Administration of drugs to food animals presents unique challenges due to veterinarians' responsibility to ensure that no drug contaminates an edible product. This challenge is compounded by changing regulations associated with treatment of food animals, the relative lack of drug options for many species, and varying considerations for meat-, milk-, and egg-producing animals. Nonetheless, it is imperative that practitioners are cognizant of the legal framework for treatment of food animals including extralabel drug use, understand the importance of withdrawal times, and can apply these concepts to a wide variety of patients that present to mixed animal practices.

The first aspect that is crucial to understand is that food-producing animals are defined by their species and class (i.e. lactating dairy goat), not by the owner's intended use (i.e. companion). Therefore, any goat, chicken, pig, etc. are all legally classified as food-producing animals and should be treated as such no matter the owner's intention of ever consuming any edible product from the animal. There are essentially two main designations within food-producing animals—major species: cattle, pigs, chickens, turkeys; and minor species—sheep, goats, rabbits, other poultry, cervids, and aquaculture. Most legal restrictions apply equally to both classifications, though some restrictions are relaxed for minor species which are detailed below.

In order to minimize the risk of drug contamination of the food supply, practitioners are legally obligated to use drugs as labeled in these species. Yet, due to the limited number of FDA-approved drugs for many of these species and some common conditions, extralabel drug use is often necessary. This is allowable in food-producing animals if the health, welfare, or life of the animal is at risk which implies that using drugs in an extralabel manner to improve production is not allowed. Extralabel drug use constitutes a use of a medication in any way that varies from its FDA-approved label. This includes altering the dose or route or frequency of administration, administering the drug for a non-labeled indication (i.e. for treatment of septicemia when labeled for respiratory disease), or giving the drug to a non-labeled species or class of animals (i.e. treating a lactating dairy cow when labeled for beef cattle).

The FDA has designated some drugs and drug classes as prohibited from extralabel use in food producing animals. These restrictions have historically been focused on concerns for toxicity in humans due to residues in edible products, but more recent additions have often been due to an effort to restrict uses of antimicrobials considered critical to human health. The intent is to reduce total usage in order to minimize transfer of antimicrobial resistant bacteria through the food chain. Note that some of these drugs have no approved uses in food animals, and therefore, all uses would be illegal (i.e. chloramphenicol), others are only restricted in certain classes (i.e. phenylbutazone in lactating dairy cattle), some have labeled uses and can be used legally in those narrow parameters (i.e. fluoroquinolones), and some restrictions only apply to major species (i.e. cephalosporins).

Extralabel use is prohibited for the following drugs:
(1) Chloramphenicol
(2) Clenbuterol
(3) Diethylstilbestrol (DES)
(4) Dimetridazole
(5) Ipronidazole
(6) Other nitroimidazoles (including metronidazole)
(7) Furazolidone
(8) Nitrofurazone (including topical administration)
(9) Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine)
(10) Fluoroquinolones
(11) Glycopeptides
(12) Phenylbutazone in female dairy cattle 20 months of age or older

(13) 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.

The following drugs, or classes of drugs, that are approved for treating or preventing influenza A, are prohibited from extralabel use in chickens, turkeys, and ducks:

(1) Adamantanes
(2) Neuraminidase inhibitors

In order for a veterinarian to use a drug in an extralabel manner in a food animal, specific criteria must be met. First, it must be done on order of a veterinarian within a valid veterinary-client-patient relationship. This means that any extralabel use of an over-the-counter drug in a food animal must be under the supervision of a veterinarian. Extralabel use of drugs in the feed is prohibited, and the extralabel use cannot cause a violative residue. The drugs used in an extralabel manner must be labeled appropriately with the veterinarian's name and address, drug name, animals to be treated, dosing regimen, and withdrawal time. Again, this means that drugs purchased over-the-counter and used in an extralabel manner must be labeled appropriately by the veterinarian recommending the treatment.

Additionally, the veterinarian must determine that there is not a labeled drug with the appropriate active ingredient that would be effective. If there is not an appropriate labeled drug (or it is deemed not clinically effective), the practitioner should preferentially use a drug labeled for food animals in an extralabel manner over a drug labeled for companion animals or humans. The veterinarian must make a "careful diagnosis" and ensure that a scientifically sound withdrawal time can be given and adhered to by the owner.

Determining a scientifically valid withdrawal interval for extralabel drug use can be challenging. An appropriate withdrawal interval is influenced by the drug dosing regimen, species being treated, disease condition, and FDA mandated tolerance for residues in specific products. The simplest example is increasing the drug dose. When doubling the dose, the withdrawal interval typically only needs to be increased by one half-life of the drug, which is approximately 10-20% of the labeled withdrawal time. When treating a different disease indication, the impact on the withdrawal time is more difficult to predict. In cases of significant hepatic or renal disease, the withdrawal interval may need to be doubled due to the delayed clearance. Extrapolation from a larger species to a related smaller species (i.e. cattle to goats) is fairly straightforward in that the small species generally metabolizes drugs faster than the larger species. This suggests that the labeled withdrawal interval for cattle would generally be adequate for small ruminants. Nonetheless, it is prudent to extend this withdrawal time somewhat due to differences in residue tolerance. In the labeled species (cattle in this example), there will be an established tolerance for the approved drug in the edible product, but in the off-label species (goat), there is no tolerance established, and therefore it is zero. Therefore, to allow for drug clearance to drop below the limit of detection, extending the cattle withdrawal time is prudent. Many situations arise in which these simplistic approaches are inadequate. In these scenarios, we recommend contacting the Food Animal Residue Avoidance Databank (farad.org) in order to determine the most appropriate withdrawal interval.

Treating laying hens presents unique challenges for veterinarians, particularly in cases of individual hens needing treatment. Few drugs are labeled for use in laying hens, and almost all of these are designed for mass medication through the feed or water. Therefore, many backyard hens are being treated in an extralabel fashion. The physiology of egg production allows for drugs to be incorporated into the yolk up to 6 weeks prior to being laid. Further, once a drug enters the yolk it does not equilibrate with the plasma, so it will persist well beyond the time the drug is cleared from the bloodstream. Therefore, egg withdrawal intervals for extralabel drug use are often quite long to allow for 6 weeks after the drug is cleared from the plasma.