Lowell Center for Sustainable Production
One University Avenue, University of Massachusetts Lowell, Lowell, MA 01854 USA

October 14, 1999

Docket No. 99D-2335
Dockets Management Branch
Division of Management Systems and Policy
Office of Human Resources and Management Services
Food and Drug Administration
5630 Fishers Lane, Room 1061 (HFA-305)
Rockville, MD 20852

Dear FDA Representative,

I am submitting comments on:

- FDA Medical Glove Guidance Manual Draft. released on July 30, 1999, and
- 21 CFR Parts 801, 878, and 880, Surgeon's and Patient Examination Gloves; Reclassification and Medical Glove Guidance Manual Availability; Proposed Rule and Notice, dated July 30, 1999

This correspondence is on behalf of the Sustainable Hospitals Project (SHP) at the University of Massachusetts Lowell Center for Sustainable Production. SHP is a university-industry partnership group which provides technical assistance to health care.

If you have any questions or would like further information on this submission, please feel free to contact me.

Sincerely yours,
Catherine J. Galligan
Catherine J. Galligan
SHP Product Engineer and Clearinghouse Manager

Mailing address: Catherine J. Galligan, Manager
Sustainable Hospitals Project, Kitson 200
University of Massachusetts Lowell
College of Engineering
1 University Avenue
Lowell, MA 01854

Phone: 978-934-3386
Email: shp@uml.edu

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Summary of Key Comments to the FDA

1. Because medical gloves purport to provide protection against blood borne pathogens (BBPs), it is essential that qualification testing include testing for penetration of BBPs. The FDA is urged to mandate that any glove marketed as a "medical glove" must pass ASTM F1671 during the entire shelf life of the gloves. (Note: ASTM F1671-97a, "Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-borne Pathogens Using Phi-X 174 Bacteriophage Penetration as a Test System).
2. Caution statements on glove labels should be made clearer, as these statements may be the only education the user gets on hazards associated with gloves.
3. There is an urgent need to evaluate a glove's viral barrier performance in a way that reflects real world conditions. Health care providers need blood borne pathogen protection under conditions of simultaneous exposure to physical stressors (e.g: flexing, stretching), perspiration, and chemicals or chemotherapy drugs. The FDA is encouraged to mandate testing for penetration of BBPs under typical clinical conditions, in addition to the unstressed condition.

Summary of the Proposed FDA Changes Regarding Medical Gloves

The FDA "Medical Glove Guidance Manual" draft dated July 30, 1999 and "21 CFR Parts 801, 878, and 880 Surgeon's and Patient Examination Gloves; Reclassification and Medical Glove Guidance Manual Availability; Proposed Rule and Notice" (CFR) spell out a variety of changes to the requirements for medical gloves.

Based upon information now available, the FDA has reevaluated its classification for surgeon's and patient examination gloves from class I to class II medical devices. This reflects FDA concerns about:

- barrier integrity
- degradation of quality during storage
- contamination
- exposure to natural latex (NL) allergens and the role of glove powder as a carrier of airborne NL allergens
- the inability of general controls to address these concerns

FDA also recognizes the concern about glove powder's capability, as a particulate material, to cause foreign body reaction, resulting in inflammation, granulomas, and adhesions of peritoneal tissues after surgery. FDA also notes that cornstarch represents a growth source for bacteria and a carrier of endotoxin, which can play a role in enhancing both delayed and immediate hypersensitivity.

This proposed rule is intended to:

1. 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
2. To reduce the adverse health effects from defects in the barrier integrity and quality of surgeon's and patient examination gloves.

C. Galligan, Sustainable Hospitals Project
University of Massachusetts Lowell
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By moving from class I to class II, gloves are required to meet special controls in addition to general controls applicable to all medical devices. The special controls are documented in the proposed document "Medical Glove Guidance Manual" and include:

- Recommended protein limits & powder limits
- New label caution statements, including protein & powder labeling requirements
- Required expiration dating

Comments On the FDA Draft Glove Manual

I. Overall

The FDA is complimented on its timely changes to the CFR and Medical Glove Guidance Manual. This effort will contribute very favorably to improved occupational safety and health and to the quality of care for both patients and health care workers. Each concern prompting these proposed changes (including barrier integrity concerns, degradation of quality during storage, contamination concerns, concerns about exposure to NL allergens and the role of glove powder, and the shortcomings of Class I general controls) is well-substantiated in the medical literature and in discussions with health care professionals.

There is an excellent checklist (in table form) starting on page 10-63 of the draft manual. It is clear, concise, and easy to pull out pertinent information. It is recommended that glove requirements be put in a similar format. The glove requirements table could be placed towards the front of the glove manual, with supporting text following. Advantages of a summary table:

- Ensure uniform criteria from one type glove to another
- Shorter text (overall) because instead of repeating same text by glove type, could have single section of text apply as appropriate to different types of glove
- Easier for reader to comprehend scope of requirements

II. Viral Barrier Integrity

Because the primary purpose for wearing medical gloves is protection against BBPs, the following modifications to the Glove Manual requirements are essential:

1. All gloves marketed and sold for medical use must pass the ASTM F1671 "Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-Borne Pathogens Using Phi-X 174 Bacteriophage Penetration as a Test System". Gloves must pass (that is, no measurable viral penetration within 2 hours) in both <u>virgin form</u> and at <u>any point during and including the end of the manufacturer-specified shelf life.</u>

2. The FDA should solicit recommendations for a testing protocol or empirical relationship that predicts glove viral integrity under conditions of actual use. It is recommended that the FDA include a provision in the Glove Manual that when appropriate evaluation protocols are developed, glove standards will be modified further to include more appropriate and comprehensive testing.

C. Galligan, Sustainable Hospitals Project
University of Massachusetts Lowell
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Discussion

Currently, the FDA does not require a manufacturer to test the BBP penetration resistance of a glove. This is unacceptable. A current FDA testing procedure, which evaluates leakage of a water-filled glove within two minutes, is inadequate for predicting BBP penetration characteristics. There appear to be at least two basic problems with the current water test method:

1. No fundamental research has been presented which validates this test method. Ideally, one would want to confirm that water serves as an appropriate surrogate for BBPs found in a health care setting , and that a visible gross water leak at 2 minutes represents the threshold for viral penetration of a glove under typical use conditions.

2. Another shortcoming is that the water leak test is conducted on virgin gloves. (Testing is done on unworn virgin or aged samples). Real-world conditions will introduce factors which by themselves or in combination may affect the viral penetration characteristics of the glove. These factors may include flexing, abrasion, perspiration, and contact with chemicals. Because protection is required in the clinical setting (rather than in the box), consideration must be given to testing in a way that is representative of practical application.

Empirical evidence shows that current medical glove standards fail to predict barrier integrity for conditions of actual use. Korniewicz and Rabussay (1,2,3) cited that surgical gloves fail more than 50% of the time during operative procedures, and gloves stressed in ICU clinical procedures leaked 16% of the time. They also note (4) that visual detection is modest, at best, for recognizing mechanical glove damage and virtually incapable of recognizing glove degradation and microperforations which allow microorganisms to pass through. Anecdotal information provided by health care professionals describes how common it is for a practitioner to find blood on her hands, although no hole was observed in the glove.

ASTM F1671 ("Standard Test Method for Resistance of Materials Used in Protective Clothing to Penetration by Blood-Borne Pathogens Using Phi-X 174 Bacteriophage Penetration as a Test System") is recommended because it closely simulates characteristics of blood, body fluids, and blood borne pathogens and their potential for penetrating the protective glove. In the ASTM test method, a glove specimen is continuously subjected to a nutrient broth containing a virus for a specified time and pressure sequence. Any evidence of viral penetration constitutes failure. The testing method uses visual detection complemented by an assay procedure. The assay detects viable viruses which penetrate the material even when liquid penetration is not evident. The Phi-X 174 bacteriophage is similar to Hepatitis C Virus (HCV) in size and shape, and also serves as a surrogate for Hepatitis B Virus (HBV) and Human Immunodeficiency Virus (HIV). Surface tension of the testing liquid is adjusted to be similar to blood and body fluids.

If one were to challenge the test method, the criticism might be that the method employs continuous contact with the simulated BBP liquid, which is unlikely in a clinical setting. While the merits of this point can be argued, it is also worth considering that testing an unused glove is much less rigorous than testing a glove subjected to stressors

encountered in a health care setting. Given the potential cost of glove failure, one would prefer to err on the side of greater protection and use the ASTM method.

A final point about the ASTM method is that it would be suitable for testing samples of gloves which had been conditioned to reflect conditions of actual use, when this become a requirement in the future.

III. Labeling and Attributes

On page 6-3 of the Glove Manual, the proposed Caution Statements should more clearly indicate each of the cautionary points. In some cases this caution statement may be the only education a user receives regarding the hazards associated with medical gloves. Therefore, each caution should be clearly visible. A suggested format is:

Caution:

- **This product contains natural rubber latex which may cause allergic reactions.**
- **This product contains glove powder which is associated with adverse reactions to wearer and patient.**
- **FDA maximum allowed powder level: 120 mg powder**
  This product contains [insert level] powder, per FDA procedures
- **FDA maximum allowed protein level: 1200 micrograms extractable protein**
  This product contains [insert level] extractable protein, per FDA procedures

Caution:

- **This product contains glove powder which is associated with adverse reactions to wearer and patient.**
- **FDA maximum allowed powder level: 120 mg powder**
  This product contains [insert level] powder, per FDA procedures

III. Labeling and Attributes

Reference: Page 6-10 of the Glove Manual, "Chemotherapy Label Claim"

If gloves are marketed for protection during administration of chemotherapy drugs, it implies that they provide an effective barrier between the chemotherapy drug and the worker. This must be backed up by conclusive data. ASTM F739, "Standard Test Method for Resistance of Protective Clothing Materials to Permeation by Liquids or Gases Under Conditions of Continuous Contact" is a recommended procedure. Therefore, the Glove Manual should be modified to require that chemotherapy gloves report a "breakthrough detection time" per this ASTM standard, that is valid throughout their entire shelf life. The glove label (e.g. on the box) should show the performance of a glove for each chemo drug (indicating breakthrough detection time) and a caution "Do not wear gloves longer than breakthrough detection time".

C. Galligan, Sustainable Hospitals Project
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IV. Other Comments

Page	*Comment*
3.3	Gloves used for chemotherapy must undergo testing per ASTM F739-96 for chemotherapy drugs
3.3	A wording change is recommended to clarify that gloves meet all requirements of ASTM D3578 *except for* thickness, which may exceed the specifications. (Technically, if a glove is thicker than specified in the standard, it doesn't meet the standard, hence the clarification).
3.3	In "Chemo/Specialty Gloves" put back in paragraph (from original glove manual) re: Chemo, Chemical, Biocompatibility testing and add ASTM # for test procedure. (ASTM F739 for Resistance to Permeation of Liquids and Gases)
3.5	In Table 3.2, why is gloving cream only under powdered gloves?
3.5	Ideally, combine Table 3.2 into single table with 6 columns
3.6	"Gloving creams should be safe and effective and should not degrade the glove material in latex or other gloves, i.e., the creams should not be oil-based". This statement needs to be accompanied by a standard test method to verify acceptability of gloving creams. Recommend that gloving creams go through minimum of testing on different types of gloves, including viral penetration & chemical permeability of gloves coated with gloving cream for 2 hours.
3.7	Radiographic gloves are no longer shown in Table 3.2. (They were in the original Glove Manual). If they are used for protection against BBPs they should meet all requirements of standard medical gloves. If they are not used for BBP barrier protection, do they belong in this manual? The text implies that this manual is for gloves that provide an effective barrier to transmission of infectious agents. Radiation gloves appear to be a protection against a physical agent.
3.8	Leak Detectors – text shows "Leak detectors are Class I devices..." while Table 3.2 shows as Class II device.
Chapter 5	Page numbering is off! (Shown as "4-x", rather than "5-x")
5-1	In the "Introduction", paragraph 2, text reads "Biocompatibility data *should be* submitted for all medical gloves...". Text in italics used to be (original Manual) "*is required*". The original stronger statement is preferable.
5-2	In the "Skin Irritation...Studies", sentence 2 reads "the gloves used for biocompatibility studies *should be* finished gloves". Text in italics used to be (original Manual) "*is required*". The original stronger statement is preferable.
6-4	In the section "Expiration Date": Point (d)(3) should clearly state the requirement of passing ASTM F1671 (Penetration of BBPs) over the entire shelf life of the product.
6-5	"Aging studies are performed with a *statistically valid number* of representative gloves...." This is too vague, and standards should be spelled out for how to establish what is *statistically valid.*

C. Galligan, Sustainable Hospitals Project
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6-6	Last paragraph of "Standards", "If the label states that a product meets a specific standard, the product delivered to the customer must meet the standard." Recommend adding the phrase shown in italics: "If the label states that a product meets a specific standard, the product delivered to the customer must meet the standard *throughout the full shelf life of the product.*"
6-5, 6-6	In reference to the national or international consensus standards: Recommend that it be made clear that the most current standard must be met.
6-7	Last sentence in paragraph 2, "affect" rather than "effect"
6-7	In "Protein Label Claims", Type I sensitivity should be defined (or refer to definition elsewhere in document).
6-10	"The minimum biocompatibility tests for chemotherapy gloves are skin irritation and dermal sensitization". It is recommended that this should be the same as for all other gloves – not clear if it is or isn't as currently shown.
9-9	"7.3 Type": Under Type 2, use more appropriate term such as "gloves compounded from non-latex compound"
9-10	"7.5 Composition of Gloves": a definition of "co-polymer" is warranted
9-10	"8.0 Specifications": A table with ASTM requirements as a reference is recommended
9-10	I recommend adding results of ASTM viral barrier testing and ASTM testing for chemo drugs and chemicals. (this would prompt changing wording in section 9.0 on page 9-11 to reflect additional testing).
9-12	Section 11.0 FORMER Release Powder or Chemical Recommend adding line "Method of Removal"
10-63	This is a really nice checklist. It is recommended that a similar format be used for glove requirements.

References

1) Korniewicz, D, "Barrier Integrity of Gloves Used in Clinical Practice", Source to Surgery, October, 1997, Ansell Healthcare Division

2) Rabussay, D and Korniewicz, DM; "The Risks and Challenges of Surgical Glove Failure", American Operating Room Nurses (AORN) Journal, November 1997, Volume 66, No. 5, pp. 867-888

3) Korniewicz, DM and Rabussay, D; "Surgical Glove Failures in Clinical Practice Settings", American Operating Room Nurses (AORN) Journal, October 1997, Volume 66, No. 4, pp. 660-673

4) Rabussay, D and Korniewicz, DM; "Improving Glove Barrier Effectiveness:, American Operating Room Nurses (AORN) Journal, December 1997, Volume 66, No. 6, pp. 1043-1063

C. Galligan, Sustainable Hospitals Project
University of Massachusetts Lowell
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C. Galligan

UMASS
University of
Massachusetts
Lowell

WORK ENVIRONMENT PROGRAM
One University Avenue
Lowell, Massachusetts 01854

TO: Docket No. 99 D-2335
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