WVU IACUC POLICY:
Residue Avoidance in Food-producing Agricultural Animals

DEFINITIONS

Adulterated (9 CFR 301.2): This term applies to any carcass, part thereof, meat or meat food product under one or more of the following circumstances:

1. If it bears or contains any such poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance, such article shall not be considered adulterated under this clause if the quantity of such substance in or on such article does not ordinarily render it injurious to health;
2.
    a. If it bears or contains, by reason of administration of any substance to the live animal or otherwise, any added poisonous or added deleterious substance other than one which is:
        i. A pesticide chemical in or on a raw agricultural commodity;
        ii. A food additive; or
        iii. A color additive which may, in the judgment of the Administrator, make such article unfit for human food;
    b. If it is, in whole or in part, a raw agricultural commodity and such commodity bears or contains a pesticide chemical which is unsafe within the meaning of section 408 of the Federal Food, Drug, and Cosmetic Act;
    c. If it bears or contains any food additive which is unsafe within the meaning of section 409 of the Federal Food, Drug, and Cosmetic Act;
    d. If it bears or contains any color additive which is unsafe within the meaning of section 706 of the Federal Food, Drug, and Cosmetic Act: *Provided,* That an article which is not deemed adulterated under paragraphs (aa)(2) (ii), (iii), or (iv) of this section shall nevertheless be deemed adulterated if use of the pesticide chemical food additive, or color additive in or on such article is prohibited by the regulations in this subchapter in official establishments;

Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA): Administered under the U.S. Food and Drug Administration (FDA) to provide greater prescribing and dispensing options for veterinarians acting within a valid veterinarian-client-patient relationship (VCPR), so that animals can receive the medications they need when they need them and be more readily relieved of suffering. **The AMDUCA allows ELDU only on the lawful order of a licensed veterinarian in the context of a valid VCPR.**

Appropriate Federal Agency: is that agency having regulatory authority over the substance in question.

1) The Federal Food and Drug Administration (FDA) has oversight over animal pharmaceuticals and animal food additives. (Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 et seq.))
2) The USDA Animal and Plant Health Inspection Service (APHIS) has oversight over substances imparting biological residues. (Virus-Serum Toxin Act (21 U.S.C. 151 et seq.))

3) The Environmental Protection Agency (EPA) has oversight over herbicides and pesticides. (Federal Insecticide, Fungicide, and Rodenticide Act, as amended (7 U.S.C. 135 et seq.))

For more information on obtaining FSIS permission for slaughter see FSIS Directive 10800.3

Food Animal Residue Avoidance Databank (FARAD): University-based national program that serves as the primary source for scientifically based recommendations regarding safe withdrawal intervals of drugs and chemicals in food-producing animals.

Veterinary Feed Directive (VFD): Administered by the FDA under the Animal Drug Availability Act of 1996. Require veterinarians to issue all VFDs within the context of a veterinarian-client-patient-relationship (VCPR).

VFD drugs: Animal drugs intended for use in or on animal feed that require the supervision of a licensed veterinarian.

Veterinary-Client-Patient Relationship (VCPR):
A *valid veterinarian-client-patient relationship* is one in which:

1. A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;
2. There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and
3. The practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.

Extra-Label Drug Use (ELDU): Deviation from the FDA-approved labeling to include:

- In a species or age not listed on the label
- For an indication not listed on the label
- At a different dose or frequency than listed on the label
- Via a different route of administration than listed on the label
- At a different dose than listed on the label

Withdrawal time: period of time from when a drug is administered to when the drug concentration falls below the tolerance.

INTRODUCTION

This policy applies to animals used in West Virginia University's agricultural teaching and research programs.

Part 1 of this policy deals with food products derived from livestock and poultry that are legally considered adulterated due to their **use in research.** The meat of these livestock used in research and

receiving experimental substances is considered adulterated according to Title 9 CFR 309.17. Likewise, the meat of poultry having received experimental substances is assumed adulterated according to Title 9 CFR 381.75. The United States Department of Agriculture (USDA) Food Safety and Inspection Services (FSIS) has established processes that allow entry of these animals into the food market after certain conditions have been met.

Part 2 of this policy defines how the adulteration of animals by the use of substances for other purposes than research, including therapeutic care under the direction of a veterinarian, can be avoided. It includes information on what substances are and are not allowed by federal regulation.

Note: While there are currently no United States markets for horse meat, international markets still exist in Mexico and Canada. No WVU-owned horse shall be sold or transferred to any entity that deals in these markets, and no horse shall be sold or transferred to any circumstance where its final disposition is unclear.

POLICY

PART 1: Substances used in research investigation involving livestock and poultry

Animals prohibited from slaughter

Any agricultural animal treated with recombinant protein, non-FDA approved vaccine adjuvant or any experimental drug, where residue clearance cannot be predicted or avoided, will not be allowed to enter the food chain, and must be euthanized upon final disposition.

A researcher can give an unapproved, experimental drug to food animals that DO NOT enter the food chain. Researchers doing so are obligated to fulfill record-keeping requirements outlined under 21 CFR 511.1(a).

Animals That May Be Sent to Slaughter Directly or through Intermediary:
As outlined in Title 9 CFR 309.17 and Title 9 CFR 381.75, animals that receive experimental substances as part of an approved WVU IACUC protocol must be approved for slaughter by the USDA Food Safety and Inspection Service (FSIS) in writing. The FSIS requires the submission of information from the *appropriate federal oversight agency attesting* to the innocuous nature of the experimental substance and/or identification of a withdrawal period where the animal becomes free of the substance through a metabolic process.

Each appropriate federal oversight agency may have formalized processes and application requirements to obtain written approval to provide to the FSIS.

Researchers may also be required to fulfill pre-study requirements for the substances in question. For example, a researcher can give an unapproved experimental drug to and market food animals only if he or she has obtained an Investigational New Animal Drug (INAD) permit (with slaughter authorization) through the Food and Drug Administration`s Center for Veterinary Medicine.

Animals sold/returned to original owner with uncertain disposition:
Circumstances may arise where the party receiving animals from the university cannot identify what their final disposition will ultimately be. In this case, the transfer or sale of the animals cannot be done unless a signed, written agreement is in place whereby the university discloses the circumstances of the use of animals in research, and the receiving party agrees to indemnify the university from the impact of the research activity on the future use of the animals.

Animal-produced products:
There are no regulations specifically addressing milk, eggs, or other animal-produced food products produced by animals used in research. The benefits of marketing such products from animals receiving experimental substances, however, would be minimal in comparison to the liability of their sale in the food market. Therefore, sale of these products from animals meeting the definition of adulteration as per Title 9 CFR 309.17 and Title 9 CFR 381.75 is prohibited.

PART 2: Substances used in the clinical care of livestock and poultry

A. Background: FDA approved compounds for clinical use will fall into two categories:

- **a.** Compounds which are used as described on label and recommended withdrawal times are adhered to.
- **b.** Compounds which are considered extra-label and must meet certain criteria to be administered to food producing animals and allow those animals to be used as food products:
  - **i.** Must be administered by or on the lawful written or oral order of a licensed veterinarian within the context of a valid VCPR.
  - **ii.** 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.
  - **iii.** Extra-label use is not permitted to enhance production.
  - **iv.** There is no approved animal drug that is labeled for such use and that contains the same active ingredient in the required dosage form and concentration, except where a veterinarian finds, within the context of a valid VCPR, that the approved animal drug is clinically ineffective for its intended use.
  - **v.** Before prescribing or dispensing an approved animal drug or approved human drug for an extra-label use in food animals, the veterinarian must:
    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 prior to marketing of milk, meat, eggs, or other edible products supported by appropriate scientific information, if applicable;
    3. Institute procedures to assure that the identity of the treated animal or animals is carefully maintained; and
    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.

B. Compounds NOT permitted in food producing animals
Under the Animal Medicinal Drug Use Clarification Act (AMDUCA) provisions, the Food and Drug Administration (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.

Drugs prohibited from use in food producing animals

Chloramphenicol	Glycopeptides
Clenbuterol	Phenylbutazone in female dairy cattle 20 months of age or older
Diethylstilbestrol (DES)	Cephalosporins (not including cephapirin) 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.
Dimetridazole	Adamantane in chickens, turkeys, and ducks
Ipronidazole and other nitroimidazoles	Neuraminidase inhibitors in chickens, turkeys, and ducks
Furazolidone and nitrofurazone	
Sulfonamide drugs in lactating dairy cattle, except for the approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine	
Fluoroquinolones	

The above list can be found in Section 530.41 of Title 21 of the Code of Federal Regulations (Drugs prohibited for extra-label use in animals, 2017).

AMDUCA excludes compounds meeting the requirements below from extra-label drug administration:

- Extra-label use in an animal of an approved new animal drug or human drug by a lay person (except when under the supervision of a licensed veterinarian);
- Extra-label use of an approved new animal drug or human drug in or on an animal feed;
- Extra-label use resulting in any residue which may present a risk to the public health; and
- Extra-label use resulting in any residue above an established safe level, safe concentration, or tolerance.

C. Compounds that ARE permitted in food producing animals

Drugs with known meat and milk withdrawal: Veterinary Drugs and other FDA-Approved Compounds

- Any veterinary drug or other FDA-approved compound that includes an FDA-prescribed withdrawal period for agricultural animals
    - Such compounds must have been manufactured utilizing Good Manufacturing Practices.
    - Such products must be administered as labeled to not fall under extra-label use category and AMDUCA.

- Any drugs used with food-producing agricultural animals must follow labeled withdrawal times for milk or meat that are species-specific. Veterinarians will provide guidance regarding product withdrawal times.
- **All drugs are to be obtained from WVU Research, Education and Outreach Centers (REOC) veterinarian service and investigators are to work with REOC staff to ensure they know when animals were last treated and when those animals have cleared withdrawal.**

- Any pharmaceutical-grade drug prescribed by a veterinarian under the Animal Medicinal Drug Use Clarification Act (AMDUCA)
  - AMDUCA permits veterinarians to prescribe extra-label uses of certain approved new animal drugs and approved human drugs for animal use under certain conditions. Under AMDUCA and its regulations published at Title 21, Code of Federal Regulations, Part 530 (21 CFR 530), any extra-label use of an approved new animal or human drug must be by or on the lawful order of a veterinarian within the context of a veterinarian-client-patient relationship (VCPR).
  - The veterinarian will provide the published withdrawal times for pharmaceuticals utilized in this manner.
  - These compounds can be administered only under the direct orders of a licensed veterinarian.
  - **All compounds that are used outside of their FDA approved label must be administered under the purview of AMDUCA and will require the direct oversight of an REOC clinical veterinarian. This includes drugs listed in the IACUC protocol which meet the requirements of extra-label use for therapeutic reasons.**

- Drugs available for use through the Minor Species Act for extra-label use must follow extended withdrawal that is available through Farm Animal Residue Avoidance Databank (FARAD) or by recommendation of the REOC clinical veterinarian who has oversight of drug treatment.

D. FARAD

FARAD can be used as a resource to guide withdrawal time recommendations on a case-by-case basis for compounds administered to animals. A withdrawal time prescribed by FARAD does not automatically indicate an animal is unadulterated or cleared to be used for food production.

- All submissions to FARAD must be done by the REOC clinical veterinarian caring for the animals.
- The FARAD website: www.farad.org.
- FARAD will respond within 72 hours and provide guidance on withdrawal times. Guidance from FARAD will detail withdrawal times specific to the scenario provided and are only to be used in the situation described in the request.
- **It is strictly prohibited to rely on withdrawal times provided by FARAD for any other instance, animal, or scenario.**
- Data from FARAD should be forwarded to the Attending Veterinarian, OAW and IACUC chair. Information from FARAD can be used to obtain the additional regulatory approvals needed for food products to be utilized from food producing animals treated for research purposes.