What's Happening with Animal Drugs?

Indiana State
Board of Animal Health

GFI #209: Judicious Use of Antimicrobials in Food Producing Animals

FDA's plan to:

1. Phase out use of medically important antimicrobials (MIAs) for growth promotion or feed efficiency.
2. Bring therapeutic uses of medically important antimicrobials under oversight of veterinarians.

Ensure safe food and sustainable long-term use of antimicrobials for humans and animals.

The Next Step Is Here

1994: Federal Animal Drug Availability Act

- Gave FDA flexibility in regulating drugs
- AMDUCA—extra label drug use allowed

2015: Veterinary Feed Directives (VFDs) Final Rule

- Clarified VFD regulations

2017: Guidance for Industry # 213

- Puts GFI #209 into effect
- Feed and water OTC antibiotics transitioned to Rx or VFD
- Removed production uses from labels

June 11, 2023: Guidance for Industry #263

- Deadline to switch remaining antibiotics from OTC to Rx

What is GFI #263?

- **CVM GFI #263 Recommendations for Sponsors of Medically Important Antimicrobial Drugs Approved for Use in Animals to Voluntarily Bring Under Veterinary Oversight All Products That Continue to be Available Over-the-Counter**
- Information for sponsors of such new animal drugs to facilitate voluntary changes to the approved conditions of use of these drugs to prescription marketing status.

- NADA (pioneer drugs)
  - Submit a supplemental application in accordance with GFI #263
    - Request to change marketing status from OTC to Rx
    - Copy of the new label
- ANADA (generics)
  - FDA contacts to align label with referenced listed new animal drug (RLNAD)
  - Will contact before NADA label is officially changed
  - Follows same steps as NADA
    - The generic drug label needs to be *the same* as the original drug's labeling.

- **Over the Counter:** Must be possible to prepare adequate direction for use under which a layperson can use the drugs safely and effectively. Safe use includes safety to the animal, safety of food products derived from the animal and safety to the persons associated with the animal. Assumes an accurate diagnosis can be made with a reasonable degree of certainty, the drug can be properly administered, and that the course of disease can be followed so that the success or lack of success can be observed.

What is the impact of GFI #263?

- FDA regulates animal and human antibiotics
  - **OTC**, over-the-counter
  - **Rx**, prescription
  - **VFD**, veterinary feed directive
- Moves all remaining **medically important antibiotics** (MIA) to prescription by June 2023:
  - injectable
  - intramammary
  - oral/boluses
  - topical antibiotics

- **Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian."**

What is an MIA?

- Medically important antimicrobials
  - –Same (or in same class) as drugs used to treat humans
  - –Most antibiotics approved for use in animals are medically important with possible exceptions:
    - bacitracin, mecadox, bambermycin, tiamulin, and monensin

Affected by GFI #263

Medically important over-the-counter drugs that will be affected:

Penicillin
Gentamicin
Lincomycin
Tetracycline
Cephapirin
Sulfa Drugs
Chlortetracycline
Tylosin
Spectinomycin
Oxytetracycline

Not Affected by GFI #263

- Non-antibiotics:
  - Dewormers
  - Some coccidiostats
  - Electrolytes
  - Probiotics
  - Aspirin

Changes to MIAs

- **96%** of MI antibiotics already have VFD or prescription status
  - –All MIA for use in feed or water of food-producing animals and some parenteral (route other than via digestive tract)
- **remaining 4%** that are currently OTCs will require prescription
  - –food-producing **and companion animals**

Take Home Message

- MIAs will no longer be available for purchase as OTC
  - –feed stores, pet stores, or online
- Must obtain prescription from a veterinarian to purchase from any source

How Does the New GFI #263 Affect Your Operation?

Will a DVM be Required to Examine Each Animal Before Prescribing an Rx?

- **No**: Veterinarians are generally not required to examine each animal for which a prescription is issued under a **veterinary-client-patient-relationship (VCPR)**.

What is a Veterinary-Client-Patient Relationship?

- Veterinarian **assumes responsibility** for making clinical judgments about patient health and owner agrees to comply with veterinarian's instructions
- Has **sufficient knowledge** of the patient by virtue of patient examination and/or visits to the premises where the animal is housed
- Provides for any **necessary follow-up** evaluation/care

The VCPR

- "sufficient knowledge"
  - Obtained through animal examination and/or visits to the facility where the animals are raised

(i) 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 followup 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.

- “Veterinarians employed by drug manufacturers or distributors may not legally dispense prescription drugs to laypersons unless they meet the above criteria.”
  - https://www.fda.gov/animal-veterinary/resources-you/fda-regulation-animal-drugs

Do You Have a Client Relationship with a Veterinarian (VCPR)?

No: **Find a veterinarian NOW.**

- *Otherwise, no legal access to any antibiotics for your animals.*
- *Veterinarians not obligated to make emergency calls for non-clients.*

Yes: **Schedule an appointment with your DVM.**

- *Makes obtaining an Rx easier, faster.*

Can I Share Prescription Antibiotics with My Neighbor?

No: **This is illegal.**

- *Contact a local veterinarian to obtain an Rx.*

Should I Stock-Up on OTCs Now, for Future Use?

No: **These medications will expire.**

- *Be prepared for when current medications will expire or be depleted.*
- *Contact your veterinarian ahead of time.*

Is this Rule Only for Food-Producing Animals?

- **No:** This rule is for **food-producing and companion animals** needing medically important over-the-counter medication.

Can I Still Buy Medications at Farm Supply Stores?

- **Probably Not:**

The FDA answers the question this way "you may be able to purchase prescription animal drug products from various suppliers or distributors with a valid prescription provided by a licensed veterinarian."

Recap

- All remaining medically important antibiotics (MIA) transition to prescription drugs by **June 2023**:
  - Injectable, intramammary, oral, and topical antibiotics.
- The prescription drugs probably won't be available at feed supply stores. They will be available online from drug supply companies, but you must have a **prescription from a veterinarian** for purchase.
- **Do not** try to stock up on OTCs now as they will expire.
  - Contact your veterinarian or find one to be prepared.

Drug Label Requirements

- Name and address of prescribing veterinarian
- Identity of animal/group
- Name of the drug and strength
- Directions for use
  - Identification of animal or group
  - Dosage
  - Frequency
  - Route of administration
  - Duration of therapy
- Cautionary statements
- Withdrawal times for food products

Some of this information may be applied by the manufacturer, and additional information may be attached to the product or provided by the veterinarian.

Prescription Record Requirements

- Identification of animal or group
  - Species
  - Number treated
- Medical condition treated
- Name of drug and active ingredient
- Dose, route of administration, duration of treatment
- Withdrawal times for food products

Records must be kept for a minimum of 2 years. FDA must be allowed access to these records if requested.

BOAH and Animal Drugs

- Not much involvement
- Tissue residues—USDA and FDA, rarely involved at state level, even if detected at state plant
- Milk drug residues

Definitions

- **Drug:** articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and articles other than food intended to affect the structure or any function of the body.
- Products that are drugs but are not FDA approved = illegal for use in animals
- Natural products
- CBD products

AMDUCA

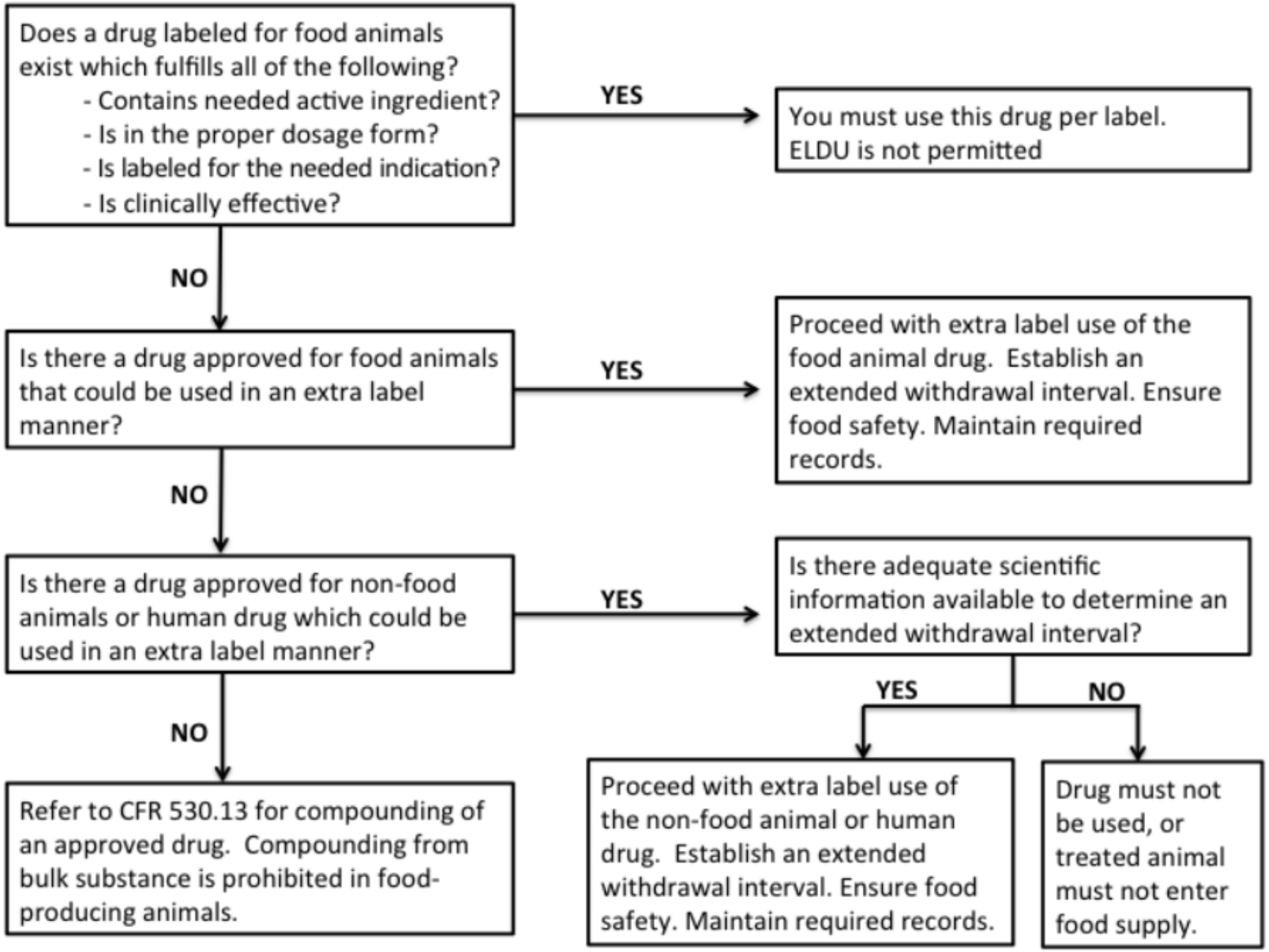
- Animal Medicinal Drug Use Clarification Act
- Provision added to the Federal Food, Drug and Cosmetic Act
- 1994
- Made extra label drug use an FDA-regulated activity
  - Federal law did not permit ELDU in animals before this act.

Extra Label Drug Use

- Deviations from the label include, but are not limited to:
  - Use in a species or production class not on the label
  - Use of a different route of administration, indication, frequency, dose, or duration

ELDU Requirements

- Allowed only for FDA-approved animal and human drugs.
- A valid Veterinarian/Client/Patient Relationship is a prerequisite.
- Therapeutic purposes only (animal's health is suffering or threatened). Not drugs for production use.
- Prohibited in feed.
- Not permitted if it results in violative food residue, or any residue which may present a risk to public health.
- FDA prohibition of a specific ELDU precludes such use.


Does a drug labeled for food animals exist which fulfills all of the following?
- Contains needed active ingredient?
- Is in the proper dosage form?
- Is labeled for the needed indication?
- Is clinically effective?
YES
You must use this drug per label. ELDU is not permitted
NO
Is there a drug approved for food animals that could be used in an extra label manner?
YES
Proceed with extra label use of the food animal drug. Establish an extended withdrawal interval. Ensure food safety. Maintain required records.
NO
Is there a drug approved for non-food animals or human drug which could be used in an extra label manner?
YES
Is there adequate scientific information available to determine an extended withdrawal interval?
YES
NO
Proceed with extra label use of the non-food animal or human drug. Establish an extended withdrawal interval. Ensure food safety. Maintain required records.
Drug must not be used, or treated animal must not enter food supply.
NO
Refer to CFR 530.13 for compounding of an approved drug. Compounding from bulk substance is prohibited in food-producing animals.

Drugs Prohibited for ELDU

- Chloramphenicol
- Clenbuterol
- Diethylstilbestrol (DES)
- Dimetridazole
- Ipronidazole and other nitroimidazoles
- Furazolidone and nitrofurazone
- Sulfonamide drugs in lactating dairy cattle, except for the approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine
- Fluoroquinolones
- Glycopeptides
- Phenylbutazone in female dairy cattle 20 months of age or older

Cephalosporin ELDU

- In cattle, swine, chickens, or turkeys
- Certain uses not allowed extra label:
  - 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.
- Rule does not include cephapirin

ELDU in Companion Animals

- In non-food animals, you may use a human drug extra label, even when an animal drug exists. Economic reasons are valid.
- Maintain required records
- Label drug appropriately
- No approved drugs are prohibited from extra label drug use in companion animals

Producer Responsibilities in ELDU

- Recordkeeping
- Identify treated animals
- Work with a veterinarian
  - –Illegal to use ELDU without veterinarian's order
  - –Even if the drug is (was) OTC
- Prevent drug residues in meat or milk

Veterinarian Responsibilites

- Diagnose condition
- Recordkeeping
- Withdrawal times
- Know specific rules

Withdrawal Time Considerations

- FARAD
- Healthy vs. sick animals
- Weight effects
- Dry cow treatment
- Use in unapproved classes

FARAD

- Food Animal Residue Avoidance Databank
- www.farad.org
- Resource for withdrawal times, drug uses and restrictions
- ELDU advice for licensed veterinarians

It is FARAD's goal to provide expert advice to veterinarians, extension specialists, and livestock producers regarding extra-label drug use and contamination emergencies to prevent drug residues in meats, milk, and eggs.

Healthy vs. Sick

- Drug approval studies performed on healthy animals, but drugs used in sick animals
- Altered metabolism
- Study on flunixin in mastitic cows

Weight Effects

- Zoetis Study
- Dairy cow weight ranges 1010 to 2265 pounds
- Underdosing
- Overdosing

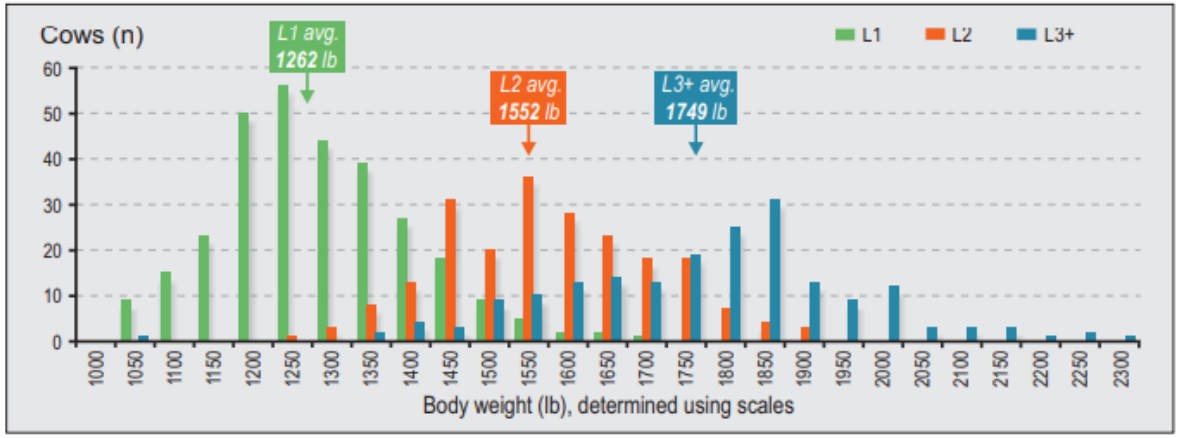


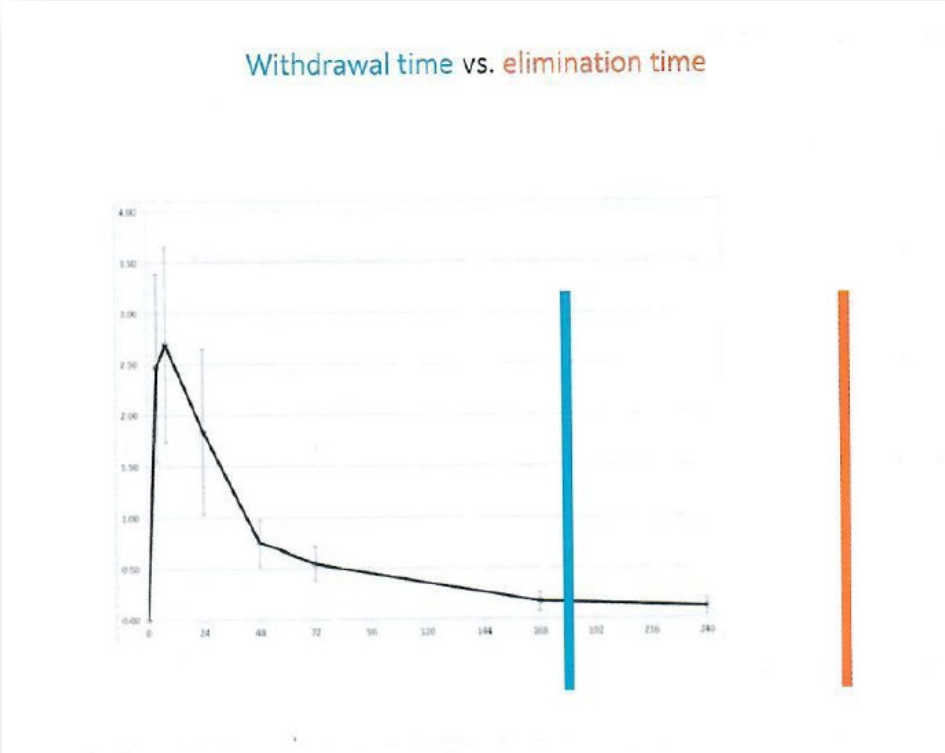
Figure 1 – *Scales:* Distribution of individual cow body weights measured at freshening using scales, by lactation number (1 dairy, n=704).

Dry Cow Treatment

- Withdrawals require minimum dry period plus milk discard after calving
- Short dry periods
- Meat withdrawal

Unapproved Class of Animals

- Zero tolerance for that food product
- Extends the withdrawal time



Graphic by Dr. Meredyth Jones

Minor Species

- Anything except horses, dogs, cats, cattle, pigs, turkeys, and chickens
- ELDU for VFD drugs
  - Compliance Policy Guide
  - FDA does not plan to take action
  - Does not make the use legal

Compounding

- Process of combining, mixing or altering ingredients to create a medication tailored to the needs of an individual animal or small group of animals
- An animal drug that is compounded using an approved human or animal drug as the starting material is not adulterated, and using such a drug is considered a legal extra-label use.
- Allowed under AMDUCA
  - Crushing tablets of an FDA-approved medication into a paste or liquid
  - Adding flavor to a medication
  - Combining two injectable medications in a syringe

Compounding

- Under the FD&C Act, an animal drug that is compounded using an unapproved drug or bulk drugs as the starting material is adulterated.
- Compounding from bulk substances is prohibited in food-producing animals.

Focus of FDA's Enforcement Activities on Compounded Animal Drugs

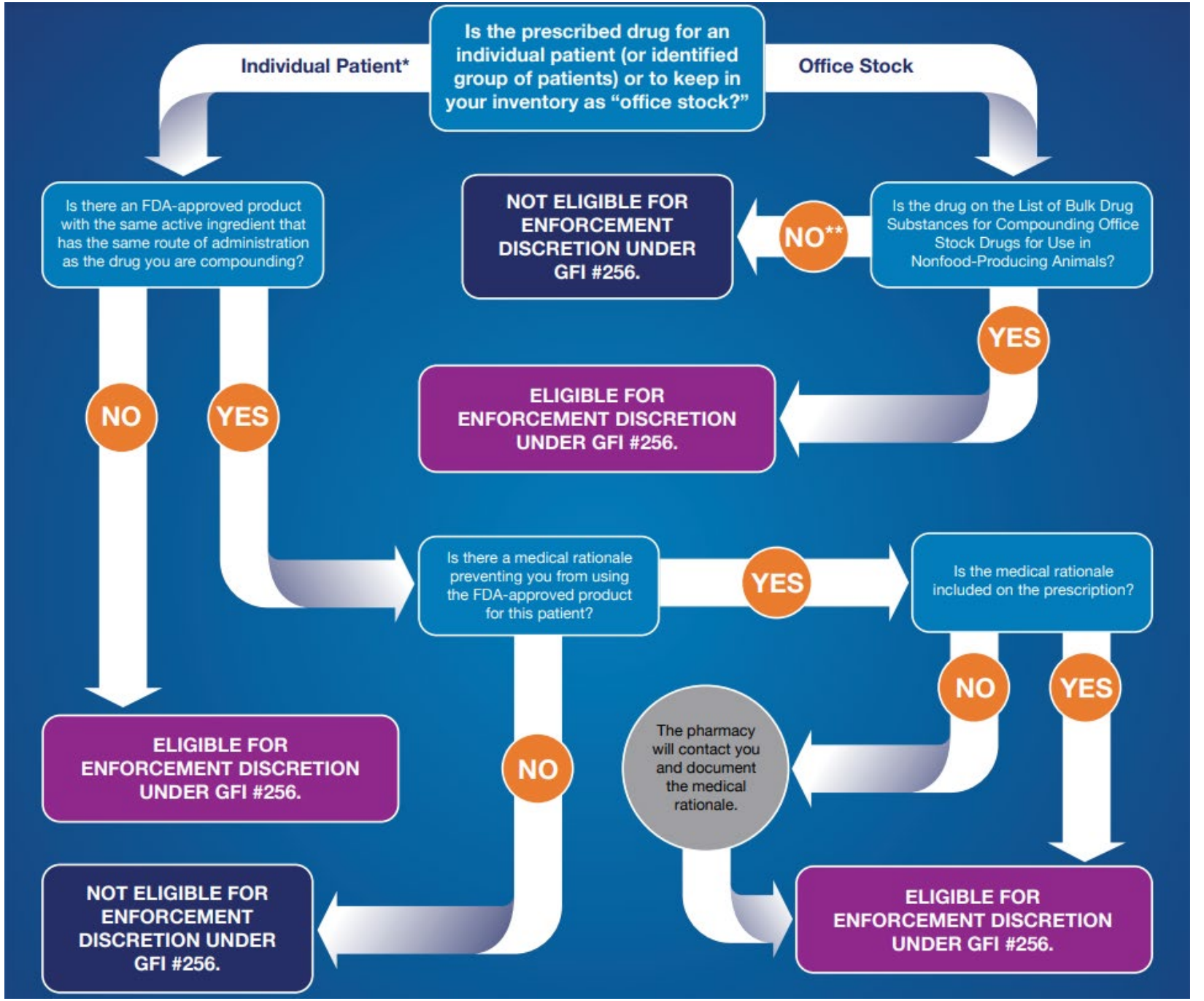
- present particular human or animal safety concerns;
- are intended for use in food-producing animals
- are copies of marketed FDA-approved or indexed drugs
- are compounded without a patient-specific prescription (i.e., office stock).

Compounding

- Guidance for Industry #256
- Finalized April 22, 2022
- Addresses situations in which the FDA does not intend to take action (enforcement discretion) for certain violations of the Food, Drug, & Cosmetic Act when pharmacists and veterinarians compound or oversee the compounding of animal drugs from bulk drug substances:
  - to fill patient-specific prescriptions for nonfood-producing animals
  - to compound “office stock” (certain drugs kept in veterinarians’ supply) for nonfood-producing animals and
  - to compound antidotes for food-producing animals.

Compounding

- Office stock from bulk drug substances can only be compounded from the FDA's *List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals*.
  - List of Bulk Drugs reviewed but not listed
  - List of Bulk Drugs under review
    - –No enforcement action until review complete


Is the prescribed drug for an individual patient (or identified group of patients) or to keep in your inventory as "office stock?"
Individual Patient*
Office Stock
Is there an FDA-approved product with the same active ingredient that has the same route of administration as the drug you are compounding?
NOT ELIGIBLE FOR ENFORCEMENT DISCRETION UNDER GFI #256.
NO**
Is the drug on the List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals?
YES
ELIGIBLE FOR ENFORCEMENT DISCRETION UNDER GFI #256.
NO
YES
Is there a medical rationale preventing you from using the FDA-approved product for this patient?
YES
Is the medical rationale included on the prescription?
NO
YES
ELIGIBLE FOR ENFORCEMENT DISCRETION UNDER GFI #256.
NO
The pharmacy will contact you and document the medical rationale.
NOT ELIGIBLE FOR ENFORCEMENT DISCRETION UNDER GFI #256.
ELIGIBLE FOR ENFORCEMENT DISCRETION UNDER GFI #256.

For More Info…

Indiana State Board of Animal Health

317-544-2400

www.boah.in.gov

animalhealth@boah.in.gov

Facebook.com/INBOAH