

PHARMACEUTICAL USE LEGAL ISSUES



BASICS

OVERVIEW

- This chapter will cover drug-related legalities present in the USA. Other countries will differ in specifics; however, the major topics are consistent.
- History
 - Pure Food and Drug Act (1906) regulated food and drug interstate commerce.
 - Federal Food, Drug, and Cosmetic Act (1938) required manufacturers to show evidence that products were safe.
 - Veterinary division of Food and Drug Administration (FDA) established in 1953, enlarged in 1958 and later became BVM (Bureau of Veterinary Medicine).
 - BVM became CVM (Center for Veterinary Medicine) in 1984.
 - Drug Enforcement Administration (DEA) established in 1973 as a single agency to enforce federal drug laws and consolidate the federal government's drug control activities.
- FDA CVM currently regulates pharmaceuticals used by veterinarians in their practice.
- DEA authorizes veterinary prescribing and dispensing of controlled medications.

LAWS GOVERNING VETERINARY DRUG USE

- Federal and state versions of the Food, Drug, and Cosmetic Act and the Controlled Drugs Act currently exist and mirror each other, with the state version differing to reflect local conditions.
- Individual state Veterinary Practice Acts (VPA) and Pharmacy Acts also apply.
- Veterinarians must follow all of the laws and, when they are in conflict or differ, the more stringent law must be followed.

IMPORTANT VETERINARY ACTS

- Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA) provided more flexibility to veterinarians to treat animals. The act made it legal for veterinarians to use, under specific

circumstances drugs that are “off-label” or “extra-label” (refer to chapter on Extra-Label Drug Use and Compounding).

- Minor Use/Minor Species Act of 2004 (MUMS) made more medications available to treat minor animal species and uncommon diseases in major animal species.
 - The term “minor species” refers to all species other than dog, cat, horse, cow, pig, chicken, and turkey. It refers to small ruminants, fish, game birds, deer, and pocket pets.
 - The bill is somewhat analogous to the orphan drug act in human drugs and has provisions for (a) conditional approval where a sponsor, after demonstrating the drug’s safety, can ask the FDA to allow it to market the drug while completing the collection of effectiveness data; (b) providing incentives for approval through grants to support approval costs and marketing exclusivity; and (c) introducing the concept of “indexing” where the potential market for a minor species drug is just too small to ever support the costs of the drug approval process. The FDA could index the drug to allow its legal marketing as an unapproved new animal drug.

ROLE OF THE FDA IN DRUG APPROVAL AND AVAILABILITY

- The FDA acts under the Federal Code of Regulations (Title 21) and Food, Drug, and Cosmetic Act.
- The FDA decides not only what drugs become approved but also their usage, label, and manufacturing.
 - Approval requires that a pharmaceutical company provide documentation to the FDA of a new drug’s efficacy, safety in the animals for which the drug is intended, safe tissue concentrations of the drug for humans who consume food products of animals that have been treated with the drug, and the impact on the environment associated with the drug’s use.
 - Once those requirements have been met, the FDA approves the label that sets out the conditions for use based on the test data submitted by the pharmaceutical company seeking FDA approval to commercially market the drug.
 - Labels define such things as species, indications, dose, route of administration and, in the case of animals whose products are consumed by humans, the time that must elapse between treatment and slaughter (meat products) or collection (milk products and eggs). This time period, termed withdrawal time, is based on tissue drug residues depleting to concentrations or tolerances that are determined by conservative algorithms to be non-toxic, even when consumed as the total source of food.
 - Label and manufacturing oversight by FDA plays a major role in drug availability.

PRESCRIBING AND DISPENSING OF PHARMACEUTICALS

- Prescription medications – labeled for use only by or on the order of a licensed veterinarian. Must be prescribed by a veterinarian licensed in the state where the drug is being prescribed or dispensed and in the context of a valid veterinarian client patient relationship (VCPR). If the drugs are controlled substances, then the veterinarian must be registered by the Drug

Enforcement Agency (DEA) and must include his/her DEA registration number on the prescription.

- Over the counter drugs (OTC) are freely available from retailers. They have a sufficiently good safety history and instructions that allow laypersons to use them safely. In recent times many drugs labeled for human use have moved from prescription-only status (also known as legend drugs) to OTC after a period of restricted use. Often, but not always, the OTC version is of a lower strength than the original prescription product.

LABELING OF DISPENSED MEDICATIONS

- State laws may vary in details, but minimal requirements are the dispensing veterinarian's name, address, and phone number; the client's name; patient's species and name/ID; clear instructions for use (dose, frequency, route, and duration), including withdrawal times; any special storage instructions; and an expiration date that cannot be greater than that of the manufacturers.
- Many states require the labeling to include the drug and quantity dispensed. This is worthy of universal use because it provides vital information in cases of accidental ingestion.
- If the drugs are intended for food-producing animals, all aspects of the drug's labeling must be complied with unless extralabel deviations are carried out in compliance with the AMDUCA, which requires more specific labeling.

VALID VETERINARIAN-CLIENT-PATIENT RELATIONSHIP

- Developed by AVMA and required by law in many states.
- The following conditions must be met:
 - The veterinarian has assumed responsibility for making clinical judgments regarding the health of the animal(s) and need for medical treatment AND the owner (client) has agreed to follow the veterinarian's instructions.
 - The veterinarian has enough knowledge of the animal(s) to initiate at least a preliminary or general diagnosis of the animal(s) medical condition. This means that the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of an examination of the animal(s) or by medically appropriate and timely visits to the premises where the animals are kept. The CVM defines "timely" as being less than 12 months.
 - The veterinarian is readily available for follow-up examination or has arranged for emergency coverage in the event of adverse reactions, unexpected response, or failure of the treatment regimen.

COMPOUNDING

- Falls under FDA Extra-label Drug Use (ELDU) regulations.
- Must be done in context of a valid VCPR.

- Defined as the customized manipulation of an FDA approved drug by a veterinarian or pharmacist for a specific patient. Common examples are crushing a tablet and mixing into a paste, mixing two injectable medications in the same syringe, or adding flavoring to a product.
- Compounding from unapproved (i.e. bulk) substances is currently illegal, although this may change in the future. Bulk substances are defined as raw, active ingredients used to make final FDA approved products.
- Use should be limited to:
 - Patients where no other route of administration is practical
 - Drugs where safety, efficacy and stability of the compounded product have been demonstrated in the intended species
 - Disease conditions where a quantifiable response to therapy or drug concentration can be measured
 - Providing the same precautions followed when using an approved drug including client counseling regarding adverse reactions, unintended human or animal exposure, and that the FDA has not evaluated the drug for potency, purity, stability, and efficacy.
 - Following ELUD label requirements and labeling the drug “not FDA approved”.



MISCELLANEOUS

SEE ALSO

Drug Residues in Milk (www.fiveminutevet.com/ruminant)

Extra-label Drug Use and Compounding (www.fiveminutevet.com/ruminant)

Food Animal Residue Avoidance Databank (FARAD) (www.fiveminutevet.com/ruminant)

Medical Waste Management: Expired Drugs (*See Appendix 3*)

ABBREVIATIONS

AMDUCA = Animal Medicinal Drug Use

AVMA = American Veterinary Medical Association

DEA = Drug Enforcement Administration

ELUD = Extra-Label drug Use

FDA = Food And Drug Administration

MUMS = Minor Use-Minor Species

OTC = over the counter drug

VCPR = Veterinarian-Client-Patient Relationship

VPA = Veterinary Practice Act

Suggested Reading

Compounding and the FDA: Questions and Answers.

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/ucm339764.htm>. Accessed 6/6/2016.

Davis JL, Smith GW, Baynes RE, et al. Update on drugs prohibited from extralabel use in food animals. Journal of the American Veterinary Medical Association. 2009; 235(5):528-34.

Teale CJ, Moulin G. Prudent use guidelines: a review of existing veterinary guidelines. Revue Scientifique et Technique-OIE. 2011; 31(1): 343-354.

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 June 6, 2016.

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