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September 28, 2016

Robert M. Califf, MD
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Ave.,
Hillandale Bldg., 4th Floor
Silver Spring, MD 20993

RE: Docket No. FDA-2016-D-2268 DRAFT GUIDANCE
"Insanitary Conditions at Compounding Facilities"

Dear Sir or Madam:

The American Academy of Allergy, Asthma and Immunology (AAAAI) appreciates this opportunity to submit comments on Docket No. FDA-2016-D-2268 DRAFT GUIDANCE **"Insanitary Conditions at Compounding Facilities".** The AAAAI represents 6,800 physicians who provide care to millions of patients suffering from asthma and allergic diseases. **We are writing to request that the proposed guidance be withdrawn and that no further action be taken until the USP process is finalized and the FDA has performed an analysis related to the impact of this proposal**.

While we appreciate the FDA actions to protect US citizens from untoward consequences from potential contaminated medical products, a-one-size-fits-all approach is over reaching, fails to incorporate any risk assessment, and will have significant negative consequences for the healthcare of patients with allergic diseases who currently receive allergen immunotherapy (AIT) or who may in the future benefit from AIT. Not only will the FDA's current draft proposal reduce patient access to critical medications, but it will also unnecessarily result in significantly increased health care costs.

This proposal requires that all sterile compounding, including allergen extract compounding, be performed in an ISO Class 5 environment. This contradicts current USP <797> guidelines and current FDA guidelines, without providing any evidence that such an approach is necessary to avoid infectious risk from mixing and administration of allergen immunotherapy. Therefore, this proposal is a solution in search of a problem, and we reject that the current standards (as previously agreed to by the U.S. Pharmacopeia Convention [USP] and FDA) are insufficient to safely provide these services in the physician's office.

We have attached comments previously provided to the FDA related to its "Draft Guidance on Mixing, Diluting or Repackaging" and comments we provided to the USP regarding its proposed changes to General Chapter <797>. We have also attached a copy of comments provided to the FDA at a recent listening session hosted by the agency for various stakeholders on compounding. To our dismay, the agency did not engage in a dialogue with stakeholders on these important issues. Rather, it has issued this draft guidance, which is contrary to the feedback we and others have provided.

Very simply, this FDA guidance, as related to allergen extract immunotherapy, is not supported by any evidence that the current allergen extract compounding rules have resulted in infectious complications in patients. In over 100 years of AIT compounding and administration, there has never been reported a single case of an infectious complication. As noted repeatedly in the comments referenced above, there is scientific data in the published medical literature that demonstrates the safety of AIT compounding in physicians' office.

To date, neither the FDA nor the USP has been able to provide any scientific data, case reports or anecdotal evidence that AIT compounding, following current USP guidelines, has resulted in an infection. Instead, the FDA has insinuated that physicians have failed to report infectious events to protect their practice and profit from AIT compounding and administration. This straw man argument lacks scientific rigor, flies in the face of appropriate scientific evidence based medical decisions, and is, frankly, frustrating. We are being told that we must prove a negative: that no infections have been caused under the current requirements, while zero evidence has been produced that this practice actually creates an infectious risk. We provide safe, potentially life-saving treatment, under current FDA approved standards and conditions. Now, FDA is suggesting that its current standards result in "insanitary compounding" and must be revised without definitive evidence supporting this change. Moreover, the draft guidance encourages State regulatory agencies to pursue regulatory action against physician's offices that do not fall within the bounds of the guidance, even though the guidance is not legally binding nor does it have the force of law, and in so doing will create a barrier to care for patients who rely on AIT. For all of these reasons, we believe that the FDA's latest actions are arbitrary and capricious.

We are concerned that the FDA is fundamentally attempting to undermine the processes in place at the USP regarding the Chapter 797 proposed revision. Last fall, the USP published a proposed revision of Chapter 797 that significantly altered the standards for sterile compounding -- from a risk assessment based series of requirements to one that treated all sterile compounding as equally and inherently dangerous, regardless of the contents or administration site of the compounded material. This over-reaching and dangerous USP proposal was met with almost 8000 comments, and the USP continues its process of reviewing and categorizing this feedback. The volume, intensity and extraordinary level of concern expressed in those comments reflects significant consideration from health care providers and patients, as well as an expectation that evidence supportive of this overreaching of a "one-size-fits-all" approach can be provided. Now, FDA is duplicating this inappropriate proposal with the current draft guidance that would require an ISO class 5 environment (among other things) or otherwise declare mixed products insanitary.

This is a broad over-reach, given that these environmental standards have not previously been applied to the much broadened category of "compounding facility" cited in the FDA's proposal.

We understand that the USP is planning to host stakeholder meetings in early 2017 to further discuss the USP Chapter 797 revisions as it relates to certain specialties that would be severely impacted by the abandonment of a risk assessment-based set of standards. We applaud the outreach by USP and request that the FDA refrain from undermining its own existing standards and currently established USP standards until the USP completes its consideration of the comments submitted and any revisions that might result. Clearly, this is a complicated process and will take time for USP to complete the review and develop any changes to USP Chapter 797.

Therefore, we respectfully request that the FDA:

(**1) Immediately withdraw Docket No. FDA-2016-D-2268 DRAFT GUIDANCE "Insanitary Conditions at Compounding Facilities"** or at the very least recognize, as they have done in "Draft Guidance on Mixing, Diluting or Repackaging" that AIT compounding is a safe and unique compounding procedure that can continue following current <797> guidelines.

(2) Produce any published scientific data / evidence that AIT compounding following current USP Chapter <797> guidelines has resulted in any infectious complication in any patient directly related to contaminated AIT compounded extract.

(3) Initiate appropriate studies to understand the risk analysis associated with AIT compounding. The FDA continues to assert that all compounding is the same, and this is simply not the case. A risk analysis study related to AIT compounding is appropriate and needs to be done.

(4) Perform the appropriate studies to understand the implications that severely limiting access to AIT will have on the health care of the citizens of the US with allergic diseases, especially in light of the fact that these is no documented case of AIT compounding causing an infectious complication. This analysis should include a thorough analysis of the economic impact associated with increased use of medications, emergency department (ED) utilizations, hospitalizations, outpatient medical visits and well as indirect costs related to lost time at school and lost time at work for example. Finally, the risk to the well being of individuals with venom hypersensitivity who are likely to be at increased risk for serious or fatal events owing to the limitation in the availability of venom immunotherapy must be carefully examined.

Sincerely,

Thomas B. Casale, MD, FAAAAI
Executive Vice President
American Academy of Allergy, Asthma & Immunology