Administering pharmaceuticals to latex-allergic patients from vials containing natural rubber latex closures

ROBERT G. HAMILTON, ROBERT H. BROWN, MICHAEL A. VELTRI, E. ROBERT FEROLI, MARIE NOEL PRIMEAU, JAMES F. SCHAUBLE, AND N. FRANKLIN ADKINSON, JR.

Am J Health-Syst Pharm. 2005; 62:1822-7

Natural rubber latex derived from the *Hevea brasiliensis* tree is widely used in the manufacturing of packaging for pharmaceuticals and medical products because of its excellent elasticity and durability. In 1991, the Food and Drug Administration (FDA) issued a medical alert on natural rubber latex allergy.[1] From that point forth, latex allergy has remained an established health problem, with a reported frequency in the 1990s of 1–6% in the general population,[2-4] 8–16% in health care workers,[5,6] and up to 50% in children with spina bifida.[7] In recent years, the number of new cases of latex allergy has decreased due to improved diagnostic methods, more extensive education, accurate labeling of medical devices containing natural rubber latex, and use of medical devices with reduced latex-allergen content.

Individuals sensitized to allergenic proteins released from natural-rubber-containing consumer (e.g., toy balloons, condoms) and medical products (e.g., medical examination and surgeon gloves, manual resuscitators, rubber dental dams) have a broad range of allergic reactions, from mild local cutaneous reactions to generalized urticaria, angioedema, allergic rhinitis, respiratory symptoms, and life-threatening or fatal anaphylaxis. The epidemiology, diagnosis, and natural history of latex allergy are more extensively discussed elsewhere in a primer for the pharmacist.[8]

Natural rubber latex in medical device packaging. Applied research in latex allergy has focused on quantifying the allergenic content of natural rubber latex in examination and surgeon gloves.[9] In 1997, FDA issued a rule requiring labeling statements on medical devices, including device packaging containing natural rubber that comes into contact with humans.[10] The rule requires that medical devices containing natural rubber latex state "Caution: This Product Contains Natural Rubber Latex Which May Cause Allergic Reactions." This rule, however, has not been adopted by FDA's Center for Drug Evaluation and Research (CDER). Thus, the rule largely remained a requirement focused on dipped rubber products, which have been shown to contain higher levels of releasable allergenic proteins than the dry, molded, natural rubber used in the packaging of medical devices and household products. However, questions have remained as to whether the dry natural rubber used in pharmaceutical vial closures or plungers in syringes releases allergenic proteins, thereby creating an allergen exposure risk for latex-allergic individuals who receive parenteral medications. Since synthetic butyl and isoprene rubber stoppers have been available since 1996, a proposal

ROBERT G. HAMILTON, PH.D., D.ABMLI, is Professor of Medicine and Pathology and Director of the Johns Hopkins University Dermatology, Allergy and Clinical Immunology Reference Laboratory, Division of Allergy and Clinical Immunology, Department of Medicine; and ROBERT H. BROWN, M.D., M.P.H., is Professor of Anesthesiology and Critical Care Medicine, School of Medicine, Johns Hopkins University (JHU), Baltimore, MD. MICHAEL A. VELTRI, PHARM.D., is Clinical Specialist; and E. ROBERT FEROLI, PHARM.D., is Director of Regulations and Safety, Department of Pharmacy, Johns Hopkins Hospital, Baltimore. MARIE NOEL PRIMEAU, M.D., is Allergist, Hospital Sainte-Justine, Montreal, Quebec, Canada. JAMES F. SCHAUBLE, M.D., is Professor of Anesthesiology and Critical Care Medicine, School of Medicine, JHU. N. FRANKLIN ADKINSON, JR., M.D., is Professor of Medicine, Division of Allergy and Clinical Immunology, Department of Medicine, School of Medicine, JHU.

Address correspondence to Dr. Hamilton at Johns Hopkins Asthma and Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD 21224 (rhamilt@jhmi.edu).

The following additional members of the Johns Hopkins Latex Task Force are acknowledged for their contributions to this paper: Kathleen M. Hale, B.S., Jay M. Frerotte, M.S., Colleen Cusick, R.N., Carla Gill, M.B.A., and Deborah Dang, R.N.

Supported by internal Johns Hopkins University funds, grant 1-RO1-AI43654 from the National Institutes of Health, and grant S1208 from the Centers for Disease Control and Prevention.

DOI 10.2146/ajhp050021

to totally exclude natural rubber from pharmaceutical vial closures was published in the *Pharmacopeial Forum*.[11]

After receiving responses from a citizen petition and communications from industry, the United States Pharmacopeia and FDA ruled that there was insufficient peer-reviewed literature to show that dry natural rubber vial closures in medication vials contribute to a significant risk for reactions in latex-allergic individuals (Mille YR, CDER, personal communication, 1997 Feb 19). FDA elected not to ban natural rubber latex in combination products such as medication vials.[12] This decision was based on the fact that total protein tests performed on natural rubber vial closures using the Lowry assay, which we now know is not sensitive enough to detect low levels of latex allergen, failed to detect leached protein. Moreover, several available reports of allergic reactions presumed to be due to natural rubber in vial closures[13,14] had been invalidated since they were later shown to involve the use of synthetic butyl rubber rather than natural rubber latex closures.[15,16]

Current hospital practices. Concerned about the safety of latex-allergic patients, health care workers responsible for establishing policy in hospitals began using several nonvalidated practices. Since latex avoidance or separation of the latex-allergic patient from any latex-allergen exposure has been the primary mode of management, health care workers first began trying to identify which medications were stored in vials containing latex. Because information regarding the precise composition of the closure was not always readily accessible, even by the manufacturer, some hospital staff began removing pharmaceutical vial closures before withdrawing the medication. By "popping the top," they avoided puncturing the latex stopper and could draw medications into glass or latex-free plastic syringes for presumably safer administration to the latex-allergic patient. The assumption underlying this action was that the puncturing event introduced rubber into the medication.[17] However, the possibility that latex allergen may have leached from the closure into the medication during shipping or storage was not considered. The practical consequences of this approach involve the technical difficulties of removing some closures and using an open system that increases the potential for microbial contamination.[18]

Other health care facilities stopped the "pop the top" practice because of these problems and adopted an alternative approach called the "one-stick" rule.[19] The rationale behind this practice is that a single stick minimizes the potential distribution of latex allergen into the medication while maintaining a closed system with a decreased potential for contamination. Importantly, it eliminates the need to determine if a vial closure is made of natural rubber before medication administration. This practice, however, does not adequately address the possibility that latex allergen can leach into medications during shipping, storage, and the single puncturing event.

Literature on the issue. No published peer-reviewed reports have clearly demonstrated that a type 1 hypersensitivity reaction can be induced in a latex-allergic individual by administering a medication from a vial containing a latex closure. A prospective, controlled, human challenge study to investigate this issue directly has not been possible because of safety concerns.

Possibly the first study to determine whether latex allergen is released into solutions from a dry natural rubber device was conducted by Melton.[20] In this study, skin puncture tests with saline extracts that had been in contact with natural rubber-containing syringe components for 1–24 hours were performed with 12 latex-allergic and 5 non-latex-allergic subjects. Three latex-allergic and zero nonallergic participants developed definite skin reactions, presumably to extracted latex allergen from natural rubber syringe components. Melton concluded that latex rubber in syringes can elicit a wheal-and-flare reaction by skin puncture test of some but not all latex-allergic subjects. Unfortunately, these data were never published as a full report in a peer-reviewed journal.

In 1996, Jones et al.[21] attempted a similar study, examining bovine collagen preparations stored for up to 45 months with natural rubber plungers in syringes. Of the 39 latex-allergic subjects, 1 had positive skin prick results, compared with none of the 31 nonallergic subjects. The authors suggested that latex allergen was eluted, but in low levels. In a different study, Thomsen and Burke[22] were unable to detect latex allergen using an insensitive inhibition immunoassay in solutions from 16% natural rubber closures in vials whose closures were punctured once.

To clarify this issue, we conducted a masked prospective clinical study in which 12 latex-allergic and 11 nonallergic volunteers underwent skin testing with masked solutions from five vials.[23] Each vial type contained a different closure formulation: A = 100% synthetic bromobutyl, B = 95.3% natural rubber latex (gum/crepe), C = 66% natural rubber latex (crepe), D = 100% synthetic isoprene, and E = 100% synthetic gum/isoprene. The vial closures used in our study were manufactured using standard formulations marketed for parenteral products. These manufacturers produce the majority of vial closures used in the pharmaceutical industry. The investigators and subjects were blinded to the composition of the closures. Sequential puncture and intradermal skin tests were performed with 0.4% phenol–

saline–0.03% human serum albumin solutions that had been stored inverted up to nine months before use. Solutions were obtained from vials with nonpunctured closures (0P) and vials with closures punctured 40 times (40P) using a 21-gauge needle 12–24 hours before testing.

The results of all skin tests (puncture and intradermal) in the non-latex-allergic subjects were negative based on the Norman criteria (<5-mm wheal and <10-mm erythema at 15 minutes).[24] Of the 12 latex-allergic subjects, 2 had clearly positive intradermal skin reactions to solutions in the 0P vials and 5 reacted to 40P solutions from vials that contained natural rubber latex. Two latex-allergic subjects also had inexplicably positive but nonreproducible results from intradermal skin tests to solutions from vial A containing bromobutyl but not vials D and E. The study data indicated that natural rubber closures release allergenic latex proteins into solutions in quantities sufficient to induce positive intradermal skin test results in up to 41% of latex-allergic patients but not in non-latex-allergic individuals. Moreover, the leaching of latex allergen can occur during shipping and storage, when the solution has direct contact with the closure, but an increase in the quantity of latex allergen results from puncturing.

Several potential limitations of this study should be considered when interpreting these data. First, the latex-allergic subjects recruited to this study had a range of sensitivities to natural rubber latex allergens as defined by varying levels of latex-specific IgE antibody in their blood. Serum IgE antibody levels were only roughly correlated with the magnitude of skin reactivity and clinical sensitivity. Moreover, there is extensive heterogeneity of the allergenic proteins and IgE antibody specificity to latex allergens among latex-allergic subjects.[25-28] This may explain why several individuals with latex-specific serum IgE antibody failed to display positive skin reactions to 0P and 40P solutions from vials containing latex closures.

Second, of the 18 latex-allergic subjects, 6 had a higher-than-expected rate of reactivity to the saline negative control and were subsequently excluded from further evaluation. The reasons for this reactivity remain unclear.

Third, while the study demonstrated the presence of latex allergen in solutions using the sensitive intradermal skin test, we have not directly shown that this level of allergen is sufficient to induce life-threatening anaphylaxis. For safety reasons, our study was confined by our institutional review board to skin testing. Schwartz and Zurowski[29] have suggested that small amounts of latex allergen administered intravenously probably induced an allergic reaction involving generalized flushing and itching, cough, and wheezing in their latex-allergic patient. We conservatively speculate that systemic administration of even lower levels of allergen from natural rubber vial stoppers could induce generalized allergic reactions in some latex-allergic individuals.

Fourth, the 40-puncture condition was used to simulate the worst-case use condition for multidose vials. Since most pharmaceutical vials are punctured once (several times, at most), the transfer of allergen from a natural rubber closure, presumably resulting from rubber cores or shavings produced by the needle, should be minimal.

Finally, 0.4% phenol is a standard ingredient in skin testing diluents, such as the elution buffer used in our study. Since phenol is not routinely present in many medications administered to patients, it is possible that its presence facilitated the extraction of latex allergen from natural rubber closures. Phosphate-buffered saline extracts prepared at the end of the study with the same study vial closures that were cut once contained extractable latex allergen as measured by immunoassay inhibition analysis. Thus, while the role of phenol in allergen extraction is unclear, aqueous solutions alone can effectively extract allergenic latex protein in the absence of phenol. The role of medication pH, excipients (e.g., preservatives, solubilizers, buffers), and vehicles in the elution of allergenic protein from natural rubber closures is unknown.

Risk in perspective. Based on the available literature, we do not know whether the amount of allergen released during shipping and storage into medications from vials with rubber closures is sufficient to induce a systemic allergic reaction. Some risk for an allergic reaction, however, may be present when vial closures contain natural rubber latex. Since medications are administered orally, intramuscularly, subcutaneously, and intravenously, the route of exposure will affect the rate and extent to which latex allergen is absorbed following drug administration. Oral and sublingual administration of gram quantities of latex C-serum protein can be effectively tolerated by latex-allergic adults undergoing desentization.[30,31] However, intramuscular administration of up to 100 µg of allergenic latex protein into sensitized individuals during immunotherapy can provoke severe systemic reactions in minutes to several hours in latex-allergic individuals.[32] The levels of allergen released by rubber closures (estimated by radioallergosorbent inhibition analysis) are much lower than those used in immunotherapy. Finally, variables related to the allergenic protein (molecular weight and isoelectric point heterogeneity), the patient's immune response (specificity, quantity, cellular versus humoral), and idiosyncratic factors (general health, genetic predisposition for atopy, releasability of mast cells and basophils) can influence the overall risk of an allergic reaction.

Identifying patients at risk for latex allergy. Special precautions should be taken when a patient is identified as (1) having a high risk for developing latex allergy or (2) latex allergic.[18,33] Individuals at high risk for latex allergy include children with spina bifida, patients who have had several surgeries, and atopic individuals. Patients who have a history of latex allergy and at least one positive diagnostic confirmatory test at the time of admission are considered latex allergic. The health care facility must have an effective triage program to identify these patients before the administration of any medications. Such a triage program should include the collection of a history using a validated questionnaire that includes questions about general allergies, allergic reactions to natural rubber products (balloons, condoms, gloves), and risk factors (hand dermatitis, history of multiple surgeries, chronic use of natural rubber latex gloves, atopy, food allergies).[34] Since there is currently no diagnostic skin-testing material licensed by FDA, a blood test conducted in a laboratory certified by the Clinical Laboratory Improvement Amendments of 1988 program using an FDA-approved assay for latex-specific IgE antibody should be considered part of the work-up to confirm a latex sensitivity.[18,35,36]

Practical approaches for pharmacy and nursing staff. Most health care facilities are aware of the general concern about the presence of latex allergen in powdered latex medical gloves and the need to limit their use to minimize patient and employee exposure.[33] However, for patients who need medications, the presence of natural rubber in the closure of pharmaceutical vials has been recognized as a practical concern for the pharmacist and other health care providers. As of 1997, it was estimated that around 20% of pharmaceutical vials manufactured contained some natural rubber (Smith E, personal communication). Many of these closures contain a mix of synthetic butyl or isoprene and 16–95% natural rubber (*H. brasiliensis*). The ultimate solution to this problem is for pharmaceutical manufacturers to eliminate natural rubber from any vial closures used in newly manufactured products. Labeling such as "contains dry natural rubber" should then be applied to existing medications. Pharmacists could also help in the effort by identifying alternative sources of medications containing synthetic closures.

Such a change to an existing pharmaceutical's packaging requires review by FDA and could be expedited if the review was fast-tracked by FDA, since changes would be limited to the packaging. Rubber vial closures, as well as intravascular equipment with latex injection ports and syringes, are medical products that should be covered by "contains dry natural rubber" labeling.[10] Proposed changes in the labeling of vial closures, syringes, and other dry natural rubber components used with drug products are routinely reviewed by CDER.[37] We believe that CDER should adopt uniform natural rubber labeling requirements for drug packaging that are analogous to those instituted by the Center for Devices and Radiological Health for medical gloves containing natural rubber latex. Presently, pharmacists must contact the pharmaceutical company directly or perform a visual inspection to determine the composition of vial closures. Both approaches have led to inaccurate identifications and lost productivity.

There are two other ways for pharmacists to protect latex-allergic patients from unnecessary and potentially risky latex-allergen exposure. The first is a catalog–avoidance approach, which requires that the pharmacy staff review the entire drug inventory and identify and catalog the medications packaged in vials containing a natural rubber latex closure. Since drug manufacturers cannot always provide timely information about the formulation of the vial closures used in the packaging of their medications, this approach can be unreliable. Moreover, hospitals that use drugs from multiple sources will require additional time to update their latex product listing when suppliers change. The primary disadvantages of the catalog–avoidance approach are the time required to prepare and maintain the listing of pharmaceuticals with latex-free closures and the potential for incomplete or inaccurate information. The advantage to the nursing staff is the minimal need to monitor latex-allergic patients during medication injections or infusions.

Many pharmacists will consider the catalog–avoidance approach to be unreliable. It is reasonable to assume that no more than 20% of all the medications administered are in vials containing a natural rubber latex closure, and only a subset of the latex-allergic subjects will be sufficiently sensitized to have a systemic reaction. Thus, some pharmacists believe it better to establish a universal policy for dispensing all parenteral medications, regardless of their packaging components. They have adopted the single-stick rule–observation approach in which (1) all vials of medications, regardless of the vial closure formulation, are punctured once, (2) the medication is drawn into a nonlatex syringe, and (3) the patient is observed after medication administration. While the single-stick rule–observation approach is advantageous to the pharmacy staff, it can require a significant time investment from the nursing staff, since nurses may need to monitor the latex-allergic patient for 30 minutes up to two hours after each medication is administered. This practice has been successfully implemented at the Johns Hopkins Hospital in Baltimore, Maryland, for more than five years with no apparent problems.[19]

Finally, for purposes of enacting appropriate procedures in medication compounding, dispensing, and administration, both approaches require a rigorous system of documentation to alert the pharmacy and nursing staff of the need for latex precautions. Moreover, only synthetic gloves should be used in the pharmacy at all times, and the pharmacy staff should participate in the hospital's latex-allergy committee.[33]

Recommendations. The following are a number of practical recommendations based on the single-stick rule–observation approach. They have been divided into actions required by hospital staff in admissions, the pharmacy, and nursing services.

Admissions. Identify all at-risk patients in which latex precautions should be practiced. This identification process occurs at the time of admission by means of a series of questions that are used to classify a patient as (1) latex allergic or (2) at risk for latex allergy. Latex-allergic patients have a clear history of latex allergy and at least one positive confirmatory diagnostic skin or blood test.[33-35] Patients at risk for latex allergy have definable risk factors and if exposed may eventually develop latex allergy. Major risk factors include more than seven actual or anticipated surgeries; allergies to avocados, bananas, or kiwis; dermatitis from rubber products; suggestive personal history; and selected patient types (e.g., spina bifida, latex-glove users with strong atopic backgrounds). Both groups of patients will be universally treated with latex precautions.

Pharmacy. The pharmacy staff should follow universal one-stick-rule precautions, which assume that every pharmaceutical vial may contain a natural rubber latex closure. This process obviates the need to develop and maintain a compendium of pharmaceuticals in inventory that contain natural rubber latex closures. All pharmaceutical vials and i.v. fluid bags or bottles will be punctured only once, and unused medications should be discarded. Alternatively, a minispike dispensing pin can be inserted into the vial closure and used to remove multiple medication doses without the need for subsequent punctures. Patient medication labels must clearly indicate "latex precautions" to alert the nursing staff who are administering the medication to the need for subsequent observation.

Nursing staff. The nursing staff should remain with any patient who is receiving medications bearing "latex precautions" labels immediately after administration of each dose or at the start of each i.v. infusion to observe for possible immediate systemic reactions (generalized hives, urticaria, bronchospasm, hypotension). Subsequently, the nurse should record the patient's vital signs and then monitor the patient for the period of time deemed appropriate by the institution. One approach is to observe the patient at 30-minute intervals for two hours and document the vital signs in the patient's chart at each observation period.

Program reevaluation at yearly intervals. The hospital policy on medication administration to patients who are at risk of or have latex allergy should be reviewed yearly.[33] If federal regulations were to require the labeling of all pharmaceutical vials that contain natural rubber latex closures, the pharmacy could easily establish a catalog of medications with natural rubber latex closures. This would permit the use of the catalog–avoidance approach. Moreover, if the use of natural rubber latex in pharmaceutical packaging is eventually banned, the need for a specific procedure to safeguard these patients will become unnecessary.

References

1. FDA medical alert: allergic reactions to latex-containing medical devices. Rockville, MD: Food and Drug Administration, 1991. FDA document no. MDA 91-1.
2. Turjanmaa K, Mäkinen-Kilijunen S, Reunala T et al. Natural rubber latex allergy: the European experience. *Immunol Allergy Clin North Am*. 1995; 15:71-8.
3. Liss GM, Sussman GL. Latex sensitization: occupational versus general population prevalence rates. *Am J Ind Med.* 1999; 35:196-200.
4. Bernardini R, Novembre E, Ingargiola A et al. Prevalence and risk factors of latex sensitization in an unselected pediatric population. *J Allergy Clin Immunol.* 1998; 101:621-5.
5. Kaczmarek R, Hamilton RG, Gross TP et al. Prevalence of latex-specific IgE antibodies in hospital personnel. *Ann Allergy Asthma Immunol*. 1996; 76:51-6.
6. Lagier F, Vervloet D, Lhermet I et al. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol.* 1992; 90:319-22.
7. Kelly KJ, Kurup V, Zacharisen M et al. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol.* 1993; 91:1140-5.
8. Hamilton RG. Natural rubber latex allergy: primer for the pharmacist. In: Swarbick J, Boylan J, eds. Encyclopedia of pharmaceutical technology. Vol. 19. Arlington, TX: Marcel Dekker; 1999:279-87.
9. Yunginger JW, Jones AT, Fransway AT et al. Extractable latex allergens and proteins in disposable medical gloves and other rubber products. *J Allergy Clin Immunol*. 1994; 93:836-42.
10. Natural rubber-containing medical devices; user labeling—FDA. Final rule. *Fed Regist.* 1997; 62:51021-30.
11. Proposal to prohibit the use of natural rubber latex for use in elastomeric closures for injection. *Pharmacopeial Forum.* 1996; 22:2886-7.
12. Natural rubber-containing medical devices; user labeling—FDA. Final rule; interpretation. *Fed Regist.* 1998; 63:24934-5.
13. Towse A, O'Brien M, Twarog FJ et al. Local reaction secondary to insulin injection. A potential role for latex antigens in insulin vials and syringes. *Diabetes Care.* 1995; 18:1195-7.
14. Vassallo SA, Thurston TA, Kim SH et al. Allergic reaction to latex from stopper of a medication vial. *Anesth Analg.* 1995; 80:1057-8.
15. Smith CC. Risk of latex allergy from medication vial closures. *Ann Pharmacother.* 1999; 33:373-4.
16. Shojaei AR, Haas DA. Local anesthetic cartridges and latex allergy: a literature review. *J Can Dent Assoc.* 2002; 68:622-6.
17. Asakura T, Seino H, Nozaki S et al. Occurrence of coring in insulin vials and possibility of rubber piece contamination by self injection. *Yakugaku Zasshi.* 2001; 121:459-63.
18. Association of Perioperative Registered Nurses. AORN latex guideline. *AORN J.* 2004; 79:653-72.
19. New one stick rule at Johns Hopkins Hospital. *Latex Allergy News*. 1999; 6(8):1.

20. Melton AL. Allergenicity of latex syringe components. In: Proceedings of the International Latex Conference: sensitivity to latex in medical devices. Rockville, MD: Food and Drug Administration; 1992:26.
21. Jones JM, Sussman GL, Beezhold DH. Latex allergen levels in injectable collagen stored in syringes with rubber plungers. *Urology.* 1996; 47:898-902.
22. Thomsen DJ, Burke TG. Lack of latex contamination of solutions withdrawn from vials with natural rubber stoppers. *Am J Health-Syst Pharm.* 2000; 57:44-7.
23. Primeau MN, Adkinson NF Jr, Hamilton RG. Natural rubber pharmaceutical vial closures release latex allergens that produce skin reactions. *J Allergy Clin Immunol.* 2001; 107:958-62.
24. Norman PS, Peebles RS. In vivo diagnostic allergy testing methods. In: Rose NR, Macario EC, Folds JD et al., eds. Manual of clinical laboratory immunology. 5th ed. Washington, DC: American Society for Microbiology Press; 1997:875-80.
25. Yip L, Hickey V, Wagner B et al. Skin prick test reactivity to recombinant latex allergens. *Int Arch Allergy Immunol.* 2000; 121:292-9.
26. Bernstein DI, Biagini RE, Karnani R et al. In vivo sensitization to purified *Hevea brasiliensis* proteins in health care workers sensitized to natural rubber latex. *J Allergy Clin Immunol.* 2003; 111:610-6.
27. Hamilton RG, Arija Mad Arif S, Yusof F et al. Heterogeneity of human IgE antibody responses to purified natural rubber latex (*Hevea brasiliensis*) allergens. *J Allergy Clin Immunol.* 2001; 107:S320. Abstract.
28. Wagner S, Breiteneder H. *Hevea brasiliensis* latex allergens. Current panel and clinical relevance. *Int Arch Allergy Immunol.* 2005; 136:90-7.
29. Schwartz HA, Zurowski D. Anaphylaxis to latex in intravenous fluids. *J Allergy Clin Immunol.* 1993; 92:358-9.
30. Toci G, Shah S, Al-Faqih A et al. Oral latex desensitization of healthcare workers. *J Allergy Clin Immunol.* 1998; 101: S161. Abstract.
31. Patriarca G, Nucera E, Pollastrini E et al. Sublingual desensitization: a new approach to the latex allergy problem. *Anesth Analg.* 2002; 95:956-60.
32. Leynadier F, Herman D, Vervloet D et al. Specific immunotherapy with a standardized latex extract versus placebo in allergic healthcare workers. *J Allergy Clin Immunol.* 2000; 106:585-90.
33. Brown RH, Hamilton RG, McAllister MA et al. How health care organizations can establish and conduct a program for a latex safe environment. *Jt Comm J Qual Saf.* 2003; 29:113-23.
34. Brown RH, Hamilton RG, Mintz M et al. Genetic predisposition to latex allergy: role of interleukin 13 and interleukin 18. *Anesthesiology.* 2005; 102:496-502.
35. Hamilton RG, Biagini RE, Krieg EF. Diagnostic performance of Food and Drug Administration-cleared serologic assays for natural rubber latex-specific IgE antibody. *J Allergy Clin Immunol.* 1999; 103:925-30.
36. Hamilton RG, Peterson E, Ownby DR. Clinical and laboratory-based methods in the diagnosis of natural rubber latex allergy. *J Allergy Clin Immunol.* 2002; 110(suppl 2):S47-56.
37. Mille RY, Center for Drug Evaluation and Research. (Letter to Marlowe D, Center for Devices and Radiological Health.) 1997 Feb 6.

Pharmacists, pharmaceutical manufacturers, and conflicts of interest

DAVID BANKS

Am J Health-Syst Pharm. 2005; 62:1827-32

Conflicts of interest (COIs) represent an expanding challenge for pharmacists as their therapeutic influence grows. Many potential COI relationships involve pharmaceutical manufacturers, who have characterized pharmacists as "a growing force to be reckoned with."[1] The expanded influence of pharmacists may increase their likelihood of being targeted for offers to become involved in ethically questionable relationships, particularly COI arrangements that may pose a threat to their relationships with patients.

COIs. The theoretical construct underlying COIs is based first on the concept of discretionary action involving professional judgment.[2] This discretionary action of a professional is widely expected to reflect fidelity. Professional fidelity involves adherence to principles of "respect for autonomy, justice, and utility, [reflected by] the obligation to act in good faith to keep vows and promises, fulfill agreements, maintain relationships, and discharge fiduciary responsibilities."[3]

A COI is defined as "a situation in which a person, such as a public official, an employee, or a professional, has a private or personal interest sufficient to appear to influence the objective exercise of his or her official duties."[4] Such situations involve a private interest (i.e., an interest based on a relationship with another person or organization) or a personal interest (self-interest) that is in conflict with an official duty and that interferes with professional responsibilities by diminishing professional judgment.

According to Latham,[5]

> A person has a conflict of interest when, in the presence of some duty to pursue the interests of another, she is motivated by self-interest to do something inconsistent with that duty. Thus a physician has a conflict

CAPT DAVID BANKS, B.S.PHARM., PH.D., Office of Special Health Issues, Food and Drug Administration, Rockville, MD 20857.

The views presented here are those of the author and do not necessarily represent the policy of the Food and Drug Administration or the U.S. Public Health Service.

DOI 10.2146/ajhp040504