

TO: State Boards of Pharmacy

FROM: Scott Brunner, CAE
Chief Executive Officer

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Director of Public Policy

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SUBJECT: Veterinary Office Stock

The Alliance for Pharmacy Compounding (“APC”) is the voice for pharmacy compounding, representing compounding pharmacists and technicians in both 503A and 503B settings, as well as educators, prescribers, researchers, and suppliers.

The purpose of this memo is to provide background and brief you on impact of regulation some states may be considering regarding compounded preparations for veterinary office use by both 503B outsourcing facilities and 503A pharmacies. In particular, we want to highlight the possible need for amending state regs to adhere to the guidance for industry document (GFI #256) on compounding animal drugs from bulk substances that was recently finalized by the Center for Veterinary Medicine (“CVM”) at the U.S. Food and Drug Administration (“FDA”) in April of this year.

Background:

As you may know, 503B outsourcing facilities were established by the amendments made to the Food, Drug and Cosmetic Act (“FDCA”) as part of the Drug Quality and Security Act (“DQSA”) passed by Congress in November of 2013. Unlike traditional compounding pharmacies, which are licensed and regulated primarily at the state level and enjoy exemptions from certain federal drug manufacturing requirements in section 503A of the FDCA, outsourcing facilities must register with FDA, are subject to risk-based FDA inspections, must be compliant with current good manufacturing practices (“cGMP”), adhere to labeling requirements, and are also subject to federal adverse event reporting requirements.¹

In addition, when an outsourcing facility is compounding using bulk substances, the bulk drug substance must appear on a list developed by FDA of bulk drug substances that can be used in compounding under section 503B, or the drug compounded from the bulk drug substance must appear on FDA’s drug shortage list at the time of compounding, distribution, and dispensing. However, outsourcing facilities are authorized to compound larger quantities of compounded preparations and to distribute those drugs to hospitals, clinics and other prescribers without a patient-specific prescription or dispense them pursuant to a patient-specific prescription as a traditional pharmacy would.²

Both section 503A and section 503B of the FDCA apply **only** to drugs compounded for human use and **do not apply to animal drug compounding**, and there is in fact no federal statute that establishes a federal regulatory framework over animal drug compounding. Compounding for veterinarians for animal use is of course a

¹ See 21 U.S.C. § 353b (2022).

² *Ibid.*

widespread practice that is integral to animal health care. It has been regulated for decades at the state level by boards of pharmacy and boards of veterinary medicine as part of the traditional practice of pharmacy. Despite clear legislative intent to the contrary, FDA and CVM take the position that the FDCA's definition of "new drug" is expansive enough to include drugs compounded for animal use and therefore **all** compounded animal drugs are "new drugs" that do not enjoy the exemptions from the drug manufacturing requirements in sections 503A and 503B of the Act applicable only to human drug compounding.³

The agency has taken the questionable legal position that provisions of the Animal Medicinal Drug Use Clarification Act ("AMDUCA") that allow for the extra-label use of certain human and animal drugs for the treatment of animals give the agency the authority to preempt state pharmacy and veterinary laws and regulate compounding for animal use.⁴ As the Board is aware, off-label use is not compounding; but nonetheless, the agency has used the off-label use language in AMDUCA to establish a federal regulatory framework for animal drug compounding for bulk substances in GFI #256, despite the lack of clear statutory authority to do so.

Guidance for Industry #256 (finalized by FDA/CVM April 2022):

GFI #256 states that *"This guidance represents the Food and Drug Administration's (FDA or Agency) current thinking on this topic. It does not establish any rights for any person and is not binding on FDA or the public."* Also, GFI #256 includes the statement that the guidance represents the agency's enforcement policy for animal drug compounding from bulk substances by "veterinarians or pharmacists in either State-licensed pharmacies or Federal facilities (i.e., facilities operated by the federal government)." Footnote 2 at the bottom of page one notes that *"Throughout this guidance, the terms "pharmacists," "pharmacies," and "veterinarians" refer to those persons or entities that are State-licensed and operate in full compliance with State laws and regulations governing their practice."*⁵ **Based on comments from CVM, we believe the agency will use this footnote to include outsourcing facilities, particularly those included in state laws and regulations as entities required to be licensed by the state pharmacy board, as is the case in many states currently.**

GFI #256 applies only to drugs compounded for animal use from bulk substances and does not apply to animal drugs compounded from FDA-approved animal or human products, which they assert is authorized under the AMDUCA off-label provisions referenced above. As it relates to non-food producing animals, the guidance establishes conditions under which CVM will exercise "enforcement discretion" from illegal manufacturing actions for pharmacies and veterinarians that adhere to its requirements. GFI #256 requires veterinarians and pharmacies to document the "clinical difference" that a drug compounded from bulk substances will have versus an FDA approved product, establishes adverse event reporting requirements, and limits animal drug compounding from bulk substances for veterinary office stock to a positive list to be developed through nominations to and consideration by CVM.⁶

APC and many other pharmacy and veterinary stakeholders,⁷ in addition to many Members of Congress,⁸ weighed in with CVM prior to the agency finalizing GFI #256 to express concerns about the legal authority of the agency to establish such a regulatory framework over animal drug compounding in a guidance document without clear statutory authority from Congress to do so. We also expressed substantive concerns and

³ See CVM GFI #256, p. 3

⁴ See 21 U.S.C. §§ 260b(a)(4) and (a)(5)

⁵ See CVM GFI #256, p. 1

⁶ See CVM GFI #256

⁷ See GFI Enforcement Extension Letter July 2022

⁸ See Congressional FDA GFI 256 enforcement extension letter (08-05-2022) and GFI_256_Letter

questions about how GFI #256 will be implemented and enforced by CVM. Although finalized in April of 2022 with a stated intention to begin enforcement on October 1, 2022, CVM responded to stakeholder and congressional concerns by announcing in September that they would delay enforcement until at least April 1, 2023.⁹ APC and other pharmacy stakeholders continue to seek clarification from CVM on certain provisions in the guidance that will be critical to compliance and that will take time to incorporate into pharmacy and veterinary standard operating procedures.¹⁰ Some of the issues we have raised that still need additional clarification from CVM include the following:

- Clinical difference: GFI #256 imposes new burdens on how veterinarians write prescriptions and communicate with compounders requiring clinical difference statements. Sufficient time to create new systems to comply with these requirements is necessary.
- Compounding from bulk: GFI #256 will require new record keeping practices for compounders and the necessity to put new systems in place to ensure documentation of rationales when bulk drug substances are being used.
- Adverse event reporting: The threshold for an “adverse event” is only described generally and needs to be clarified by the agency prior to enforcement.
- FDA’s list for office stock drugs: Until veterinarians and compounders have clarity on the process and have an adequate opportunity to nominate products for the list – and CVM has had time to review the nominations – this requirement will likely result in many drugs being immediately unavailable.
- Labeling: Compounded products are not FDA-approved drugs so there is no FDA-approved indication for use; therefore, compounders cannot identify an indication on the label, though this is required by GFI #256.
- Outsourcing Facilities: CVM removed from final GFI #256 references to 503B outsourcing facilities that were included in earlier versions of the guidance. However, the agency has indicated that outsourcing facilities will be required to meet GFI #256’s requirements and will be limited in compounding animal drugs from bulk substances for office stock to the positive list of substances now under development. Stakeholders have inquired whether additional or separate guidance applicable to outsourcing facilities is necessary.

APC recommendations for future state regulations:

APC supports authorizing both 503A state licensed pharmacies and 503B outsourcing to compound drugs for animal use, including drugs needed by veterinarians to administer to their animal patients or to dispense to the animal patient’s owner or caretaker.

The location and unique circumstances of a veterinarian practice and the wide variety of animal patients treated by that practice affect whether they may need to order compounded drugs from a pharmacy or from an outsourcing facility. Outsourcing facilities must comply with cGMP standards that make providing smaller batches of compounded drugs on shorter timeframes to veterinarians much more difficult than for pharmacies. State laws and regulations should reflect the need for that flexibility and access while not conflicting with the requirements put on pharmacies and outsourcing facilities in federal law, regulation, and agency policy guidance.

APC’s position is that quantity caps on pharmacy compounding of animal drugs for office stock based on arbitrary percentages or days of supply are inappropriate both for 503A pharmacies and for 503B outsourcing facilities and points out that FDA/CVM intend to apply GFI #256 to both types of entities and the guidance contains no such limitations. FDA has never stated or issued guidance asserting that only outsourcing facilities can provide animal drug office stock or that the agency “prefers” outsourcing facilities over pharmacies to

⁹ See Response to Joint Pharmacy Request for Delay 9_9_22

¹⁰ See GFI 256 Questions for CVM Letter

provide animal drug stock to veterinarians. To the contrary, GFI #256 sets forth the conditions and limitations on animal drug compounding from bulk substances for office stock for both pharmacies and outsourcing facilities and does not contain any such quantity limitations; but rather, limits both entities to bulk substances on a positive list under development by CVM. ¹¹

Therefore, as APC and other pharmacy and veterinary stakeholders continue to seek further clarification from CVM about GFI #256 (and seek to work with NABP toward model regulations that are consistent with the federal guidance on animal drug compounding), the State Boards should be prepared to consider additional revisions to these sections based on that clarification of GFI #256 and any model regulations that should be developed by NABP. APC is committed to keeping Boards of Pharmacy informed of these efforts and to make further recommendations as necessary. We hope you will see our organization as a helpful resource on this and other pharmacy compounding matters.

Recap of APC Suggested Board Actions:

- When considering state regulations, there should be no arbitrary quantity limitation on pharmacies or outsourcing facilities providing vet office stock to protect animal patient access and maintain consistency with federal law as expressed in GFI #256.
- Boards should track GFI #256 and any clarifications, revisions or extensions of enforcement made by CVM and prepare to revise regulations to align with federal law as expressed in GFI #256.
- Boards should urge NABP to work with other pharmacy and veterinary stakeholders to create model regulations on animal drug compounding, both patient specific and non-patient-specific, that align with federal law as expressed in GFI #256 to provide vets and pharmacists consistency and predictability in the regulations of animal drug compounding which will improve both animal patient safety and access to needed compounded animal drugs.

We're grateful for your attention to these important requests. If I may be helpful, please contact Savannah@a4pc.org.

Resources

- CVM GFI 256 – [Link](#)
- Congressional Letters
- Congressional FDA GFI 256 enforcement extension letter (08-05-2022) - [Link](#)
- GFI_256_Letter – [Link](#)
- Industry Letters
- GFI Enforcement Extension Letter July 2022 - [Link](#)
- GFI 256 Questions for CVM Letter – [Link](#)
- CVM Response to Joint Pharmacy Request for Delay 9_9_22 - [Link](#)

¹¹ See CVM GFI #256, p. 1, footnote 2