Medical devices with latex become easier to identify

Workplace decisions remain unclear

New labeling mandated by the Food and Drug Administration (FDA) calls for manufacturers of medical devices, including gloves, to identify which products have natural rubber latex and which have dry natural rubber. Not only must the products containing natural rubber latex state so, they must remind users that the substance may cause allergic reactions. Disappearing from labels are any claims of hypoallergenicity.

Manufacturers received one year’s notice, from September 1997, to deplete stocks bearing the old labeling and add new labeling to inventory. The FDA rule, effective September 30, does not affect medical devices already purchased. It also does not give health care workers and consumers help in deciding which options to take in making an environment latex-safe.

Differentiation of allergy from other reactions.

Estimates vary on the prevalence of latex allergy, a reaction mediated by immunoglobulin E (IgE) and involving the skin and respiratory systems. According to the FDA, 5–17% of health care workers are sensitive to latex proteins.

The actual prevalence is closer to 2.5%, says Edward L. Petsonk, medical officer in the division of respiratory disease studies at the National Institute for Occupational Safety and Health (NIOSH). Speaking at the 1998 Frontline Healthcare Workers Conference in Washington, D.C., in August, he said the best study on the subject involved a follow-up challenge. In that study, Belgian researchers first exposed health care workers to latex gloves. Those who initially had symptoms of asthma were then exposed to airborne latex particles and observed for confirmatory evidence of an allergy.

A diagnosis of latex allergy should be made on the basis of a person’s history and test results, Petsonk said. Although three types of tests are in use—glove-use testing, skin-prick testing with latex extracts, and in vitro serum assays for IgE antibodies to latex proteins—none has been declared the standard procedure.

In glove-use testing, a person dons a latex finger cot, waits, and then takes it off. A visible reaction on the finger suggests the person is allergic to latex. Alternatively, the tester exposes a person to airborne latex particles by snapping a latex glove and then observes whether the person has a respiratory reaction such as airway edema. Because of the chance for severe reactions, these tests must be done only by people who strictly follow the testing protocols, Petsonk said.

Beyond the new labeling.

Health care workers can ask glove manufacturers about the protein content of their products, Petsonk said, but must bear in mind that not all the proteins in a latex glove are allergenic. U.S. manufacturers report protein content as the findings of the modified Lowry test, the only FDA-approved test for measuring natural rubber latex protein in gloves.

Since FDA considers the test’s limit of detection to be 50 µg of protein per gram of glove, no manufacturer can report a lower protein content in its U.S. labeling. Even a latex glove advertised as having a “reduced protein” content cannot have U.S. labeling claiming a protein content of less than 50 µg/g. Independent researchers, however, can and do report lower amounts.

Despite the availability of an FDA-accepted method for measuring the protein content of latex gloves,
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there is no standard method for measuring allergens that can be reported in glove labeling, Petsonk said. The popular latex enzyme-linked immunosorbent assay for antigenic protein, or LEAP, remains unaccept-
ed by FDA and the American Society for Testing and Materials. Developer Donald H. Beazhold, of the Guthrie Foundation for Medical Research in Sayre, Pennsylvania, has achieved reliable test results with LEAP, but glove manufacturers have not, said Petsonk. The test relies on immunization of a group of rabbits with latex proteins and use of a nonstandardized reagent.

Efforts to develop a technique that reliably measures antigenic latex proteins are under way at NIOSH and FDA, Petsonk said. Until such a technique becomes available, “the use of powder-free [latex] gloves will very likely reduce the exposure of an individual to the important antigens that are associated with latex allergies,” a conclusion Petsonk reached from his review of studies of airborne latex antigens. The powder acts as a “vector” for latex proteins and serves only to deliver the antigen of concern.

“When we can get a better measure of latex allergens,” Petsonk said, “we may be able to do better in helping you make purchasing decisions.” He said the U.S. Public Health Service held its first meeting in July 1998 to develop a document that will offer criteria for selecting gloves and address other latex-related issues. That document, he said, will not be available for two years because of the amount of information to be processed.

Elsewhere in the government sector, the Occupational Safety and Health Administration will soon issue the hazard information bulletin “Potential for Sensitization/Allergy and Life-Threatening Reactions to Natural Rubber Latex Gloves and Other Products.” In 1997, NIOSH issued a statement calling for the use of only reduced-protein, powder-free latex gloves, according to one study, protect better than latex gloves against viruses, Wilburn said. Well-known in the manufacturing industry, nitrile gloves protect workers against exposure to chemicals and antineoplastic drugs. Tactylon, neoprene, and elastryn gloves provide the same barrier protection as latex gloves or better, she said.

Recommendations for a Latex-Safe Pharmacy Protocol

- Use i.v. medications available in ampuls.
- For i.v. medications not available in ampuls, “it is recommended that stoppers be removed”; the clinical risk of latex antigens leaking from vial stoppers into medication solution during storage has not been substantiated.
- Do not use puncture-through latex injection ports on i.v. bags, bottles, and tubing.
- Dispense syringe products in latex-free or glass syringes, or draw up medication doses into latex-containing syringes less than 24 hours before the doses are scheduled to be given.
- Wear nonlatex gloves and use latex-free syringes to prepare the patient’s i.v. medications and fluids.
- Wipe the inside surfaces of the laminar-airflow hood with 70% isopropyl alcohol before preparing i.v. products.


Protection of patients.

In the March 1998 issue of AORN Journal, from the Association of Operating Room Nurses, a multidisciplinary team led by Kenneth T. Kim, president of the Foundation for Latex Allergy Research and Education (FLARE), published recommendations for making health care facilities latex-safe. “Whenever possible,” the authors state, “i.v. medications and solutions should be prepared in a latex-safe manner for a patient with known latex allergy. Exceptions to this policy are chemotherapy medications and total parenteral nutrition (TPN) solutions because possible latex exposure can be reduced but not totally eliminated in the preparation of these two products.” Included in the article are directions for pharmacies to use making their products latex-safe (see box) and a list of supplies for a latex-free cart, equipped with anaphylactic medication trays, to be placed inside the room.
Anti-TNF antibody approved for Crohn’s disease

FDA has licensed infliximab (Remicade, Centocor), a chimeric monoclonal antibody that neutralizes the biological activity of tumor necrosis factor alpha (TNF-α), for treatment of moderately or severely active Crohn’s disease in patients who have not responded adequately to conventional therapy. It is also indicated for use by patients with fistulizing Crohn’s disease to reduce the number of draining enterocutaneous fistulas.

In a dose-ranging study in patients with moderately or severely active Crohn’s disease, 22 (82%) of 27 patients who received a single 5-mg/kg dose of infliximab showed clinical improvement at four weeks, compared with 4 (16%) of 25 patients who received placebo. One placebo recipient and 13 patients treated with infliximab 5 mg/kg were in clinical remission. Most patients took the assigned treatment along with stable doses of one or more conventional therapies. The maximum response to infliximab was seen two to four weeks after the dose. Doses larger than 5 mg/kg were not associated with higher response rates.

In a study of patients with fistulizing Crohn’s disease and fistulas of at least three months’ duration, 21 (68%) of 31 patients given three 5-mg/kg doses of infliximab, 18 (56%) of 32 patients given three 10-mg/kg doses, and 8 (26%) of 31 patients given placebo had at least a 50% reduction in the number of draining fistulas. As in the previous study, most patients continued to receive conventional therapies. The median onset of response to infliximab was 2 weeks and the duration 12 weeks. Between 8 and 16 weeks after the last dose, 12% of infliximab-treated patients and 3.5% of placebo-treated patients had an abscess developed in the area of the fistula.

Adverse events associated with infliximab therapy include infusion-related reactions (e.g., rash, hypotension, chills, chest pain), infections, and autoimmune antibody development, which has been accompanied in rare cases by reversible lupus-like symptoms.

When given as a 5-mg/kg i.v. infusion, infliximab has an apparent distribution volume of 3 L and a terminal half-life of 9.5 days.

The recommended dose for moderately or severely active Crohn’s disease is a single 5-mg/kg i.v. infusion. Patients with fistulizing disease should receive two additional doses, at two and six weeks.

Remicade is supplied as a lyophilized powder for i.v. infusion. Each vial contains infliximab 100 mg. Doses should be prepared in glass or polypropylene or polyolefin containers and administered through polyethylene-lined administration sets. An infusion time of at least two hours is recommended. The solution should not be stored for more than three hours before the infusion.

The list price is $450 per vial. Most patients will require three or four vials per dose.

Study raises question: Are we harming patients with albumin?

Because a low serum albumin concentration has been associated with an increased risk of mortality, albumin is often administered to critically ill patients with hypoalbuminemia, burns, or hypovolemia from trauma or surgery. However, a recent meta-analysis calls into question this practice.

The authors included in their analysis randomized, controlled clinical trials comparing albumin or plasma protein fraction (PPF) one additional death occurs.1

The authors found that critically ill patients treated with albumin or PPF had a higher risk of death than the comparison group. The relative risk of death after albumin or PPF administration was 1.46 (95% confidence interval, 0.97–2.22) for patients with hypovolemia, 2.40 (1.11–4.30) for patients not treated with albumin or PPF, and 2.71 (1.12–6.50) for patients treated with albumin or PPF. These differences were statistically significant (p < 0.05).

In a meta-analysis of 32 randomized, controlled trials involving 97% of all critically ill patients treated with albumin or PPF, the authors found a relative risk of death of 1.46 (95% confidence interval, 1.11–2.22) for patients treated with albumin or PPF. The relative risk of death was 1.46 (95% confidence interval, 0.97–2.22) for patients treated with albumin or PPF and 2.40 (1.11–4.30) for patients not treated with albumin or PPF. These differences were statistically significant (p < 0.05).

The authors concluded that albumin is not associated with increased mortality. However, they noted that the number of patients in the meta-analysis was limited, and further research is needed to confirm these findings.