

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

As a practicing veterinarian, you've likely prescribed a drug for an extra-label use. What does that mean? What gives you the legal ability to do so? What conditions must be met? By explaining FDA's requirements for extra-label drug use in animals, this [article](#) answers these questions and more.

In 1994, Congress added provisions to the Federal Food, Drug, and Cosmetic Act (FD&C Act) that give veterinarians the legal ability to use approved human and animal drugs in an extra-label manner. This means you can use an approved drug in a way that isn't listed on the drug's labeling. Extra-label drug use is sometimes called off-label because the use is "off the label."

To prescribe drugs in an extra-label manner, you need to follow FDA's extra-label drug use requirements, as stated in the FD&C Act and FDA regulations. You should also educate your clients, particularly food animal producers, on these requirements and on FDA's recommendations for the [judicious use of antimicrobial drugs](#).

## Extra-Label Drug Use in Animals

Before Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) in 1994, federal law did not permit extra-label drug use in animals. The [AMDUCA provisions](#) amended the FD&C Act to allow veterinarians to prescribe approved human and animal drugs for extra-label uses in animals under specified conditions. The key points are:

- [Valid Veterinarian-Client-Patient Relationship](#)
- [General Conditions for Extra-Label Drug Use](#)
- [Conditions for Extra-Label Drug Use in Food-Producing Animals](#)
- [Compounding](#)
- [Drugs Prohibited from Extra-Label Uses in Animals](#)

We'll look at each point separately as well as touch on how [FDA's judicious use recommendations affect extra-label drug use in food-producing animals](#).

## Valid Veterinarian-Client-Patient Relationship

The AMDUCA provisions of the FD&C Act allow extra-label drug use only on the lawful order of a licensed veterinarian in the context of a valid veterinarian-client-patient relationship. A valid veterinarian-client-patient relationship has three parts:

- You have assumed responsibility for making medical judgments about the health of an animal, or animals, and the need for medical treatment. In turn, the client (the owner or other animal caretaker) has agreed to follow your instructions;

- You have sufficient knowledge of the animal, or animals, to develop a general or preliminary diagnosis of the medical condition; and
- You are readily available for follow-up in case of adverse drug reactions or treatment failure.

Such a relationship can exist only when you have recently seen the animal and are personally acquainted with its care. This means you have recently examined the animal, have made “medically appropriate and timely visits” to where the animal is kept (usually the case for food-producing animals), or done both.

### **General Conditions for Extra-Label Drug Use**

Before you can legally prescribe an approved human or animal drug for an extra-label use, one of these general conditions must be met:

- There is no animal drug approved for the intended use; or
- There is an animal drug approved for the intended use, but the approved drug does not contain the active ingredient you need to use; or
- There is an animal drug approved for the intended use, but the approved drug is not in the required dosage form (for example, you need a liquid dosage form, but the approved drug is only available as a tablet dosage form); or
- There is an animal drug approved for the intended use, but the approved drug is not in the required concentration (for example, you need 5 mg, but the approved drug is only available at 50 mg); or
- You have found, in the context of a valid veterinarian-client-patient relationship, that the approved drug is clinically ineffective when used as labeled.

In companion (non-food-producing) animals, you can prescribe an approved human drug for an extra-label use even if an approved animal drug is available. This is not the case for food-producing animals. FDA’s extra-label drug use requirements prohibit you from prescribing an approved human drug if there’s a drug approved for food-producing animals that you can prescribe for the particular extra-label use instead.

Thorough recordkeeping is vital. You must maintain records that identify the treated animals. In food animal practices, this can be done on a group, herd, flock, or per-client basis. The records must include the:

- Established name of the drug or, if formulated from more than one active ingredient, the established name of each active ingredient. Ordinarily, the [established name of the drug](#) is the name listed in the [United States Pharmacopeia \(USP\)](#) , and is made up of the active ingredient, route of administration, and dosage form (for example, “fenbendazole oral suspension”);
- Condition treated;
- Animal species treated;
- Dosage administered;
- Treatment duration; and

- Number of animals treated.
- For food-producing animals, the records must include the withdrawal, withholding, or discard period for food products made from treated animals, such as meat, milk, or eggs.

You must keep these records for two years or as required by federal or state law, whichever is longer. The records must be made available to FDA-designated personnel, at all reasonable times, for copying and verifying.

Thorough labeling is critical. The labeling for a drug dispensed on your order for an extra-label use must state your name and address. If the drug is dispensed by a pharmacy on your order, the labeling must state your name, and the name and address of the dispensing pharmacy. The labeling must also include information similar to what is required in the record:

- Established name of the drug or, if formulated from more than one active ingredient, the established name of each active ingredient.
- The class/species or identity of the treated animal. Animals should be identified individually (usually for companion animals) or by herd, flock, pen, or lot (usually for food-producing animals);
- Directions for use, including dosage, frequency, route of administration, and duration of therapy; and
- Any cautionary statements (for example, “Not for use in veal calves”).
- For food-producing animals, the labeling must also include the withdrawal, withholding, or discard period for food products made from treated animals.

### **Conditions for Extra-Label Drug Use in Food-Producing Animals**

Before prescribing an approved human or animal drug for an extra-label use in food-producing animals, you must:

- Carefully diagnose and evaluate the condition for which you are prescribing the drug;
- Have an appropriate medical rationale for using the drug;
- Make sure your client maintains the identity of the treated animal, or animals, in the record;
- Establish a substantially extended withdrawal period supported by appropriate scientific information. You may get this information from such sources as scientific literature, academia, or the [Food Animal Residue Avoidance Databank \(FARAD\)](#) ; and
- Take measures to assure that no illegal drug residues occur. Your client must follow your established withdrawal period before marketing food products made from treated animals.
- If scientific information on the safety of food products made from an animal treated with a human drug or an animal drug that is approved only for companion animals is not available, you must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

Remember, you may not prescribe an approved human drug for food-producing animals if there's an animal drug approved for food-producing animals that you can prescribe for the particular extra-label use instead.

The FD&C Act doesn't allow the extra-label use of any drug in animal feed.

## **Compounding**

Under the FD&C Act, an animal drug that is compounded using an unapproved drug or bulk drugs as the starting material is adulterated. An animal drug that is compounded using an approved human or animal drug as the starting material is not adulterated, and using such a drug is considered a legal extra-label use as long as all other conditions required by law are met. You can find these requirements in [Sections 512\(a\)\(4\) and \(5\) of the FD&C Act](#) and [Title 21 of the CFR, Part 530.13](#). It's important to note that Part 530.13 specifically states, "Nothing in this part shall be construed as permitting compounding from bulk drugs."

## **Drugs Prohibited from Extra-Label Uses in Animals**

Under the AMDUCA provisions, FDA has the right to prohibit extra-label uses of certain drugs in animals. The following drugs (both human and animal), families of drugs, and substances are prohibited from extra-label uses in all food-producing animals, including horses intended for human food:

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dimetridazole
- Iprnidazole and other nitroimidazoles
- Furazolidone and nitrofurazone
- Sulfonamide drugs in lactating dairy cattle, except for the approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine
- Fluoroquinolones
- Glycopeptides
- Phenylbutazone in female dairy cattle 20 months of age or older
- Cephalosporins (not including cephalixin) in cattle, swine, chickens, or turkeys:
  - For disease prevention purposes;
  - At unapproved doses, frequencies, durations, or routes of administration; or
  - If the drug is not approved for that species and production class.

The following drugs, or classes of drugs, that are approved for treating or preventing influenza A are prohibited from extra-label uses in chickens, turkeys, and ducks:

- Adamantane
- Neuraminidase inhibitors

The above list can be found at [Title 21 of the CFR, Part 530.41](#). Currently, no approved drugs are prohibited from extra-label uses in companion animals.

### **Judicious Use of Medically Important Antimicrobial Drugs and Extra-Label Drug Use in Food-Producing Animals**

In 2012, FDA issued a [guidance document](#)<sup>1</sup> that discussed the agency's concerns about antimicrobial resistance and recommended the following judicious use principles in food-producing animals:

- Limit medically important antimicrobial drugs to uses that are necessary for assuring animal health (in other words, therapeutic uses to treat, control, or prevent specific diseases); and
- Limit medically important antimicrobial drugs to uses that include veterinary oversight or consultation.

(The term “medically important antimicrobial drugs” generally refers to antimicrobial drugs that are important for therapeutic uses in people.)

In light of the public health risk posed by antimicrobial resistance, FDA stated in this 2012 guidance document that the agency doesn't think using medically important antimicrobial drugs for production purposes in food-producing animals is a judicious use of these drugs. Animal drugs currently approved for production purposes, such as increased rate of weight gain and improved feed efficiency, are typically given in feed or water on a herd- or flock-wide basis.

In a 2013 [guidance document](#),<sup>2</sup> FDA recommended that drug sponsors begin to voluntarily phase out the use of medically important antimicrobial drugs for production purposes in food-producing animals. Both veterinarians and food animal producers need to be aware that after a sponsor removes a production claim from the approved labeling of a medically important antimicrobial drug, the continued use of that drug in animal feed for a production purpose is an illegal extra-label use (remember, the FD&C Act specifically prohibits the extra-label use of any drug in animal feed).

Keep in mind that using a medically important antimicrobial drug that's approved for a therapeutic use in food-producing animals (to treat bovine respiratory disease, for example) in an extra-label manner for a production purpose (to increase rate of weight gain, for example) goes against FDA's judicious use principles. Also remember that under FDA's requirements for extra-label drug use in food-producing animals, you must carefully diagnose and evaluate the condition for which you are prescribing the drug. This means you must diagnose a medical condition and any drug you prescribe in an extra-label manner must be for a therapeutic use, which wouldn't include increased rate of weight gain (or any production claim).

### **Conclusion**

The Animal Medicinal Drug Use Clarification Act of 1994 added provisions to the Federal Food, Drug, and Cosmetic Act legalizing the extra-label use of approved human and animal drugs in

animals under certain conditions. You can ensure proper extra-label use by complying with FDA's requirements and by understanding what's allowed and what's not under the law.

For more information, please call FDA's Center for Veterinary Medicine at 240-276-9300, or send an email to [AskCVM@fda.hhs.gov](mailto:AskCVM@fda.hhs.gov).

<sup>1</sup> [Guidance for Industry #209: The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals.](#)

<sup>2</sup> [Guidance of Industry #213: New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209.](#)

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