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**SUMMARY MINUTES**

**OF THE**

**32<sup>nd</sup> MEETING OF THE**

**GENERAL HOSPITAL & PERSONAL USE DEVICES PANEL**

September 15, 1997

**OPEN SESSION**

**Holiday Inn**  
**Gaithersburg, MD**

**General Hospital & Personal Use Devices Panel Meeting**

**September 15, 1997**

**Attendees**

Jacqueline Simmons, M.D.  
Chairperson

Martha T. O'Lone, LCDR  
Executive Secretary

Voting Members

Charles Edmiston, M.D.

Joseph R. Fowler, M.D. (deputized)

Elaine Hylek, M.D.

Marcia Ryder, M.S.N

Frederick Whitehouse, M.D. (Deputized)

Consumer Representative

Christine Chandler, M.S.N, R.N., C.S., A.N.P.

Industry Representative

Otis J. Bouwsma, Ph.D., D.M.D.

FDA Representatives

Chiu Lin, Ph.D.

Vesna Tomazic-Jezic, M.D.

Ronald Kaczmarek, M.D.

## CALL TO ORDER

Executive Secretary Martha O'Lone opened the meeting and read the conflict of interest statement. The following panelists were granted waivers because of affiliation or employment with certain firms: Jacqueline Simmons, M.D.; Charles Edmiston, Ph.D.; Elaine Hylek, M.D.; Frederick Whitehouse, M.D.; Joseph R. Fowler, M.D.; Christine Chandler, M.S.N., R.N., C.S., A.N.P.; and Marcia Ryder, M.S.N. Introductions followed.

## OPEN PUBLIC MEETING

Chief of the Infection Control Devices Branch, Chiu Lin, Ph.D., asked the panel to advise FDA on its proposed guidance document for "Testing for Skin Sensitization to Chemicals in Latex Products." He said that latex allergy is a growing public health issue, and FDA wants to ensure that its guidance is as scientifically based as possible. The document will provide recommendations to industry on how to test and generate the appropriate data, he said.

Roberta Carlin, Associate Executive Director of Spina Bifida Association of America, stressed the need for educating people about Type I latex allergies, latex use in the home, and latex use in the medical field. Ms. Carlin described exposure risks and a list of latex products and substitutes. She added that sensitive persons should obtain practitioners' information on what to do when experiencing a reaction and should always wear a medical alert device. According to Ms. Carlin, it is possible to live a latex-safe, but not latex-free life. Following examples of how hospitals and dental offices offer latex-safe environments, Ms. Carlin

concluded her presentation with a video.

A dentist, Lee R. Shapiro, related experiences that led him to sell his 20-year-practice because of his type IV allergy to latex. His disability claim is under review. He noted that for him, vinyl gloves are not a safe alternative and do not fit well; cotton liners make the problems worse. He is concerned that although the Type IV allergy is primarily a quality-of-life issue, it could overlap into Type I allergy, which can be life threatening.

## **FDA PRESENTATIONS**

Dr. Lin described the regulatory background and claims issues pertaining to latex sensitivity in medical devices. The first death reports appeared in 1990, and the problems faced by healthcare workers who used gloves were highlighted in May 1990. According to Dr. Lin, in December 1991, OSHA promulgated regulations governing blood-borne pathogens. Workers' reactions have since been exacerbated. Of the three types of reactions to latex (irritation, and Type IV and Type IV allergies), FDA is currently addressing the Type IV allergy. Dr. Lin characterized it as a delayed-type hypersensitivity, caused by residual manufacturing chemicals. He said it is a serious public health problem that causes allergic contact dermatitis. Furthermore, some people do not know they are allergic to latex, the allergy may be induced by residual processing chemicals or latex proteins, and manufacturers who do not use state-of-the-art equipment leave high concentrations of residue on the gloves, he said.

Dr. Lin outlined FDA's activities from 1991 until its proposed rule issued in 1996. FDA

proposed (1) requiring a labeling statement such as "rubber latex products may cause allergies," (2) prohibiting "hypoallergenic" claims on latex product labels, and (3) requiring manufacturers to supply test data to support a claim of "negative results" from the modified Draize test (MDT) conducted on 200 volunteers selected from the general public. Dr. Lin concluded that to encourage manufacturers to make low-protein devices, FDA must issue a guidance document "Testing for Skin Sensitization to Chemicals on Latex Products" that outlines standard measurements for analyzing proteins in natural rubber.

According to Dr. Vesna Tomazic-Jezic, OST, this document has been in development since 1994. After providing details on the labeling issues raised by Dr. Lin, she asked the panel to consider FDA's proposed new claims and recommended tests. Dr. Tomazic-Jezic outlined the history/development of the MDT, the testing procedure, characteristics of test subjects, testing criteria, and exclusionary criteria. She concluded that a negative MDT on 300 nonsensitized subjects warrants a claim of "reduced potential to induce Type IV allergy in the general population." A negative patch test on 25 allergic subjects warrants the claim "reduced potential to cause reaction in allergic individuals."

Dr. Ronald Kaczmarek, OSB, discussed statistical issues of the guidance document. He outlined the rationale for requiring 300 participants and insisted an adequate confidence level (95%) in results is maintained. He acknowledged there may be difficulties in locating and recruiting the sensitized individuals as well as the health risks in testing them.

*Discussion*

Industry representative Otis Bouwsma, Ph.D., DMD, inquired about the exclusion of pregnant subjects, the rationale for choosing 300 subjects, and the study methodology. Dr. Tomazic-Jezic responded that the immunosuppressive system is compromised in pregnancy, and standard results can only be obtained on a uniform population. Continuing, she said the range of health care workers who may have latex allergy is 5.5 - 20%, whereas in the general population the range may be 1 - 6%. Dr. Kaczmarek added that 450 patients would be required for a confidence level of 99%; however, 300 subjects reflect a 95% confidence level, which is standard in the field of medicine. Dr. Lin said the guidance document does not require all studies to be conducted in the U.S., and FDA wants multiple data sets submitted as well.

**OPEN COMMITTEE DISCUSSION***Invited Speakers*

Jay Slater, M.D., Children's Hospital, claimed that individuals with Type IV allergy are at risk of developing Type I allergy. The latter should therefore be discussed as well. He described the history of Type IV and the range of reactions experienced by sensitive patients. Characterizing latex allergy as a lifelong disease, with no spontaneous remission, he said, avoidance is the only way to prevent it.

After providing background information on latex (its sources, components, allergens,

range of reactions, and the prevalence and scope of the problem), Timothy Sullivan, M.D., Emory Clinic, concluded powdered latex should not be used. Noting the "tremendous confusion" with the term "hypoallergenic," he said, FDA should be careful of the words it allows manufacturers to put on packages.

Safeskin Corporation's representative, Wava Truscott, Ph.D., disagreed. Latex is an excellent barrier and should not be discarded. He recommended the following: manufacturers should slow the development process and choose appropriate chemicals to earn the right to have a "low-chemical" claim; FDA should expand its guidance document to include all synthetics used to make gloves; manufacturers should not be required to test for chemicals not in their product; and FDA should consider requiring 300 subjects for tests of cosmetics and other products. Regarding the patch test, the concentration, not the size of the patch, is what makes a difference, he said. Dr. Truscott said the product label should specify the presence of thiurams, thiazoles, and carbamates; the language should be minimal and user friendly such as "reduced sensitization potential" or "reduced reaction potential"; and the label should list the manufacturer's phone number. The guidance document should specify which side of the glove should be tested.

Frank Perella, Ph.D., American Society of Testing Materials (ASTM), described the organization, its standards-approval process, the current standards for medical gloves; and the recently approved repeat insult patch testing (RIPT) of medical gloves (PS 77-97). ASTM recommends a sample size of 200, a 2- x 2-inch patch, the inclusion of subjects 65 and older, and

a minimum of 100 subjects per clinical location. Dr. Perella discussed a recently convened Chemical Sensitivity Task Group and its function. He then read several statements/recommendations he received from colleagues on previous ASTM Work Groups: FDA should use more specific terms (not "allergy" or "hypoallergenic"); concentration per unit area determines sensitization, and the size of the patch is of no importance; use of 300 subjects does not provide greater assurance of safety; and there is no need to discriminate against age.

Health Industries Manufacturers Association representative Anne Baldwin found FDA's labelling unworkable. She said the association recommends that FDA adopt the ASTM standard PS 77-97; work with ASTM to establish a method for patch-testing (with glove pieces) individuals with Type IV hypersensitivity; and allow manufacturers to state on their labeling that their product meets the applicable ASTM numerical designation. Manufacturers would then take responsibility for training the user community about the testing, she said.

Howard Maibach, M.D., USC, reiterated the importance of mass per unit area (not patch size). He said getting 25 sensitized subjects would not be difficult and that the ASTM document is better than the "other guideline." He said the scoring method in the guidance document is "totally confusing" and FDA needs to get across the appropriate terminology for allergy.

#### *Panel Deliberations*

Dr. Maibach told Dr. Edmiston that the MDT can give false negatives. To get a warning for risk assessment you must increase the concentration. Drs. Edmiston and Fowler then

discussed the sensitivity of the Draize methodology. Dr. Sullivan disagreed with Dr. Whitehouse's suggestion to omit the terms thiazoles, carbonates, and thirams on the label. He said the objective of the label is to prevent reactions and avoid disease for individuals with sensitivities. The objective "does not lend itself to a three-word explanation," he said.

According to Dr. Maibach, the Draize test will identify egregious gloves, but there will be a decrease in Type IV allergy when industry starts to pay attention to it. Lowering the offending allergens found in latex is a viable option, he said, citing a Finnish study. In response to Dr. Hylek's question, Dr. Sullivan followed with a discussion on the immunologic responses in people over age 65. He said they can be tested for IgE safely. Dr. Fowler continued. In his experience, half of the people with Type I allergy to latex protein also are allergic to the chemical additives. However, those allergic to the chemicals are not necessarily Type I allergic. The panel was told that the skin of elderly people offers an increased barrier to certain chemicals. Also, it is less reactive to irritants and experiences less redness and swelling than younger skin. Dr. Maibach stated it would be outlandish to refute testing in this case.

### *Discussion*

The panel addressed a series of questions posed by FDA. FDA's recommendation for having 300 test subjects to provide a 95% confidence level regarding the chemical sensitization potential of latex products is appropriate. Individuals with other forms of contact dermatitis should be excluded from study.

Discussion ensued on the issues of patch size, geographic locations, and scoring methodologies. According to Dr. Lin, the 1- x 1-inch has been used most often in the Draize test. Dr. Whitehouse said the 2- x 2-inch is more common in clinical practice and the former is used to equate dosage. He added that some reactivity to the allergen relates to the local concentration. The 2- x 2-inch is reasonable though, and is closer to how things are tested. It was stated that the 1- x 1-inch size is empirically the better size for reactivity.

Regarding locations, Dr. Fowler said it would be easier to obtain 25 sensitized subjects if 2 or more locations were used. Dr. Edmiston, however, asked how would FDA deal with the differences in scores by location.

During the discussion on scoring, it was stated that although the ASTM scoring is different than what is used clinically, some classification is needed. Dr. Hylek said that in the guidance document, the symptoms of irritation are indistinguishable during the first 72 hours. This puts more weight on the second reaction 2 to 4 days later, which is more relevant than at 24 hours. The irritation fades and the allergy accelerates, he said. This should be clarified when reactions are being scored. Panelists agreed that the scoring method should be standardized, and needs a closer look.

Different wording for the labelling claims was discussed. Dr. Hylek said that although

the speakers asked for more specifics and the use of chemical names, only people with severe cases would understand the language. Ms. Christine Chandler, consumer representative, described her experience with callers who had Type I and Type IV allergies. She would like to see the powder in gloves treated as second-hand smoke. She recommended that the labelling clearly state that the product can be hazardous without listing the chemicals and that the term "hypoallergenic" not be used. Ms. Chandler would also like more hospitals to create latex-free environments. She also characterized the problem as epidemic and stated her patients even complain of latex allergy to condoms. Dr. Fowler said for the second claim the chemical names are useful for those tested. Although they constitute a small minority, the information is critical. The names would not be useful for the first claim.

#### *Discussion Points*

Following the group's discussion, Dr. Simmons stated the panel's opinion: FDA should not change the proposed sample sizes (300 and 25); it should exclude contact dermatitis patients; and should leave the patch size as is. The scoring methodology should be revisited, and Dr. Fowler and others will followup. The second labelling claim needs more specificity and should have the chemical names.

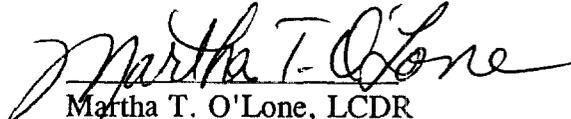
Discussion again ensued. Dr. Fowler said manufacturers should not have to conduct tests for chemicals not used in their products. The labelling should not be shortened. There should be a caution statement added about the presence of proteins, said Dr. Simmons. It was noted that

FDA is working with NIAASH to educate health care workers. A teleconference is being planned with downlinks to hospitals for educating staffs.

#### **ADJOURNMENT**

The meeting was adjourned at 4:43 p.m.

I certify that I attended the meeting of the  
General Hospital & Personal Use Devices  
Panel on September 15, 1997, and that  
these minutes accurately reflect what  
transpired.

  
Martha T. O'Lone, LCDR  
Executive Secretary, FDA

I approve the minutes of this meeting  
as recorded in this summary.

*see fax sheet - Martha T. O'Lone  
for signature*   
11/18/97

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Jacqueline Simmons, M.D.  
Chairperson

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