

EXTRA LABEL DRUG USE AND COMPOUNDING



BASICS

OVERVIEW

- Extralabel Drug Use (ELDU) is the use of a Food and Drug Administration (FDA) approved drug in a way that deviates from the label, but meets specific conditions set by the FDA and the 1994 Animal Medicinal Drug Use Clarification Act (AMDUCA).
 - Deviations include use in another species, other indication(s), different dose or frequency, or another route of administration.
- Compounding is described as combining, mixing, or altering the ingredients of an FDA approved drug by a licensed veterinarian or pharmacist to meet the specific needs of an individual patient.
 - Compounded drugs are not FDA approved nor are they generic equivalents.
 - If poor procedures are followed, compounded drugs may be more or less potent than expected or can be contaminated or adulterated.
 - Compounding animal drugs from bulk drugs or substances is illegal under the Federal Food, Drug and Cosmetic Act (FFDCA), but the FDA acknowledges the need for such compounding under certain limited circumstances. Bulk drugs are raw, active pharmaceutical ingredients used to make final FDA approved drugs.
 - It is currently illegal for compounded products to be manufactured in large quantities and sold to licensed veterinarians or wholesalers for resale.
- Animal biologics (vaccines) are regulated by the United States Department of Agriculture Center for Veterinary Biologics (USDA CVB) and not subject to ELDU.
- Pesticide use is under the jurisdiction of the Environmental Protection Agency (EPA) and not subject to ELDU.
- The regulations described in this chapter are specific to the United States

VETERINARY CLIENT PATIENT RELATIONSHIP (VCPR)

- Occurs when the veterinarian has:
 - Assumed responsibility for medical decisions and the client has agreed to follow the instructions
 - Has sufficient knowledge of the animal(s) to initiate a diagnosis
 - Is readily available for problems or questions involving medical treatment, and
 - Has examined the animal(s), and/or has made medically appropriate and timely visits to the premises.

EXTRA LABEL DRUG USE

- Allowed under the following circumstances:
 - Use of FDA-approved animal or human drugs
 - Health of the animal is threatened or suffering/death may result from failure to treat
 - Performed within the context of a valid VCPR
- EXCLUDES the following uses:
 - Initiation by a non-veterinarian (e.g., producer, animal caretaker)
 - Production drugs (e.g., weight gain, estrus synchronization)
 - In or on an animal feed
 - Resultant drug residues that present a public health threat or are above established limits
- Veterinarians must:
 - Diagnose and evaluate conditions for which the drug is used
 - Correctly identify the specific animal(s) and maintain identification

- Determine that no FDA approved drug labeled for use in the particular species is available or one that has the same active ingredient, concentration, and dosage form **OR** find that the FDA approved version is ineffective for medical needs.
- Provide a long withdrawal interval with scientific backing (refer to Food Animal Residue Avoidance Databank or FARAD)
- If human food safety information is unavailable, ensure that the treated animal will not enter the human food supply
- Label the product accordingly
 - Veterinarian's name and address (or pharmacy's name and address)
 - Name of drug and/or active ingredients
 - Complete directions for use (e.g., species, animal identification, dosage, frequency, duration of therapy)
 - Cautionary statements
 - Veterinarian's specified withdrawal period
- Keep adequate records so the FDA can determine whether ELDU practices present a public health risk. Records must include:
 - Drug name and/or active ingredients
 - Medical condition treated
 - Species and number of treated animals, either a group or individuals
 - Dosage administered
 - Duration of treatment
 - Specified withdrawal, withholding, or discard times

PROHIBITED USE

- In food producing animals, extralabel use of an approved human drug is **NOT** permitted if an extralabel use of approved animal drug can be used to treat the condition.
- ELDU where analytical methods for tissue detection have not been or cannot be established is prohibited
- Where ELDU poses a public health risk
- The following drugs are prohibited from any extralabel use in food-producing animals:
 - Chloramphenicol
 - Clenbuterol
 - Diethylstilbestrol (DES)
 - Dimetridazole
 - Ipronidazole
 - Other nitroimidazoles
 - Furazolidone
 - Nitrofurazone
 - Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine)
 - Fluoroquinolones
 - Glycopeptides
 - Phenylbutazone in female dairy cattle 20 months of age or older
 - Cephalosporin (excluding cephalixin) in cattle, swine, chickens, turkey when:
 - Cephalosporin drugs are used at unapproved dose rates, frequencies, routes of administration, or duration
 - Cephalosporin drugs are used in cattle, swine, chickens, or turkeys and not approved for use in that species
 - Cephalosporin drugs are used for disease prevention

COMPOUNDING ANIMAL DRUGS

- Drugs may be legally compounded for use in a single animal under ELDU regulations provided:
 - There is no approved animal or human drug available to treat the condition
 - Only FDA approved animal or human drugs are used.

- Special Note: Compounding from an FDA approved human drug for use in food-producing animals is not permitted if an approved animal drug can be used for compounding
- Compounding is performed by a licensed pharmacist or veterinarian within the scope of their professional practice
- Adequate procedures are utilized to ensure safety and efficacy of the compounded drug
- Scale of compounding is commensurate with the need for the product
- All relevant state compounding laws are followed
- All other provisions of ELDU use regulations are met
- Bulk compounding
 - Compounding animal drugs from bulk substances is illegal. Bulk substances are the actual active ingredients used to manufacture finished FDA approved drugs
 - The American Veterinary Medical Association (AVMA) believes that bulk compounding is necessary for some specific instances such as poison antidotes and euthanasia compounds
 - The FDA has a draft proposal on compounding drugs from bulk substances that describes the conditions under which the FDA does not intend to take action. It is not yet implemented in 2016, but may be in the near future.
- All compounded drugs must be prescribed for a single, individual animal.
 - It is currently illegal for compounded products to be manufactured in large quantities and sold to licensed veterinarians or wholesalers for resale.
 - The AVMA, however, believes that licensed veterinarians should be able to have enough compounded products to meet urgent/emergency needs.
- Generally, the FDA will defer to states regarding the day-to-day regulation of animal drug compounding.
- In determining whether significant violations of FDA law by veterinarians have occurred, CVM will consider any combination of the following factors:
 - Compounding of drugs for use in situations where the health of the animal is not threatened or where suffering or death of the animal is unlikely to result from failure to treat.
 - Compounding of drugs that are prohibited under the ELDU regulation
 - Compounding from bulk drug substances
 - Compounding from approved human drugs for which the FDA has implemented a restricted distribution system.
 - 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.
 - Failing to operate in conformance with applicable state law regulating the practice of pharmacy.
 - Instances where illegal residues occur in food-producing animal products and were caused by the use of a compounded drug.
 - Labeling a compounded drug with a withdrawal time established by the pharmacist instead of the prescribing veterinarian.
 - Labeling of compounded drugs with insufficient ELDU information



MISCELLANEOUS

ABBREVIATIONS

- **AMDUCA**= Animal Medicinal Drug Use Clarification Act
- **CVB** = Center for Veterinary Biologics
- **CVM**= FDA/Center for Veterinary Medicine
- **ELDU**= Extra-label Drug Use
- **EPA**= U.S. Environmental Protection Agency
- **FARAD** = Food Animal Residue Avoidance Databank

- **FDA**= U.S. Food and Drug Administration
- **FFDCA**= Federal Food, Drug and Cosmetic Act
- **USDA**= United States Department of Agriculture
- **VCPR** = Veterinarian-Client-Patient Relationship

Suggested Reading

Compounding from Unapproved (Bulk) Substances in Food Animals. Available at:

<https://www.avma.org/kb/policies/pages/compounding-from-unapproved-bulk-substances-in-food-animals.aspx>. Accessed 5/15/2016.

Compounding and the FDA: Questions and Answers.

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm>. Accessed 5/12/2016.

Drug Compounding for Animals. FDA Could Improve Oversight with Better Information and guidance.

September 2015. Available at: <http://gao.gov/assets/680/672749.pdf>. 5/14/2016.

Extralabel Drug Use (ELDU) Resource Page. Available at: <http://www.farad.org/eldu/eldumain.asp>. Accessed 5/8/2016.

Extralabel drug use and facts. Available at: <https://www.avma.org/KB/Resources/FAQs/Pages/ELDU-and-AMDUCA-FAQs.aspx>. Accessed 5/10/2016.

The Ins and Outs of Extra-Label Drug Use in Animals: A Resource for Veterinarians. Available at:

<http://www.fda.gov/animalveterinary/resourcesforyou/ucm380135.htm>. Accessed May 9, 2016.

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