

VETERINARY Compounding

Veterinarians occasionally use compounded preparations to meet a specific patient's medical need. The purpose of this brochure, created jointly by the Animal Health Institute (AHI), the American Veterinary Distributors Association (AVDA), and the American Veterinary Medical Association (AVMA), is to explain the Food and Drug Administration (FDA) requirements for compounding preparations for veterinary use and the distinction between drug products approved by the US FDA and compounded preparations.¹



Table of Contents

Federal Regulations to Follow	1
Compounding from Unapproved Substances	2
Compounded Preparations Are Not Generic Drug Products	3
How to Identify an FDA-Approved Animal Drug Product	3
Inappropriate Compounding Pharmacy Practices	4
Questions to Ask Your Pharmacist	5-7
Characteristics of FDA-Approved Products vs. Compounded Preparations	8-9
Additional Resources	Back Cover

What is compounding?

Compounding that is consistent with the FDA Extra-Label Drug Use regulations is the customized manipulation of an approved drug(s) by a veterinarian, or by a pharmacist upon the prescription of a veterinarian, to meet the needs of a particular patient. For example, mixing two injectable drugs is compounding. Preparing a paste or suspension from crushed tablets is another example of compounding. Likewise, adding flavoring to a drug is compounding. Be aware, however, that products are being promoted to veterinarians under the guise of compounding that do not fit this definition. According to the FDA, legal compounding is not the formulation of preparations from bulk or raw active ingredients. Compounding should not be used as a way of circumventing the drug approval process or producing a product so it can be sold for less cost than an FDA-approved drug.

Federal Regulations to Follow

The FDA regulations and Compliance Policy Guide 608.400 “Compounding of Drugs for Use in Animals” describe specific circumstances under which FDA will either permit compounding for use in animals or may exercise its enforcement discretion:

- A valid Veterinarian-Client-Patient relationship exists.
- The health of an animal is threatened, or suffering or death may result from failure to treat.
- Compounding is performed by a licensed veterinarian or a licensed pharmacist on the order of a veterinarian within the scope of professional practice.
- There is no approved animal or human drug that, when used as labeled or in conformity with the extralabel drug use regulations, will, in the available dosage form and concentration, appropriately treat the condition diagnosed.
- Preparations are compounded from FDA-approved animal or human drugs. Nothing in the regulations permits compounding from bulk (raw pharmaceutical ingredient) drugs.
- Compounding from a human drug for use in food-producing animals is not permitted if an approved animal drug can be used for the compounding.
- For animals produced for human consumption, the veterinarian institutes procedures to assure the identity of treated animals, establishes a substantially extended withdrawal interval for the compounded preparation supported by appropriate scientific information, and ensures food safety. Compounding is not permitted if it results in violative food residue or any residue that may present a risk to public health.
- No drug may be compounded for food animals from drugs listed on the prohibited list (go to www.fda.gov/AnimalVeterinary/ and enter “530.41” in the search engine).
- Veterinarians comply with all aspects of the federal extralabel drug use regulations including record-keeping and labeling requirements.
- Adequate procedures and processes are followed that ensure the safety and effectiveness of the compounded product.
- The scale of compounding in advance of receiving prescriptions is limited and commensurate with the established need for compounded products.
- All relevant state laws relating to the compounding of drugs for use in animals are followed.

Compounding from Unapproved Substances

Federal regulations describe specific circumstances under which veterinarians, or pharmacists upon veterinarians' prescriptions, are legally permitted to compound drugs for extralabel use in animals. Under these regulations, compounding for non-food animals may only be performed using FDA-approved animal or human drug products and only when there is no approved animal or human drug product available in the relevant dosage form and concentration to appropriately treat the diagnosed condition. Compounding from human drugs for use in food animals is not allowed if an approved animal drug can be utilized.

However, veterinarians may occasionally face situations where they diagnose conditions for which no FDA-approved product is available for use to relieve the animal's suffering or prevent the animal's death. 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. Although FDA considers it a violation of the Federal Food, Drug and Cosmetic Act, it acknowledges the need for compounding from bulk active or raw ingredients within certain areas of veterinary practice. For example, the FDA published a list of bulk drug substances for compounding and subsequent use in animals to which FDA would exercise enforcement discretion and not ordinarily object, specifically poison antidotes available only as bulk chemicals. In these situations or others, veterinarians may find it necessary to compound, or prescribe for a pharmacist to compound, from the bulk chemical to satisfy the requirements of good veterinary medical practice. The veterinarian and/or pharmacist are then responsible for the safety and efficacy of the compounded drug. In cases where no approved drug or combination of approved drugs can adequately address a specific patient's need, veterinarians and pharmacists must carefully assess whether the use of an unapproved substance in a compounded veterinary drug is consistent with state and federal law and FDA policy.

Compounded Preparations are not Generic Drug Products

Generic drug products are very different from compounded preparations. Generic drug products are FDA-approved, which requires a demonstration of bioequivalence of safety and efficacy with the pioneer drug product. Generic animal drug products are identified by an Abbreviated New Animal Drug Application (ANADA) number on their label or in FDA drug references. In contrast to generic drugs, compounded preparations lack FDA approval.

How to Identify an FDA-Approved Animal Drug Product

FDA-approved animal drug products can be identified by the six-digit New Animal Drug Application (NADA) number for brand-name drug products or the six-digit ANADA number for generic drug products. The NADA or ANADA number and the statement "Approved by FDA" can usually be found on the drug product's label including the package insert. It may also be helpful to cross-check with a drug reference, such as the FDA's online databases, Animal Drugs @ FDA and FDA Orange Book, which list approved animal and human drug products, respectively. The presence of a National Drug Code (NDC) number on a product label does not confer FDA approval.

Inappropriate Compounding Pharmacy Practices Include the Following:

- **Compounded preparations that mimic FDA-approved drug products.**

Beware of pharmacies that purport to sell compounded preparations that are the same as commercially available FDA-approved products or similar but with a minor difference, such as a slightly different concentration. Often these are marketed as a cheaper alternative to the approved drug. FDA has not identified price as a legitimate reason for prescribing a compounded preparation. Legitimate compounding is prescription-driven and predicated upon the need to customize a preparation to meet an individual patient's needs.

- **Manufacturing under the guise of compounding.**

The use of commercial scale equipment and preparation of large quantities of compounded products in anticipation of receiving orders.

- **Promotion and advertising of unapproved new animal drugs.**

FDA considers products compounded from bulk active ingredients to be unapproved new animal drugs.

- **Wholesale distribution of compounded preparations.**

It is not legal for compounded preparations to be developed in large quantities and sold to third parties (including veterinarians and companies) or wholesalers, to resell to individual patients.

Questions To Ask Your Pharmacist

- Q:** What are your credentials for preparing compounds for use in animals?
- A:** Pharmacy undergraduate education offers varying degrees of compounding instruction, and training in veterinary pharmacotherapy may be limited. Postgraduate pharmacy training can include continuing education certificates and membership in veterinary pharmacy professional organizations. Consider whether the pharmacy is compliant with United States Pharmacopeia (USP) standards, such as General Chapters <795> and <797> for non-sterile and sterile compounding for both humans and animals.
- Q:** Are you licensed as a pharmacy in my state? Is the pharmacy accredited by an independent body?
- A:** Most state boards of pharmacy require that an out-of-state pharmacy register with their state prior to filling prescriptions to be mailed into their state. Veterinarians can inquire with their state board of pharmacy to ascertain the status of a pharmacy's license and to gain valuable information including the pharmacy permit number. Also, consider whether the pharmacy is certified by an independent body. Examples include the National Association of Boards of Pharmacy's Vet-VIPPS and the Pharmacy Compounding Accreditation Board.
- Q:** What sources will you use for the components and formula for the compound I am prescribing?
- A:** FDA-approved products should be used to make compounded preparations. In cases where no approved drug or combination of approved drugs can adequately address a specific patient's need, veterinarians and pharmacists must carefully assess whether the use of an unapproved substance in a compounded veterinary drug is consistent with state and federal law and FDA policy. If medical necessity dictates that a bulk active ingredient be used in the formulation, the pharmacist should ensure the integrity of all components used (e.g. certificates of analysis, USP National Formulary grade substance, or substances obtained from an FDA-registered supplier.) The pharmacist can also identify the company from which products are purchased as well as the domestic or international location of the company. Formulas used for compounding should be obtained from a peer-reviewed source (e.g. published studies in primary literature, textbooks, or the USP) when possible.

Questions To Ask Your Pharmacist

Q: What assurances can be offered regarding the quality and stability of the preparation?

A: There are both benefits and risks associated with compounded preparations used in animals. While they may be useful when medically necessary, the reality is that no assurances can be given without sufficient scientific data backing the preparation method of each active ingredient. However, some assurances of the quality of active ingredients and preparation methods can be offered by the pharmacy to help mitigate certain risks that are also associated with compounding, such as poor quality ingredients or unstable preparations.

Q: How do I know that the compounded preparations such as drug delivery systems or drug combinations will be safe and effective?

A: You don't. There is no assurance, like there is with an FDA-approved drug, that a compounded preparation will be safe or effective for the condition you are treating. Extensive laboratory and clinical studies are needed to assure that these preparations achieve adequate blood and tissue levels on a consistent basis from batch to batch as well as being safe to the animal. Sponsors of FDA approved products must conduct in vivo pre-market testing. Veterinarians should seek results from scientifically designed studies demonstrating the efficacy and safety of a particular preparation, including drug delivery systems in the target species. These study results showing suitable stability, relative efficacy, and safety in the target species can be considered in the benefit-risk analysis a veterinarian performs when deciding whether to use the particular preparation in the patient.

Q: What data or other sources will you use for the assigned beyond-use date for the compound I am prescribing?

A: Veterinarians should inquire as to how the beyond-use date was established. Beyond-use dates and expiration dates are not the same. Expiration dates for the chemical and physical stability of manufactured products are determined from results of rigorous analytical and performance testing, and they are specific for a particular formulation in its container and at stated exposure conditions. According to the USP (e.g. General Chapters <795> and <797>), the compounding pharmacist is responsible for setting the beyond-use date within the conservative default parameters established by USP.

Q: Will you prepare a compound specifically for my patient, or is it prepared in advance?

A: Pharmacies should compound medications pursuant to the receipt of a valid prescription.

Q: How would I report an adverse event that I think is associated with use of a compounded preparation?

A: Veterinarians should report suspected adverse events or product failures involving compounded preparations to the compounding pharmacist, the State Board of Pharmacy and the FDA Center for Veterinary Medicine. Instructions for reporting adverse events to FDA can be found at the FDA website:

<http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm>

Pharmacists should instruct pet owners to contact both the prescribing veterinarian and pharmacist immediately if a compounded preparation has caused an adverse event.

¹ *The information in this brochure should not be construed as legal advice or legal opinion on specific facts, and is not intended as a definitive statement on the subject of compounding preparations for veterinary use. Rather, this brochure is intended to serve as a tool for veterinarians and other readers, providing practical information on the subject of veterinary compounding.*

Characteristics of FDA-Approved Products vs. Compounded Preparations

CHARACTERISTICS	BENEFIT	FDA APPROVED DRUG PRODUCT: NEW ANIMAL DRUG (NADA)/ GENERIC ANIMAL DRUG (ANADA)	COMPOUNDED DRUG
FDA approval	Agency substantiation of manufacturers' drug label claims that are supported with substantial scientific evidence and language that are sufficiently clear to ensure safe and effective use of the product.	YES	NO
Tested in labeled animal species in laboratory and field trials	Drug's safety and efficacy must be scientifically demonstrated	YES	NO
Manufactured according to current Good Manufacturing Practices (cGMPs)	Ensures each batch is manufactured within specification for therapeutic consistency	YES	NO
Manufacturing facilities inspected and approved by FDA	Ensures manufacturer compliance with FDA regulations governing product quality	YES	NO
Ongoing stability testing of drugs	Ensures drug shelf life matches labeled expiration date	YES	NO

CHARACTERISTICS	BENEFIT	FDA APPROVED DRUG PRODUCT: NEW ANIMAL DRUG (NADA)/ GENERIC ANIMAL DRUG (ANADA)	COMPOUNDED DRUG
Prescription drug advertising and promotional material submitted to and reviewed by FDA	Means nothing is false or misleading about the materials	YES	NO
Adverse events or lack of efficacy reported to FDA	Permits unanticipated yet significant post-marketing experiences to be communicated back from FDA to the veterinarian	YES	YES
Analytical testing of product prior to release for <i>Strength</i> <i>Identity</i> <i>Purity</i>	Ensures that product contains what is represented on the label	YES YES YES	UNKNOWN UNKNOWN UNKNOWN

Resources

- FDA Center for Veterinary Medicine
<http://www.fda.gov/AnimalVeterinary/default.htm>
- FDA Extralabel Drug Use Rules (21 CFR 530.3, 530.20, 530.41)
<http://www.gpo.gov/fdsys>
- CPG Sec. 608.400 Compounding of Drugs for Use in Animals
<http://www.fda.gov>
- Animal Drugs @ FDA
<http://www.accessdata.fda.gov/scripts/animaldrugsatfda>
- Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations
<http://www.accessdata.fda.gov/scripts/cder/ob/docs/queryai.cfm>
- United States Pharmacopeia National Formulary (USP-NF)
<http://www.usp.org>
- Papich, MG. Drug Compounding for Veterinary Patients. AAPS J 2005; 07(02):E281-E287
- National Association of Boards of Pharmacy – <http://www.nabp.net>
- American Veterinary Medical Association – <http://www.avma.org>
- American Association of Bovine Practitioners – <http://www.aabp.org>
- American Association of Equine Practitioners – <http://www.aaep.org>
- Pharmacy Compounding Accreditation Board – <http://www.pcab.info>
- American Association of Feline Practitioners – <http://www.catvets.com>

This document was prepared by the Animal Health Institute (AHI), the American Veterinary Medical Association (AVMA), and the American Veterinary Distributors Association (AVDA).

For additional copies of this brochure, contact AVDA headquarters at 443-640-1040 or avda@ksgroup.org.