

**Guidance for FDA Staff and
Industry**

Compliance Policy Guides Manual

Sec. 608.400

Compounding of Drugs for Use in Animals

Submit written comments regarding this guidance document identified with **Docket No. 2003D-0290** to the Dockets Management Branch (HFA-305), 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

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U.S. Department of Health and Human Services
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Compliance Policy Guide
Compliance Policy Guidance for FDA Staff and Industry

CHAPTER – 6
SUBCHAPTER - 600

Sec. 608.400 - Compounding of Drugs for Use in Animals

This compliance policy guidance is intended to provide guidance and instructions to FDA staff, industry, and the public for obtaining information to help fulfill the Agency's plans regarding the compounding of drugs for use in animals. The compliance policy guidance does not create or confer any rights for or on any person and does not operate to bind the Food and Drug Administration (FDA) or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute and regulations. It is intended for FDA personnel, industry, and the public and is available electronically to the public.

INTRODUCTION

This document provides guidance to drug compounders, veterinarians, and the staff of the Food and Drug Administration (FDA) on how the Agency intends to address compounding of drugs intended for use in animals. This guidance describes FDA's current thinking on what types of compounding might be subject to enforcement action.

BACKGROUND

FDA announced the availability of Compliance Policy Guide (CPG) section 608.400 entitled "Compounding of Drugs for Use in Animals" on July 3, 1996 (61 FR 34849), to provide guidance to FDA's field and headquarters staff with regard to the compounding of animal drugs by veterinarians and pharmacists for use in animals. There is a potential for causing harm to public health and to animals when drug products are compounded, distributed, and used in the absence of adequate and well-controlled safety and effectiveness data or adherence to the principles of contemporary pharmaceutical chemistry and current good manufacturing practices. Use of compounded drugs in animals can result in adverse reactions and animal deaths. Furthermore, because the pharmacokinetics and depletion times for residues from compounded products intended for use in food-producing animals are not known, the assignment of an extemporaneous withdrawal time may result in potentially harmful residues in food. Inactive ingredients, such as excipients and vehicles, from unapproved or unknown origins may also pose additional risk (e.g., Freund's adjuvant, a carcinogen).

FDA is updating this guidance to be consistent, to the extent practicable, with the scope of compounding permitted under regulations implementing the Animal Medicinal Drug Use Clarification Act of 1994, to describe what factors FDA will consider in exercising its enforcement discretion regarding compounding of drugs intended for use in animals, and to

ensure the consistency of its policies with regard to compounding of drugs intended for use in humans and in animals.

DISCUSSION

The Federal Food, Drug, and Cosmetic Act (**the Act**) does not distinguish compounding from manufacturing or other processing of drugs for use in animals. FDA acknowledges the use of compounding within certain areas of veterinary practice. The current state of veterinary medicine requires products to treat many conditions in a number of different species, some of which are known to have unique physiological characteristics. Furthermore, FDA regulations specifically permit the compounding of products from approved animal or human drugs under the conditions set forth in 21 CFR 530.13. This activity is not the subject of this guidance.

However, FDA is greatly concerned about veterinarians and pharmacies that are engaged in manufacturing and distributing unapproved new animal drugs in a manner that is clearly outside the bounds of traditional pharmacy practice and that violates the Act (e.g., compounding that is intended to circumvent the drug approval process and provide for the mass marketing of products that have been produced with little or no quality control or manufacturing standards to ensure the purity, potency, and stability of the product). These activities are the focus of this guidance. Pharmacies and veterinarians who engage in activities analogous to manufacturing and distributing drugs for use in animals may be held to the same provisions of the Act as manufacturers.

With regard to compounding from bulk drug substances, two Federal Appeals Court decisions, *United States v. Algon Chemical Inc.*, 879 F.2d 1154 (3d Cir. 1989) and *United States v. 9/1 Kg. Containers*, 854 F.2d 173 (7th Cir. 1988), affirmed the FDA position that the Act does not permit veterinarians to compound unapproved finished drug products from bulk drug substances, unless the finished drug is not a new animal drug. The principle established by the court applies equally to compounding by pharmacists.

Neither the Act nor its implementing regulations exempt veterinarians or pharmacists from the approval requirements in the new animal drug provisions of the Act, 21 U.S.C. Section 360b. In the absence of an approved new animal drug application, the compounding of a new animal drug from any unapproved drug or from bulk drug substances results in an adulterated new animal drug in violation of section 21 U.S.C. Section 351(a)(5). The compounding of a new animal drug from an approved human or animal drug also results in an adulterated new animal drug in violation of 21 U.S.C. Section 351(a)(5), unless the conditions set forth in 21 CFR 530.13(b) are met.

DEFINITIONS

1. “Bulk drug substance,” as defined in 21 CFR 207.3(a)(4), means any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or

packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances.

2. "Compounding" does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling
3. A "valid veterinarian-client-patient relationship" (**valid VCPR**), as defined in 21 CFR 530.3(i), is one in which:
 - a. A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;
 - b. There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and
 - c. The practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.

POLICY:

Generally, FDA will defer to state authorities regarding the day-to-day regulation of compounding by veterinarians and pharmacists of animal and human drugs that are intended for use in animals. FDA anticipates that, in such cases, cooperative efforts between the states and the Agency will result in coordinated investigations, referrals, and follow-up actions by the states.

However, when the scope and nature of activities of veterinarians and pharmacists raise the kinds of concerns normally associated with a drug manufacturer and result in significant violations of the new animal drug, adulteration, or misbranding provisions of the Act, FDA has determined that it will seriously consider enforcement action. In determining whether to initiate such an action, the Agency will consider whether the veterinarian or pharmacist engages in any of the following acts:

1. Compounding of drugs for use in situations (a) where the health of the animal is not threatened; and (b) where suffering or death of the animal is not likely to result from failure to treat.
2. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities in relation to the amounts of drugs compounded after receiving prescriptions issued within the confines of a valid VCPR.

3. Compounding of drugs that are prohibited for extralabel use in food-producing or nonfood-producing animals, under 21 CFR 530.41(a) and (b) respectively, because the drugs present a risk to the public health.
4. Compounding finished drugs from human or animal drugs that are not the subject of an approved application, or from bulk drug substances, other than those specifically addressed for regulatory discretion by the FDA, Center for Veterinary Medicine, e.g., antidotes (see **Appendix A**). Inquiries about compounding from unapproved drugs or bulk drug substances should be directed to CVM, Division of Compliance, 301-827-1168.
5. Compounding from approved human drugs for which FDA has implemented a restricted distribution system.
6. Using commercial scale manufacturing equipment for compounding drug products.
7. Compounding drugs for third parties who resell to individual patients, or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
8. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.
9. Compounding of drugs for use in animals where an approved new animal drug or approved new human drug used as labeled or in conformity with 21 CFR Part 530 will, in the available dosage form and concentration, appropriately treat the condition diagnosed.
10. Compounding from a human drug for use in food-producing animals if an approved animal drug can be used for the compounding.
11. Instances where illegal residues occur in meat, milk, eggs, honey, aquaculture, or other food-producing animal products, and such residues were caused by the use of a compounded drug.
12. Labeling a compounded drug with a withdrawal time established by the pharmacist instead of the prescribing veterinarian.
13. Labeling of compounded drugs without sufficient information, such as withdrawal times for drugs for food-producing animals or other categories of information that are described in 21 CFR 530.12.

The foregoing list of factors is not intended to be all inclusive. Other factors may be appropriate for consideration in a particular case.

REGULATORY ACTION GUIDANCE:

District offices are encouraged to consult with state regulatory authorities to assure coherent application of this guidance to establishments that are operating outside of the traditional practice of pharmacy.

Follow FDA's laws and procedures prior to sharing non-public information with the public, or federal, state, local, and foreign government officials.

FDA-initiated regulatory action may include issuing a warning letter, seizure, injunction, and/or prosecution. Charges may include, but need not be limited to, violations of 21 U.S.C. Sections 351(a)(2)(B), 351(a)(5), 352(a), 352(f)(1), and 352(o) of the Act. Tissue residue violations are covered under 21 U.S.C. Section 342(a)(2)(C)(ii) of the Act.

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APPENDIX A

LIST OF BULK DRUG SUBSTANCES FOR COMPOUNDING AND SUBSEQUENT USE IN ANIMALS TO WHICH CVM WOULD NOT ORDINARILY OBJECT

Ammonium molybdate
Ammonium tetrathiomolybdate
Ferric ferrocyanide
Methylene blue
Picrotoxin
Pilocarpine
Sodium nitrite
Sodium thiosulfate
Tannic acid