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An interview with
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Negotiating extra label drug use rules

> "[The Animal Medicinal Drug Use Clarification Act] applies to extra label use in animals of any FDA-approved human or animal drug, not just antibiotics."

Q: Extra label drug use in swine and other animals is sometimes essential, but there are quite a few regulations governing extra label use. Are swine veterinarians up to speed with all the rules?

RS: We still get questions. That indicates uncertainty remains about what's permitted and what's not.

Q: Hasn't the law permitting extra label use been around a long time?

RS: It has. Congress passed the Animal Medicinal Drug Use Clarification Act (AMDUCA) in 1994. Before then, federal law prohibited extra label drug use in animals. AMDUCA added provisions to the Food, Drug and Cosmetic Act that made it possible for approved human and animal drugs to be used extra label by licensed veterinarians, but under certain conditions.

Q: If the law is that old, why is there still uncertainty about extra label drug use?

RS: For one, there are a lot of conditions to adhere to. I also think the restrictions imposed by the Food and Drug Administration (FDA) in recent years regarding the use of medically important antibiotics has obscured the basics of AMDUCA, which applies to extra label use in animals of any FDA-approved human or animal drug, not just antibiotics.

Q: Let's review the definition of extra label drug use.

RS: Extra label means using an approved drug in any way that's not listed on the drug's label — the species, indications, dosage levels, frequency of treatment, route of administration and anything else on that label.[1]

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> "Extra label use is limited to circumstances when the health of an animal is threatened, or suffering or death may result from failure to treat."

Q: What situations justify use of an extra label drug?

RS: Extra label use is limited to circumstances when the health of an animal is threatened, or suffering or death may result from failure to treat.[2] There are additional conditions:

- There must be no animal drug already approved for the disease or condition you want to treat.
- There's an approved drug available, but it doesn't have the active ingredient you need.
- The drug you need isn't available in the dosage form or concentration you need.
- The approved drug is clinically ineffective when used as labeled.[3]
- You have an established veterinarian-client-patient relationship (VCPR) before prescribing a drug extra label.[4]

Q: Are there additional FDA requirements or restrictions for using an extra label drug in food animals?

RS: There are. You must carefully diagnose and evaluate the condition. Extra label drugs absolutely cannot be used to enhance production or be used in or on feed. Your producer clients must clearly keep track of the treated animals.[5]

A major concern for FDA is making sure there are no extra label drug residues that are a public health risk or that leave a residue above an established safe level, concentration or tolerance. Consequently, FDA says you need to establish a "substantially extended" withdrawal period — supported by scientific information — and take measures to make sure no illegal drug residues turn up.[6] Help with withdrawal times can be found on the Food Animal Residue Avoidance Databank.[7]

Q: You mentioned an established VCPR. Do livestock veterinarians have to make farm visits to maintain a VCPR in the eyes of the FDA?

RS: They do — usually. FDA says a VCPR can only exist when you have "recently seen and are personally acquainted with the keeping and care of the animal or animals."[8] However, due to the coronavirus disease 2019 pandemic, FDA wants to facilitate telemedicine and won't enforce the requirement for visiting premises and examining animals. It will reassess the situation periodically and, at some point, resume enforcement.[9]

Q: Is it correct that extra label use of some drugs is completely forbidden in food-producing animals?

RS: That's true. Those drugs include chloramphenicol, fluoroquinolones and glycopeptides to name a few. All food-animal veterinarians should have the list of drugs they cannot use extra label, which is easily accessible on FDA's website.

Cephalosporins — excluding cephapirin since it is not used in humans — cannot be used for preventing disease. You can use it for an extra label indication but only if it is approved for that species and production class — and it's used according to the labeled dose, frequency, duration and route of administration.

Q: Say a swine veterinarian needs to use a drug approved for use in people or companion animals but not in swine. What does FDA require?

RS: In this case, FDA says you have to have an appropriate medical rationale and, again, make sure the drug doesn't enter the food chain if scientific information isn't available about the safety of food products made from animals given a particular drug.

Q: What about off label drug use? Is it the same as extra label use?

RS: FDA says extra label drug use is sometimes called off label because the use is "off the label,"[10] indicating it considers extra label and off label to be the same. The American Veterinary Medical Association says the term "off label" has no legal or regulatory definition and that extra label is the appropriate term.[11]

However, the late James D. McKean, a veterinarian and attorney with Iowa State University, studied the legal history for veterinary drug use, which is lengthy and complex. He maintained there could be veterinary drugs used in food animals in such a way that does not conform to either the label or to the allowances granted by AMDUCA, constituting "off label," illegal use.[12]

Q: Can you give an example of drug use in swine that might be considered off label versus extra label?

RS: Take penicillin. It's an over-the-counter drug labeled for 1 mL/100 pounds bodyweight — which today is considered antiquated and ineffective. Swine producers who administer penicillin would very likely use 1 mL/20 pounds bodyweight — 5 times the dose on the label. Under AMDUCA, a veterinarian could legally administer penicillin at this dosage and extend the withdrawal time accordingly.

However, AMDUCA applies to veterinarians, not producers. Administration by a layperson such as a producer is illegal.

Q: It's a given that good recordkeeping is important, but do you have any tips regarding recordkeeping for extra label drug use in case FDA comes calling?

RS: When an extra label drug is dispensed, your records need to be really thorough.[13] You have to identify the treated animals, the name of the drug and its active ingredient or ingredients,

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> "Extra label drugs absolutely cannot be used to enhance production or be used in or on feed."

the condition treated, the species, dosage, treatment duration and number of animals treated. Since swine are food-producing animals, you also have to include the withdrawal, withholding or discard period.

The label you provide has to have your name and address and include information similar to what's in the record — and that's whether you or a pharmacy dispense the extra label drug.

> "To ensure their own compliance, swine veterinarians need to make sure their producer clients also comply."

Q: Do you have any other advice for swine veterinarians to help them adhere to FDA regulations regarding extra label drug use?

RS: FDA rightly emphasizes the importance of educating food-animal producers about the rules for extra label drug use. To ensure their own compliance, swine veterinarians need to make sure their producer clients also comply.

For more information, contact Richard Swalla (richard.swalla@zoetis.com) or your Zoetis representative.

[1] Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA). FDA.

[2] The Ins and Outs of Extra Label Drug Use in Animals: A Resource for Veterinarians. FDA.

[3] Ibid.

[4] Ibid.

[5] Ibid.

[6] Ibid.

[7] Food Animal Residue Avoidance Databank.

[8] Ibid.

[9] FDA Guidance for Industry #269. Enforcement Policy Regarding Federal VCPR Requirements to Facilitate Veterinary Telemedicine During the COVID-19 Outbreak. March 2020.

[10] The Ins and Outs of Extra Label Drug Use in Animals.

[11] Extralabel drug use and AMDUCA: FAQ. AVMA.

[12] McKean J. Legal issues for drug usage in practice and production. Am Assoc Swine Vet. Annual Meeting, Omaha, Nebraska. 2010.

[13] Animal Medicinal Drug Use Clarification Act of 1994.

Toolbox is a series of interviews with veterinarians about their experiences managing antimicrobials, vaccines and other tools for swine health. It is produced by the editors of *Pig Health Today*® on behalf of the US Pork Business of Zoetis.

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