**MEETING WITH FDA CENTER FOR VETERINARY MEDICINE**
**May 4, 2022 / May 18, 2022**

Alliance for Pharmacy Compounding
Formerly IACP

**General**

DQSA, the most recent federal law to address compounded medication, establishes clear allowances for the broad use of API for compounding human medication under section 503A. There are far fewer FDA-approved or indexed products available for various animal species. Why does FDA take a much more restrictive approach to animal compounding from API when there are already fewer products available and vastly greater needs to customize medications for various species and individual patients?

- USP has published examples of formulation failures when using FDA-approved products, which are successful when made from API. Can FDA provide us with some examples of instances where they have seen higher levels of safety or efficacy when starting with FDA-approved and indexed drugs vs API?
- Labeling for FDA-approved and indexed drugs does not include excipients in the formulations, which would potentially interfere with a compounder's ability to fully investigate/determine the root cause of a reported ADR if the patient had a reaction to some unknown excipient. What is the liability if a pharmacist is following the GFI and patient harm occurs due to toxic or inappropriate ingredients when the pharmacist has no ability to identify them?
- What concerns does FDA have with the manufacturing and supply chain of API used in animal health compared to API used in human health?

**Compounding for Office Stock**

GFI #256 prohibits pharmacies from compounding from bulk drug substances (BDS) for office stock or food animals unless the BDS is on either the ***List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals*** or the ***List of Bulk Drugs Substances for Compounding Drugs for Use in Food-Producing Animals or Free-Ranging Wildlife Species*** (each, a "positive list).

1. FDA states that it is "concerned that compounded office stock potentially exposes large numbers of animals to drugs of unproven safety, effectiveness, and quality." What is the basis for this assumption?
   - Can FDA describe their experience with or perception of compounded veterinary office stock?
   - Can FDA point to specific instances where large numbers of animals were harmed by drugs compounded for veterinary office use? How would those situations have been prevented with the current GFI?"

2. The proposed positive lists accompanying the final GFI do not list Bulk Drug Substances, but rather an API in a specific strength and dosage form, for a specific indication used in a specific species. Allowances for a limited number of finished products rather than an allowance for the BDS for all applications that a veterinarian determines are appropriate (and assuming they are not copies) defeats the purpose of compounding.
   - What is FDA's rationale for taking this approach?
   - This format for the positive list will be seen as a de facto "approval" from FDA for those formulations when used for those indications. Has FDA considered how facilities may mass-produce and market those specific formulations?

- Would FDA consider adopting an approach where only the BDS is listed and utilized according to a veterinarian's documented therapeutic judgement?

3. When issued as draft guidance in 2019, GFI#256 referred to a list of ***Nominated Bulk Drug Substances That May NOT Be Used to Compound Office Stock Drugs or Antidotes for Use in Animals*** (a negative list). This list has been retitled as ***Bulk Drug Substances Reviewed and Not Listed*** in the final guidance. As such, these bulk drug substances are not covered by the enforcement discretion policy described in GFI#256.

a. Are these BDS allowed for patient-specific compounding?
b. Since most of these BDS were submitted following the release of GFI#230 in 2015, who reviewed these BDS and when?
    i. Can FDA briefly describe the review process, not only the process itself but also who will do the review and under what criteria?
    ii. Why wasn't a committee like PCAC formed?
    iii. Was input solicited from practicing veterinarians and compounding pharmacists?
    iv. How can FDA assure the absence of bias in the decision-making process?
c. What is the process and timeline for review of nominated substances to the list going forward?
    i. How quickly between submission of any nomination of a bulk substance will you add that bulk substance to the Nominated Bulk Drug Substances Currently Under Review list?
    ii. Has FDA estimated the number of BDS it expects to be nominated for the positive list and evaluated the time it will take to make a determination on each nomination?
    iii. Will there be a reasonable phase-out period for drugs that are nominated and rejected for veterinarians to plan for adequate patient care?

4. An example: FDA has declined to add apomorphine ophthalmic because ropinirole is FDA-approved. Does FDA only intend to allow compounding for office stock in situations where nothing is approved, even as a therapeutic alternative when the veterinarian determines it to be appropriate?

- Apomorphine hydrochloride –
    - *Indication:* For the induction of emesis in dogs.
    - *Dosage forms:* 3.125-6.25 mg/mL subconjunctival solution, 6.25 mg subconjunctival tablets.
    - *Reason:* Clevor (ropinirole ophthalmic solution) 30 mg/mL (NADA 141-534) is now FDA-approved for induction of emesis in dogs.

**Adverse Event Reporting**

GFI #256 requires reporting of "adverse events," but "adverse events" is not defined with any specificity. Likewise, GFI #256 requires reporting of "product defects," but "product defects" is not defined with any specificity.

1. Would FDA be willing to work with stakeholders to develop specific definitions for each of these reportable events?

2. Adverse events and product defects are required to be reported within 15 days. We believe that this time period may not permit a full investigation by the compounder and, therefore, could lead to confusion as to the severity of the issue. Adverse events and product defects should be reported within a reasonable time period after conclusion of an investigation.

3. Form 1932a is cumbersome and has been subject to criticism. Does FDA plan to revise Form 1932a and the reporting process?

**Other Concerns**

1. On page 10 of GFI #256, FDA states that "FDA intends to prioritize enforcement of these provisions [when]…(3)the compounded drugs do not meet other manufacturing, product quality, labeling or packaging requirements of the FD&C Act…" Can you be specific as to what provisions of the FD&C Act FDA will be using to prioritize enforcement?

2. In Section B.4, FDA states that enforcement discretion does not apply to drugs that are transferred to a veterinarian at another physical location.

- Is the movement of medication from one location to another restricted if the clinic is under the same ownership?
- Is FDA's intention to conduct audits of veterinarians' offices? If so, will FDA be developing internal audit guidelines to ensure consistency in these audits?

3. The Guidance requires a significant amount of information on the product label, much of which might not fit on a standard prescription label. Is providing some of the required information on a supplemental product insert adequate?

4. Section A. 4 requires all BDS, inactive ingredients and finished drug products used in compounding to meet applicable USP-NF monograph standards and to comply with other FD&C Act requirements for drug components. Flavorings, fillers and many other inactive ingredients do not necessarily have USP monographs and currently do not have to be made in FDA registered facilities. Does GFI#256 change the standards currently applicable to inactive ingredients?

5. OMB Paperwork Reduction Act: FDA CVM estimates the "time required to complete this information collection is one minute per response." How did you derive that number?

6. Most State Boards of Pharmacy will view this guidance as settled law and use it to inform their own rule making and regulations. Furthermore, when Boards of Pharmacy reach out to FDA with questions, they generally contact CDER, not CVM, which can lead to them receiving inaccurate or inappropriate information. What plans does FDA CVM have to educate State Boards of Pharmacy as to what the guidance is and is not? Likewise, will CVM engage with CDER to develop appropriate responses to State Board of Pharmacy questions?