Dear Dr. Califf:

On behalf of the Drug Quality and Security Act (DQSA) Coalition, we write to thank the Food and Drug Administration (FDA) for its recent announcement on inspections put forth in the Agency’s notice of the change in procedure for inspections for pharmacies and other health care facilities compounding in accordance with section 503A of the Federal Food, Drug and Cosmetic Act (FD&C Act), effective as of August 1, 2016. We commend FDA’s effort to change the procedure for inspections of 503A pharmacies and are encouraged by the FDA’s openness to stakeholder input.

Our organizations represent patient advocates, physicians, pharmacists, and other healthcare providers who are united in a mission to preserve patient safety and access to needed compounded medications, consistent with state and federal laws and regulations. Since 2014, our organizations have been meeting and working together as part of a coalition of over 30 organizations (the DQSA Coalition) to provide input to the FDA, to State Boards of Pharmacy, and to the Congress about our concerns with the Agency’s implementation of the Drug Quality and Security Act (‘DQSA’, P.L. 113-54) and to seek solutions that maintain a balance between public safety and patient access to compounded medications.

The DQSA Coalition is seeking clarification on certain policies announced in the notice to ensure that compounding pharmacies operate in good faith compliance with the DQSA as well as FDA policies that provide guidance for the DQSA. In this letter, we will focus on the following topics:

- Determination of 503A status;
- Inspection standards;
- FDA’s 501(a)(2)(A) authority with regard to 503A pharmacies;
- 503A Facility Records Exemption; and
- General implementation issues.

**Determination of 503A Status**

* Determination of Status Timing
The FDA indicated in the notice that it will determine whether a facility is a 503A pharmacy before closing an inspection. In addition, the notice states that “FDA investigators will continue to include observations on Form FDA-483 that appear to constitute ‘insanitary conditions’ without regard to the investigator’s preliminary assessment of a health care facility’s status under section 503A.” We have concerns with both policy statements.

We believe the proper time for the determination of 503A status is at the beginning of the inspection, because that finding will determine which standards should be applied to the facility – the current good manufacturing standards (cGMPs) that govern the activities of drug manufacturers and 503B outsourcing facilities, or 503A-specific standards that are distinct from the cGMPs. Section 503A status also triggers exemptions from three federal FDCA provisions, 351(a)(2)(B), 352(f)(1), and 355. Thus, the beginning of the inspection is a vital point that acts as the lynchpin for all subsequent interactions between the FDA and the compounding pharmacy during the inspection.

Likewise, we are concerned about the FDA’s retention of authority to conduct a thorough review of the evidence that could overturn the investigators assessment of 503A status. While efforts should be made to ensure 503A health care facilities are acting as such, an open-ended, post inspection review of an investigator’s assessment of a facility’s 503A status will leave any facility that has been inspected in limbo with regard to the true conclusion of the inspection process. The DQSA Coalition urges the FDA to empower its investigators to make the determination of 503A status on-site and if the investigators determine the facility to be in compliance with 503A, the facility should immediately be referred to the proper State Board for follow up. Regardless, if a post inspection review of evidence is necessary, the DQSA Coalition urges the FDA to ensure that the post review period is of limited duration, the timeframe of which is transparent to the public, and that it provides a mechanism for the facility to be able to respond to any questions or concerns, before any action is taken.

Factors of Determining 503A Status

The FDA cites the conditions that a facility must meet to obtain 503A status. While the FDA has finalized a general guidance on this issue entitled “Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act,” there are currently several guidances that are not finalized with regard to the various standards in section 503A that would lead to determination of 503A status, most notably:

- “Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act”;
- “Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic Act”;
- “Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the State of [insert STATE] and the U.S. Food and Drug Administration”;

Insanitary Conditions at Compounding Facilities Draft Guidance.

The individual members of the DQSA Coalition, as well as the DQSA Coalition itself, have expressed concerns about the draft versions of these guidances and we remain steadfast in our efforts to work with you to resolve those concerns.

Because this inspection notice went into effect on August 1, 2016, it is unclear what factors FDA inspectors will be using to make a determination of 503A status and subsequently what factors the FDA will use after the inspection during the “thorough review of the evidence” discussed in the notice. It has come to our attention that investigators apply items outlined in the draft guidances in their determination, including, but not limited to, compounding for office administration, compounding essential copies of commercially available drug products, anticipatory compounding and interstate commerce of compounded drug products.

Inspection Standards for 503A Facilities

Generally speaking, the DQSA Coalition recommends that the FDA consider the prevailing community standard (i.e. United States Pharmacopeia (USP) or other state regulations) to be the base standard for inspections to ensure a 503A facility is not being inspected using 501(a)(2)(B) (cGMP) standards that are inapplicable to section 503A facilities. By using prevailing community standards, the FDA could deduce what observations are deviations solely from inapplicable FDA cGMPs and which are not. This recommendation will greatly decrease the issue with skewed perceptions of 503A facilities if their FDA Form 483 is posted to the FDA website, as observations made by the investigators will reflect issues with either USP standards or applicable state regulations instead of cGMP standards, from which these facilities are exempt.

503A Facility Records Exemption

With regard to the determination of 503A status, the DQSA Coalition would like to remind the FDA that a finding of insanitary conditions during the course of a pharmacy inspection does not revoke a pharmacy’s 503A status and as such does not remove any of the 503A exemptions, including but not limited to the 503A Facility Records Exemption within Section 704 of the FD&C Act. Section 704(a)(2)(A) of the FD&C Act outlines that a 503A health care facility has a records exemption. This exemption has long been upheld by courts as an intended Congressional distinction between a 503A health care facility and a pharmaceutical manufacturer. As part of the determination process the FDA should recognize the records exemption as outlined by Congress in Section 704 of the FD&C Act and adhere to the records exemption during the initial determination of a health care facility as well as throughout the entirety of an inspection for a 503A health care facility. The inspector’s ability to inspect a facility’s “equipment, finished and unfinished materials, containers, and labeling” pursuant to section 704(a)(1) amply enables the inspector to assess a facility’s 503A compliance, without the need to violate the Congressionally-enacted records exemption.

General Implementation Issues
The DQSA Coalition urges the FDA to ensure that all investigators that conduct inspections of compounding pharmacies after August 1, 2016 are applying the notice’s policy guidance uniformly. We urge the FDA to publish an inspection checklist that would guide industry and FDA inspectors through every inspection of a compounding facility, from determination of 503A status to application of inspection standards to issuance of inspection observations and warning letters. A publicly available document to guide the process will provide a platform for compounding facilities and the FDA to have a smooth inspection process where all parties are informed of the appropriate processes and what to expect.

We would also like to express our concern regarding the FDA questionnaire being sent to pharmacies and how it will be used by the agency in making the initial determination as to whether the pharmacy will be inspected under cGMP standards or under USP or other state-adopted standards. We urge the FDA to provide further clarification on the purpose and intended use of the questionnaire and to make it clear to the pharmacies receiving the questionnaire that they are under no legal obligation to complete and return the questionnaire.

Additionally, we recommend that the FDA investigators be granted the ability to determine compliance with 503A when inspecting pharmacies. This would prevent an arduous inspection process on both the pharmacy and the investigator, caused by confusion between the field inspector’s notes and the central FDA office.

We thank you for your work on these issues and your efforts to ensure inspections of 503A pharmacies are conducted in a manner consistent with the intent of the DQSA. We stand prepared to work with you to ensure compounding pharmacies are producing safe and effective products for Americans who need compounded drugs.

Sincerely,

Alliance for Natural Health
American Pharmacists Association
Fagron
International Academy of Compounding Pharmacists
National Alliance of State Pharmacy Associations
National Community Pharmacists Association
National Home Infusion Association
PCCA