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ADVOCACY COUNCIL OF THE AMERICAN COLLEGE OF ALLERGY, ASTHMA AND IMMUNOLOGY

FDA STAKEHOLDER LISTENING SESSION
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Good Afternoon. My name is Dr. Kathleen May and I am speaking to you today on behalf of the Advocacy Council of the American College of Allergy, Asthma and Immunology, a physician specialty organization that represents over 3500 allergists – physicians who are board-certified in allergy and immunology. I am also an allergist practicing in Cumberland, Maryland. We appreciate the opportunity to present our views today on issues related to physician compounding, and, in particular, on the safety of compounding of allergen extracts.

It is estimated that there are 2.6 million people in the United States who receive allergen extracts through subcutaneous injection, totaling approximately 16 million injections per year. Yet, in the millions of injections administered, and with a safety record of more than 100 years, there are no reported infections in the medical literature. Nor do we see this in our clinical practice.

We agree that safety concerns exist whenever compounded materials are introduced into the human body as was tragically demonstrated several years ago in the case of the New England Compounding Center. We also

agree that compounding incorrectly has the potential to cause harm and should be performed according to specific protocols.

Allergists who prepare allergen extracts in their offices currently adhere to either the special protocol established by USP in its current Ch. 797 sterile compounding section or to published allergy specialty vaccine preparation guidelines. Allergen extract preparation begins with FDA-approved allergen extracts. Most of these are 50% glycerinated. These extracts or "concentrates" are combined in a sterile vial using sterile syringes. Serial dilutions are then made from the vial concentrate using sterile saline typically containing 0.4% phenol. The use of glycerinated extracts and the addition of phenol are extremely effective in ensuring that there is no bacterial growth. Beyond use dates are assigned based on the most recent expiration date of any of the component antigens. Allergen extracts are only administered subcutaneously. They are never injected intravenously or into body cavities or the central nervous system.

We are very concerned that the USP has proposed to eliminate its protocol for allergen extract preparation and is proposing that allergen extract preparation meet the same strict standards applicable to other more

dangerous compounded products, including an ISO Class 5 environment, environmental sampling for airborne particles, ongoing sterility testing requiring culturing of vials based on USP specifications, and discarding of multi-dose vials after 28 days. FDA Draft Industry Guidance entitled "Mixing, Diluting or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application, published last year, but before the USP announced its proposed changes to Ch. 797, would indirectly incorporate these new requirements. We do not believe the FDA intended this result, or intended to eliminate allergen extract compounding by physicians. In fact, the Draft Guidance, which sets forth special rules for allergen "prescription sets" makes it clear that the FDA intended to preserve allergen extract compounding by physicians as long as they adhered to specific protocols. This is also consistent with what Congress intended when it enacted the Drug Quality and Safety Act.

If the USP adopts its proposed rules and the FDA Industry Guidance is not changed, allergy immunotherapy as a treatment option for patients will no longer exist. Our organizations are working very hard to convince USP to modify its proposal and we hope we are successful. But if we are not, and if those rules are incorporated in FDA guidance, patients will be deprived of

the only treatment that actually presents the possibility of a cure for allergic rhinitis and asthma. There is no patient safety justification for this. In fact if these rules are adopted, the public will actually be less safe.

The proposed 28-day beyond use date has a critical impact. If allergists prepare new patient-specific vials every 28 days, instead of for up to 12 months, it is inevitable that antigens would come from different lots. Because of variability among lots there is always the risk of a systemic reaction, including anaphylaxis, when a patient is moved to extracts prepared from different lots. Our practice parameters recommend consideration of a 50-90% dose decrease for lot changes from the same manufacturer for this reason.

This risk of allergic reaction is especially acute during the initial 3-6 months of desensitization, as doses are being advanced. So under the new proposal, with a new extract every 28 days, the dose or concentration would be additionally reduced for safety. This creates a significant barrier to ever achieving a maintenance dose. And even if an individual is already on

maintenance therapy, it will be necessary to reduce the dose when a new lot is introduced.

This is not a problem resolved by compounding moving to facilities equipped to meet the proposed USP 797 sterile compounding rules..

Effectively, adoption of USP rules would mean the end of subcutaneous allergy immunotherapy. Public safety would be directly impacted, with people deprived of the only proven disease modifying therapy for asthma, allergic rhinitis and allergic conjunctivitis that offers a possibility for cure. The public health consequences of this would be enormous, impacting millions.

Thank you.