

# New Draft Guidance on Veterinary Drug Compounding from Bulk Drug Substances

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Food & Drug

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In late May, the United States Food and Drug Administration (FDA) Center for Veterinary Medicine (CVM) published Draft Guidance for Industry No. 230 “Compounding Animal Drugs from Bulk Drug Substances” (Guidance), and withdrew its 2003 Compliance Policy Guide (CPG) 608.400 “Compounding of Drugs for Use in Animals”. The new draft Guidance describes CVM’s current thinking on scenarios in which the Center will agree to exercise regulatory discretion for bulk-active-based drug compounding for non-food-producing animals. The comment period on the draft Guidance ends August 17, 2015 and animal health companies should consider submitting comments.

## Background

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The sections of the Federal Food, Drug, and Cosmetic Act (FDCA) that regulate human drug compounding, sections 503A and 503B (21 U.S.C. §§ 353a and 353b), do not apply to animal drug compounding. Instead, drug compounding for animals is regulated under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA), which also regulates extra-label drug use in animals. FDA codified 21 C.F.R. § 530.13 to formalize the conditions under which it would permit drug compounding for use in animals. That regulation allows drug compounding for animal use by modification of approved animal or human drugs under specific circumstances. It says: “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.” Section 530.13(a).

CVM recognized, however, that there were situations in which no approved human or animal drug existed that could be modified through compounding for use in the particular animal for which the medication was needed. Accordingly, CVM has explained that it will allow drugs to be compounded from bulk pharmaceutical active ingredients under limited circumstances. The CPG listed thirteen issues it would consider in determining whether to take enforcement action against compounding from bulk, including compounding of drugs for use when the health of the animal is not threatened; compounding in anticipation of receiving prescriptions, except in very limited quantities; using commercial scale manufacturing equipment for compounding drug products; compounding for resale or offering compounded drug products at wholesale for resale; compounding where an approved new animal drug or approved new human drug will, in the available dosage form and concentration, appropriately treat the condition; and compounding from a human drug for use in food-producing animals if an approved animal drug can be used for the compounding. Notably, the CPG signaled that CVM would not object to compounding from bulk actives for use in food-producing animals under the conditions listed in the CPG. The CPG also listed certain substances, including methylene blue and sodium

thiosulfate, to which CVM generally did not object if used in veterinary drugs compounded from bulk.

## Draft Guidance

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CVM's new draft Guidance for Industry reflects the Center's revised thinking about types of compounding from bulk actives to which the Center does not intend to object.<sup>1</sup> The Guidance is divided into three sections respectively directed to compounding by pharmacies, veterinarians and "outsourcing facilities".<sup>2</sup> Essentially, the draft Guidance says FDA will evaluate conditions including the following in deciding whether to take enforcement action against compounding animal drugs from bulk actives:

- That the drug is not intended for use in a food producing animal and, for those drugs compounded by pharmacies or outsourcing facilities, the veterinarian's prescription itself or documentation that accompanies the prescription reflects that fact. For these purposes, cattle, swine, chickens, turkeys, sheep, goats, and non-ornamental fish are always considered to be food-producing animals, whether or not the specific animal is intended for food use.
- That the drug is dispensed either by the veterinarian who compounds it or following the receipt of a valid veterinary prescription, and, except for outsourcing facility-compounded drugs, for an individually-identified animal patient. Before receiving a prescription, a pharmacy may compound the drug in a quantity that does not exceed the amount it compounded pursuant to patient-specific prescriptions received over any consecutive 14-day period within the previous 6 months.
- For drugs compounded by either the veterinarian or a state-licensed pharmacy, that there is a change between the compounded drug and the comparable FDA-approved animal or human drug that will produce a clinical difference for the individually-identified animal patient for which the compounded drug is intended. If the veterinarian orders but does not perform the compounding, that the prescription or documentation that accompanies it says, for example: "Compounded drug X would produce a clinical difference for the individually identified animal patient because the approved drug is too

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<sup>1</sup> Because it had withdrawn the CPG before the draft Guidance was finalized, FDA advised stakeholders in the Federal Register Notice announcing the availability of the draft Guidance, "Stakeholders should be aware that, until this draft guidance is finalized, FDA intends to look at the totality of the circumstances when determining whether to take enforcement action for unlawful animal drug compounding activities." 80 Fed. Reg. 28624, 28625 (2015).

<sup>2</sup> The FDCA defines "outsourcing facility" as "a facility at one geographic location or address that is engaged in the compounding of sterile drugs; has elected to register as an outsourcing facility; and complies with all of the requirements of section 503B [of the FDCA]." <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm393571.htm>. FDCA Section 503B requires outsourcing facilities to register annually with FDA, file reports regarding the drugs the facility compounds, and be subject to FDA inspections. Drugs the facility compounds can qualify for exemptions from FDA approval and labeling requirements, but must be produced in accordance with current good manufacturing practices (cGMPs).

large a dose for the animal and cannot be divided or diluted into the small dose required.”

- For drugs compounded by a state-licensed pharmacy, if there is an FDA-approved animal or human drug with the same active ingredient(s), that the pharmacy determines the compounded drug cannot be made from the FDA-approved drug(s), and documents that determination.
- That the bulk drug substance(s) used to compound the drug is(are) manufactured by an establishment registered under section 510 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 360), and accompanied by a valid certificate of analysis, and, for drugs compounded by a state-licensed pharmacy or veterinarian, the drug is compounded in accordance with Chapters <795> and <797> of the United States Pharmacopeia and National Formulary.
- Within 15 days of becoming aware of any product defect or serious adverse event associated with a drug it compounded from bulk, that the person or entity compounding the drug reports it to FDA.
- That the drug is not sold or transferred by an entity other than the pharmacy or outsourcing facility that compounded it, except that a veterinarian compounding the drug may dispense or administer it.
- For drugs compounded by an outsourcing facility, that the bulk drug substance(s) from which the outsourcing facility compounds the drug appear(s) on Appendix A of the draft Guidance. As published, however, the draft Guidance did not list any substances in Attachment A and requests comments to populate the list. FDA intends to include substances on the Appendix for which 1) there is no approved animal or human drug that could be used extra-label or from which a drug could be compounded to treat the condition in the animal, 2) immediate treatment is necessary to avoid animal suffering or death, and 3) FDA has not identified a significant safety concern.

## Summary

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The period to submit comments on the draft Guidance ends August 17, 2015. Companies may want to consider whether the draft Guidance is sufficiently robust in protecting approved veterinary drugs from unapproved copying by compounders. We note that the Guidance is limited to compounding for use in non-food-producing animals and that it requires veterinarians to assert that the compounded drug represents a difference with an approved product. Companies should, however, consider situations in which products compounded from bulk are competing with approved products and whether the draft Guidance appropriately addresses all such scenarios.

FDA also specifically seeks comments on the following subjects<sup>3</sup>:

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<sup>3</sup> 80 Fed. Reg. at 28625-26.

- Whether the final guidance should address the issue of FDA-approved animal and human drugs that are in shortage or are otherwise unavailable and, if so, how and when?
- Whether United States Pharmacopeia and National Formulary (USP–NF) chapters <795> and <797> provide suitable standards for animal drugs compounded by veterinarians, and if not, what standards should apply?
- Whether veterinarians should be able to sell or transfer an animal drug a pharmacy or outsourcing facility has compounded from bulk?
- How FDA should apply the condition to identify an individual patient when it is not possible to identify an individual animal (such as for koi in a koi pond)?
- Whether and how the final guidance should limit the amount of compounded animal drugs a pharmacy or outsourcing facility can ship in interstate commerce?
- Whether registered outsourcing facilities should be able to compound for an individually-identified animal patient animal drugs from bulk drug substances that do not appear on Appendix A?
- Whether additional guidance is needed to address drug repackaging for animal use; how widespread the practice is; what drug types are involved and why; and what problems have been identified?
- Whether additional guidance is needed regarding compounding animal drugs from approved animal or human drugs and regarding compounding from bulk for food-producing animals?
- Regarding the 15-day reporting condition in the draft Guidance, how many state-licensed pharmacies and veterinarians might file such reports; whether these entities are filing the same or similar information with any state regulatory agency and, if so, how many are filed annually; how FDA should define the terms “product defect” and “serious adverse event”; and whether FDA can achieve the same objective through other means and, if so, what are they?

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Food & Drug practice group:

Jeannie Perron  
MaryJoy Ballantyne

+1 202 662 5687  
+1 202 662 5933

[jperron@cov.com](mailto:jperron@cov.com)  
[mballantyne@cov.com](mailto:mballantyne@cov.com)

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