brava

March 23, 2023

Maria Serpa, Licensee Member, Chair
Enforcement and Compounding Committee
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

RE: Proposed Sterile Compounding Regulations

Dear Ms. Serpa:

My name is Erik Clausen and I serve as the Pharmacist-in-Charge for Brava CA, LLC, a compounding pharmacy located in Novato, CA specializing in veterinary medicine. I would like to take the opportunity to thank the committee for the opportunity to provide comments to the proposed updates to California's compounding regulations. Brava is committed to provide high quality compounded medications to veterinary patients both in California and throughout the United States.

As a compounding pharmacy specializing in the veterinary space, Brava adheres to the many of the same standards as a pharmacy compounding human medications, however, our patients do have unique needs which require additional consideration to ensure that the unique differences between veterinary patient and human patient needs are being met appropriately.

General Comments:

While we support the efforts to update the regulations to harmonize California's regulations with recent change to both federal guidance and industry standards (USP), we believe the approach presented create regulatory burdens on compounding pharmacies which will result in the disruption of patient care thereby negatively impacting the quality of care enjoyed by California residents and their pets.

a. Many sections of the proposed rules include new language with subjective terms thereby overriding the plain language of the standard that the Board is attempting to adopt. Terms such as "comparable" or "suitable" are subject to professional judgment and open to interpretation which makes maintaining a compliance plan for the pharmacy difficult at best.

b. The proposed rules fail to take into full consideration a number of provisions allowed under federal law such as interim bulk lists which will put California patients at a disadvantage to continue to receive compounded medications that they rely upon which are otherwise allowed under federal law.

For these reasons, we strongly encourage the committee to reconsider the approach to formally adopt the USP standards by simply referencing the actual standards into the regulations as written by USP which almost all other states have done (or are in the process of doing). This preserves the original plain language of the standard thereby providing clearer guidance for a pharmacy's compliance program.

Please note our comments to the following specific provisions.

1. <u>General USP References</u>:

There are numerous references to USP Chapters 1000 and above which would establish them as a regulatory requirement. These USP Chapters are not the actual standards, but are intended to be informational. We are concerned that the manner in which they are referenced exceeds the intent of the USP Board as it would in effect establish those chapters as requirements for pharmacies to adhere to. Our recommendation is that the regulations should clearly reflect the informational nature of these chapters which correspond to the intent of their use by USP.

2. 1736 (a) "Certificate of Analysis" definition as proposed would require a COA to be produced by a manufacturer...demonstrates that the component confirms to the specifications....manufactured under cGMP, is suitable for use in pharmaceuticals and meets the requirements of USP.

   We are very concerned about the term "suitable for use in pharmaceuticals". Who makes that determination? Is it the pharmacist in exercising their professional judgment or is it at the determination of an inspector? How are they reconciled without formal disciplinary action if there is a disagreement as to what is suitable or not?

   Our pharmacies collect Certificates of Analysis for our APIs and other pharmaceutical components used in compounding, they are often provided by our wholesale supplier and as such may not be an original COA from the manufacturer. We trust that this practice still meets the requirements under this definition. It should be noted that the FDA regards the original COA as confidential commercial information which is one of the reasons that it is not always provided in its original format from the manufacturer.

Further, specifically for veterinary compounding, not all components (which we interpret to mean an actual ingredient, whether active or inert), that we use have a USP monograph for APIs specific to veterinary preparations. Because of this any COA we receive may not fully conform to the proposed definition.

3. 1736 (d) Essentially a copy definition...means all preparations that are ***comparable*** in active ingredients to commercially available drug products.

   We are concerned that the inclusion of the word "comparable" will create ambiguity and conflict with established definitions provided by the FDA in their regulations and guidance documents. The determination of what is considered comparable is open to any number of determinations and places pharmacies at risk should an inspector disagree with the professional judgment of the pharmacist.

   As the FDA retains enforcement rights under the FDCA and manufacturers themselves have private rights of action, we question whether this is an area that the State would want to focus its enforcement resources which are likely to occur due to interpretations of the definition being proposed.

4. 1736.1 Sterile Compounding Scope (d)(1)(A)

   (d)(1)(A) ....drug product appears on an ASHP or FDA list of drugs that are in short supply...

   We recognize that this is the current regulation, however these lists do not cover veterinary drug shortages. The FDA animal drug shortage page is not updated in a timely enough manner to reflect animal drugs that are in short supply. Manufacturers of animal drugs are not required to report shortages as manufacturers of human drugs are required to do. Therefore, these lists would not be accurate for a pharmacy engaged in veterinary medicine.

   We recommend also allowing wholesaler BO reports to satisfy documentation requirements that the drug is in short supply. Compounding pharmacies, particularly in the veterinary space, are a viable solution to ensuring continuity of care when these shortages occur.

5. 1736.1 Sterile Compounding Scope (d)(2)

   (d)(2) Is made with any component not intended for use in a CSP for the intended patient population.

Many medications prescribed by veterinarians are prescribed as "off-label". We are not sure how we would meet this requirement for our veterinary patients since the prescription is for a drug approved for human use, but recognized by veterinarians for treatment of animals. Assuming component means ingredient, who determines what component is "intended" for use in compounded sterile preparation for the patient population? Will documented human standards apply to veterinary patients? Is the prescription and medical opinion of the prescribing veterinarian the standard?

6. 1736.3 Personnel Hygiene and Garbing (b)

   (b)...shall not allow personnel to enter the compounding area with non-removable piercings...

   We ask that this be modified to include "visible" non-removable piercings. Without this clarification we are concerned about meeting the requirement while balancing privacy protections and rights of our employees.

7. 1736.9(d) Equipment, Supplies, and Components

   (d) All *components* .... Shall be manufactured by an FDA-registered facility and *suitable for use* in sterile pharmaceuticals.

   Compounding pharmacies use a number of inactive ingredients that are not manufactured in an FDA registered facility, but have been approved by FDA for pharmaceutical purposes.

   In addition, use of the phrase "suitable for use in sterile pharmaceuticals" is vague and open to interpretation. Who would determine suitability? Is this left to a pharmacist's professional judgement? We are very concerned that there would be differences in opinions even between inspectors which will make compliance difficult at best.

8. 1736.12(b): Establishes that an alternative method for sterility testing can be used so long as it is validated according to USP Chapter 1223.

   We support the inclusion of the alternative method for sterility testing, however are unsure if the validation must be completed by the pharmacy or if the lab performing the testing may provide it.

9. 1736.17(d): Failure to follow written SOPs shall constitute a basis for enforcement action.

The current rule contains a similar provision but it provides for disciplinary action for a "material" failure. As proposed, "any" failure, whether material, single occurrence or multiple occurrences could all trigger enforcement action. We strongly recommend maintaining the current language which provides that a material failure to serve as the impetus for disciplinary action, not the mere occurrence of an event, no matter how insignificant or minor.

Compliance to SOPs within a pharmacy is important but there are any number of examples where it would be excessive to bring an enforcement action against a pharmacy for an identified gap in following an SOP. There could be periods where the pharmacy is changing a procedure and the actual update to the SOP could occur a few days later (as well as training on the new procedure). Another example is there may be a miss of a minor detail in an SOP that has no impact on the quality or efficacy of the compounded product and this may be remedied immediately. Would identification of this miss during an inspection give rise to full enforcement action? SOPs are internal working policies and procedures. If there is a pattern of non-adherence to the pharmacy's SOPs, then it could be indicative of a problem. We recommend modifying this language to reflect a pattern of inconsistency or material events and not single event occurrences.

Again, thank you for the time to present these comments to the committee for consideration.

Sincerely,

Erik Clausen, PharmD
General Manager and Pharmacist-in-Charge