November 23, 2018

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane; Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2018-D-2268; "Insanitary Conditions at Compounding Facilities."

To Whom It May Concern:

The National Home Infusion Association (NHIA) appreciates the opportunity to comment on the September 26, 2018, Draft Guidance: "*Insanitary Conditions at Compounding Facilities*" (hereinafter referred to as "Draft Guidance"). NHIA is the trade association representing 503A home infusion pharmacies that provide sterile, parenteral medications and services to patients able to be treated at home.

NHIA is committed to ensuring patients receive high quality sterile medications and supports the FDA's efforts to eliminate the potential for patient harm from adulterated compounded products. However, NHIA has grave concerns with several of the conditions described in the Draft Guidance and fears there will be negative impacts on patient access and safety should the guidance be finalized in current form. The vast majority of compounding activities performed by home infusion pharmacies involve the preparation of a conventionally manufactured sterile product according to the instructions provided in the approved labeling. These products are prepared after receiving a physician order, and subsequently dispensed to the patient for administration in the home setting. Examples of sterile medications administered at home include: anti-infectives, parenteral nutrition, analgesics, and various biologics.

Scope

Even though the majority of compounds made by home infusion pharmacies are conventionally manufactured products prepared in accordance with the FDA approved labeling, home infusion providers adhere to the sterile compounding standards published by the United States Pharmacopeia (USP). USP standards provide a clear framework for states to regulate pharmacies engaged in compounding incident to a physician order for an individual patient. This draft guidance, if enacted, will result in creating an inconsistent, subjective, and confusing standard that intermingles elements of good manufacturing practices with accepted 503A standards.

Therefore, NHIA feels the FDA should limit the scope of this guidance to include the examples of obvious, visible contamination, such as those in III.A(1) and III.B. The conditions cited in these sections are serious, easily identified, and can be universally applied to any compounding facility. The conditions

cited in this document related to gowning, aseptic practices, facilities, environmental monitoring, sterilization, and cleaning and disinfecting are not comprehensive, and cannot be effectively combined into a single guidance that applies to both 503A and 503B pharmacies.

Additionally, this Draft Guidance sets an extraordinarily high standard for pharmacies engaged in compounding sterile products, including the aseptic preparation of conventionally manufactured products; while exempting physicians despite their being engaged in the same activity (Draft Guidance footnote 3, page 1). Some physicians are also providers of home infusion services where compounded drugs are dispensed from the office, stored for extended periods, and administered at home by the patient/caregiver or nurse[1]. To exempt physicians from adhering to the same standards for dispensing compounded sterile products (CSPs) does not sufficiently protect patients from potential harm caused by adulterated CSPs. NHIA finds the broad physician exemption confusing and inconsistent with the mission of the FDA. NHIA agrees that *all* practitioners must be allowed to prepare a single dose of a conventionally manufactured, sterile medication for *administration* without being cited for insanitary conditions according to the Draft Guidance. However, *all* compounding facilities that *dispense* CSPs to patients, including those owned and operated by physicians must not dispense adulterated medications.

Recommendations for the scope of the Insanitary Conditions Guidance:

1. Do not exempt physicians from the scope of the guidance if they dispense CSPs to patients for use at home.

2. Limit the scope of the guidance to the examples of obvious, visible contamination as stated in sections III.A(1) and III.B with a high potential to result in adulterated products if present.

3. Refer to accepted USP standards for 503A pharmacies for aseptic practices, garbing, facility design, environmental monitoring, and cleaning and disinfecting.

Subjective wording

NHIA has serious concerns with the potential for subjective interpretation and application of this Draft Guidance. The use of ambiguous terminology makes it impossible for a provider to know explicitly when corrective action is required. Words used frequently throughout the Draft Guidance such as, "adequate, routine, frequently, periodically, regularly, improper, difficult, insufficient, and unnecessary" leave a compounder without a clear understanding of when an insanitary condition exists. The actions and consequences associated with the presence of insanitary conditions are serious and have the potential to disrupt patient care. NHIA agrees that if the conditions in III.A(1) and III.B are present, then immediate corrective actions are warranted and appropriate; however to include subjective variations of certain elements of practice standards in this document gives the appearance that FDA intends to take authority for regulating compounding of 503A entities away from the states and replace the current USP standard with an incomplete, vaguely written guidance that has the potential to be inconsistently applied. For example, USP standards have clear requirements for employee qualification and training; specific frequencies for personnel testing and facility certification; and definitive action levels indicating when corrective action must be taken. NHIA believes the FDA can avoid inconsistent application of the guidance by adopting the recommendations stated above regarding the scope of the document.

[1] 2018 IDSA Clinical Practice Guideline for the Management of Outpatient Anti-microbial Therapy

Application of good manufacturing practices (GMP) to 503A pharmacies
As written, NHIA fears this draft guidance lists elements not required under the accepted USP standards used by state authorities to license, regulate, and inspect 503A pharmacies. Several conditions cited in the document are sourced from the manufacturing sector and will create undue barriers to providing individual patients with sterile IV products. Few 503A pharmacies across the healthcare spectrum today could meet the requirements identified in this document, and as a result, nearly every hospital and home infusion pharmacy would likely be cited for insanitary conditions by FDA inspectors. NHIA believes the application of GMP requirements would impede a 503A pharmacy's ability to fulfill a physician order for a compounded sterile product. NHIA strongly urges the FDA to consult with state boards of pharmacy and the USP regarding appropriate standards for 503A pharmacies, and not refer to manufacturing standards when describing insanitary conditions.

NHIA offers the following examples of insanitary conditions that represent conflicts with existing standards of practice for 503A pharmacies, and/or contain ambiguous language:

- *The requirement for complete and comprehensive segregation for "open processing" of beta-lactam products.*

There is no clear definition for "open processing" and NHIA is concerned that this condition would place an unnecessary expectation on 503A compounders that preparing conventionally manufactured beta-lactam products requires separate facilities. Requiring 503A pharmacies to build special facilities to prepare patient-specific doses of commercially available beta-lactams will prevent patient access to these anti-infectives. The risk of contamination from sterile, FDA approved, conventionally manufactured components is insignificant compared to the risks of handling raw materials as occurs in the manufacturing setting. FDA can clarify the condition by referencing the use of active pharmaceutical ingredients as components if the intent is to limit the condition to such processing.

- *Inability to gown in a non-classified area.*

Some 503A pharmacies have invested in garbing rooms that utilize an unclassified space to conduct hand washing and garbing. This arrangement has the potential to improve environmental control of the classified areas by moving the sink further from the buffer room or SCA where compounding occurs. This condition would prevent compounders from placing the sink outside the ISO classified area.

- *Handling hazardous, "sensitizing", or "highly potent" drugs with inadequate controls to prevent cross-contamination.*

This particular section contains terminology that is ill defined, exceeds the requirements of *USP <800> Hazardous Drugs – Handling in Healthcare Settings*, and leaves providers with no clear reference for how to identify the drugs that trigger this condition. This is another example of FDA attempting to re-create an existing 503A standard in an incomplete and ambiguous manner.

- *Engaging in aseptic processing wearing critical gown components that are non-sterile, and performing aseptic manipulations with exposed skin.*

503A pharmacy standards only require gloves to be sterile; and do not require all exposed skin (forehead) to be covered. Requiring all garb to be sterile, and restricting exposed skin are GMP standards and unnecessary for aseptic processing of conventionally manufactured, FDA approved products for individual patient use. Again, FDA seems to be blending requirements from manufacturing sector with "patient care compounding" practice. The financial investment 503A pharmacies make to comply with USP standards is not insignificant, goes largely unrecognized as a professional service, and is not adequately reimbursed. If a 503A pharmacy has to meet GMP standards, then some providers will decide to stop offering home infusion services, resulting in a negative impact on patient access to home infusion medications, particularly in rural areas.

- *Using non-sterile disinfecting agents and cleaning pads/wipes in ISO classified areas.*

Current 503A standards only require cleaning and disinfection agents and supplies to be sterile when used in the primary engineering control, not in all classified areas.

The escalation of environmental monitoring, personnel testing, and facility certification to condition level.
The references in section III.A(2)(b) regarding equipment and facilities (specifically lines 217 to 228) escalate the elements of environmental monitoring, personnel testing, and facility certification to the level of eligible insanitary conditions. Unfortunately, in doing so the FDA offers no clear guidance as to when a compounder would be cited for such conditions. Again, NHIA strongly urges FDA to limit the scope of this guidance to visible contamination that is easily identifiable and described, and leave assessing compliance of 503A compounders with accepted USP standards for environmental monitoring, personnel testing, and facility certification to the states.

In Summary
NHIA and its members are strongly committed to maintaining the highest standards for compounding quality, promoting patient safety, and assuring patient access to safe and effective infusion therapies in the home and outpatient settings. NHIA applauds the FDA for providing a guidance that serves to educate compounders and regulators about insanitary conditions that may cause patient harm. NHIA encourages the FDA to work with representatives of the 503A compounding community, state regulators, and USP in developing a clear and objective guidance document that describes and identifies insanitary conditions in all settings, and that does not conflict with accepted 503A standards for preparing CSPs.

NHIA appreciates the opportunity to comment on this Draft Guidance. Please feel free to contact Connie Sullivan, BSPharm, at connie.sullivan@nhia.org should you want to discuss our comments further. Thank you for your consideration of NHIA's comments.

Thank you for your consideration.

Sincerely,

Connie Sullivan, BSPharm
National Home Infusion Association