

Good Afternoon. My name is Dr Andrew Murphy. I am a Board Certified Allergist-immunologist and I am representing the American Academy of Allergy, Asthma and Immunology, and the over 6800 physicians, research scientists, and millions of patients with allergic diseases. Thank you for the opportunity to present comments on behalf of the Academy on proposed regulations impacting allergen extract compounding in physician offices.

In February 2015, the FDA issued “Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application Guidance for Industry.” Those FDA draft guidelines suggest in-office allergen extract compounding should follow the USP < 797> instructions specific to allergen extracts. The Academy submitted comments generally in support. However, we were unaware that USP was crafting a significant revision to the <797> chapter that, if approved, could significantly alter the process of allergen immunotherapy compounding and administration that could significantly decrease access to and safety of this treatment.

In the fall of 2015, USP released a proposed draft revision of Chapter <797> that does not include a separate section for allergen immunotherapy extract compounding, as had been included in the previous version. The proposed changes to the USP for allergen compounding are not based on published scientific data in which any infectious clinical

problem(s) with allergen extract compounding has occurred. However, these proposed changes have the potential to significantly decrease the safety of allergen immunotherapy and place patients at increased risk for adverse outcomes. The Academy and other stakeholders provided formal comments to USP earlier this year and those are attached for your review.

Allergen immunotherapy has been safely compounded and administered in allergists' offices for over 100 years. This precision medicine technology is life altering and at times life saving. And unlike many other compounded treatments, allergen immunotherapy is administered subcutaneously and NOT parenterally or intrathecally, essentially eliminating any risk of systemic infection. Indeed, the medical literature is clear; there is no documented evidence of an infectious risk from compounding allergen extracts in the office setting.

The safety of allergen immunotherapy is demonstrated in a 2016 publication in the Journal of Allergy and Clinical Immunology providing evidence that immunotherapy using allergen extract compounding based on current guidelines is safe and does not put patients at risk for infectious complications. In this retrospective study, 3,242 patients received a total of 136,322 allergen immunotherapy injections over the 10 year study period with no infections related to the allergy immunotherapy injection. In addition, in over 40 years of practice, the United States Military's centralized allergen extract lab has not identified any infectious complication related to allergen extract compounding and administration. These data clearly support the conclusion that allergen extract preparation following current <797> guidelines is safe and does not place patients at risk for infectious complications related to allergen immunotherapy.

Anaphylaxis is the major risk in an allergen immunotherapy treatment. This risk is carefully managed under current requirements by having the extract mixed onsite by physicians and staff with a personal knowledge and experience with each and every patient. Outsourcing extract preparation removes this important safeguard and severely limits a physician's ability to respond to any adverse allergic reactions to allergen immunotherapy. The proposed revisions require patients to start new extract vials every month, potentially changing source material in the extract, and thus significantly increasing risk for adverse and potentially fatal allergic reactions. These changes therefore decrease the safety and increase the risk to the patient, forcing physicians and patients to decide if the newly increased risk is actually worthwhile, all based on a hypothetical but undocumented risk of infection. Furthermore, this will severely compromise the life saving application of venom immunotherapy to patients with a history of anaphylaxis to stinging insects.

Moreover, the proposed changes potentially undermine ongoing Congressional initiatives to support the use of and develop further research into the effectiveness of allergen immunotherapy. In 2011 a bi-partisan group of US Senators wrote to then-Secretary of Health And Human Services Kathleen Sebelius regarding research showing significant health and cost saving benefits of allergen immunotherapy in children and adults. The research showing these patient benefits and healthcare utilization savings are well documented. The recent proposed changes by USP undermine this bi-partisan effort by making allergen immunotherapy, which currently is a proven, safe and effective, disease modifying therapy, into a higher risk treatment that would be less accessible and less effective treatment option.

Finally, the proposed changes will directly and negatively impact the ability of our active duty military to receive this therapy with potentially profound consequences. Men and women whose allergic disease were controlled with immunotherapy would be forced to rely on medications that may impact their ability to fulfill mission critical activities.

The FDA needs to carefully weigh proposed regulations and the impact that they have on patient care. The FDA has recognized the important and vital role of allergen immunotherapy in managing patients with allergic diseases. However, proposed changes in USP <797> decrease the safety of and increase the risk of allergen immunotherapy all in an effort to prevent a non-event. This proposed change is overreaching, not based on any data suggesting a risk of infectious complication from allergen extract compounding and ignores the current scientific data that supports the safety of allergen extract compounding. Failure to keep the current USP <797> guidelines for allergen extract compounding will significantly increase the risk/benefit ratio of allergen immunotherapy and needlessly place patients in danger of medical complications and potential death.