Additives and Ingredients Subcommittee of the Food Advisory Committee Center for Food Safety and Applied Nutrition Food and Drug Administration

Food-Mediated Latex Allergy

Executive Summary

August 26-27, 2003
The St. Regis Hotel
Washington, DC

On August 26th and 27th CFSAN convened a meeting of the Additives and Ingredients Subcommittee of its Food Advisory Committee to assist in gathering information, and to get independent expert consideration of questions that CFSAN has raised regarding natural rubber latex (NRL) allergy as it relates to food safety. In accordance with Title 21 CFR 177.2600 *Rubber articles intended for repeated use*, natural rubber is an approved indirect food additive when used as a component of a repeat-use, food-contact article such as a food-service glove. Nevertheless, FDA has received reports of latex allergic individuals experiencing allergic reactions to foods believed to have been prepared by workers wearing NRL food-service gloves. FDA has been gathering and analyzing information from a variety of sources relating to the incidence of food-mediated latex allergic reactions and presented that information to the Additives and Ingredients Subcommittee.

During the two day meeting, the Subcommittee heard from a variety of sources, including experts from Center for Devices and Radiologic Health and Center for Biologics Evaluation and Research, as well as experts from outside of FDA. The Subcommittee reached a consensus that a potential hazard may exist, but concluded that the science establishing a risk from the use of NRL food-service gloves is very weak. The committee recommended that FDA consider establishing specifications for food service gloves (for example, residual protein and/or donning powder levels) to address the potential hazard, and that well-designed clinical studies would be helpful to better understand the levels of exposure that would be required to elicit a systemic response in a latex allergic individual.

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Summary Minutes

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Johanna Dwyer, D.Sc., R.D.	Tufts New England Medical Center and Tufts University	*Chair*
Richard Bonnette	Center for Food Safety and Applied Nutrition	*Executive Secretary*

Subcommittee Members

Jeffrey Blumberg, Ph.D.	Tufts University	
J. Antonio Torres, Ph.D.	Oregon State University	
Rachel Johnson, Ph.D.	University of Vermont	
Lawrence Fischer, Ph.D.	Michigan State University	
Brandon Scholz	Wisconsin Grocers Association	*Industry Representative*
Goulda Downer, Ph.D.	Metroplex Health and Nutrition Services	*Consumer Representative*
Anthony Gaspari, M.D.	University of Maryland School of Medicine	*Temporary voting member*
Steve Taylor, Ph.D.	University of Nebraska	*Temporary voting member*
Robert Hamilton, Ph.D.	Johns Hopkins University School of Medicine	*Temporary voting member*

FDA Speakers

Alan Rulis, Ph.D.	Center for Food Safety and Applied Nutrition (CFSAN)
Laura Tarantino, Ph.D.	Center for Food Safety and Applied Nutrition
George Pauli, Ph.D.	Center for Food Safety and Applied Nutrition
Mark Hepp, Ph.D.	Center for Food Safety and Applied Nutrition
Anna Shanklin, Ph.D.	Center for Food Safety and Applied Nutrition
Jay E. Slater, M.D.	Center for Biologics Evaluation and Research
Melvin E. Stratmeyer, Ph.D.	Center for Devices and Radiologic Health (CDRH)
Vesna Tomazic-Jezic, Ph.D.	Center for Devices and Radiologic Health

Guest Speakers

Don Beezhold, Ph.D.	National Institute for Occupational Safety and Health
Lise Borel, DMD	Consumer Advocate
John Schulz	Marriott Corporation
Charles Reed, M.D.	Emeritus Professor of Medicine, Mayo Clinic, for the Glove Industry
Don Herrington	Arizona Department of Environmental Health (by telephone)
Michael Heumann	Oregon Department of Human Services
Marie Stoeckel	Rhode Island Department of Human Services (by telephone)

Public Comment

Christine Andrews	American Restaurant Association
Karen Jakpur	Consumer, (comments read by Lise Borel, D.M.D.)
Doris Rittenmeyer	Food Handler, Inc.
Rochelle Spiker	Potomac Latex Allergy Association
Wava Truscott	Kimberly Clark
Esah Yip	Malaysian Rubber Export Promotion Council

The Additives and Ingredients Subcommittee of FDA's Food Advisory Committee met on August 26, and 27, 2003, at the St. Regis Hotel in Washington, D.C. to discuss the available scientific data relating to reported food-mediated latex allergic reactions. Dr. Johanna Dwyer, Chair, called the meeting to order and welcomed the subcommittee members. Dr. Dwyer also reviewed the charge and questions provided to the committee by FDA. The Executive Secretary read the conflict of interest statement into the record, and announced the appointment of three temporary voting members, Dr. Anthony Gaspari, Dr. Robert Hamilton, and Dr. Steve Taylor.

Invited Presentations

Dr. Alan Rulis of the FDA's Office of Food Additive Safety (OFAS) thanked the committee for their participation and stressed the importance of advisory committees in assisting FDA to make objective, balanced, and scientifically sound decisions.

Dr. George Pauli described for the Committee the organization and responsibilities of the Office of Food Additive Safety. Dr. Pauli also described the authority, granted to FDA by the Federal Food, Drug and Cosmetic Act to ensure the safety of food. Finally, the standard of review and the safety standard established by the FFDCA, that FDA employs in its decision making process were described.

Dr. Laura Tarantino, Acting Director of the Office of Food Additive Safety, reviewed the charge and questions posed to the subcommittee, and stressed that FDA is looking for advice relating to the strength of the evidence and whether it establishes a link between the use of the gloves and food-mediated latex allergic reactions. Dr. Tarantino indicated that any regulatory action FDA might take will have to rely on that scientific evidence which must be documented and must withstand scientific challenge.

Dr. Jay Slater defined latex allergy as a specific clinical syndrome and differentiated it from other reactions like delayed-type hypersensitivity and contact dermatitis. Dr. Slater also described the history of latex allergy, the production of latex gloves, and the role of donning powder as a vehicle for the dissemination of latex proteins. Finally, Dr. Slater discussed the importance of a proper diagnosis, and how that relates to data regarding the prevalence of latex allergy. He stated that in his opinion, avoidance remains the best treatment, but that because latex has some important benefits, focus should be on creating latex safe environments rather than latex free environments. Dr. Slater's comments focused on the latex allergy experience in the clinical healthcare setting.

Dr. Melvin Stratmeyer described the process by which FDA ensures the safety and effectiveness of natural rubber-containing medical devices. He stated that the adverse event monitoring system was the first indication that there may be an allergy problem with the use of surgeon's and patient examination gloves. Dr. Stratmeyer further stated that research in his laboratory, in collaboration with other clinical labs, has served as a basis for risk assessment, methods development, and regulatory actions. CDRH actions including the publication of a Medical Alert (1991), a protein content guidance document (1995), a natural rubber labeling regulation (1997), and a proposal to reclassify medical gloves from Class I to Class II medical devices were discussed.

Dr. Anna Shanklin described in detail the provisions of the Federal Food, Drug and Cosmetic Act (FFDCA) that provide FDA's authority for regulating food additives. Dr. Shanklin further described the scope and limitations of the food additive provisions of the law, and clarified the meaning of the FFDCA's standard of review and its standard of safety. Dr. Shanklin explained that food additive regulations are issued based solely on safety data relating to the additive itself, that food additive provisions do not provide a mechanism for FDA to consider risks versus benefits relative to other options.

Dr. Mark Hepp discussed additional regulatory and scientific background regarding latex allergy. Dr. Hepp further discussed the increasing use of latex gloves in the food service industry as a result of the Food Code recommendations for limited bare hands contact with ready-to-eat foods. He also reviewed all of the scientific data of which the Agency was aware relating latex allergy directly to food safety. This information consisted of three research papers, (one that quantified protein transfer from gloves to food, an oral desensitization study, and one oral challenge study), and five case reports of individuals that experienced an allergic reaction to food believed to be contaminated with latex allergen. Dr. Karl Klontz, (CFSAN) answered several questions regarding adverse event reports he received through a latex allergy support group website.

Dr. Vesna Tomazic-Jezic presented data on the trends in latex medical glove use, as well as trends on medical glove protein and powder levels, and described how these trends have impacted the incidence of latex allergy. Recent decreases in glove powder and protein levels in medical gloves have led to an important decrease in the incidence of latex allergy. Dr. Tomazic-Jezic stated that standards for latex gloves, developed or currently under development, would be beneficial in continuing to reduce exposure to latex allergens. Dr. Tomazic-Jezic also noted that such standards could not be developed before validated methodology for determining powder and protein levels became available.

Dr. Donald Beezhold described research he conducted prior to joining National Institute of Occupational Safety and Health that was designed to test whether latex proteins could be transferred from gloves to food by contact. Dr. Beezhold described his work and addressed certain criticisms of that work for the subcommittee. Dr. Beezhold concluded that latex proteins could be transferred to food, in amounts that could be quantified, from gloves that were high in protein levels. Dr. Beezhold presented data that showed there was no detectable transfer to the food in the small number of low protein powder-free gloves tested. He also stated that although donning powder and protein levels in medical gloves have decreased dramatically in recent years, consumer and food service gloves which are not required to meet medical device standards may or may not have low protein levels.

Mr. Michael Heumann, from the Oregon Department of Human Services, described the State of Oregon's work to ban latex gloves in food service. Mr. Heumann described the basis for the action as a combination of occupational exposure incidents documented through worker's compensation claims, including contact dermititus and delayed type reactions, and some reports of consumers experiencing reactions they believed to be due to latex in their food.

Following this presentation, the chair adjourned the meeting at 5:15 pm.

Wednesday, August 27, 2003

The chair called the meeting to order at 8:00 am.

Dr. Lise Borel described everyday challenges faced by those with latex allergy and illustrated them with individual examples and accounts. Dr. Borel also stated that only about 30-35% of those who are latex

allergic have cross-reacting food allergies; therefore cross reactions with food do not represent the bulk of reactions associated with latex allergy. Further, Dr. Borel stated that although avoidance is the best treatment, certain rubber articles need to be avoided more rigorously than others because of differences in availability of protein. She recommends avoiding gloves and balloons most rigorously. She also related concerns about the adverse event reporting systems used by FDA, especially the program used by CFSAN.

Dr. Charles Reed stated that latex allergy came to the attention of the Mayo clinic in the 1980's. He also stated that the clinic identified and purchased only low protein gloves, and patients returned to work with out incident. By 1998, the clinic began seeing patients who were affected by an unrealistic fear of a latex allergic reaction. He said that this was due in part to the imprecise use of the terms like "anaphylaxis" and "sensitization"and concluded that the significance of mild allergic reactions is therefore overstated. Dr. Reed differentiated local reactions from systemic reactions and stated that there exists no proof that tiny exposures to latex allergen can cause systemic reactions. Because biologic responses to allergen are known to follow a classic s-shaped dose response curve, trivial exposures will result in trivial responses. He compared the exposures expected to result from the use of latex food service gloves to the much higher exposures determined to be threshold doses of allergen that cause severe allergies to foods like peanuts.

Mr. John Shulz described Marriott Corporation's worldwide experiences with latex gloves at Marriott and their associated food service brands. Mr. Shulz stated that Marriott has been using latex food service gloves for 13 years as a deterrent to hand transmitted pathogenic organisms. Marriott has been requiring examination quality, powder-free latex gloves be used when food service workers are handling ready-to-eat foods because of the low protein content. Mr. Schluz also stated that Marriott is aware of only one complaint of a minor allergic reaction to food in the past ten years. Marriott could not confirm that the reaction was due to latex allergen in the food.

Ms. Marie Stoeckel described the State of Rhode Island's rationale for banning latex gloves in food service establishments in Rhode Island.. Ms. Stoeckel noted that occupational exposure and worker's compensation claims were a major factor in the ban, not food safety.

Mr. Don Herrington explained his state's ban on latex gloves in food service as a response anecdotal reports and an article in the medical literature where latex gloves were implicated in allergic reactions to foods. Mr. Herrington reported the ban was introduced in the State's food code regulations.

Public Comment

Ms. Doris Rittenmeyer, of Food Handler, Inc. voiced support for voluntary standards in improving gloves and reducing allergenic potential.

Dr. Wava Truscott, of Kimberly-Clark, described the manufacturing process for latex gloves and explained how this can result in gloves of differing quality.

Ms. Rochelle Spiker, of the Potomac Latex Allergy Association, related the experiences of individuals around the country she has spoken with that believe they have experienced latex allergic reactions from food exposures.

Dr. Karen Jacpor, a latex allergic physician, described her personal experience with latex allergic reactions she believes were caused by food exposures. (Letter read by Dr. Lise Borel)

Ms. Christine Andrews, of the American Restaurant Association, voiced her organization's opposition to a proposal to ban the use of latex gloves in food service establishments.

Dr. Esah Yip, of the Malaysian Rubber Export Promotion Council, described the efforts of Malaysian glove manufacturers to reduce glove protein content and questioned the efficacy and safety of alternative glove materials.

Review of Charge and Questions, Discussion, and Responses to Questions

The chair read the charge and questions to the committee and each member voiced an opinion in response to each question. No formal vote was taken but, the committee members were in general agreement in their responses to the questions.

Question 1.

Has a positive relationship been established between the use of natural rubber latex gloves in food service and allergenic reactions to food served in food establishments, or sold at the market, based on the available data? If it exists, what is the strength of that relationship, and has it been shown to be causative?

The committee agreed that scientific evidence demonstrates that NRL allergens can be transferred to food from natural rubber latex gloves. However, the evidence is very weak regarding whether those allergens are transferred to food in amounts sufficient to elicit systemic allergic reactions in variably sensitive individuals. In addition, the absence of any good information about the dose required to elicit an allergic reaction in a sensitized person makes it difficult to extrapolate whether such a transfer would have any clinical significance. Therefore, the evidence is suggestive of a weak positive relationship between the use of natural rubber latex gloves and food-mediated latex allergic reactions. The data linking the presence of these proteins in foods to allergic reactions is based primarily on anecdotal evidence, and is very weak.

Question 2.

If a positive relationship has been established and shown to be causative, can the Advisory Committee suggest science-based options to mitigate food-mediated latex allergy risk?

The committee felt the evidence was sufficiently weak to preclude recommending a ban on latex gloves. However, the committee agreed that there exists evidence demonstrating that the cornstarch donning powder serves as the vehicle for the transmission of allergenic proteins, and that elimination of the powder could eliminate most of the possible exposure to the allergen. The committee suggested the adoption of a food service glove standard that specified glove powder and/or protein limits on food service gloves, but acknowledged that the data to properly establish such limits may not exist. The committee agreed that these suggestions should apply to all producers of food and not be limited to retail food and food service establishments. The committee also suggested that FDA employ a public education project to heighten public awareness.

Question 3.

If current evidence isn't sufficient to establish a relationship, what additional questions need to be addressed to adequately understand this issue?

The committee agreed that a well designed, double-blind, placebo-controlled low-dose oral challenge study would be necessary to determine the threshold doses for such a reaction, and to better understand what percentage of the latex-allergic population is at risk of a reaction to food contaminated with low

levels of latex allergen. In addition, experiments designed to determine the amount of allergen to which a consumer may be exposed as a result of consuming food prepared by a worker wearing latex gloves are needed, as well as studies on the fate of the antigenic proteins in the gastrointestinal tract. The committee agreed that the FDA should more rigorously follow up the case reports and adverse event reports but, acknowledged that even if followed up, the adverse event reports would not address the deficiencies in data. The committee also suggested more thorough epidemiological studies among high-risk individuals to better document the frequency of the reactions and the variables that are common to such events.

I certify I attended the August 26-27, 2003, meeting of the Additives and Ingredients Subcommittee of the Food Advisory Committee, and these summary minutes accurately reflect what transpired.

11-17-03

Richard Bonnette Date
Executive Secretary

Nov 10, 2003

Johanna Dwyer, D.Sc., R.D. Date
Chair