california **pharmacists** association

October 23, 2020

Maria Serpa, Pharm, D
Chair, Enforcement and Compounding Committee
California Board of Pharmacy
2720 Gateway Oaks Dr, Ste. 100
Sacramento, CA 95833

Dear Dr. Serpa,

The California Pharmacists Association (CPhA) thanks you for placing an agenda item to the Enforcement and Compounding Committee's agenda related to compounding animal drugs from bulk drug substances and related federal guidance.

As stated in our August 26 letter to your committee, several of our member pharmacists have received "orders of correction" from Board inspectors stating that licensees are to "update the practice", "please state how pharmacy will comply with this law", "please find a path for compliance" and "PIC educated on 21 CFR 530.13(a)." As noted in the meeting materials, the Committee acknowledges such orders as a means to educate licensees on this regulation and its meaning. While we are grateful for the education route that inspectors have taken, CPhA remains concerned that Board inspectors are taking this regulation text and making conclusions about federal law that are not entirely accurate.

By way of background, the Federal Food, Drug and Cosmetic Act (FD&C) was passed and signed into law in 1938 by President Franklin Roosevelt. The FD&C, through various amendments passed over the years, never addresses compounding animal drugs from bulk drug substances. In 1994, Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) which regulates, among other things, the extralabel use of drugs in animals.

Specifically, within AMDUCA, 21 CFR 530.13(a) states that "*This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine. Nothing in this part shall be construed as permitting compounding from bulk drugs.*"

As noted in the meeting materials, CPhA consulted with legal experts and the phrase "*Nothing in this part shall be construed as permitting compounding from bulk drugs"* is meant to reflect that this individual regulation should not be used as a basis for the allowance compounding from bulk drug substances. However, as we noted earlier, the FD&C is silent on the compounding of animal drugs from bulk substances.

The concern that CPhA has is that Board inspectors are issuing Orders of Correction with the intent of making a policy decision that this practice is forbidden or outlawed altogether. In fact, the FDA's current draft Guidance for Industry (GFI) document proposes conditions in which compounding from bulk drug substances is appropriate. The FDA's Center for Veterinary Medicine (CVM), which issued the GFI, is in its second iteration because the first iteration, published in 2015, had to be withdrawn due to stakeholder feedback about impact to patients. Even the email from Michelle Adams, MPH, (of the Office of the Commissioner of the FDA) which the meeting materials reflect, states that "The regulation at 21 CFR 530.13(a) is not what explicitly prohibits compounding from [bulk drug substances]." The email further goes on to say that "*FDA recognizes that a drug compounded from BDS may be the only treatment option for an animal because there may not be an FDA-approved product that can be used on-label or extralabel to treat the variety of illnesses and conditions that can*

occur in the many different species of animals treated by veterinarians. Therefore, FDA has issued a draft guidance for industry to address such circumstances, draft GFI #256, Compounding Animal Drugs from Bulk Drug Substances."

While the GFI states that the FDA intends "to generally defer to State licensing boards for day-to-day oversight", CPhA would ask the Board to take into consideration the effect on patients that this practice has brought forth. The practice of furnishing compounded medications for animals involves different aspects of medically appropriate healthcare provider judgements. A licensed veterinarian uses his or her education and professional judgement in prescribing appropriate drugs and dosages for their animal patients. The veterinarian will determine that a compounded drug is medically necessary when an animal is suffering from a medical condition and there is no FDA-approved human or veterinary product available and medically appropriate to treat the patient. The pharmacist, using their education and professional judgement, also makes necessary clinical decisions as to the appropriateness of drugs that may need to be compounded. For example, a dog may be prescribed Gabapentin, which is used as an anti-seizure and pain medication. Cats may also be prescribed Gabapentin for anxiety. The commercially available oral liquid form of Gabapentin contains "xylitol" which is a sugar-free sweetener and is a sugar alcohol. While it may provide health benefits for humans, it is toxic for dogs. According to the American Veterinary Medical Association, "*In dogs, xylitol stimulates insulin release that can result in severe, and sometimes deadly, hypoglycemia (low blood sugar) and causes liver damage that can result in bleeding problems and liver failure.*"

Fillers and binders in commercially available products may also interfere with the potency and stability of compounded products for animals. The Board has historically taken, and continues to take, enforcement action against compounders who cannot prove stability of compounded drug preparations in humans as outlined in California regulation. By the same token, the Board may be putting these same compounders in a situation where by only being able to use commercially available products for compounded veterinary drugs can result in medication with substandard stability. For example, methimazole, a commonly used medication in felines for the treatment of hyperthyroidism, has been shown not to maintain stability within the limits of labeled potency after initial testing and at 24 hours when compounded with the FDA approved tablets. This, in turn, can result in patient harm.

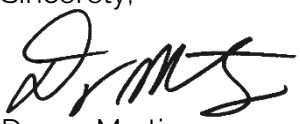
Palatability is also an issue when it comes to compounded medication for animals. In the instance of gabapentin, the commercially available capsules many times cannot be used as the source of the active ingredient due to the excess amount of fillers that are in the capsule. Due to the high powder load, suspending the fillers with the active ingredient creates too large of a volume for administration. This leads to the animal refusing the medication and thus a medication failure.

Magnesium stearate is another filler that is found in a lot of commercially manufactured tablets. When a commercially available product containing this is used to formulate a suspension, especially an oil, it tends to thicken the suspension as it sits over time, which can in turn affect the amount that is measured out as a dosage. This, in turn, can cause inaccurate dosing and can result in either subtherapeutic or super potent dosage being delivered. Fillers can especially be a problem when it comes to the sterile compounding of these medications. They are known to be detrimental when creating sterile preparations.

CPhA is asking the Board to reconsider the actions being done by Board inspectors. At best, these Orders of Correction being given to pharmacists are premature while the FDA is in the process of finalizing the GFI. We expect, based on known feedback to the FDA, the GFI will undergo further revision either later this year or early next year. CPhA believes it to be appropriate to bring this issue back to a future Committee meeting if the GFI becomes finalized so that licensees are clear on what is and isn't allowed. Until then, CPhA believes it's not advisable to continue issuing these orders, as it may result in patients being left without proper medications without any good reason for doing so.

Once again, CPhA appreciates the Committee's willingness to place this item on the agenda for discussion and consideration. If you have any questions about our statements, please don't hesitate to contact me at dmartinez@cpha.com or at (916) 779-4519. Thank you.

Sincerely,



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