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ANIMAL HEALTH

FDA Guidance for Industry #256 –

Compounding animal drugs from bulk drug substances

What you need to know

September 20, 2023

What is Guidance #256?

- FDA issues guidance to provide their current thinking about a particular topic and their expectations.
- Guidance #256 is intended to protect human and animal health:
  - Limiting the use of animal drugs compounded from bulk drug substances.
  - Should only use when veterinarian determines there is **no medically appropriate** human or animal drug that is FDA approved, conditionally approved, or indexed to treat the animal.
- This presentation will only focus on animal drugs.
- Guidance highlights the FDA's enforcement activities on animal drugs compounded from bulk drug substances that present the most significant concerns:
  - Safety,
  - Bulk drug substances intended for use in food-producing animals,
  - Copies of marketed FDA-Approved or Indexed Drugs or
  - **Office Stock:** Compounded drugs kept on hand by veterinarians for patients without a patient-specific prescription.

What is Guidance #256?

Meeting the requirements of the Federal Food, Drug, and Cosmetic Act (FD&C Act), a drug must be legally marketed under the animal drug approval requirements of the FD&C Act (approved, conditional approval, or Index Drug.)

Compounded drugs do not go through any of the pre-market review processes required to be legally marketed.

What does "meeting FD&C Act requirements" mean?

- Data is submitted to FDA demonstrating that the animal drug is safe and effective,
- Drug is manufactured under cGMP's and meeting product specifications,
- Sponsor of drug provides instructions and information regarding safety risks and how to properly administer the drug.

FDA's Concerns about Compounded Drugs

- Safety:
  - Superpotency, microbial contamination, and drug formulations that present safety risks for the treated animals or for people handling or administering the drug.
- Compounded drugs sold as office stock (as opposed to dispensed by a pharmacy upon receipt of a prescription for an identified patient):
  - The concern is exposing large number of animals to drugs of unproven safety, effectiveness, and quality.
  - Exception: FDA recognizes that in some limited cases an animal drug is urgently needed, and the time needed to compound a drug in response to an individual patient prescription may result in animal suffering or death.

FDA's Decision on Buprenorphine

- FDA recently decided that BUPRENORPHINE is not one of these exceptions that can be manufactured and used as office stock.
- Thus, enforcement action against compounding buprenorphine for office stock is at risk if not meeting the exceptions for being able to compound the drug as office stock.

Manufacturing Requirements for an Indexed Drug

Drug is properly manufactured under cGMP's, including:

- ✓ Validated analytical methods: accurate testing methods.
- ✓ Validated manufacturing process: ensuring reproducibility and integrity of the quality of the product.
- ✓ Specific active and inactive ingredients are to be used in the manufacturing process and all vendors and ingredients have been qualified by sponsor.

Note: Buprenex is an approved drug for human use; however, once diluted, it is no longer considered cGMP and the integrity of the product is not assured.

Regulatory Requirements of an Indexed Drug

- The animal drug is accurately labeled.
  - ✓ Drugs indication(s) and intended species is properly identified.
  - ✓ Warnings and safety information is adequately presented in the labeling and proper instructions on how to administer or use the product.
  - ✓ Indexed drugs will always contain a Package Insert with detailed information and safety and use
- Sponsors must have a pharmacovigilance program to monitor adverse events, as well as a product complaint program ensuring appropriate action can be taken throughout the life of the drug.

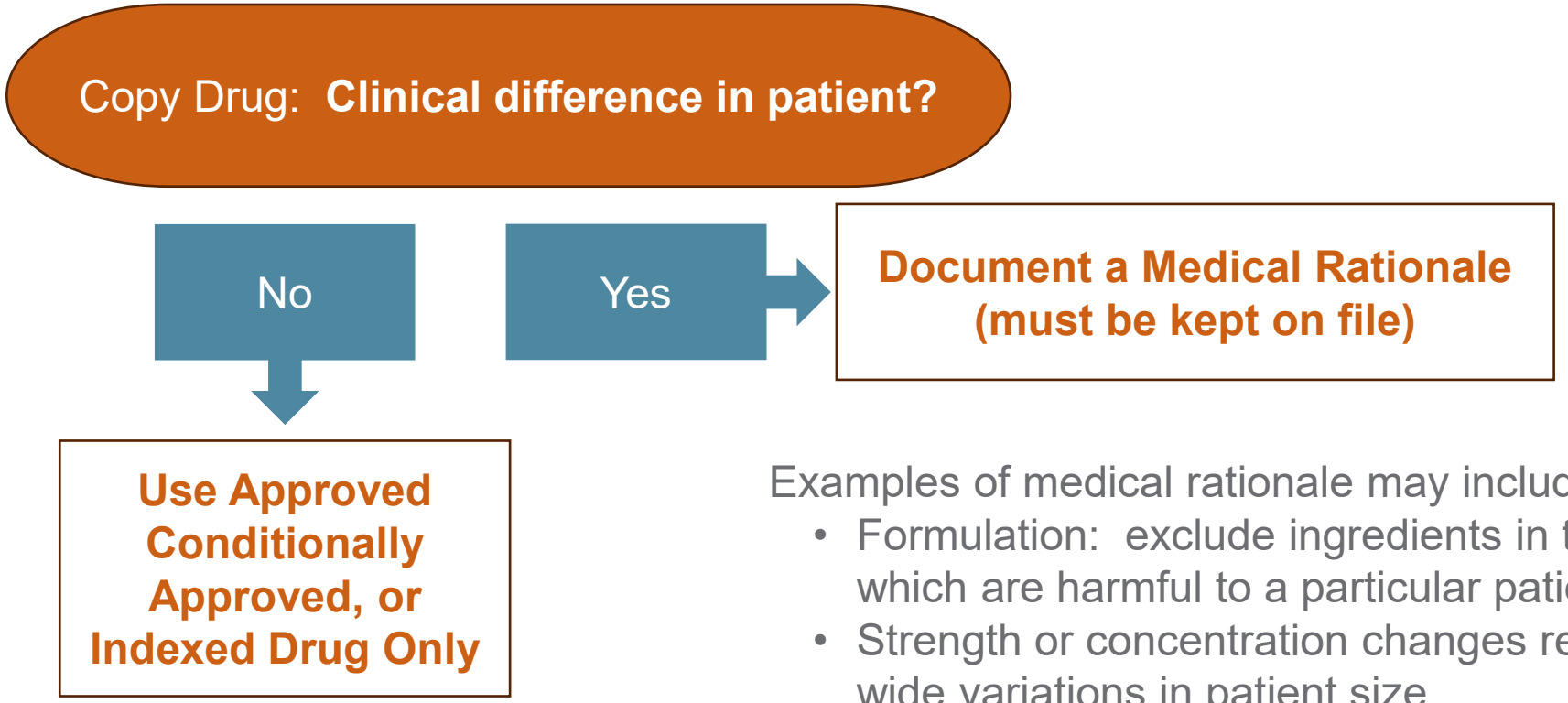
When is compounding acceptable?

One of the key points when enforcement action will not be taken:

The compounded drug is NOT a copy of a marketed FDA-approved or Indexed Drug.

If it is a copy, then the following conditions must be met:

When is compounding acceptable?



Examples of medical rationale may include:

- Formulation: exclude ingredients in the approved or index drug which are harmful to a particular patient or species
- Strength or concentration changes required to accommodate wide variations in patient size
- Changes in flavoring or dosage from needed to achieve patient compliance or protect individuals administering the drug.

Note: Price Difference is not a medical rationale.

Medical Rationale Required

FDA intent is not to challenge the prescriber

- FDA will check to ensure that the medical rationale describing the clinical difference is detailed enough to make the determination of needing a compounded drug.

CONSEQUENCES OF NON-COMPLIANCE

FDA will take a risk-based approach for initiating inspections and determining which pharmacies and compounding facilities to visit first.

If violations are found, fines could be issued. The actions taken will depend upon the severity of the violations.

SUMMARY

- Approved, conditionally approved and indexed drugs must be used unless there is a clinical difference and documented medical rationale.
- Office stock drugs are only acceptable if listed by FDA or under review.
  - **Buprenorphine was reviewed and not accepted as a bulk drug substance for compounding office stock for nonfood-producing animals.**
- Compounded drugs:
  - Do not go through a review process ensuring the drug's safety, efficacy, and quality.
  - Are not made under cGMP's. Example: Buprenex, cannot be diluted. If it is, it is no longer GMP compliant.
  - Do not provide adequate directions for use.
- Compounded drugs violate the FD&C Act because they are not approved or Indexed drugs.
  - Compounded drugs cannot be presumed to have the same effect as the approved or Indexed drug.
  - Focus is not only on the API but the manufacturing of the finished drug product.

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QUESTIONS?

Please direct post-webinar questions to: info@FidelisAH.com

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