labeling special control provides essential decisionmaking information for health professionals, patients, and lay users. The information required under the proposed regulations would assist health care professionals, patients and lay users to select a lower risk device by providing information about protein and glove powder levels.

The proposed caution statements would be required to appear on all device labels and other labeling, including the principal display panel of the device packaging, the outside package, container or wrapper, and the immediate device package, container or wrapper. The proposed caution statements for powdered and powder-free NL gloves (surgeon's and patient examination) would supersede the caution statements in § 801.437(d) for devices containing NRL currently required in the regulation published in the **Federal Register** of September 30, 1997 (effective September 30, 1998).

Labeling for powdered surgeon's and patient examination gloves containing NL that contacts humans would be required to bear the following statement:

“Caution: This product contains natural rubber latex which may cause allergic reactions. FDA recommends that this product contain no more than 120 mg powder and 1,200 µg extractable protein per glove. This product contains no more than [insert level] mg powder and no more than [insert level] µg extractable protein per glove.”

Labeling for powder-free surgeon's and patient examination gloves containing NL that contacts humans would be required to bear the following statement:

“Caution: This product contains natural rubber latex which may cause allergic reactions. FDA recommends that this product contain no more than 1,200 µg extractable protein per glove. This product contains no more than [insert level] µg extractable protein per glove.”

FDA is also proposing new labeling requirements for powdered gloves made of synthetic material. FDA proposes that labeling for those gloves bear the following statement:

“Caution: Glove powder is associated with adverse reactions. FDA recommends that this product contain no more than 120 mg powder per glove. This product contains no more than [insert level] mg powder per glove.”

FDA is proposing no new labeling for powder-free surgeon’s gloves and patient examination gloves made of synthetic materials.

FDA is also proposing to require expiration dating on the labeling of all powdered surgeon’s and patient examination gloves and powder-free surgeon’s and patient examination gloves. Previously, expiration dating has not been required for surgeon’s or patient examination gloves, although it is customary for surgeon’s gloves to bear an expiration date for sterility. A few glove manufacturers have voluntarily used expiration dates based on real-time data to support the integrity of the gloves throughout the shelf-life period.

In view of the quality concerns discussed in section IV of this document, especially those relating to degradation of barrier integrity over time, FDA believes that expiration dating is necessary to allow users to correctly store and use stock of gloves, and to allow users to avoid gloves that may have degraded. Users must be aware of the potential for degradation of gloves in order to safely use such products to provide a barrier from infectious agents. Accordingly, FDA believes that shelf life is a fact material to the consequences of use of surgeon’s and patient examination gloves. Therefore, FDA is now proposing that all surgeon’s and patient examination gloves be required to bear an expiration date on their primary and retail packaging and shipping carton. The expiration date should consist of the month and year for which data exists to support the shelf-life of the gloves. The time period upon which the expiration date is based starts with the date of manufacture.

This expiration date must be based on testing conducted according to a validated stability study protocol to determine the shelf-life of the gloves. The stability study protocol should employ

tests commonly used by industry to demonstrate the physical and mechanical integrity of the gloves over their claimed shelf-life.

Manufacturers will not be required to provide new section 510(k) of the act submissions to demonstrate the shelf-life of gloves. However, for each distinct glove design, the records of study protocols and test data must be retained for a period equivalent to the design and expected life of the gloves, and must be made available for inspection by FDA personnel.

Expiration dates for sterile surgeon's or patient examination gloves should either be based on the shelf-life determined by stability studies as outlined in the proposed rule, or on the sterility shelf-life, whichever is shorter. Only one expiration date should appear on each product.

FDA does not intend to require a new submission under section 510(k) of the act based upon labeling changes or reductions in glove powder or NL protein made to comply with any final regulation based upon this proposed regulation, provided that no other changes requiring a new 510(k) submission under § 807.81 are made to the device.

Section 510(m) of the act allows FDA to exempt a class II device from the requirement of premarket notification in section 510(k) of the act. FDA does not intend to exempt powdered or powder-free surgeon's or patient examination gloves from premarket notification because of FDA's concerns regarding the effective maintenance of barrier properties and adverse health effects associated with NL allergens, glove powder and residual chemical sensitizers and irritants.

This proposed rule would not impose requirements on glove users or user facilities. Therefore, it would not affect the authority of the Secretary of Labor, under the Occupational Safety and Health Act (OSH act), to enforce regulations, standards, or other directives issued under the OSH act.

VI. Specific Request for Comments

FDA recognizes that this regulation affects surgeon's and patient examination gloves in different ways, depending on glove powder level. FDA also recognizes that manufacturing

processes for powdered and powder-free gloves vary. FDA welcomes comments on all aspects of the proposed regulation, but particularly invites comments on the following issues:

1. FDA requests comments on the timeframe for implementation of the proposed rule considering the need for changes in production, technology, and labeling, as well as the immediate need to address adverse health concerns associated with medical gloves. Although FDA prefers a 1-year effective date, FDA is proposing a 2-year effective date based on indications from industry that the necessary changes could not be made in 1 year and that a shortage of medical gloves could result.

2. In the proposed guidance document, FDA recommends a limit of no more than 120 mg powder per powdered glove, regardless of size, as the maximum level in order to reduce exposure to particulates and airborne allergens. FDA requests comments on the recommended limit with regard to the minimum level of powder needed for adequate donning of gloves.

3. FDA requests comments on the feasibility and desirability of additional labeling requiring manufacturers to state the primary ingredients in glove powder in the product labeling.

4. In the proposed guidance document, FDA is recommending no more than 2 mg powder per glove, regardless of size, as the recommended powder level for those surgeon's and patient examination gloves labeled "powder-free." FDA requests comments on the proposed limit. FDA is also seeking comments on the possible impact of this powder limit on barrier properties and shelf-life of NL gloves.

5. FDA is also considering a future requirement that all surgeon's and patient examination gloves marketed in the United States be powder-free. FDA requests comments as to whether a continued need for powdered gloves exists, and, if so, the reason for this need.

6. FDA considered restrictions on the sale (advertising), distribution, and use of powdered surgeon's and patient examination gloves. FDA is seeking comments on the feasibility of such restrictions.

7. In the proposed guidance document, FDA is recommending an upper limit of no more than 1,200 µg protein per NL glove, regardless of size, as the maximum level for NL surgeon's and patient examination gloves. FDA is seeking comments on the proposed recommended limit.

8. FDA's objectives in this proposed rulemaking are to reduce adverse health effects from allergic reactions and foreign body reactions by controlling the levels of water-extractable protein and glove powder on NL gloves. FDA requests comments as to whether there are feasible alternative approaches to achieve these objectives. If other alternatives or data submitted present feasible methods to protect the public health or suggest that different powder or protein levels are adequate to protect the public health, FDA may incorporate such data or approaches in a final rule.

9. FDA also invites comments on the issue of whether the recommended limits on powder and protein proposed in this rule should be recommended limits or required limits.

10. FDA considered allowing manufacturers to establish an initial tentative shelf-life up to a certain duration based on accelerated aging data, provided that manufacturers initiate concurrent real-time shelf-life studies to confirm and extend the tentative shelf-life. FDA has been unable, however, to determine whether any validated stability study protocols exist employing accelerated aging methodologies. The agency invites comments or information on the availability of accelerated aging stability study protocols which are predictive of glove shelf-life. If convincing information concerning such protocols is available, FDA may incorporate such an approach in a final rule.

11. FDA considered requiring the use of a special air handling system at the point of use for those facilities using powdered surgeon's and patient examination gloves with powder levels over 120 mg per glove, regardless of glove size. FDA is seeking comments on the appropriateness of this restriction.

12. FDA seeks comments as to whether a provision permitting affected persons to request exemptions or variances from the labeling requirements or restrictions on distribution and use proposed in this rule should be added.

VII. General Request for Comments

Interested persons may submit written comments regarding this proposed rule by (*insert date 90 days after date of publication in the **Federal Register***), to the Dockets Management Branch (address above). Comments regarding the information collection provisions should be submitted by (*insert date 30 days after date of publication in the **Federal Register***), to the Office of Information and Regulatory Affairs, Office of Management and Budget (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number 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.

VIII. Access to Special Control

The availability of the special control entitled “Medical Glove Guidance Manual” is being announced elsewhere in this issue of the **Federal Register**. A copy of the “Medical Glove Guidance Manual” may be seen by interested persons in the Dockets Management Branch (address above) between 9 a.m. and 4 p.m., Monday through Friday.

Persons interested in obtaining a copy of the guidance may also do so using the World Wide Web (WWW). FDA’s Center for Devices and Radiological Health (CDRH), maintains an entry on the WWW for easy access to information including text, graphics, and files that may be downloaded to a PC with access to the Web. The CDRH home page is updated on a regular basis and includes the draft “Medical Glove Guidance Manual;” device safety alerts; **Federal Register** reprints; information on premarket submissions (including lists of approved applications and manufacturers’ addresses); small manufacturers’ assistance; and information on video conferencing and electronic submissions, mammography matters, and other device-oriented information. The CDRH home page may be accessed at “<http://www.fda.gov/cdrh>”.

Submit written requests for single copies of the draft guidance to the Division of Small Manufacturers Assistance, Center for Devices and Radiological Health (HFZ-220), Food and Drug

Administration, 1350 Piccard Dr., Rockville, MD 20850. Send two self-addressed adhesive labels to assist that office in processing your request, or fax your request to 301-443-8818.

To receive the directions via fax machine on receiving the proposed guidance document, call CDRH Facts-on-Demand system at 800-399-0381, or 301-827-0111 from a touch-tone telephone. At the first voice prompt, press 1 to access the Division of Small Manufacturers Assistance (DSMA) Fax, at the second voice prompt, press 2, and then enter the document number 852 followed by the pound sign (#). Then follow the remaining voice prompts to complete your request.

IX. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866, under the Regulatory Flexibility Act (5 U.S.C. 601-612), and under the Unfunded Mandates Reform Act (Public Law 104-4). 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). Unless the agency certifies that the rule is not expected to have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant economic impact of a rule on small entities. Section 202 of the Unfunded Mandates Reform Act requires that agencies prepare an assessment of anticipated costs and benefits before proposing any rule that may result in an expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million in any one year (adjusted annually for inflation).

The agency believes that this proposed rule is consistent with the principles set out in the Executive Order and in these two statutes. The rule is an economically significant regulatory action as defined by the Executive Order. With respect to the Regulatory Flexibility Act, FDA does not believe that this proposal will have a significant effect on a substantial number of small entities, but recognizes the uncertainty of its estimates. Therefore, the agency has prepared an IRFA. FDA

is not required to conduct a cost-benefit analysis according to the Unfunded Mandates Reform Act, because the rule will not impose any mandates on State, local, or tribal governments, or the private sector, that will result in an annual expenditure of \$100 million or more.

Furthermore, in accordance with the Small Business Regulatory Enforcement Fairness Act of 1995 (Public Law 104–121), it has been determined that this proposed rule would be a major rule for the purpose of congressional review.

A. Objectives of the Proposed Regulations

The objectives of this proposed regulation are to reduce the adverse health effects from allergic and foreign body reactions caused by the NL protein allergens and glove powder found on surgeon's and patient examination gloves, and from defects in the barrier integrity and quality of surgeon's and patient examination gloves. The rule will accomplish these objectives by encouraging manufacturers to limit both the level of water-extractable protein allowed on gloves and the level of powder packaged with the gloves, and by requiring the inclusion of caution statements and the actual level of protein and powder in the labeling of the gloves. In addition, labeling will include expiration dates to ensure that the gloves provide adequate barrier protection and that all medical gloves meet quality standards specified in the special control guidance referenced elsewhere in this preamble. FDA believes that by reducing the amount of powder dispersed, these special controls will reduce the incidence and severity of the allergic reactions caused by NL proteins without compromising the barrier performance of these products.

B. Risks of NL Protein Allergic Reactions

FDA recognizes that no systemic epidemiological data exist to identify the risk of airborne NL protein allergens. However, several sources indicate that a proportion of the U.S. population have developed NL sensitivity (Refs. 1 to 8) due to increased exposure to NL proteins. The increased use of NL gloves with unlimited powder and protein levels in recent years is believed to contribute to these adverse events.

FDA's Adverse Experience Reporting System received a total of 330 NL allergy Medical Device Reports (MDR's) associated with medical gloves for the 12-month period of August 15, 1996, through August 15, 1997 (Ref. 9). These reports included reactions of 435 affected persons. Despite the lack of representative sampling and the unconfirmed nature of these reports, FDA believes these data may provide a reasonable measure of the magnitude of existing risk. Table 1 classifies these reports by type and severity of reaction and shows the results by number of affected patients.

TABLE 1.—NUMBER OF PATIENTS REPORTING TO FDA NATURAL RUBBER LATEX ALLERGIES REACTIONS ASSOCIATED WITH MEDICAL GLOVES BETWEEN AUGUST 15, 1996, AND AUGUST 15, 1997

	Type of Allergic Reaction ¹			
	Local Topical	Systemic Topical (i.e., rash not in area with direct contact)	Systemic Respiratory (e.g., wheezing, shortness of breath)	Respiratory Requiring Aggressive Treatment (e.g., anaphylaxis, hospitalization)
Number of Patients Reporting Reaction	20	21	294	100

¹Includes 40 patients with unclassified reactions that were distributed by proportion of reported reactions.

FDA has long been aware that MDR's received by the agency may account for as little as one percent of the actual events (Ref. 37). If true, the reports received for allergic reactions associated with medical gloves could represent as many as 43,500 allergic incidents during the 12-month period. Because patients may often fail to connect an allergic incident to use of gloves, FDA believes that this estimate better reflects the true number of incidents associated with medical gloves. Given that approximately 22.0 billion gloves (Ref. 38) were used and 2.16 billion patient visits occurred during that period (Ref. 39), the projected baseline rate of annual allergic reaction incidents to the total population (0.0001626) at current protein/powder levels does not seem unreasonable.

Despite the widespread under-reporting cited in the General Accounting Office (GAO) report, FDA believes that those allergic reactions that require the most aggressive treatment would be subject to less under-reporting. For this analysis, FDA has assumed that MDR's for patients with severe allergic reactions are under-reported by 33 percent, and the other three categories are proportionally increased to account for the total under-reporting (Table 2). Specifically, FDA

believes that the 100 reported incidents of respiratory allergic reactions requiring aggressive treatment (from Table 1) represent only 150 actual such incidents; not 1,000 as would be indicated by MDR underreporting. The difference of 850 expected incidents were distributed to the remaining three categories to result in 43,500 total incidents. Table 2 also shows the proportion of each category of reactions reporting long-term and short-term effects, based on reported lost work-time due to recovery. As expected, only 6 percent of all topical local reactions were considered long-term, while almost half of the serious systemic reports were long-term. As discussed in the benefits section (section IX.F of this document), FDA has assumed, based on discussions with clinicians, that short-term impacts have a duration of 1 day and long-term impacts a duration of 2 months.

Table 2 also presents FDA's estimated annual number of each type of allergic reaction. Although no mortalities were reported in the MDR's for this period, anaphylaxis carries a risk of mortality that FDA statisticians place at up to 2 percent, even in health care settings. Because not all reported serious systemic respiratory reactions were anaphylaxis, FDA assigned a probability of 0.002 to the adjusted reports to account for potential fatalities due to anaphylactic shock caused by NL allergens. (This assumes that only 10 percent of all respiratory reactions that require aggressive treatment were due to anaphylaxis.) Given the estimated under-reporting rate, this implies an annual risk of 0.3 mortalities. FDA expects that by encouraging lower protein and powder levels for medical gloves, the proportion of allergic reactions to NL protein allergens will be reduced.

TABLE 2.—ESTIMATED NUMBER OF PATIENTS EXPERIENCING NATURAL RUBBER LATEX ALLERGIC REACTION ASSOCIATED WITH MEDICAL GLOVES FROM AUGUST 15, 1996, TO AUGUST 15, 1997, AND PROPORTION EXPERIENCING SHORT- AND LONG-TERM EFFECTS

	Type of Allergic Reaction				
	Local Topical	Systemic Topical	Systemic Respiratory	Respiratory Requiring Aggressive Treatment	
				Other Reactions	Mortality
Estimated Number of Patients Experiencing Reaction	2,588	2,717	38,045	149.7	0.3
Proportion Exhibiting Short-Term Effects (duration of 1 day)	94%	74%	73%	51%	NA
Proportion Exhibiting Long-Term Effects (duration of 2 months)	6%	26%	27%	49%	NA

C. Costs of the Proposed Regulation

This section develops estimates of the costs of compliance with the proposed rule by comparing the expected costs of using surgeon's and patient examination gloves after the rule is in effect to the costs that would have been incurred in the absence of the rule. Regulatory costs occur in four categories. First, the proposed regulation is expected to accelerate the trend of the glove market towards more costly, powder-free products. Second, higher average glove purchase prices will result from the increased cost of gloves with recommended levels of powder and NL proteins compared to the cost of gloves with unregulated levels of powder and NL proteins. Third manufacturers will be required to conduct shelf-life testing on gloves in order to support expiration dates. Fourth, increased labeling costs will result from the addition of protein and powder levels and/or expiration dating to each package of surgeon's and patient examination gloves. Because many of the estimates are derived from uncertain projections based on limited data, sensitivity analyses are presented for the most critical variables and assumptions.

D. Baseline Conditions

1. Annual Number of Gloves

To measure the incremental costs of the regulation against a baseline of nonregulation, FDA first projected future glove sales. An estimated 22.0 billion surgeon's and patient examination gloves were used in the United States in 1997, more than an 11-fold increase from the approximately 2.0 billion gloves used in 1987 (Ref. 38). The major contributors to this growth were the recognition of the potential risk from AIDS infection and the publication of Occupational Safety and Health Administration (OSHA) regulations requiring barrier protection for patients and employees exposed to blood borne pathogens (Ref. 40).

FDA assumed that the demand for surgeon's and patient examination gloves will continue to grow as a result of expected increases in employment within the health services industry (Standard Industrial Classification (SIC) 80). The Bureau of Labor Statistics has suggested that employment within this industry may continue to grow at an annual rate of 3.9 percent (Ref. 41).

Assuming that annual glove use per employee remains at current levels of approximately 10 pairs per day, the agency projected that the annual demand for gloves will increase over the next 10 years at an approximate rate of 3.9 percent per year (see Table 3). As expected growth in employment or patient health service visits may also predict future glove use. FDA tested this assumption by forecasting alternative rates of growth in the sensitivity analyses presented in section IX.G of this document.

About 65 percent of the current glove market consists of powdered gloves (Ref. 38), but both health service facilities and glove manufacturers agree that the market share of powdered gloves is decreasing rapidly as facilities gain awareness of the potential adverse health effects associated with NL protein allergens. Manufacturers, however, explain that powdered gloves will not soon disappear, because new chlorinators and production lines associated with powder-free glove production take at least 18 months to install and because powdered gloves are still desired by a proportion of customers. However, manufacturers have estimated that even in the absence of this regulation, the market share of powder-free gloves could reach as high as 60 percent within 18 months (Ref. 38). For this analysis, FDA assumed that, even in the absence of regulation, the market share for powdered gloves would decrease from the current 65 percent down to 20 percent within 4 years. Concurrently, the market share for powder-free gloves would increase from 35 percent up to 80 percent over the same period (see Table 3).

Next, FDA estimated that gloves manufactured with synthetic materials (referred to as synthetic gloves), which are available in both powdered and powder-free varieties, account for approximately 10 percent of the current market. Most synthetic gloves are manufactured of vinyl, but other polymers are also used. Synthetic gloves are generally believed to provide less acceptable barrier protection after extended use and reduced tactile sensitivity compared to NL. FDA assumed that, in the absence of regulation, this market share would increase slightly each year, accounting for 20 percent of the market within 5 years. Table 3 includes the projected market shares for each glove type.

Because these projections contain considerable uncertainty, FDA analyzed several alternative assumptions in the sensitivity analysis section presented in section IX.G of this document. These scenarios assume that, in the absence of this rule, the anticipated baseline market adjustments would take either 10 years, or would not occur at all.

TABLE 3.—SURGEON'S AND PATIENT EXAMINATION GLOVE MARKET SHARES—BASELINE ESTIMATE

Year	All Surgeon's and Patient Examination Gloves	Synthetic Gloves			Natural Rubber Latex Gloves		
		Number for Powder-Free (billion)	Number of Powdered (billion)	Total (billion)	Number of Powder-Free (billion)	Number of Powdered (billion)	Total (billion)
Current	22.00	0.77	1.43	2.20	6.93	12.87	19.80
1	22.86	1.37	1.37	2.74	10.06	10.06	20.12
2	23.75	1.99	1.33	3.32	12.25	8.17	20.42
3	24.68	2.76	1.18	3.95	14.51	6.22	20.73
4	25.64	3.69	0.92	4.61	16.82	4.20	21.02
5	26.64	4.26	1.07	5.33	17.05	4.26	21.31
6	27.68	4.43	1.11	5.54	17.71	4.43	22.14
7	28.76	4.60	1.15	5.75	18.40	4.60	23.00
8	29.88	4.78	1.20	5.98	19.12	4.78	23.90
9	31.04	4.97	1.24	6.21	19.87	4.97	24.83
10	32.25	5.16	1.29	6.45	20.64	5.16	25.80

2. Baseline Glove Cost

There are an estimated 198 current marketers of surgeon's and patient examination gloves in the United States, 10 of which are domestic manufacturers. Approximately 95 percent of all gloves purchased in the United States are imported. Although individual marketers of surgeon's and patient examination gloves operate in a highly competitive industry and face highly elastic demand curves, the aggregate market demand for the gloves is assumed to be price inelastic, because of workplace regulations that require gloves as barrier protection (Ref. 42). Demand is inelastic if the percentage increase in price exceeds the percentage decrease in quantity sold. Consequently, most glove manufacturing cost increases would be passed on to health care facilities in the form of industry wide price increases. Although over 95 percent of the manufacturing facilities are located overseas and the world wide demand for gloves is high, the United States market dominates global sales. According to Malaysian manufacturers (Ref. 38), about 80 percent of their gloves are for U.S. customers.

Current prices of powdered NL gloves average \$3.90 per 100, while powder-free NL gloves average \$5.80 per 100 (Ref. 38). Prices were reported as averages of both surgeon's and patient examination gloves. The price difference of \$1.90 per 100, or almost \$.02 per pair, is attributable to a number of factors, but the predominant reason is the increased cost of removing former-release powder and/or applying other lubricants to produce powder-free gloves. The estimated cost for synthetic gloves is \$4.15 per 100 for powdered and \$5.03 per 100 for powder-free. Vinyl gloves account for 90 percent of the synthetic glove market, with the remaining gloves manufactured from polymers and other materials.

The nation's annual expenditures for surgeon's and patient examination gloves are currently estimated at over \$1.0 billion. Even in the absence of regulation, FDA expects that these outlays would increase to \$1.1 billion within 1 year and \$1.7 billion within 10 years.

E. Estimation of Compliance Costs

The net costs of compliance with the proposed regulation is the difference between glove-related costs with and without the regulation. As noted earlier, industry comments suggest that even in the absence of this regulation, the market share of powder-free gloves is expected to increase from 35 percent to about 80 percent over a 4-year period. With regulation, this trend will be accelerated. Although the market effects of the rule cannot be known with certainty, FDA estimates that powder-free gloves will achieve the 80 percent market share 2 years earlier, or within 2 years of the rule's implementation. In addition, manufacturers would experience increased costs due to the recommendation to limit the level of protein to 1,200 g per glove and the level of powder on NL and synthetic powdered gloves to 120 mg per glove. These costs would be passed through to health care facilities in the form of higher prices. Finally, each package of NL gloves must include labeling that includes protein and powder levels and expiration dating, and shelf-life testing must support this labeling.

1. Accelerated Market Share for Powder-Free and Synthetic Gloves

Figure 1 illustrates FDA's forecast that powder-free gloves would gain 80 percent of the surgeon's and patient examination glove market share within 4 years without regulation and within 2 years with regulation. Manufacturers have indicated (Ref. 38) that if U.S. facilities are willing to bear the market price for powder-free gloves, the powder-free supply to other parts of the world could be shifted to meet U.S. demand and powder-free market shares could reach as high as 60 percent within 18 months. FDA forecasts that the proposed regulations will accelerate this trend by reinforcing incentives for facilities to use powder-free gloves. The shaded area of the chart measures the expected substitution of powder-free for powdered gloves caused by facilities choosing to increase use of powder-free gloves in response to regulatory controls. In addition, FDA projects that the synthetic market share will rise from 10 to 20 percent within 5 years without regulation, but within 2 years with regulation. The expected market shares with the proposed regulation in place are shown in Table 4.

FDA also examined the potential of this regulation to result in domestic shortages of latex gloves and concluded that there would be minimal disruption to the U.S. market, as it constitutes such a major proportion of global sales (up to 80 percent (Ref. 38)). If other countries do not restrict glove powder, it is possible that the number of powder-free gloves sold in those markets would fall in the short-term, while producers adjusted to the demand shift. FDA solicits public comment on how manufacturers would respond to these altered market forces.

TABLE 4.—SURGEON'S AND PATIENT EXAMINATION GLOVE MARKET SHARES WITH REGULATION

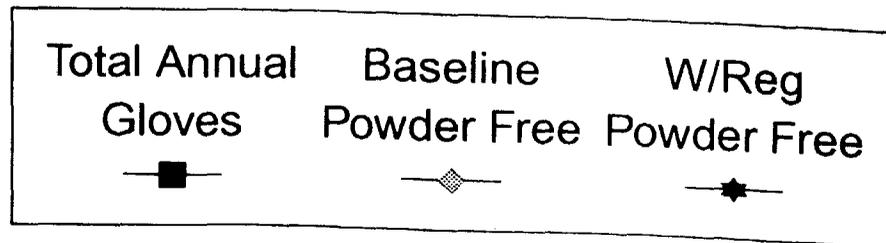
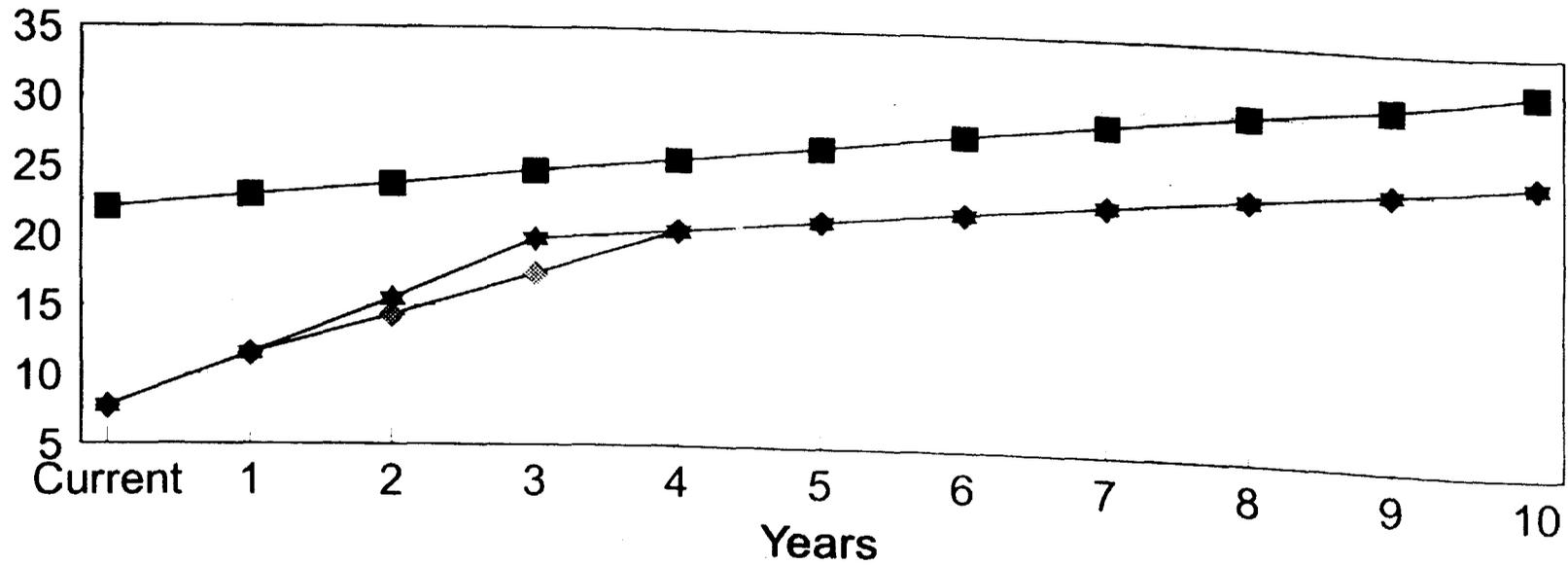
Year	Surgeon's and Patient Examination Gloves	Synthetic Gloves			Natural Rubber Latex Gloves		
		Number of Powder-Free (billion)	Number of Powdered (billion)	Total (billion)	Number of Powder-Free (billion)	Number of Powdered (billion)	Total (billion)
Current	22.00	0.77	1.43	2.20	6.93	12.87	19.80
1	22.86	1.37	1.37	2.74	10.06	10.06	20.12
2	23.75	2.47	1.33	3.80	12.97	6.98	19.95
3	24.68	3.95	0.99	4.94	15.79	3.95	19.74
4	25.64	4.10	1.03	5.13	16.41	4.10	20.51
5	26.64	4.26	1.07	5.33	17.05	4.26	21.31
6	27.68	4.43	1.11	5.54	17.71	4.43	22.14
7	28.76	4.60	1.15	5.75	18.40	4.60	23.00
8	29.88	4.78	1.20	5.98	19.12	4.78	23.90
9	31.04	4.97	1.24	6.21	19.87	4.97	24.83
10	32.25	5.16	1.29	6.45	20.64	5.16	25.80

Because the regulation would not be implemented until 2 years after publication of the final rule (as shown in Figure 1), no costs would be incurred in the first year. Moreover, there would be no market share-associated costs expected after the fourth year, because, by that time, there would be no difference in the respective market shares of powdered and powder-free gloves. Based on these assumptions, the accelerated increase in the powder-free market share results in increased regulatory costs of \$18.9 million in the second year and \$37.3 million in the third year. In the fourth year following implementation of the rule, costs would fall by \$2.9 million due to the increased use of lower cost synthetic gloves. As shown in Table 5, the average annualized costs (at a 7 percent discount rate over a 10-year period) attributable to the accelerated market share for powder-free gloves are calculated at \$6.4 million.

Figure 1

Annual Glove Sales

Gloves (in Billions)



2. Increased Costs for Powdered Gloves

Limiting the amount of protein and powder permitted on gloves would increase the production cost and therefore raise the purchase price of gloves to health care facilities. Although the limits are only recommended, both the actual and recommended levels of protein and powder must be included on the product label. Thus, FDA believes it likely that most glove manufacturers will meet the recommended levels. According to tests conducted by FDA, current powder levels on powdered gloves vary between 50 mg and 426 mg per glove. For this analysis, FDA assumed that a typical powdered NL or synthetic glove contains 260 mg of powder (based on the observed distribution). Current glove protein levels vary widely.

Several manufacturers indicated that even minimal recommendations on powder and protein would result in cost increases of as much as five percent. These increases would be due to the increased testing and validation required to ensure that gloves did not exceed limits, the slower production times resulting from more controlled processes, the increased inventory damage when stripping gloves from molds, the increased controls for slurry mixtures, the increased time spent cleaning or replacing filters and other equipment, and the other costs associated with more careful controls for the entire manufacturing process. Manufacturers stated that limiting powder is more a question of adding controls in the production process than adding new production lines or facilities. Equipment such as slurries and tumblers are currently in place, and controls are likely to consist of simply weighing finished gloves or weighing the slurry filters. However, these costs are expected to result in increased contract prices for U.S. health facilities, because there are no substitute products for medical gloves.

To calculate the costs of alternative permissible powder limits, FDA estimated an average cost function where the cost of reducing each mg of powder increases as the proportion of powder remaining on the manufactured glove decreases. Because current powdered NL gloves cost \$3.90 per 100 and powder-free gloves cost \$5.80 per 100, FDA calculated that the \$1.90 cost of removing the average 260 mg of powder per 100 gloves is about \$0.0073 per mg ($\$1.90/260$ mg). If the

cost function were linear, the incremental cost of reducing powder levels by 140 mg (i.e., from the current average 260 mg of powder to the recommended level of 120 mg) would be calculated as \$0.0073 times 140, or \$1.022 per 100 gloves. However, FDA believes that the relationship is unlikely to be linear as several manufacturers indicated that significant control costs would be needed to achieve even modest reductions in powder levels, after which average costs would rise slowly and then more steeply as powder concentrations approach zero. Such a functional form is typical of many manufacturing processes and illustrated by the solid sigmoid curve shown in Figure 2 (Refs. 44 and 45). A cost equation fitting this illustrated functional form is:

$$Y = 0.00365 + 0.0292(X - 0.5)^3$$

Where:

Y equals the cost per mg removed per 100 gloves, and

X equals the proportion of powder removed.

Figure 2 includes the estimated cost function for removing powder from synthetic gloves as the hashed line. The expected costs per mg removed are less than for NL gloves because the current price difference between powder-free and powdered synthetic gloves (\$0.88 per 100) is less than the difference for NL gloves (\$1.90 per 100).

On the assumption that these equations approximate the actual relationships, FDA estimates that the cost of limiting powder to 120 mg per 100 NL gloves is about \$0.003652 per mg removed, or about \$0.511 per 100 NL gloves. For synthetic gloves, the estimated costs are \$0.001693 per mg removed, or about \$0.237 per 100 synthetic gloves. As shown in Figure 3, the control costs rise sharply for limits below 120 mg. For example, a proposed powder limit of 100 mg per NL and synthetic glove would result in costs over 15 percent greater than the proposed 120 mg limit. Because of the control processes required, FDA assumes that the previous estimates would also account for the cost of limiting protein levels for NL gloves.

Table 5 shows these estimated costs over a 10-year period. Because the regulation is expected to be implemented 2 years after publication of the final rule, no increased powdered glove costs

are incurred in the first year. In year 2, the higher prices for powdered NL gloves result in increased costs of \$35.7 million. In year 3, these costs fall to \$20.2 million. Thereafter, the yearly incremental compliance costs associated with NL glove powder and protein limits vary between \$21.0 and \$26.4 million. The average annualized contribution of this cost category (at a 7 percent discount rate over 10 years) equals \$21.4 million.

Within 2 years, higher costs for powdered synthetic gloves will equal \$3.1 million. The yearly incremental compliance cost for powdered synthetic gloves is expected to decrease to \$2.3 million in year 3, and then increase slightly each year throughout the evaluation period. The average annualized contribution of this cost category (at a 7 percent discount rate over 10 years) equals \$2.4 million.

Figure 2. Cost per mg of Powder Removed from 100 Gloves by Proportion of Powder Removed

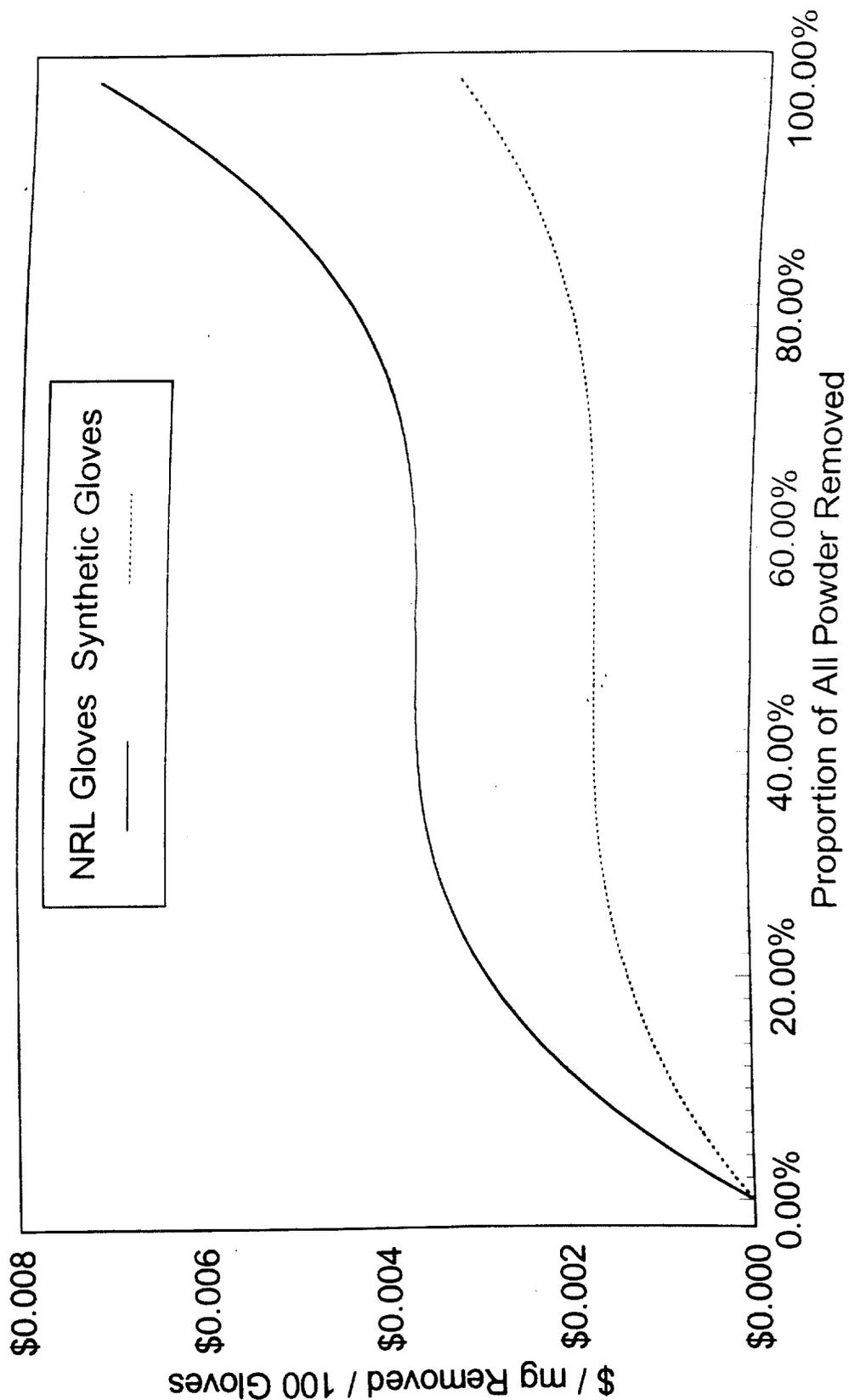


Figure 3. Increased Cost per 100 Gloves by Powder Level

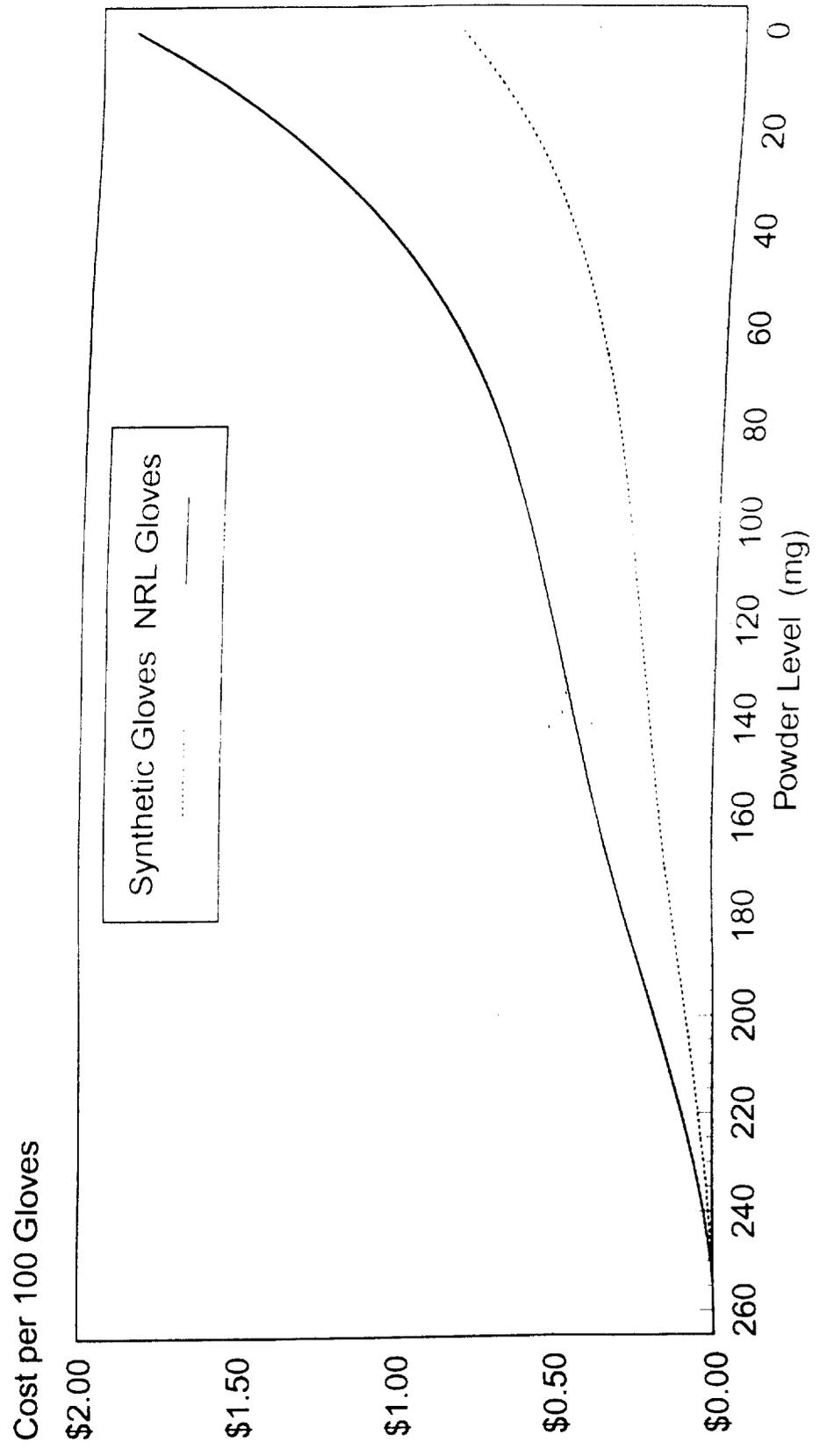


TABLE 5.—COMPLIANCE COSTS OVER 10-YEAR PERIOD

Year	Cost of Accelerated Market Share (\$ million)	Increased Powdered NRL Gloves (\$ million)	Cost of Synthetic Gloves (\$ million)	Cost of Shelf-Life Testing		Labeling Cost (\$ million)	Total Cost (\$ million)
				Test Cost (\$ million)	Lost Inventory (\$ million)		
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	18.9	35.7	3.1	1.6	3.0	1.6	63.9
3	37.3	20.2	2.3	1.2	1.3	0.6	62.9
4	2.9	21.0	2.4	1.2	1.1	0.5	23.3
5	0.0	21.8	2.5	1.3	1.4	0.7	27.7
6	0.0	22.6	2.6	1.3	1.2	0.5	28.2
7	0.0	23.5	2.7	1.5	1.1	0.6	29.4
8	0.0	24.4	2.8	1.5	1.6	0.8	31.1
9	0.0	25.5	2.9	1.4	1.3	0.6	31.7
10	0.0	26.4	43.1	1.5	1.3	0.6	32.9
Total	53.3	221.0	24.6	12.5	13.3	6.5	331.2
Average Annualized (7 percent discount rate)	6.4	21.4	2.4	1.2	1.3	0.7	33.4

3. Costs of Shelf-life Testing and Inventory Loss

The proposed regulation will require manufacturers of patient examination and surgical gloves to develop and affix labeling to their products that will include expiration dating. To ensure that medical gloves will maintain adequate barrier protection for the entire stated period, manufacturers will likely conduct real-time shelf-life testing of gloves. The compliance costs of this testing includes both the actual cost of conducting laboratory tests, and the lost revenues of inventory lost due to sampling.

a. *Shelf-life testing.* FDA contracted with the Eastern Research Group (ERG), an economic consulting firm, to contact domestic and foreign glove manufacturers and research laboratories to determine the expected unit costs of shelf-life testing, and to determine current levels of industry compliance. ERG developed a cost model that estimated compliance costs according to the size of the manufacturer (Ref. 45a).

ERG estimated that the expected marketing life for each glove model is approximately 3 years. During this period, stability testing is likely to occur at 6-month, 1-year, 2-year, and 3-year intervals. The actual tests were assumed to consist of a combination of real-time and accelerated tests. Overall, the estimated costs of a shelf-life test was found to approximate \$265 for foreign tests and \$865 for domestic tests. (The difference in testing costs are attributable to the lower purchasing power parity per capita in foreign countries that produce medical gloves.)

As explained in Ref. 45a, almost 3,000 separate glove models are currently produced by 198 separate manufacturers. Only 160 models are marketed by the 10 domestic manufacturers. Given the expected growth in the demand for gloves, and the shift to powder-free and synthetic glove models, the estimated costs of shelf-life testing varies with FDA's projected number of future glove models. It was assumed that new models would have two shelf-life tests during the year of introduction while models already marketed would have one annual shelf-life test. Finally, ERG and industry sources estimated the current level of shelf-life testing based on both domestic/foreign and size characteristics.

Based on these assumptions, the greatest increase in shelf-life testing is expected during year 2, with over 6,000 additional tests due to this proposed regulation. The total cost of conducting these tests equals \$1.6 million, of which \$0.1 million is incurred by domestic glove manufacturers. Amortizing the annual testing costs by 7 percent over 10 years, the average annualized costs of conducting the required shelf-life tests equals \$1.2 million.

b. *Inventory losses.* As part of these tests, manufacturers will be required to set inventory aside from which test samples will be selected. ERG, with discussions with laboratories and manufacturers, has determined that small glove manufacturers would be likely to set 10,000 gloves per model aside for shelf-life testing while large manufacturers would set 30,000 gloves per model. Given the industry characteristics as discussed in Ref. 45a, this implies that over 115 million gloves would be set aside in year 2. In addition, the relative market shares of synthetic, NL, powdered and powder-free gloves is expected to change over time which will affect the average lost revenue per sample. FDA analyzed the impact of this future inventory loss and found that during year 2 of the evaluation period, the value of lost inventory for testing is expected to equal over \$3.0 million for the entire industry. The average annualized cost of this lost inventory (as shown in Table 5) at 7 percent over 10 years equals \$1.3 million.

4. *Costs of Labeling.* ERG also developed estimates of the costs of developing the proposed enhanced labeling for gloves. These estimates included the costs of artwork, design, regulatory

review, production and application, as shown in Ref. 45a. Overall, the average cost of developing a label for a foreign medical glove model was estimated to equal \$411, while a domestic model would cost \$1,444. The number of domestic and foreign glove models expected to be introduced throughout the 10-year evaluation period and the market characteristics as discussed in Ref. 45a, indicate that the costs of labeling will equal \$1.4 million in year 2. These yearly costs will then decrease to as low as \$0.3 million by the 10th year. The average annualized cost of developing and producing labeling for medical gloves attributable to this proposed regulation is estimated to equal \$0.7 million, as shown in Table 5.

5. Total Incremental Costs

Figure 4 presents the estimated annual expenditures imposed by the proposed rule. Overall, costs of \$63.9 million are expected in year 2. These costs decreased to \$62.9 million in year 3, and then decrease to \$23.3 million in the third year. Costs are expected to increase slightly for each subsequent year. Most of the incremental costs, as shown in Table 5, are due to increases in glove costs (powdered NL and synthetic gloves with limited powder levels). The estimated average annualized cost over a 10-year period (at a 7 percent discount rate) is \$33.4 million.

Figure 4. Total Annual Compliance Costs

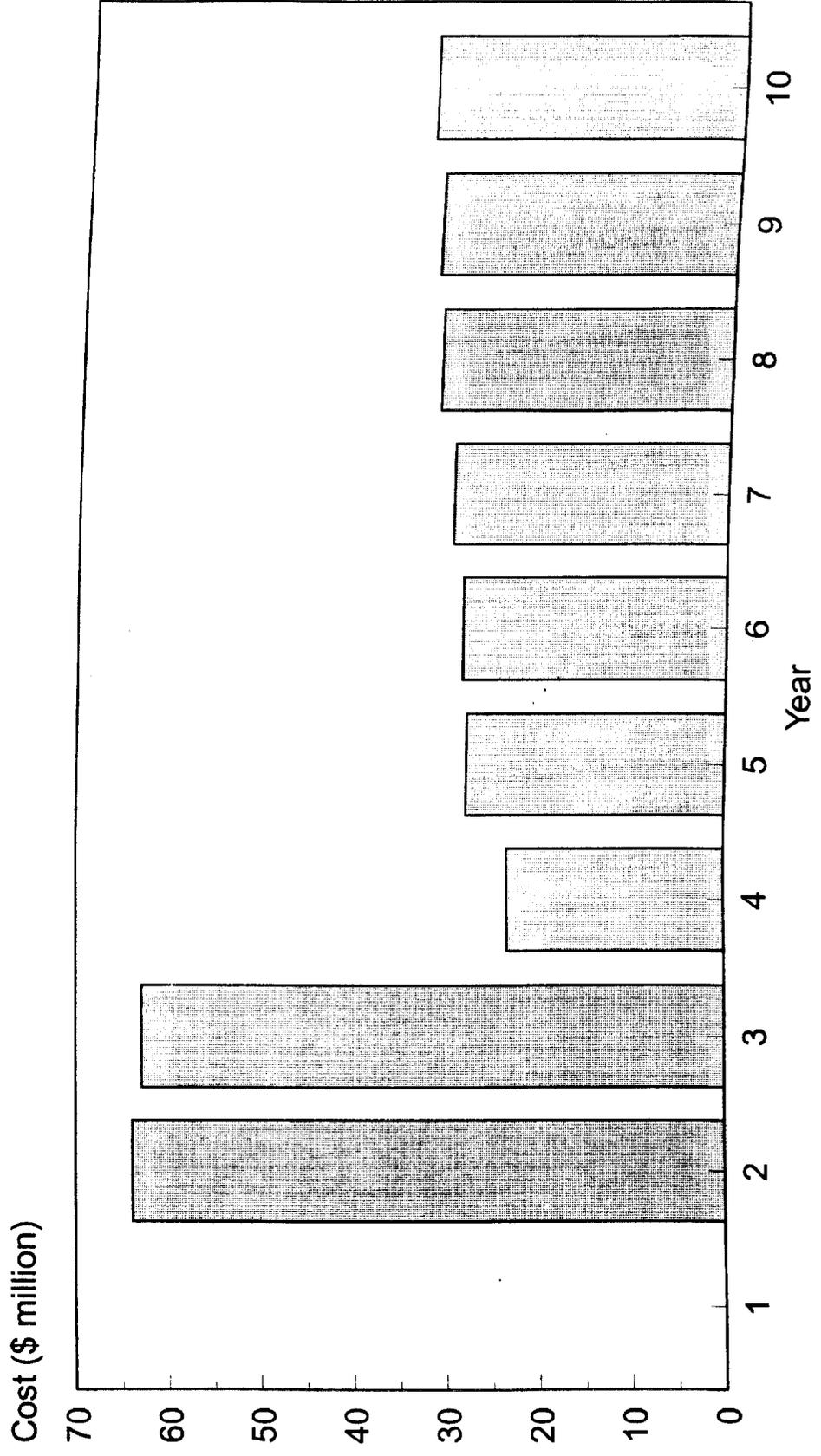
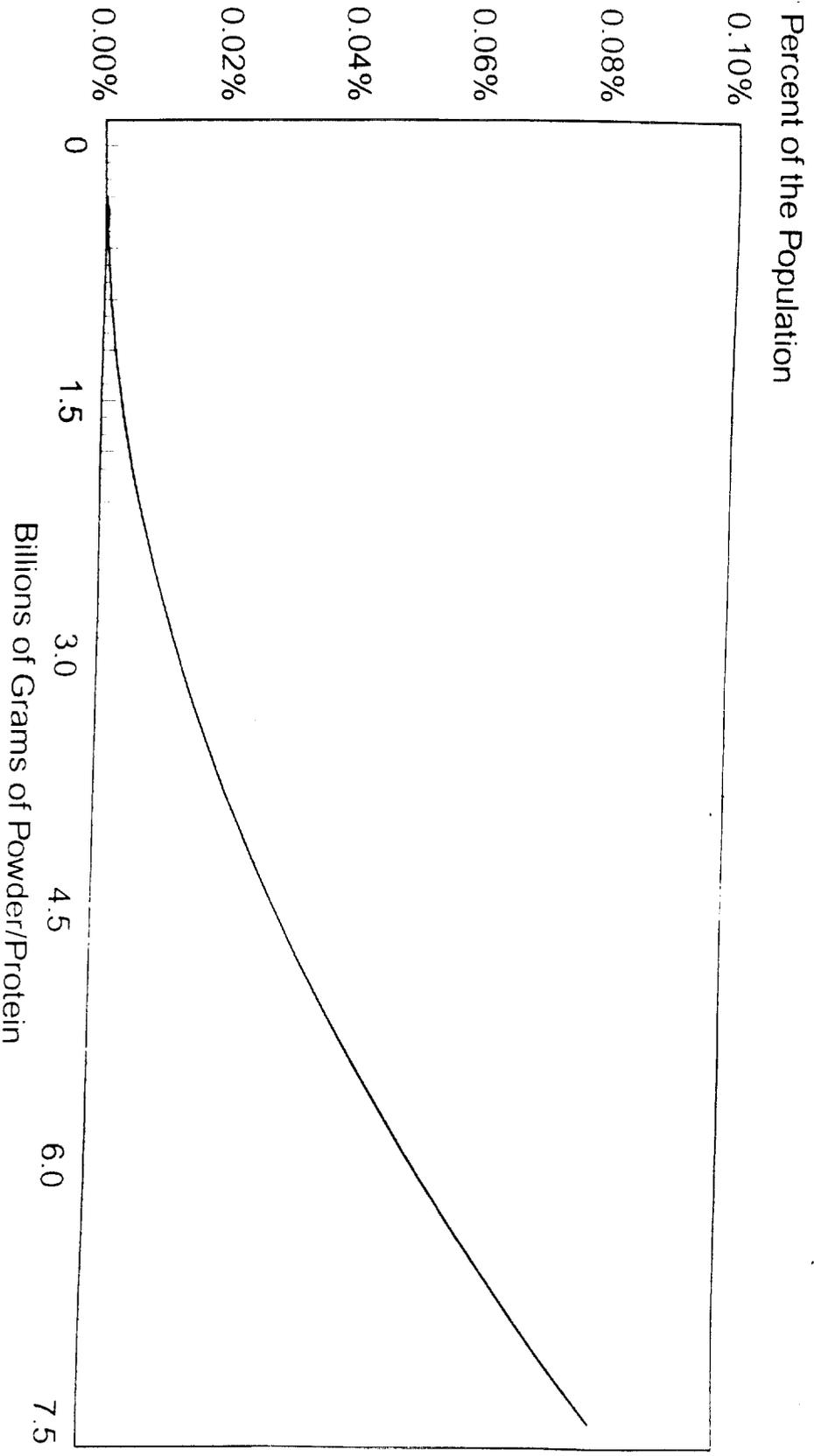


Figure 5
Percent of the Population Experiencing Allergic Reaction to Natural Latex Proteins in Relation to the Level of Powder



F. Benefits of the Proposed Regulations

1. Expected Risk Reduction

As discussed previously, the estimated annual proportion of the population (0.0001626) that experiences allergic reactions associated with medical gloves is assumed to be related to the prevalence of environmental protein and powder. Consequently, reducing protein and powder levels would reduce the proportion of the population expected to experience an allergic reaction. Decreases would be expected in NL sensitization as well as allergic reactions.

To estimate this relationship, FDA assumed that the proportion of the population affected would vary directly with the total quantity of environmental protein/powder. The annual level of environmental protein/powder was calculated from the expected annual number of powdered NL gloves multiplied by the average level of powder per glove. The current market share of powdered NL gloves (Table 3) and the current average level of glove powder (260 mg) yield an aggregate estimate of 3.346 billion g of protein/powder. This quantity of protein/powder is associated with allergic reactions in 0.0001626 of the population, or 0.000049 reactions per billion g. If the relationship between the number of reactions and the quantity of protein/powder were linear, the model implies a 30 percent reduction in allergic prevalence for each billion g of powder reduction. Alternatively, the function relationship may take other forms, and FDA suspects that the increasing number of reports of allergic reactions to NL in recent years likely indicates a nonlinear relationship. Figure 5 presents a polynomial projection that FDA tentatively adopts as a plausible estimate for this analysis. The equation of the function illustrated in Figure 5 is:

$$Y = (0.0000143)X^2$$

Where:

Y equals the proportion of the population with NL allergic reactions, and

X equals the level of environmental protein/powder (in billions of g).

Although the exact relationship is speculative, FDA believes that an exponential relationship as shown in Figure 5 is most likely. As shown in section IX.G of this document, the agency's

sensitivity analysis indicates that due to the rising baseline projection, this polynomial projection yields smaller benefits than a linear model.

Table 6 shows the expected number of allergic reactions associated with protein/powder levels with and without the proposed regulation. The protein/powder amounts are derived from the expected numbers of powdered NL gloves shown in Tables 3 and 4, the current average glove powder level (260 mg per glove), and the new recommended glove powder level (120 mg per glove). Powdered synthetic gloves do not affect this relationship because no NL proteins are associated with those products. Table 6 shows that in the absence of the proposed regulation, the expected increased market share of powder-free gloves would reduce the number of annual allergic reactions attributable to medical gloves from 43,500 to only 4,800 within 4 years. With the proposed regulation in place, the expected number of allergic reactions would decrease to only 900 within 3 years, and consistently remain several thousand fewer than those expected without regulations.

2. Benefits

To estimate the potential benefits of the proposed rule, the number of reduced expected allergic reactions shown in Table 6 were distributed in proportion to the categories shown in Table 2. Assuming that the decreased number of reactions would not modify the severity distribution as reported in the MDR's (as adjusted to account for under-reporting), the proposed regulation would reduce annual allergic reactions by 15,100 within 2 years. The characteristics of these second year avoided reactions are shown in the first four columns of Table 7.

TABLE 6.—EXPECTED NUMBER OF ALLERGIC REACTIONS

Year	In the Absence of Regulation ¹			With Regulation ²			Difference in Allergic Reactions with Regulation (000)
	Number of Powdered Natural Rubber Latex Gloves (billion)	Level of Powder (billion g)	Estimated Number of Allergic Reactions (000)	Number of Powdered Natural Rubber Latex Gloves (billion)	Level of Powder (billion g)	Estimated Number of Allergic Reactions (000)	
Current	12.87	3.35	43.5	- NA -	- NA -	- NA -	- NA -
1	10.06	2.62	26.9	10.06	2.62	26.9	0.0
2	8.17	2.13	17.9	6.98	0.84	2.8	(15.1)
3	6.22	1.62	10.4	3.95	0.47	0.9	(9.5)
4	4.20	1.09	4.8	4.10	0.49	1.0	(3.8)
5	4.26	1.11	5.0	4.26	0.51	1.1	(3.9)
6	4.43	1.15	5.4	4.43	0.53	1.2	(4.3)
7	4.60	1.20	5.9	4.60	0.55	1.3	(4.7)
8	4.78	1.24	6.4	4.78	0.57	1.4	(5.1)
9	4.97	1.29	7.0	4.97	0.60	1.5	(5.5)
10	5.16	1.34	7.6	5.16	0.62	1.6	(6.0)

¹ Powder level of 0.260 g per glove

² Powder level of 0.120 g per glove

There is no methodology that permits a precise assignment of monetary values to regulatory health benefits. However, one approach recently described in the health economics literature (Refs. 47 and 48) combines relative states of well-being with observed willingness to pay for risk avoidance. FDA adopted this methodology and used the Kaplan-Bush Indices of Well-Being (Refs. 49 and 50) to estimate the value of reducing the number of allergic reactions.

The first step was to assign to each category of reaction a functional index based on mobility/physical/sociability scales. The index of relative well-being (as described in Refs. 49 and 50) utilize functionality levels as a basis for estimating well-being. The functionality scales are described in Table 8. Baseline levels of well-being were defined for 43 distinct combinations of mobility, physical activity, and sociability. For example, if a hypothetical patient could drive a car and use transportation without help (mobility equals 5), could walk without a physical problem (physical activity equals 4), and had no morbidity symptoms or problem, then this patient would have an assigned well-being of 1.0000. However, if this hypothetical patient could perform all of these activities, but suffered from any morbidity (including requiring eyeglasses), the assigned baseline level of well-being was found to equal 0.7433. The baseline levels of well-being are then adjusted, either up or down, based on the predominant symptom or problem that is on-going. This methodology is described in detail in Refs. 49 and 50. For example, a local topical reaction is unlikely to interfere with normal activities, such as driving a car or performing housework. A patient suffering from a local topical reaction is expected to continue to be able to interact with others in a normal manner. This functional state is assigned a relative well-being rate of 0.7433, or roughly 74 percent of optimum well-being. This baseline functional index is based on the prevailing medical problem. In this case, the problem/symptom is identified as “burning and/or itching of skin” and the 0.0171 value for this problem/symptom (from Refs. 49 and 50) is added to the basic functional state. Thus, by combining these indices, a person suffering a local, topical allergic reaction is expected to have a relative well-being of 0.7604. Each of the categories of reactions have been assigned values, as included in Table 7. Mortalities are valued as 0.0000.

Next, optimum values of well-being were derived for both short-term durations (1 day) and long-term durations (2 months). The economic literature includes many attempts to quantify society's willingness-to-pay (WTP) to avoid risks. Various methodologies have resulted in an average value of approximately \$5.0 million as a measure of the WTP to avoid a statistical death (Refs. 51, 52, and 53). By amortizing this value to account for life expectancy and expected disability-days (Refs. 54 and 55), FDA estimates that a quality-adjusted life-year (QALY) has an approximate value of \$373,000. Using this estimate, the expected value of a quality-adjusted life-day is approximately \$1,022 and the expected value of two quality-adjusted life-months is \$62,166.

The relative wellness values for each category shown in Table 7 represent the proportion of wellness relative to an optimum level. The willingness of society to pay for avoiding each incident were reflected as the difference between the wellness state and an optimum level multiplied by the duration of the event. For example, a local topical allergic reaction has an expected wellness value of 0.7604, or 0.2396 below optimum. This difference is used to calculate the amount that society is willing to pay to avoid a reaction of this type.

TABLE 7.—CHARACTERISTICS OF REDUCTIONS IN SECOND YEAR ALLERGIC REACTIONS

Category of Reaction	Number of Avoided Reactions (000)	Number of Avoided Short-Term Reactions (000)	Number of Avoided Long-Term Reactions (000)	Functional State ¹	Problem/Symptom Weight ²	Relative Wellness	Value per Short-Term Reaction	Value per Long-Term Reaction (\$ 000)	Value per Short-Term Reaction Avoided (\$ 000)	Value per Long-Term Reaction Avoided (\$ 000)	Total Value (\$ 000)
Local Topical	0.89	0.84	0.05	0.7433	0.0171	0.7604	245	14,900	205	794	999
Systemic Topical	0.94	0.69	0.24	0.6065	0.0171	0.6236	385	23,400	267	5,709	5,976
Systemic Respiratory	13.24	9.66	3.57	0.525	-0.0075	0.5175	493	30,000	4,764	107,194	111,958
Respiratory Requiring Aggressive Treatment	0.05	0.03	0.03	0.5284	-0.1507	0.3777	636	38,700	17	972	989
Mortality	0.00	NA	NA	0	0	0	NA	NA	NA	NA	514 ³
Totals	15.11	11.22	3.90								120,436

¹ Functional states: Mobility - 5; Physical activity - 4; Social - 5 = 0.7433
 Mobility - 4; Physical activity - 4; Social - 4 = 0.6065
 Mobility - 4; Physical activity - 3; Social - 3 = 0.525
 Mobility - 4; Physical activity - 1; Social - 2 = 0.5284
 Mortality = 0.0000

² Problem/Symptom Adjustments:
 Burning or itching rash on body = +0.0171
 Wheezing or shortness of breath = -0.0075
 Loss of consciousness, fainting = -0.1507

³ Value per mortality is \$5 million. May not add due to rounding.

For 1 day, this value is \$245 ($\$1,022 \times .2396$) and for 2 months, the estimated value per reaction is \$14,895. The derived values for each of the reaction categories and terms are shown in Table 7.

The values for each category, when multiplied by the number of decreased reactions expected due to this regulation, result in the expected annual benefit. Table 7 includes this estimate for only the second evaluation year. It indicates that society would be willing to pay a value of approximately \$120.4 million to avoid 15,100 allergic reactions to NL protein.

Taking these steps for each year in the evaluation period yields estimates of the willingness to pay to avoid these reactions as shown in Table 9. The undiscounted benefits equal \$120.4 million in year 2, then decrease to \$30.4 million in year 4. Between years 4 and 10, the estimated annual benefit increases to a value of \$47.5 million. The estimated annualized benefit of avoiding these reactions is \$46.9 million.

FDA notes that other potential benefits, such as the avoidance of third-party payments as a result of treating fewer allergic reactions, the value of reduced anxiety due to lowering NL sensitization, the reduction in defects in glove barrier integrity, and the reduction in other foreign body reactions caused by glove powder have not been quantified at this time. FDA recognizes the considerable uncertainty of all of these estimates, however, and requests comment on all of the data and assumptions.

TABLE 8.—DESCRIPTION OF INPUTS TO FUNCTIONALITY LEVELS

Mobility	Physical Activity	Social Activity
5-Drove car and used transportation without help		5-Did work, school, or housework and other activities
4-Did not drive, needed help with transportation	4-Walked without physical problem	4-Did work, school, or housework, but other activities limited
3-In house	3-Walked with physical problem	3-Limited in work, school or housework
2-In hospital	2-Moved own wheelchair without help	2-Performed self-care
1-In special unit	1-In bed or chair	1-Had help in self-care

Source: Kaplan, Bush, et. al. (Refs. 49 and 50)

TABLE 9.—Expected Benefit of Decreased NRL Allergic Reactions Due to Regulation

Year	Decreased Reactions (000)	Value of Decreased Reactions (\$ million)	Net Present Value of Decreased Reactions (\$ millions)
Current	NA	NA	NA
1	0.0	NA	NA
2	(15.1)	120.4	105.2
3	(9.5)	76.0	62.0
4	(3.8)	30.4	23.2

TABLE 9.—Expected Benefit of Decreased NRL Allergic Reactions Due to Regulation—Continued

Year	Decreased Reactions (000)	Value of Decreased Reactions (\$ million)	Net Present Value of Decreased Reactions (\$ millions)
5	(3.9)	31.1	22.2
6	(4.3)	34.0	22.7
7	(4.7)	37.1	23.1
8	(5.1)	40.3	23.4
9	(5.5)	43.7	23.8
10	(6.0)	47.5	24.2
Average Annual Benefit (\$ million)			46.9

G. Sensitivity Analyses

FDA examined the impact of various assumptions that affect future conditions. These analyses are as follows:

1. Growth Rate of the Demand for Surgical and Patient Examination Gloves

FDA used 1992 to 1994 rates of employment growth within the health services industry (SIC 80) to project a 3.9 percent annual growth in the future demand for surgical gloves (Ref. 41). However, more recent data obtained for the period up to 1998 suggest the more modest growth rate of 2.7 percent for this industry (Ref. 55a). Examining the expected costs and benefits after lowering the expected growth for surgical and patient examination gloves to 2.7 percent indicates that average annual costs decrease from \$33.4 to \$31.5 million and average annual benefits decrease from \$46.9 to \$42.1 million. If the forecast relied instead on the growth of total employment hours in the health service industry (Ref. 55b), the rate in recent years has been approximately 2.0 percent. Using this rate as the expected growth rate for surgical and patient examination gloves results in average annual costs of \$30.4 million and average annual benefits of \$39.6 million.

FDA notes that under the alternative assumptions, both costs and benefits are lower than under the scenario presented earlier, but the regulation would still be justified.

2. Market Shares of Powder-Free and Synthetic Gloves

FDA has estimated that in the absence of regulation, within 4 years, 80 percent of the glove market would consist of powder-free gloves; and within 5 years, 20 percent of all gloves would

be manufactured of synthetic material. The proposed regulation is expected to accelerate these trends to within 2 years of implementation.

To examine the sensitivity of these assumptions, FDA calculated the costs and benefits of the rule assuming that, in the absence of regulation, it would take 10 years rather than 4 years for powder-free gloves to account for 80 percent of the market and 10 years rather than 5 years for synthetic gloves to account for 20 percent of the market. The expected average annual costs in this scenario equal \$72.7 million, and the average annual benefits equal \$112.1 million. FDA also examined the impact of assuming no expected change in baseline market share from the first implementation year, in the absence of regulation. In this case, the average annual costs equal \$135.7 million, and the average annual benefits equal \$283.2 million.

3. Linear Relationship between Environmental Protein/Powder and Allergic Reactions

FDA expects that an exponential relationship exists between protein/powder levels and allergic reactions, but the agency also examined the effect of a linear relationship. The linear model increased the expected average annual benefit of reducing exposure from \$46.9 million to \$75.7 million, by increasing the number of avoided incidents as protein/powder levels were decreased. Table 9 indicates the magnitude of the expected decrease in NL reactions using the expected exponential relationship. A total of 57,900 avoided reactions were forecast. If the actual relationship were linear, the rule would be expected to result in the avoidance of 88,100 incidents over the same period.

4. Conclusion

FDA has tested several key assumptions used in the analysis of impacts. Each simulation resulted in estimated benefits exceeding costs. Nonetheless, FDA recognizes the significant uncertainty in this analysis and requests any additional information that would improve the projections.

H. Small Business Impact

1. Initial Regulatory Flexibility Analysis

FDA believes that the proposed regulation will not have a significant impact on a substantial number of small entities, but conducted an initial regulatory flexibility analysis (IRFA) to ensure that impacts on small entities were assessed and to alert any potentially impacted entities to the opportunity to submit comments to the agency.

2. Description of Impact

The objectives of the proposed regulation are to reduce the adverse health effects attributable to allergic and foreign body reactions from NL allergens and glove powder and to defects in barrier protection and quality of surgeon's and patient examination gloves. The proposed regulation will accomplish these objectives by reclassifying surgeon's and patient examination gloves into class II products, and requiring product labeling. In addition, the proposed regulation recommends protein and powder levels for surgeon's and patient examination gloves. FDA's statutory authority for the proposed rulemaking under the act is discussed in section II of this document.

Two separate industries will be affected by the proposed regulation: Manufacturers of surgeon's and patient examination gloves (found in Standard Industrial Classification 3842, Medical Equipment and Supplies) and Health Facilities (found in SIC 80).

TABLE 10.—NON-HEALTH CARE INDUSTRIES THAT USE GLOVES AS PROTECTION

Industry Sector	SIC Code	Number of Establishments	Number of Employees
Government	9,461	10,893	56,345
Residential Care	836	2,423	NA
Personal Services	7,362	1,348	163,477
Funeral Services	726	19,890	57,013
Health Units in Industry	NA	202,540	178,732
Non-Health Research Laboratories	8,221	1,453	89,159
Linen Services	7,218	1,250	50,000
Medical Equipment Repair	384	1,076	6,185
Law Enforcement	9,221	4,946	341,546
Fire and Rescue	9,224	3,174	252,048
Lifesaving	9,229	100	5,000
Schools	9,411	6,321	4,132
Waste Removal	4,953	940	13,300

Source: OSHA (Ref. 40)

FDA considered the potential impact of the proposed regulation on a number of nonhealth industries, but found that any impact would be insignificant. When OSHA issued its final regulations on blood-borne pathogens (Ref. 40), it considered a wide-range of establishments including: Law enforcement agencies, schools, linen services, and funeral parlors (see Table 10). While a substantial number of these establishments are small under the Small Business Administration definition, this proposed regulation does not require the use of FDA-regulated medical gloves at these sites. OSHA assumed that many of these industries would use utility gloves or consumer-grade gloves to provide barrier protection. For example, janitorial services and waste removal establishments were assumed to use utility work gloves, while law enforcement agencies were expected to use consumer-grade vinyl gloves. Few industries or establishments were expected to use FDA-regulated medical gloves in nonmedical settings. However, even in settings where medical gloves may be used, the frequency of glove usage was much less in these sectors. OSHA estimated that an average school would use approximately eight pairs of gloves per day. In contrast, a small physician/dental office would be expected to use 30 pairs of gloves per day. Both the relative frequency of glove use and the concentration of FDA-regulated medical gloves convinced FDA to focus on the Health Services Industry (Table 11) as the area of largest potential impact.

TABLE 11.—ESTABLISHMENT AND EMPLOYMENT IN THE HEALTH SERVICES¹

Establishments and (Standard Industrial Classification Codes)	Number of Establishments (thousand)	Number of Employees (thousand)	Average Number of Employees per Establishment
Total Health Services (80)	1,030.0	11,000.0	10.7
Clinics and Offices of MD's (801)	328.9	1,908.4	5.8
Clinics and Offices of Dentists (802)	138.5	709.4	5.1
Clinics and Offices of Osteopathy (803)	18.4	60.6	3.3
Other Health Practitioners (804)	243.0	483.6	2.0
Nursing Facilities (805)	57.7	2,011.8	34.9
Hospitals (806)	7.1	4,496.5	633.3
Medical/Dental Laboratories (807)	29.4	229.3	7.8
Home Health Services (808)	99.9	743.9	7.4
Other Allied Services (809)	107.7	356.5	3.3

¹ 1992 Census of Service Industries and Bureau of Labor Statistics projections of employment trends in the health services industries.

Glove manufacturers will be affected by labeling that requires additional warnings and statements concerning recommended protein and powder limits, testing and validation measures that are necessary to ensure the accuracy of this information, and limitations on the use of powder for mold release. Health facilities will face increased expenditures for surgeon's and patient

examination gloves by either shifting from powdered gloves to more expensive powder-free products or continuing to use powdered gloves that cost more due to production cost increases.

Manufacturers classified within the four-digit SIC code 3842 are typically small. Only 38 percent of all establishments had 20 or more employees in 1992 (Ref. 56), and companies had an average of 1.12 separate establishments. The manufacturers are highly specialized, with over 92 percent of their products considered within the medical equipment and supplies industry, and 94 percent of all medical equipment and supplies manufactured by these firms. The Small Business Administration classifies as small any entity within this industry with 500 or fewer employees (Ref. 57), capturing the majority of establishments. However, the affected manufacturers of surgeon's and patient examination gloves have some product-specific characteristics that distinguish them from the average establishment in this industry.

FDA's registration system for medical devices shows 198 manufacturers of surgeon's and patient examination gloves, the vast majority of which are located outside the United States and operate in a world-wide market, although the U.S. constitutes the most significant regional market. FDA examined the records of current manufacturers and identified 10 domestic manufacturers of surgeon's and patient examination gloves out of the total 198 marketers. Only 1 of these 10 domestic manufacturers reported employment of fewer than 1,200 employees. However, FDA acknowledges that additional small domestic manufacturers could enter the market in the future.

The main impacts of the proposed regulations on small manufacturers would occur if the manufacturer had to conduct additional validation tests to ensure the accuracy of protein and powder levels displayed on the product labeling and if increased inventory loss or slower production times occurred due to limited uses of powder as a mold release. Although FDA does not stipulate the acceptable validation test method in the regulation, and is soliciting comments on this issue in order to minimize its impact, it is possible that a chemist would be required on a contract basis to ensure that the actual levels of protein and powder matched the levels on the label. FDA is working with industry groups to ensure that an acceptable and reliable test method is chosen.

Despite this outreach, the selected test method could impose additional and disparate costs to a small manufacturer. Similarly, increased inventory loss because of tearing in the production process due to limited powder would affect small production runs to a greater degree than large production runs. Discussions with manufacturers have indicated that any additional validation testing or negative impacts on production capability could increase the production costs of medical gloves by 5 percent or more.

As discussed earlier in the analysis of impacts section (section IX.D of this document), the demand for medical gloves is highly price inelastic due to the regulatory requirement for health facilities (SIC 80) to provide barrier protection (Ref. 40) and the lack of substitute products (Ref. 42). The characteristics of the medical glove market therefore indicate that production cost increases resulting from the proposed rule are likely to be passed through in the form of higher contract prices. In addition, many facilities are currently accepting increased glove prices by establishing powder-free environments in the absence of any rule-making. Thus, production cost increases by glove manufacturers are likely to be offset by revenue gains for these same manufacturers, with the result of shifting the cost impact to the health facilities.

Small health facilities therefore will also bear some regulatory impact. The Small Business Administration has defined as small any “for-profit” health facility with annual revenues of \$5 million or less (Ref. 57). Most hospitals and nursing facilities would be considered large under this definition. However, nonprofit facilities not dominant in their field are also considered small entities. Industry characteristics of the health facility industry are shown in Table 11. Approximately 95 percent of the hospitals and nursing facilities are considered as small entities (6,700 hospitals and 54,800 nursing facilities).

FDA examined the potential impact of the proposed regulations on two types of health care user facilities: Small physician/dental facilities and small hospitals. A small physician or dental facility may use as many as 25,000 (based on 120 patient visits per week) gloves each year. If

the facility substitutes powder-free for powdered gloves as a result of this regulation, costs would increase by \$475 per year $((25,000/100) \times \$1.90)$.

Similarly, a small hospital is also likely to experience increased annual costs of acquiring gloves. An extremely small hospital with only 6 beds and a staff of 11 might use about 22,000 gloves annually. If the facility faced increased glove costs, the total increase in costs could amount to about \$950.

FDA wishes to collect additional information on the nature of the impacts on small entities in order to ensure that all such impacts are noted. In addition, other public facilities such as prisons, and police or fire departments may face higher glove prices due to this regulation. FDA does not expect these costs to be significant, but solicits comments on this potential burden.

3. Analysis of Alternatives

FDA has examined and rejected the following alternatives to the proposed rule: (1) Banning powdered gloves; (2) mandating protein and powder levels on medical gloves; (3) requiring all users of powdered gloves to comply with restrictions on distribution and use; (4) retaining the class I classification for all (or some) of the medical gloves; and (5) excluding powdered synthetic gloves from this rulemaking; and (6) providing for a shorter or longer compliance period. FDA has rejected the alternatives at this time for the following reasons:

Alternative 1: A ban of all powdered medical gloves has been requested in a citizen petition submitted to FDA. FDA considered banning powdered gloves because that action would meet the stated objective of eliminating airborne powder and greatly reducing exposure to airborne allergens associated with the use of medical gloves. However, FDA did not select this alternative because a ban would not address exposure to NL allergens from medical gloves with high levels of NL proteins. Moreover, such a ban of powdered gloves might compromise the availability of high quality medical gloves and greatly increase the annual costs by almost as much as \$64 million over the selected alternative.

Alternative 2: FDA also considered mandating powder and protein levels for medical gloves because this alternative would accomplish the stated objectives more completely than banning. FDA rejected mandating powder and protein levels for medical gloves because the agency believes that the increased regulatory flexibility of the proposed rule may reduce the costs of compliance by allowing for more efficient methods of reaching the goal. Inventories could be lowered and industry capacity could be assured. Mandating specific protein and powder levels, as well as the acceptable test method, may preclude all parties from developing a more efficient system. In addition, FDA inspectional and compliance costs are minimized by relying on recommended levels of powder and protein. By ensuring user access to relevant information, the agency believes that users will move the market to a more efficient level.

Alternative 3: FDA considered restricting the distribution and use of powdered NRL or synthetic material medical gloves by requiring that establishments using powdered gloves establish and maintain written procedures for selecting, purchasing and distributing gloves. FDA further considered restricting the distribution and use of powdered NRL or synthetic material medical gloves by requiring establishments using powdered gloves with more than the recommended powder levels to establish and maintain written procedures to evaluate, monitor and control airborne particulate matter at the point of use, through the use of an externally exhausted air handling system, HEPA filtration, or other system. FDA believes that these restrictions would reduce the risk of adverse foreign body and allergic reactions associated with powdered glove use. However, the extent of the expected reduction is uncertain. The expected costs of complying with these restrictions was estimated to be over \$21 million. Furthermore, any such workplace restrictions may impede or preempt the authority of OSHA to regulate gloves and glove powder in the workplace.

Before rejecting this alternative, the agency had examined the feasibility of exempting small facilities from the requirements of developing written procedures and air quality measures. Based on the expectation that small establishments with 10 or fewer employees would be able to

communicate and control risks associated with powdered medical easier than larger institutions. Exempting small medical facilities from these controls lowers the added costs to \$6.6 million. However, FDA rejected this alternative because the expected benefits of restricting glove use remained uncertain, and the potential overlap of authority with OSHA would still exist.

Alternative 4: FDA considered retaining the class I classification for all or some of the medical gloves. This alternative was rejected because it did not meet the stated objectives. In light of new information concerning barrier integrity, degradation of quality during storage, contamination concerns and concerns about exposure to foreign bodies and allergens, FDA found that general controls are no longer sufficient to provide reasonable assurances of the safety and effectiveness of medical gloves. Moreover, such concerns were not limited to only powdered gloves. To require a device to meet special controls as well as general controls, a device must be classified (or reclassified) into class II. Consequently, although compliance costs would have been reduced by this alternative, retaining some or all gloves as class I devices was rejected.

Alternative 5: Alternative 5 (excluding powdered synthetic gloves for this rulemaking) was considered in order to reduce cost by as much as \$2.4 million per year. FDA rejected this alternative because it would not meet the stated objective of the applicable statutes. While synthetic gloves do not contain NL proteins, FDA is concerned about foreign body reactions caused by glove powder. These reactions occur whether the powder is present on a NRL or synthetic glove. Consequently, FDA is rejecting exempting powdered synthetic gloves from this regulation.

Alternative 6: FDA considered providing a shorter compliance period for implementation of the regulation. A compliance period of 90 days or 1 year would significantly increase the expected benefits of the rule by decreasing the number of annual allergic reactions. FDA estimates that a 90-day or 1-year implementation period would result in between 3,300 and 3,600 fewer annual allergic reactions to NL proteins than the number expected with the selected 2-year compliance period. However, FDA is concerned that the lead times necessary to manufacture limited powder gloves would make compliance difficult. As stated earlier, manufacturing equipment used to control

glove powder levels is currently backordered as much as 18 months, and short compliance periods may result in inadequate supplies of medical gloves. Not including the potential of shortages, FDA has estimated that average annualized costs of shorter compliance periods could equal \$10 million to \$16 million more than the selected alternative. The 2-year compliance period allows firms to combine recommended changes with any other market driven changes, and will allow firms to deplete their supply of existing labels. As set forth above, however, FDA is soliciting comment on the timeframe for implementation to determine whether a 2-year compliance period is really needed. FDA also rejected providing a longer compliance period. FDA has tentatively determined that the decrease in costs is outweighed by the decrease in benefits if the compliance period is lengthened to as many as 3 years. While annual costs would decrease by almost \$9 million, allowing such a long compliance period would result in about 1,800 additional average annual allergic reactions as compared to the selected alternative and benefits would be reduced to \$32.0 million. Since glove manufacturers would have ample opportunity to comply within the selected 2-year period, FDA does not believe that additional time is justified.

FDA solicits comments on other alternatives that meet the stated objectives.

4. Assuring Small Entity Participation in Rulemaking

At this time, FDA does not believe that the proposed regulation will have a significant economic impact on a substantial number of small entities. However, the agency recognizes that many facilities will be affected. The impact may range from increased glove manufacturing costs due to validation testing and control of mold powder to increased contract prices of powdered gloves used by health facilities. FDA solicits comments from affected entities to ensure that this impact is analyzed.

FDA plans to provide for access to the **Federal Register** analysis through FDA's website on the Internet. Notice of the availability of this proposed rule and request for comment will be communicated to all glove-related associations and include a request for comments.

FDA is currently preparing an article for publication in latex-related trade publications that will highlight the proposed requirements. In addition, notice of the proposed rulemaking and request for comments will be available in health-related publications and sent to trade organizations. FDA actively seeks input into this proposal and requests comments on all aspects of the analysis of impacts and the regulatory flexibility analysis.

X. Conclusion

FDA has examined the impacts of the proposed regulation of protein and powder levels of NL gloves. Based on these estimates, the average annual quantifiable benefits (\$46.9 million) exceed the average annual quantifiable costs (\$32.5 million). Given the high level of uncertainty and the existence of unquantified benefits, FDA solicits comment on this analysis and all of its assumptions and projections.

XI. Environmental Impact

FDA has determined under 21 CFR 25.30(k) and 25.34(b) that this action is of the 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.

XII. Paperwork Reduction Act of 1995

This proposed rule contains information collections provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). A description of these provisions is given below with an estimate of the annual reporting burden. Included in the estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on: (1) Whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of

information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Title: Labeling and Written Procedures Requirements for Powdered and Powder-Free Patient Examination Gloves, and Powdered and Powder-Free Surgeon's Gloves.

Description: The proposed rule intends to provide users with material information to safely use patient examination and surgeon's gloves. The proposed rule expands the labeling for medical gloves to include: (1) Caution statements including the actual levels of protein and powder on the gloves, and (2) expiration dating.

The proposed labeling requirements would require manufacturers to conduct tests to support the protein and glove powder levels and expiration date. The proposed special control, a guidance document entitled "Medical Glove Guidance Manual," recommends that protein levels be measured by the ASTM D 5712 modified Lorry method and that glove powder levels be measured by the ASTM D6124-97 method. The labeling requirements also require stability testing to support the expiration date. The special control recommends that stability testing include tensile strength, elongation and water leak tests.

The labeling is intended to communicate useful information to users about FDA's guidance recommending the use of gloves with no more than 1,200 µg of protein and 120 mg of glove powder (or 2 mg of powder, for powder-free gloves) and to ensure that the labeling contains adequate directions for use. The labeling would require manufacturers to indicate the actual levels of protein and powder on the gloves so that the user can ascertain if the gloves meet the recommended limits on protein and powder, which are intended to reduce exposure to particulates and airborne allergens. The expiration date labeling is intended to ensure that medical glove users have appropriate information regarding shelf life to enable them to use medical gloves safely by avoiding products that may have degraded.

*Description of Respondents: Businesses or other for profit organizations.*TABLE 12.—ESTIMATED ANNUAL REPORTING BURDEN¹

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours	Total Capital Costs
801.440(a)	180	1	180	22	3,960	\$985,248
801.440(b)	18	1	18	14	252	
801.440(c)	178	1	178	16	2,848	
801.440(d)	376	4 ²	1,504	72	108,288	
Total					115,348	\$985,248

¹ There are no operating and maintenance costs associated with this collection of information.

² The annual burden reported here represents the first year in which a manufacturer would have conducted testing at 0 days, 3 months, 6 months, and 1 year. FDA expects in any succeeding years, testing would only be done at 6-month intervals.

For the proposed labeling requirements, the hours per response included the hours estimated, based upon communications with industry, to run the tests to support the powder and protein levels and the expiration date, as well as the hours estimated to change the respondent's labeling. The total capital costs were derived from multiplying the total annual responses for protein testing and multiplying it by the estimated costs of buying a spectrometer and a plate reader, instruments that are necessary to conduct the protein testing. That cost was then annualized over a 5-year period.

Based on communication with industry, FDA estimates that a respondent would take approximately 8 hours to run the protein tests necessary to obtain a protein level to add to the labeling. FDA bases its estimate on the ASTM D 6124-97 protein test.

Based on communication with industry, FDA estimates that a respondent would take approximately 6 hours to run the powder tests necessary to obtain a powder level to add to the labeling. FDA bases its estimate on the ASTM D 5712 modified Lowry method powder test.

Based on communication with industry, FDA estimates that a respondent would take approximately 16 hours to run the elongation, tensile strength, and waterleak tests recommended to support the expiration date. In the first year, FDA estimates that the tests would be run 4 times, at 0 days, 3 months, 6 months, and 1 year (16 X 4 = 64). In the second, or succeeding years, FDA expects the tests to be run twice a year.

FDA estimates that a respondent would take approximately 8 hours to change the labeling and approximately 8 hours to change the promotional materials to include the appropriate caution

statement and the expiration date. This 16 hours is divided between the labeling changes proposed in § 801.440(a) and (d) resulting in 8 hours being assessed for the caution statement and 8 hours being assessed for the expiration date.

FDA estimates the number of burden hours per response for § 801.440(a) is 22. That burden comes from the sum of the hours for running the powder and protein tests (8 hours plus 6 hours) and the hours for changing the labeling (8 hours).

FDA estimates the number of burden hours per response for § 801.440(b) is 14. That burden comes from the sum of the hours for running the powder tests (6 hours) and the hours for changing the labeling (8 hours).

FDA estimates the number of burden hours per response for § 801.440(c) is 16. That burden comes from the sum of the hours for running the protein tests (8 hours) and the hours for changing the labeling (8 hours).

FDA estimates the number of burden hours per response for § 801.440(d) is 72. That burden comes from the sum of the hours for running the elongation, tensile strength, and waterleak tests four times in the first year (64 hours) and the hours for changing the labeling (8 hours).

FDA believes that manufacturers already have the equipment necessary to do the tests to support the powder levels and expiration dating because such equipment is currently being used to test the gloves. In order to do the protein tests recommended by FDA, FDA believes a manufacturer would need to obtain a spectrometer and a plate reader. FDA estimates that buying this equipment would cost approximately \$22,000 (approximately \$10,000 for the spectrometer and \$12,000 for the plate reader). In addition, FDA assumed a 7 percent discount on the price of the equipment and that the equipment would be annualized over a 5-year period. In order to obtain a per annualized year estimate, FDA multiplied the cost by the discount ($\$22,000 \times .244$). FDA added the discounted amount (\$5,368) to the cost of the equipment (\$22,000) for a total equipment cost of \$27,368. That cost annualized over a 5-year period is \$5,473.60. FDA multiplied

that cost by the number of respondents testing for protein levels (180) for a total capital cost of \$985,248.

In compliance with the Paperwork Reduction Act of 1995 (44 U.S.C. 3507(d)), FDA has submitted the information collection provisions of this proposed rule to OMB for review. Interested persons are requested to send comments regarding information collection by (*insert date 30 days after date of publication in the Federal Register*), to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn.: Wendy Taylor, Desk Officer for FDA.

XIII. References

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List of Subjects

21 CFR Part 801

Labeling, Medical devices, Reporting and recordkeeping requirements.

21 CFR Parts 878 and 880

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 801, 878, and 880 be amended as follows:

PART 801—LABELING

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

Authority: 21 U.S.C. 321, 331, 351, 352, 360c, 360i, 360j, 371, 374.

2. Section 801.437 is amended by revising paragraph (d) to read as follows:

§ 801.437 User labeling for devices that contain natural rubber.

* * * * *

(d)(1) As described in paragraph (b) of this section, devices containing natural rubber latex that contacts humans, except natural rubber latex surgeon's and patient examination gloves shall bear the following statement in bold print on the device labeling:

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

This statement shall appear on all device labels, and other labeling, and shall appear on the principal display panel of the device packaging, the outside package, container, or wrapper, and the immediate device package, container, or wrapper.

(2) Natural rubber latex surgeon's and patient examination gloves shall bear the appropriate caution statement delineated in § 801.440(a) or (c). This statement shall appear on all device labels, and other labeling, and shall appear on the principal display panel of the device packaging, the outside package, container, or wrapper, and the immediate device package, container, or wrapper.

* * * * *

3. Section 801.440 is added to subpart H to read as follows:

§ 801.440 User labeling for powdered and powder-free surgeon's and patient examination gloves.

The caution statements required in this section shall appear on all device labels, and other labeling, and shall appear on the principal display panel of the device packaging, the outside package, container, or wrapper, and the immediate device package, container, or wrapper.

(a) Natural rubber latex powdered surgeon's gloves and powdered patient examination gloves shall bear the following statement: “Caution: This product contains natural rubber latex which may cause allergic reactions. FDA recommends that this product contain no more than 120 mg powder and 1,200 µg extractable protein per glove. This product contains no more than [insert level] mg powder and no more than [insert level] µg extractable protein per glove.”

(b) Synthetic material powdered surgeon's or powdered patient examination gloves shall bear the following statement: "Caution: Glove powder is associated with adverse reactions. FDA recommends that this product contain no more than 120 milligrams powder per glove. This product contains no more than [insert level] mg powder per glove."

(c) Natural rubber latex powder-free surgeon's gloves and powder-free patient examination gloves shall bear the following statement: "Caution: This product contains natural rubber latex which may cause allergic reactions. FDA recommends that this product contain no more than 1,200 µg extractable protein per glove. This product contains no more than [insert level] µg extractable protein per glove."

(d) All surgeon's and patient examination gloves shall bear an expiration date as follows:

(1) The expiration date shall state the month and year of the shelf-life as supported by data from the studies described in paragraph (d)(3) of this section;

(2) The expiration date must be prominently displayed on the exterior of the primary and retail package, and on the shipping carton;

(3) The expiration date must be supported by stability studies demonstrating acceptable physical and mechanical integrity of the product over the shelf-life of the product from its date of manufacture;

(4) For each glove design, the testing data and stability study protocol supporting an expiration date must be maintained by the manufacturer for a period equivalent to the design and expected life of that glove type, and shall be made available for inspection and copying by FDA; and

(5) Sterile surgeon's and patient examination gloves that have a date of expiration based on sterility that is different from the expiration date based upon physical and mechanical integrity testing shall bear only the earlier expiration date.

PART 878—GENERAL AND PLASTIC SURGERY DEVICES

4. The authority citation for 21 CFR part 878 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360l, 371.

5. Section 878.4460 is revised to read as follows:

§ 878.4460 Surgeon's gloves, powdered.

(a) *Identification.* A powdered surgeon's glove is a disposable device made of natural rubber latex or synthetic material that bears powder to facilitate donning, and it is intended to be worn on the hands, usually in surgical settings, to provide a barrier against potentially infectious materials and other contaminants. The lubricating or dusting powder used on these gloves is classified separately in § 878.4480.

(b) *Classification.* Class II special controls are as follows:

(1) *Guidance document.* The Center for Devices and Radiological Health, FDA, "Medical Glove Guidance Manual," as revised. The guidance document is available from the Division of Small Manufacturers Assistance (HFZ-220), Center for Devices and Radiological Health, Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850.

(2) *Labeling.* User labeling requirements in § 801.440 of this chapter.

6. Section 878.4461 is added to subpart E to read as follows:

§ 878.4461 Surgeon's gloves, powder-free.

(a) *Identification.* A powder-free surgeon's glove is a disposable device made of natural rubber latex or synthetic material that may bear a trace amount of glove powder and is intended to be worn on the hands, usually in surgical settings, to provide a barrier against potentially infectious materials and other contaminants.

(b) *Classification.* Class II special controls are as follows:

(1) *Guidance document.* The Center for Devices and Radiological Health, FDA, "Medical Glove Guidance Manual," as revised (see § 878.4460(b)(1)).

(2) *Labeling.* User labeling requirements in § 801.440 of this chapter.

PART 880—GENERAL HOSPITAL AND PERSONAL USE DEVICES

7. The authority citation for 21 CFR part 880 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 371.

8. Section 880.6250 is revised to read as follows:

§ 880.6250 Patient examination gloves, powdered.

(a) *Identification.* A powdered patient examination glove is a disposable device made of natural rubber latex or synthetic material that bears powder to facilitate donning and is intended to be worn on the hand or finger(s) for medical purposes to provide a barrier against potentially infectious materials and other contaminants.

(b) *Classification.* Class II special controls are as follows:

(1) *Guidance document.* The Center for Devices and Radiological Health, FDA, “Medical Glove Guidance Manual,” as revised. The guidance document is available from the Division of Small Manufacturers Assistance (HFZ-220), Center for Devices and Radiological Health, Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850.

(2) *Labeling.* User labeling requirements in § 801.440 of this chapter.

9. Section 880.6251 is added to subpart G to read as follows:

§ 880.6251 Patient examination gloves, powder-free.

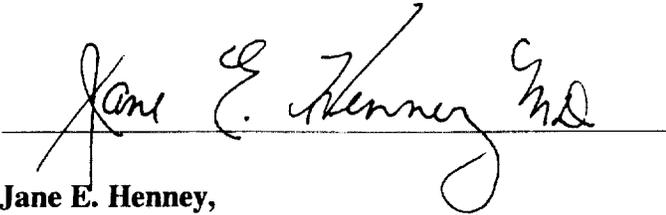
(a) *Identification.* A powder-free patient examination glove is a disposable device made of natural rubber latex or synthetic material that may bear a trace amount of glove powder and is intended to be worn on the hand or finger(s) for medical purposes to provide a barrier against potentially infectious materials and other contaminants.

(b) *Classification.* Class II special controls are as follows:

(1) *Guidance document.* The Center for Devices and Radiological Health, FDA, “Medical Glove Guidance Manual,” as revised (See § 880.6250(b)(1)).

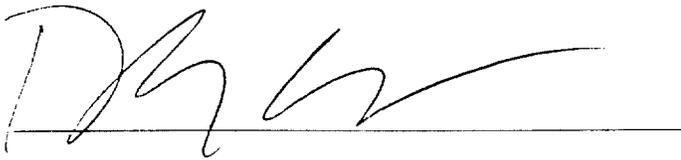
(2) *Labeling*. User labeling requirements in § 801.440 of this chapter.

Dated: MAR 2 1998



Jane E. Henney,

Commissioner of Food and Drugs.



Donna E. Shalala,

Secretary of Health and Human Services.

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