

Extra-Label Drug Use In Free-Ranging Wildlife: Rules, Regulations, & Realities

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2022 ILAR Roundtable Wildlife Workshop

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- ▶ UC Davis School of Veterinary Medicine
- ▶ Western Region Director of the Food Animal Residue Avoidance and Depletion Program (FARAD).
- ▶ USDA sponsored national program to provide guidance on residue avoidance following extra-label drug use.

Overview

- ▶ On-Label versus Extra-Label Drug Use (ELDU)
- ▶ Rules and Regulations for ELDU in Animals Destined for Human Food Consumption
- ▶ Requirements for Extra-Label Drug Use
- ▶ Challenges with establishing ELDU withdrawal intervals for Free-Ranging Wildlife
- ▶ Resources



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Residue Challenges With Drug Use: Free-Ranging Wildlife

- ▶ Drug use = potential for drug residues in edible tissues from free-ranging wildlife (hunted or scavenged)
- ▶ What is a residue?
 - ▶ Parent or metabolite that can accumulate in edible tissues or products (eggs, milk, honey) from an animal.
- ▶ Withdrawal Time/Interval
 - ▶ Time required after administering a drug for concentrations deplete to a safe concentration (tolerance) for human consumption.

Why Are Withdrawal Times/Intervals Important?

► Direct Impacts

- Toxicity
- Allergic reactions
- Bone marrow suppression



"Wildlife - Animal - Dall Sheep in Denali National Park" by blmiers2 is licensed under CC BY-NC-SA 2.0

► Indirect Impacts

- Occurs over a longer time period
- Carcinogenicity, mutagenicity, reproductive disorders, etc.

FDA Approved Medications: On-Label Drug Use

Cervidae (**Fallow Deer, Mule Deer, Sika Deer, White-Tailed Deer and Elk**)

Amount: Administer **IM**, by either hand syringe or syringe dart, in the heavy muscles of the croup or shoulder. Fallow Deer- **2.0 to 4.0mL/100lbs** body weight. Mule Deer, Sika Deer, White-Tailed Deer – **1.0 to 2.0mL/100lbs** body weight. Elk- **0.25 to 0.5mL/100lbs** body weight.

Indications: To calm and facilitate handling of fractious animals. For diagnostic procedures. For minor surgical procedures. Therapeutic medication for sedation and relief of pain following injury or surgery. As a preanesthetic to local anesthesia, AnaSed at the recommended dosages can be used in conjunction with local anesthetics, such as procaine or lidocaine.

Limitations: **Do not use in Cervidae less than 15 days before or during hunting season.** Federal law restricts this drug to use by or on the order of a licensed veterinarian.



FDA Approved Drugs For Wildlife Species

Approved Products Species		Active Ingredient (Approved FDA formulations)
Cervids (n=14)	Deer (Fallow, Mule, Silka, White tail)	Xylazine hydrochloride (4)
	Elk	Yohimbine hydrochloride (1); Xylazine hydrochloride (1); Naltrexone hydrochloride (1)
	Reindeer	Ivermectin (5)
	Cervidae, all use classes	Gelatin-Sodium chloride (1); Fenbendazole (1)
	Moose	Naltrexone hydrochloride (1)
American Bison (n=5)	Bison, American	Ivermectin (5)
Game Birds (n=19)	Pheasants	Bacitracin zinc (2); Amprolium (1); Bacitracin methylenedisalicylate (2); Thiabendazole (1)
	Quail	Bacitracin zinc (3); Salinomycin (1); Bacitracin methylenedisalicylate (3); Monensin sodium (2); Salinomycin (1); Salinomycin sodium (1)
	Ducks	Novobiocin (1); Calcium chlortetracycline (1); Chlortetracycline (1); Iodinated casein (1); Ormetoprim-sulfadimethoxine (1)
	Partridges, Chukar	Lasalocid sodium (1); Ormetoprim-sulfadimethoxine (1)
Other Wildlife Species (n=10)	Weasels, mink	Novobiocin (1); Melatonin (1)
	Rabbits	Lasalocid sodium (1); Sulfaquinoxaline (1)
	Pigeons	Carnidazole (1)
	Foxes	Ivermectin (1)
	Wildlife, not specified	Diprenorphine hydrochloride (1)
	Bears	Fenbendazole (1)
	Wildcats	Fenbendazole (1)
	Goats, wild	Fenbendazole (1)
	Sheep, bighorn	Fenbendazole (1)
	Swine, feral	Fenbendazole (1)
	Amphibians	Tricaine methanesulfonate (1)

Withdrawal Times

FDA approved Products

Product	Species	Meat Withdrawal Time
Anased®, Chanazine® (xylazine)	Deer, Elk	Do not use less than 15 days before or during hunting season
Antagonil® (yohimbine)	Deer, Elk	Do not use less than 30 days before or during hunting season
Ivermectin	Reindeer	56 days
Fenbendazole	Cervids, Bighorn Sheep, Wild Goats	Do not use less than 14 days before or during hunting season

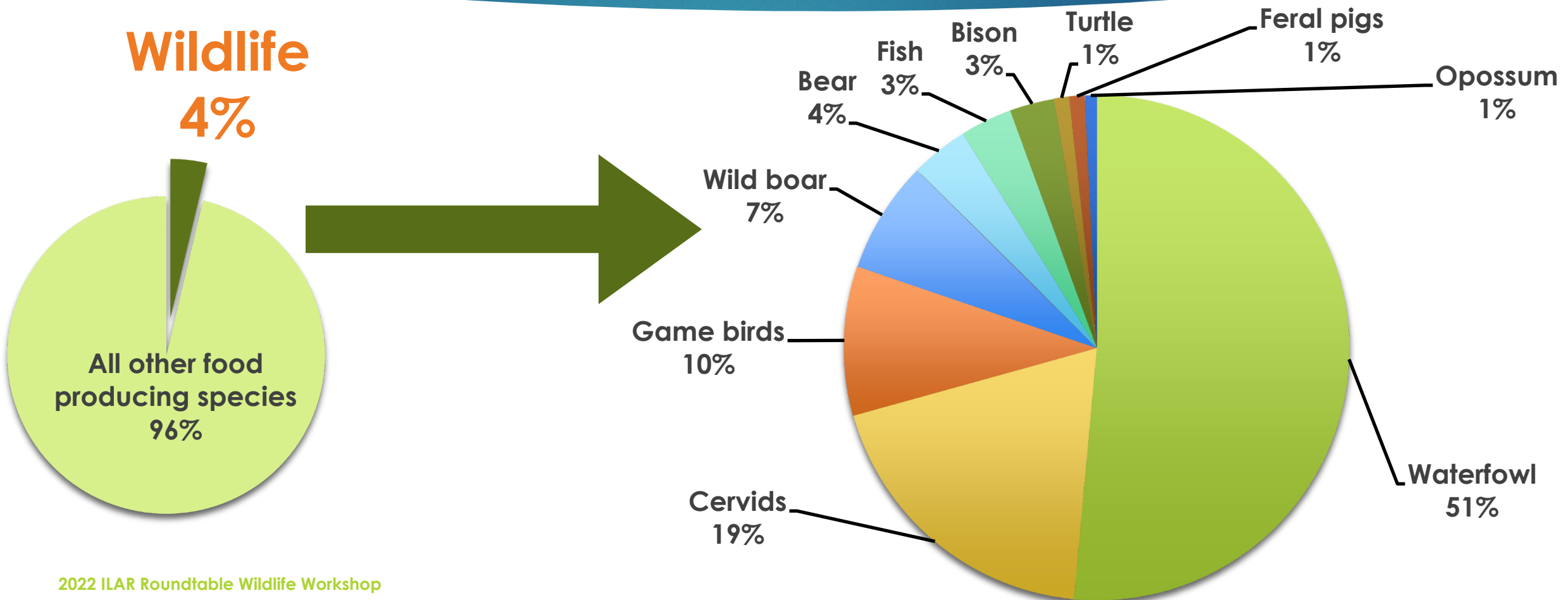
Extra-Label Drug Use (ELDU)

- ▶ **Legalized** by Animal Medicinal Drug Use Clarification Act (AMDUCA; 1994)
- ▶ **Differs** from the **FDA-approved label** by:
 - ▶ **Animal species/class**
 - ▶ **Administration route**
 - ▶ **Dose, dosing frequency/interval, duration**
 - ▶ **Treatment indication**
 - ▶ **Limitations** (injection volume/site, WDT, etc)



Limitations: **Do not use in Cervidae less than 15 days before or during hunting season**

ELDU Wildlife Requests Submitted To FARAD 10 years (2012-2022)



Top Drug Requests Submitted to FARAD

Active Ingredient

Meloxicam (pain medication)

Amoxicillin trihydrate- clavulanate (antibiotic)

Enrofloxacin* (antibiotic)

Oxytetracycline (antibiotic)

Carprofen (pain medication)

Fenbendazole (antiparasitic)

Xylazine (anesthetic agent/sedative/tranquilizer)

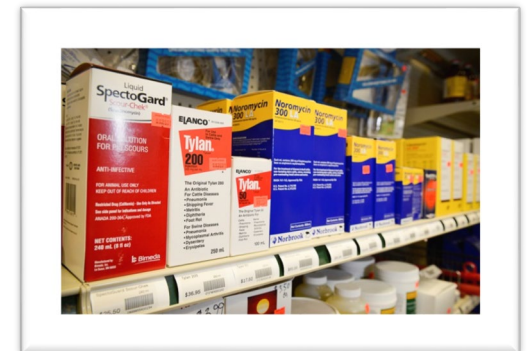
Butorphanol (pain medication)

Tiletamine hydrochloride- zolazepam HCL (anesthetic agent)

Clindamycin hydrochloride (antibiotic)

AMDUCA: ELDU Requirements

- ▶ Need to **use FDA approved product first**
- ▶ Requires **a VCPR with a licensed veterinarian.**
- ▶ **FDA approved** (not EPA) OTC or RX human or veterinary drug; not all OTC medications are FDA approved and ELDU of unapproved FDA drugs is not allowed
- ▶ Only for **therapeutic use**
- ▶ ELDU **not for convenience/\$** purposes



AMDUCA: ELDU Requirements

► Therapeutic Use

- Cannot be used for production purposes
- Therapeutic means situations where suffering or death may occur if treatment is not administered.
- Wildlife: FARAD would consider several situations to fit into the category of “death may occur if treatment is not administered” (behavioral management)



"Grizzly Bears at the National Elk Refuge" by USFWS
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AMDUCA: ELDU Requirements

1

Treated animal
or animals must
be **IDed**

2

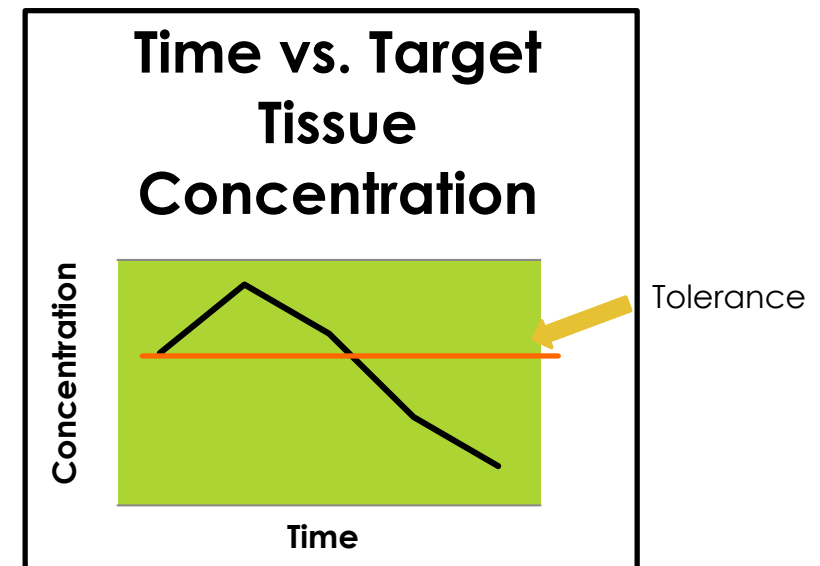
Establish a
substantially
extended
scientific
withdrawal
interval

3

Protect human health:
assure that no illegal
drug residues will be
present

Methods for Establishing Extra-Label Withdrawal Intervals For Wildlife

- ▶ Published Pharmacokinetic Data
- ▶ Extrapolate from an Approved FDA Product
- ▶ Foreign Drug Approvals
- ▶ Pharmacokinetic models
- ▶ No data = No WDI



Establishing Extra-Label Withdrawal Intervals: Route of Administration & Volume per Injection Site

- ▶ Administering an injectable drug by a different route of administration may lead to prolonged drug residues
- ▶ Larger volume per injection site/dart administration → tissue damage, inflammation and delayed absorption and elimination



Photo Credit: Mark Drew



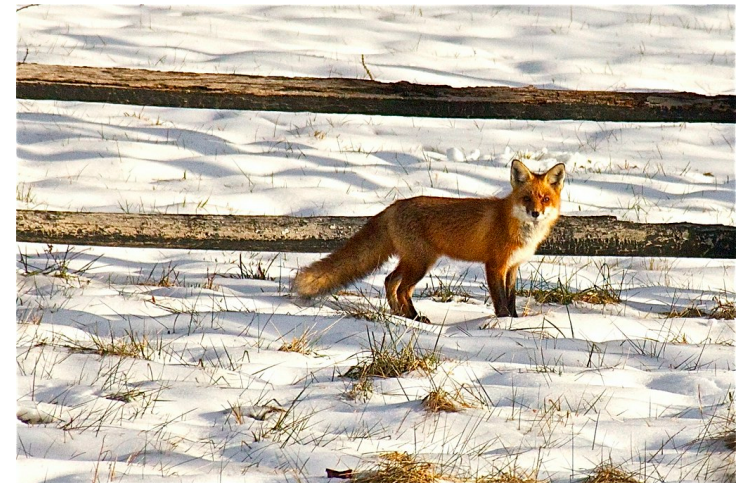
Photo Credit: Mark Drew

Establishing Extra-Label Withdrawal Intervals: Animal Species Extrapolation

- ▶ Extrapolation between species can be complicated
 - ▶ Drug metabolism might differ
 - ▶ Marker residue might differ
 - ▶ % of parent drug/metabolites might differ



Photo Credit: Don Preisler



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Prohibited Drugs and Prohibited ELDU Food Producing Animals

- ▶ Several drugs are prohibited from any use and several drug classes are prohibited from ELDU
- ▶ ELDU of FDA Indexed Drugs is prohibited. Required labeling language:

“This product is **not to be used in animals intended for use as food for humans or food-producing animals.**”

Compounding

- ▶ Definition: combining, mixing, or altering ingredients to create a medication tailored to the needs of an individual patient
- ▶ Must follow ELDU stipulations
- ▶ Allowed under AMDUCA if made from an FDA approved animal or human drug.
- ▶ Use in food producing animals should be rare.
 - ▶ Sufficient data is needed in order to establish a withdrawal interval and PK data for compounded formulations typically does not exist
- ▶ Compounded preparations are viewed as unapproved new animal drugs

Resource:
www.farad.org

[FARAD](#) [About Us](#) [VetGRAM](#) [Quick Links](#) [Resources](#) [References](#) [Contact Us](#)



[Request Extra-label Advice](#)

Food Animal Residue Avoidance Databank

a component of the Food Animal Residue Avoidance & Depletion Program

[Banco de datos para evitar residuos en animales de consumo en Español](#)



[Request ELDU Advice](#)

If you are a licensed veterinarians, please use our FREE online submission form for questions regarding accidental chemical contamination or drugs used in an extralabel manner in food animals.

FARAD Resource: Bibliographic Database

[Search FARAD Bibliographic Database for Citations](#)

[Go To FARAD Homepage](#)

This database only contains documents that have time versus concentration data for live animals with a focus on food animal species. Freedom of Information and European Medicine Agency summaries have been harvested into the database.

Chemical Filter

Enter a Chemical: TradeName, Active Ingredient, Pesticide, Vitamin, Environmental Contaminant, etc., then click Search

- ☒ Xylazine ☒ Xylazine (hydrochloride) ☒ xylazine hydrochloride
☒ Xylazine (2,6-dimethylaniline DMA metabolite)

Species Filter

- ☒ unspecified or not coded ☒ Birds ☒ Cattle ☐ Dogs ☒ Horses ☐ Cats
☒ Sheep

Matrix Filter

- ☒ unspecified or not coded ☒ Inj Site ☒ Kidney ☒ Liver ☒ Milk ☒ Muscle ☒ Plasma ☒ Serum

Route Filter

- ☐ unspecified or not coded ☒ Intramuscular ☒ Intravenous ☒ Other

51 records found.

FARAD Resource: Digests

FARAD Digest

Extralabel drug use in wildlife and game animals

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"Bull moose eating Coyote Willow on Seedskaadee National Wildlife Refuge" by USFWS Mountain Prairie is licensed under CC BY 2.0

Summary: Extra-Label Drug Use in Wildlife

- ▶ Only FDA approved over the counter and prescription medications can be used ELDU
- ▶ ELDU of Indexed Drugs is Prohibited
- ▶ ELDU requires veterinary oversight; document basis for ELDU use
- ▶ Protect HUMAN health: all animals should be tagged or marked following ELDU



"Mule deer bucks in velvet Seedsdakee National Wildlife Refuge"
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