



July 18, 2016

Robert Califf, MD, MACC, FACP
Commissioner
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; Availability

Dear Commissioner Califf:

On behalf of the American College of Physicians (ACP) and allergy and immunology, a subspecialty of internal medicine, I am writing to encourage the Food and Drug Administration (FDA) to carefully consider the safety record associated with sterile preparation of allergen extracts and negative impact on patient access that may be associated with elimination of the current in-office compounding procedures. ACP members include 148,000 internal medicine physicians (internists), related subspecialists, and medical students. Internal medicine physicians are specialists who apply scientific knowledge and clinical expertise to the diagnosis, treatment, and compassionate care of adults across the spectrum from health to complex illness.

As the FDA considers revisions to its policies governing compounding of drugs, the Agency should prioritize patient safety and consider in any discussion of modifications to compounding policies the safety record that is associated with the type of compounded drug and the criteria governing its preparation. Any revision to regulations governing compounding should reflect documented safety issues related to the compounding of a specific type of drug rather than a broad policy that ignores special considerations that have been given to specific circumstances such as those related to sterile preparation of allergen extracts.

Current standards from the U.S. Pharmacopeial Convention's (USP) General Chapter <797> Pharmaceutical Compounding – Sterile Preparation are based on a graduated set of requirements that are reflective of the actual risk associated with specific procedures. The current rules, established in 2008, include a distinct set of standards for allergen immunotherapy (AIT): "allergen extracts as [compounded sterile preparations] CSPs are single-dose and multiple-dose intradermal or subcutaneous injections that are prepared by specially

trained physicians and personnel under their direct supervision. Allergen extracts as CSPs are not subject to the personnel, environmental, and storage requirements for all CSP Microbial Contamination Risk Levels in this chapter only when all of the following criteria ...” These distinct standards that allow for in-office compounding for the provision of AIT were established based on there being no reported instances of adverse infectious events related to allergy shots.

In September 2015, USP posted a notice of intent to revise General Chapter <797> Pharmaceutical Compounding – Sterile Preparation.¹ This proposed revision eliminates the special treatment that allergen extract preparations receive in the current standards and instead applies an overly broad determination that all sterile compounding must be treated as equally and inherently dangerous without any documented justification for this change. ACP strongly opposes the removal of the special criteria regulating allergen extracts as CSPs and encourages the FDA to retain the standards for allergen extracts in the current 2008 version of USP Chapter <797>. While we support revisions to policies to protect patient safety, removing the policies for AIT when there is no documented evidence showing that patient safety is in question based on preparation techniques will negatively impact patient access and increase the cost of care without contributing to improvements in patient safety.

Allergen extracts have been safely prepared by physicians using aseptic techniques for more than one hundred years, and there is no evidence that current practice poses any threat to patient safety. A Harvard Medical School study² published in the *Journal of Allergy and Clinical Immunology* this year found that there is no documented risk of infection associated with AIT. This study, which involved more than 3,000 patients who received more than 130,000 subcutaneously administered AIT injections over a 10-year period, led the authors to conclude that “These findings suggest that the sterility and safety practices in place during the study period are adequate to prevent adverse infectious outcomes related to the preparation and administration of AIT.”

If the FDA were to remove the special criteria that currently exist for in-office compounding of allergen extracts, patient access to AIT will be drastically reduced, if not eliminated, because physicians will no longer be able to prepare individualized AIT vials for their patients. For example, patients often have allergic reactions to their immunotherapy injections that require allergists to change the content or dilution of the vials in response to specific sensitivities prior to the next injection to avoid life-threatening systemic allergic reactions. These adjustments would need to occur while the patient is in the allergist’s office to avoid interruptions in the treatment schedule. Off-site compounding pharmacies would not be able to make these adjustments in a timely fashion, delaying treatments and creating patient safety and efficacy concerns. This will negatively impact patient access to essential treatments for the approximately 2.6 million individuals who rely upon AIT to treat their asthma and allergic rhinitis each year as well as those who may need it in the future.

¹ <http://www.usp.org/usp-nf/notices/general-chapter-797-proposed-revision>

² Balekian DS, Banerji A, Blumenthal K, Camargo Jr. CA, Long AA, Allergen Immunotherapy: No Evidence of Infectious Risk, *Journal of Allergy and Clinical Immunology* (2016), doi: 10.1016/j.jaci.2016.03.021.

Therefore, ACP recommends that the FDA encourage that regulations that incorporate USP-established standards prioritize patient safety, but within a balanced approach that includes patient access to well-established, evidence-based specialty care that relies upon individualized treatments provided through in-office compounding by maintaining the 2008 USP Chapter <797> policies pertaining to compounding of allergen extracts.

Thank you for considering our comments. Please contact Stacey Harms, by phone at 202-261-4556 or e-mail at sharms@acponline.org if you have questions or need additional information.

Sincerely,

Nitin S. Damle MD MS FACP

Nitin S. Damle, MD, MS, FACP
President