Compounding Guide for the Food Animal Veterinarian

What is Compounding?

Compounding is the term used for combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient.[1] Since compounding was grandfathered into law following the passing of the Food Drug and Cosmetic Act, compounded products do not have to undergo the required safety and efficacy testing that is required of new FDA approved drugs. Therefore, in virtually all cases, FDA regards compounded medications as unapproved new drugs.[1] Using compounded medications is considered to be extra label drug use (ELDU) of an approved animal or human drug and is permissible under the Animal Medicinal Drug Use Clarification Act (AMDUCA). Currently, the FDA is developing a new draft guidance on compounding drugs for animals.[2]

When may a veterinarian consider using a compounded product in a food animal?

Veterinarians may consider using a compounded medication when there is no approved new animal or approved new human drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed. [21CFR530.13].

The veterinarian must also ascertain that there is sufficient data on which to base a withdrawal interval. This is the legal responsibility of the veterinarian and it is particularly important if the pharmacy compounding the medication is not aware of all the legal ramifications. If there is not sufficient data to establish a withdrawal interval, then the veterinarian must assure that the animal and its products never enter the food chain.

Overall, compounding for food animals should be rare. When treating an animal whose tissues or products have the potential to enter the human food chain, it's important to remember that Food Safety and Public Health come first.

What are the requirements for legal use of a compounded product in food animals? [21CFR530.13]

1. All requirements for ELDU under AMDUCA are met
2. Additional stipulations specific for compounding:
    a. An approved animal drug should be used for compounding before using an FDA approved human drug

1. https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm339764.htm
2. https://www.fda.gov/animalveterinary/resourcesforyou/ucm268128.htm#compounding

b. Compounding is done by the veterinarian or pharmacist within their scope of practice
c. Adequate procedures are followed to ensure the safety and effectiveness of the compounded product
d. Scale of compounding is in line with the need for the product and is for a particular patient. Compounding in anticipation of receiving prescriptions, except in limited quantities, is illegal. The compounding of large quantities can fall under "manufacturing" and thus the compounded product would be considered a drug in need of FDA approval. Also, compounding for third parties to resell or selling it at wholesale to another individual or entity for resale is illegal. So, it would not be legal for a compounding pharmacy to make a product for a veterinarian to sell to clients, for example, keep on his truck to sell to dairies. Products can be compounded "for office use". This mean that the drug is to be administered or applied in the prescriber's office and if dispensed, only a limited supply, generally defined as up to a 72 hour supply, of the drug is to be given to the client. However, state laws may vary, and it is advised to check with your state board.
e. All state laws relating to compounding are followed

Compounding falls under AMDUCA, so what are the requirements for ELDU and Compounded Medications under AMDUCA?

a. Therapeutic Purpose
ELDU can only occur for therapeutic purposes when an animal's health is suffering or threatened. This means that utilization of medications for reproductive purposes, growth promotion and efficiency, or research (with animals intended to enter the food chain) is not permissible by the AMDUCA. Use for prophylaxis is a gray area and would require thorough documentation and justification of ELDU.
b. No Effective Labeled Drugs
ELDU should not occur unless FDA approved drugs as labeled are clinically ineffective for their intended use.
c. VCPR
A valid veterinarian-client-patient relationship (VCPR) must exist.
d. Veterinarian's Supervision
ELDU is permitted only under the supervision of a veterinarian. If a producer gives a drug, including Over the Counter (OTC) products, in an extralabel manner, then calls a veterinarian for a withdrawal interval, this would not be considered legal ELDU, as ELDU needs to be under the direction of a veterinarian. If the veterinarian gives a withdrawal interval recommendation (which must be documented in the records), he/she are assuming responsibility for the ELDU and can be held responsible, along with the producer, if there are any residues.
e. Approved Drugs

ELDU is permitted using only FDA approved animal and human drugs. Medications approved for other food animal species should be used before using medications approved for non-food animal species. Medications approved for animals should be used preferentially over drugs approved for humans only. Using bulk chemicals is not allowed as they are not FDA approved.

1. What are bulk chemicals? Defined in 21 CFR207.3 "Bulk drug substance means any substance that is represented for use in a drug and that, when used in the manufacturing, processing, or packaging of a drug, becomes the active ingredient or a finished dosage form of the drug, but the term does not include intermediates used in the synthesis of such substances." In other words, it is the drug in powdered chemical form, often used for research purposes and may not be of pharmaceutical grade.
2. Compounding with bulk chemical can be less expensive than using an FDA approved medication.
    a. ELDU is legal for therapeutic purposes only in food producing animals, thus, cost is not an acceptable reason for ELDU under AMDUCA.
3. This bulk chemical is often manufactured in foreign countries with potentially less oversight than there is in the United States. As only a portion of states require a drug pedigree or a certificate of origin, there is no assurance that the product is safe and unadulterated and not a potential contamination to our food supply.

f. Not in Feed

Extra label use of an approved animal drug or human drug or feed additive in or on an animal feed is prohibited. Also, using combinations of medicated feed or feed additives not approved to be used together is considered illegal. ELDU in water is permitted.

Exceptions: CPG Sec. 615.115 Extra Label Use of Medicated Feeds for Minor Species specifies that regulatory action will not be taken in some instances of ELDU of medicated feeds in minor species. The requirements to use feed ELDU in minor species are similar to the requirements for ELDU of medications. Some of the differences include:

a. A written recommendation that includes the medical rationale, dated within 3 months prior to use is required. The producer and vet must keep copies that are available for FDA inspection.
b. The medicated feed is approved in a major food producing species and is to be used in a food producing minor species.
c. ELDU of medicated feed in aquaculture is limited to medicated feeds approved for use in aquatic species.

Refer to the FDA's Compliance Policy Guide on the extra label use of medicated feeds for minor species, available at:
https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-ice/documents/webcontent/ucm074659.pdf

g. Prohibited Drugs

ELDU is prohibited in food producing animals with the following drugs:

1. Chloramphenicol
2. Clenbuterol
3. Diethylstilbestrol (DES)
4. Nitroimidazoles such as metronidazole
5. Nitrofurans- including topical applications
6. Sulfonamides in adult lactating dairy cattle
7. Fluoroquinolones such as enrofloxacin
8. Glycopeptides such as vancomycin
9. Dipyrone
10. Gentian Violet
11. Phenylbutazone in adult dairy cattle (defined by the FDA as dairy cattle 20 months of age or older, regardless of whether they are milking or dry).
12. Antiviral medications including adamantine and neuraminidase inhibitors in poultry
13. Cephalosporins, not including cephapirin, must be used on label in cattle, swine, chickens, and turkeys. They may be used extra label only to treat a disease indication not labeled.

Please note that regulations related to the Pasteurized Milk Ordinance (PMO) also prohibits the presence of non-medical grade dimethyl sulfoxide (DMSO) and colloidal silver on dairies.

h. No Residues

ELDU must not result in violative residues.

i. Additional Food Animal Requirements

1. Make a careful diagnosis and evaluation of the conditions for which the drug is to be used.
2. Establish a substantially extended withdrawal period supported by scientific information, if applicable. Unfortunately, the variability in the chemical make-up of compounded products and lack of pharmacokinetic data makes this difficult. As previously mentioned, this is the main reason not to use compounded medications, as we do not have the data necessary to establish an appropriate withdrawal interval to ensure the food supply is safe.
3. Institute procedures to assure that the identity of the treated animal(s) is/are carefully maintained. If the individual animal cannot be identified for the extended withdrawal interval, then the extended withdrawal interval must be applied to the entire group.
4. Take appropriate measures to assure that assigned time frames for withdrawal are met and no illegal drug residues occur in any food-producing animal subjected to extra label treatment.

What needs to be in the records for ELDU and compounded products?

1. Identify the animals, either as individuals or as a group

2. Animal species treated
3. Number of animals treated
4. Conditions being treated
5. The established name of the drug and active ingredient
6. Dosage prescribed or used
7. Duration of treatment
8. Specified withdrawal, withholding, or discard time(s), if applicable, for meat, milk, eggs, or other animal-derived food
9. Keep records for 2 years
10. FDA may have access to these records to estimate risk to public health

What information should be on the prescription label?

1. Name and address of the prescribing veterinarian
2. Established name of the drug
3. Any specified directions for use including the class/species or identification of the animal or heard, flock, pen, lot, or other group; the dosage, frequency, route of administration, and duration of therapy
4. Any cautionary statements
5. The veterinarian's specified withdrawal, withholding, or discard time for meat, milk, eggs, or any other animal-derived food

Commonly Asked Questions:

What is FARAD's stance on compounding in food producing animals?

FARAD discourages the use of compounded medications in food producing animals. Compounded drugs do not undergo the same quality assurance testing as commercially manufactured medications and there is a lack of pharmacokinetic data on compounded formulations from which to base scientifically sound withdrawal intervals.

Can a product be compounded for use on Dairy X?

No, products can only be compounded for an individual patient with whom the veterinarian has a valid VCPR. They should not be compounded for general use, such as mastitis cases, on the farm. The farm is not considered an individual patient.

Where can I get more information on compounding?

The AVMA has compounding resources that can be found at:
https://www.avma.org/KB/Resources/Reference/Pages/Compounding.aspx

More details of the published law on compounding and AMDUCA may be found at:
http://www.farad.org/amduca-law.html

More details on state laws related to compounding may be found at:
https://www.avma.org/Advocacy/StateAndLocal/Pages/compoundinglaws.aspx

Regulations and requirements for compounding products set by USP can be found at: http://www.usp.org/compounding

The Society of Veterinary Hospital Pharmacists' statement on animal compounding, which includes helpful information for pharmacists and veterinarians, may be found at: https://svhp.org/position-statements/

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