U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR VETERINARY MEDICINE

Office of Surveillance & Compliance
FDA Center for Veterinary Medicine

DRAFT GUIDANCE FOR INDUSTRY (GFI) #256 COMPOUNDING ANIMAL DRUGS FROM BULK DRUG SUBSTANCES

Welcome

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Challenges That Veterinarians Face

Balance

- Unproven safety, effectiveness, and quality of animal drugs compounded from bulk drug substances
- The need for those drugs when no FDA-approved or indexed drug can be used to treat the animal

Legally Marketed New Animal Drugs

- FDA-approved
- Conditionally approved
- Listed on the *Index of Legally Marketed Unapproved Drugs for Minor Species*
  https://www.fda.gov/animal-veterinary/minor-useminor-species/index-legally-marketed-unapproved-new-animal-drugs-minor-species

New Animal Drug Approvals

- Pre-approval: FDA reviews data demonstrating safety, efficacy, manufacturing quality, and labeling adequacy.

- Post-approval: FDA monitors adverse events, product defects, advertising, and changes in manufacturing and labeling.

Compounding from Approved Drugs

- The federal Food, Drug, and Cosmetic Act permits veterinarians to use approved animal or human drugs in an extralabel manner.

- Compounding an animal drug using finished, approved drugs as the source of the active ingredient can be a legal extralabel use (ELU) if ELU regulations are followed (21 CFR Part 530).

Compounding from Bulk Drug Substances

- The federal Food, Drug, and Cosmetic Act does not authorize compounding animal drugs from bulk drug substances.

- Compounding an animal drug from bulk drug substances creates a product that requires FDA approval or index listing under the federal Food, Drug, and Cosmetic Act.

Compounding from Bulk Drug Substances
continued

- Animal drugs compounded from bulk drug substances are **not** FDA-approved brand-name (i.e., pioneer) drugs (even if they contain the same bulk drug substance as an approved animal drug).
- Animal drugs compounded from bulk drug substances are **not** FDA-approved generic drugs (even if they contain the same bulk drug substance as an approved animal drug).

Compounding from Bulk Drug Substances

continued

- Drugs compounded from bulk drug substances have not been evaluated by FDA.
- Drugs compounded from bulk drug substances do not have the same assurances of safety, efficacy, manufacturing quality, and labeling adequacy as FDA-approved drugs.
- Drugs compounded from bulk drug substances are not routinely monitored by FDA for adverse events, product defects, advertising, and changes in manufacturing and labeling.

Regulatory Priorities

FDA is most concerned with drugs compounded from bulk drug substances that

- Present human or animal safety concerns
- Are for use in food-producing animals
- Are copies of approved, conditionally approved, or indexed marketed animal drugs
- Are compounded without a patient-specific prescription and sold to veterinarians as “office stock”

Draft GFI #256

- **Does not** make the marketing and use of drugs compounded from bulk drug substances legal

- Describes when FDA **does not intend** to take action against animal drugs compounded from bulk drug substances

Draft GFI #256

continued

Under Draft GFI #256:

- Only veterinarians and pharmacists can compound from bulk drug substances
- Drugs compounded from bulk drug substances should only be prescribed and dispensed when:
  - A veterinarian is acting within a valid veterinarian-client-patient relationship **and**
  - There is no medically appropriate FDA-approved drug or option for lawful extralabel use of an FDA-approved drug.
- Veterinarians and pharmacists who compound from bulk drug substances should report adverse events and product defects to FDA by following instructions for Form FDA 1932a at www.fda.gov/reportanimalAE

Categories of Compounding from Bulk Drug Substances

- Patient-specific prescriptions for nonfood-producing animals
- Office stock for nonfood-producing animals
- Antidotes for food-producing animals

Patient-specific Prescriptions for Nonfood-producing Animals

FDA does not intend to take action against drugs compounded from bulk drug substances for **nonfood-producing animals with patient-specific prescriptions** when the compounded drug

1. Is not a copy of a marketed, FDA-approved human or animal drug; and
2. Cannot be made using an approved drug as the source of the active ingredient; and

Patient-specific Prescriptions

continued

FDA does not intend to take action against drugs compounded from bulk drug substances for **nonfood-producing animals with patient-specific prescriptions** when the compounded drug

3. Is dispensed to the patient's owner or caretaker or the prescribing veterinarian, and not to a distributor, retailer, or other third party; and
4. Is compounded according to the standards in the United States Pharmacopeia and National Formulary (USP-NF), at a minimum

Compounding Office Stock for Nonfood-producing Animals

FDA does not intend to take action against drugs compounded from bulk drug substances for **nonfood-producing animals as office stock** when the drug

1. Is compounded from a bulk drug substance on FDA's "List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food-Producing Animals"; and

Office Stock

continued

FDA does not intend to take action against drugs compounded from bulk drug substances for **nonfood-producing animals as office stock** when the drug

2. Is not dispensed or transferred to a third party (except for a veterinarian dispensing to an animal's owner); and
3. Is compounded according to the standards in the United States Pharmacopeia and National Formulary (USP-NF), at a minimum

Antidotes for Food-producing Animals

FDA does not intend to take action against drugs compounded from bulk drug substances for **food-producing animals** only when

1. The drug is an antidote; and
2. The drug is compounded from a bulk drug substance on FDA's "List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals or Antidotes for Food-Producing Animals"; and

Antidotes for Food-producing Animals

continued

FDA does not intend to take action against drugs compounded from bulk drug substances for **food-producing animals** only when

3. The veterinarian either
   - Establishes and documents a scientifically based withdrawal, withholding, or discard time(s) for meat, milk, eggs, and any food that may be derived from the treated animal(s); or
   - Ensures the animal does not enter the food supply

Requests for Nominations to the List of Bulk Drug Substances

- The public may submit nominations for bulk drug substances to be included on the office stock/antidotes bulk list.
- Nominations may be submitted electronically or in writing.
- Nominations should include all requested information or FDA may be unable to determine if the bulk drug substance meets the criteria for inclusion on the list.
- For a complete list of requested information and directions on how to submit, see the appendix in Draft GFI #256 or the *Federal Register* notice inviting nominations.

Key Points for Veterinarians

- Compounded drugs are not FDA-approved, and FDA has not evaluated their safety and efficacy.
- Veterinarians will be able to compound or prescribe drugs compounded from bulk drug substances, under circumstances described in Draft GFI #256, if finalized, when no legal (FDA-approved or indexed) treatment options exist that would be appropriate to treat a patient.

Key Points for Veterinarians

continued

- We are interested in your input and suggestions. Please submit comments on the draft guidance by 2/18/2020. Nominations for office stock and antidotes may be submitted at any time.
- Reminder: Draft GFI #256 is draft guidance; its provisions only take effect if finalized.

Key Points for Pharmacists

- Pharmacists will be able to compound drugs from bulk drug substances when prescribed by a veterinarian under circumstances described in Draft GFI #256, if finalized.
- If there is an approved product with the same active moiety, compounders should only use a bulk drug substance if the approved drug cannot be used as the source of active ingredient.
- We will prioritize action against compounded copies of approved drugs, except in cases where a prescribing veterinarian has documented that there is a clinical difference for a specific patient.

Key Points for Pharmacists

continued

- GFI #256 limits the BDS that can be used for office stock compounding to the bulk drug substances on the Bulk Drug Substances List.

- We will prioritize action against drugs compounded from bulk drug substances for food-producing animals, except for antidotes compounded from bulk drug substances on the Bulk Drug Substances List.

- We are interested in your input and suggestions. Please submit comments by 2/18/2020.

- Reminder: Draft GFI #256 is draft guidance; its provisions only take effect if finalized.

Key Points for the Pharmaceutical Industry

- FDA is prioritizing action against compounding copies of approved or indexed products.

- GFI #256 limits compounding copies of FDA-approved or indexed drugs to situations where the veterinarian documents a clinical difference for a specific patient.

Key Points for the Pharmaceutical Industry
continued

- Draft GFI #256, if finalized, expects the compounder will consider using an FDA-approved drug(s) as the source of the active ingredient and will document the reason they cannot be used when compounding from BDS.

- We are interested in your input and suggestions. Please submit comments by 2/18/2020.

- Reminder: Draft GFI #256 is draft guidance; its provisions only take effect if finalized.

Thank you!

Questions?

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