The Animal Drug Compounding Debate

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Agenda

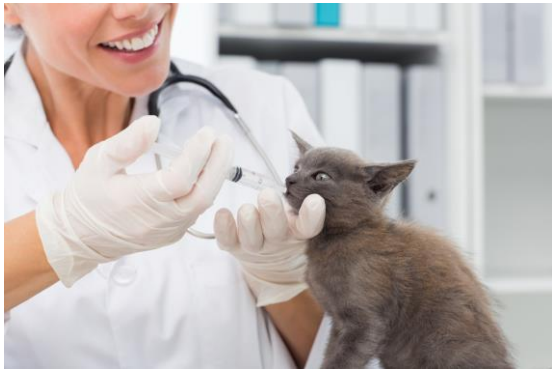
- Legality of Animal Drug Compounding / Historical Context
- FDA's View of Animal Drug Compounding
- FDA's Regulation and Oversight of Animal Drug Compounding
- Views Regarding Animal Drug Compounding and FDA's Guidance
- Defining the Controversy / Areas of Agreement and Disagreement

Legality of Animal Drug Compounding: Historical Context

- Panel Discussion

FDA's View of Animal Drug Compounding

- FDA believes the Federal Food, Drug and Cosmetic Act (FD&C Act) does not distinguish between animal compounding and animal drug manufacturing
- As a result, animal drugs not approved, conditionally approved, or on the Index of Legally Marketed Unapproved New Animal Drugs for Minor Species under Section 572 of the FD&C Act, FDA views as generally "unsafe," "misbranded", and "adulterated"
- Section 512(a)(4) and (5) provides for exemptions for animal drug compounding from approved animal and human drugs when *extralabel use* requirements set forth in 21 C.F.R. Part 530 are met



FDA's View of Animal Drug Compounding (cont'd)

- Extralabel Use: Part 530 Requirements
  - Implements the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994
  - On the lawful order of a licensed veterinarian within the context of a valid veterinary-client-patient relationship
  - New animal drugs and approved new human drugs, limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat
  - Actual use or intended use of a drug in an animal in a manner not in accordance with approved labeling, including use in species not listed in the labeling, use for indications (disease or other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from the labeled withdrawal time based on these different uses

FDA's View of Animal Drug Compounding (cont'd)

- Extralabel Use: Part 530 Requirements (cont'd)
  - No approved new animal or human drug that will, in available dosage form and concentration, treat the condition diagnosed
    - Compounding from a human drug for use in food-producing animals is not permitted if an approved animal drug can be used
  - Compounding only by a licensed pharmacist or veterinarian within the scope of a professional practice
  - Adequate procedures and processes followed to ensure the safety and effectiveness of the compounded product
  - Scale of the compounding operation commensurate with the established need for compounded products (e.g., similar to that of comparable practices)
  - All relevant State laws relating to the compounding of drugs for use in animals followed

FDA Regulation and Oversight of Animal Drug Compounding

- Previously
  - 1996 CPG 608.400 (Compounding of Drugs for Use In Animals), updated in 2003, withdrawn May 19, 2015
    - Compliance Policy Guides (CPGs) are FDA expressions of non-binding policy
    - FDA would primarily defer to States' authorities day-to-day as states regulate compounding for animal as a traditional part of pharmacy practice
    - FDA would consider acting where compounding raised "concerns normally associated with a drug manufacturer" and could result in new animal drug, adulteration, or misbranding violations of the FD&C Act

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- Previously
  - 1996 CPG 608.400 (Compounding of Drugs for Use In Animals), updated in 2003, withdrawn May 19, 2015 (cont'd)
    - FDA set out the follow factors to determine when compounding raised these concerns:
      - Compounding for situations where health of animal not threatened or suffering or death of animal not likely if animal not treated
      - Compounding in anticipation (i.e., in advance of receiving prescriptions)
      - Compounding for uses prohibited for extralabel use due to public health risks
      - Compounding using commercial-scale manufacturing equipment
      - Compounding where an approved animal or human drug was available and could appropriately be used to treat the condition

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- Previously (cont'd)
  - CPG 608.400 called into question by *Franck's Lab* case (*U.S. v. Franck's Lab, Inc., et al.*,816 F. Supp. 2d 1209 (M. D. Fla. 2011), *appeal filed but later jointly dismissed as moot*)
    - FDA asserted that it could prohibit veterinary compounding from bulk drug substances, because all compounds are "new drugs" under the FD&C Act, and as such, FDA could enforce its regulatory authority over animal compounds and prohibit compounding from bulk drug substances
    - But Franck's Lab practiced "traditional animal compounding", i.e., compounded animal drugs under State-regulated guidelines, including patient-client-veterinarian relationship, only for non-commercially-available drugs, and placed warnings on drugs prohibiting use for non-food animals

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- Previously (cont'd)
  - CPG 608.400 called into question by *Franck's Lab* case (*U.S. v. Franck's Lab, Inc., et al.*,816 F. Supp. 2d 1209 (M. D. Fla. 2011), *appeal filed but later jointly dismissed as moot*)
    - Court found that the FDCA's new drug approval process did not give FDA the authority to prohibit compounding from bulk, because veterinary compounding is a traditionally state regulated practice, and Congress would not displace the state regulation of a traditional part of the practice of pharmacy in such a cryptic manner
    - As such, court held FDA did not have authority to enjoin the "long-standing, widespread, state-regulated practice of pharmacists filling a veterinarian's prescription for a non-food producing animal by compounding from bulk substances"

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- May 2015, FDA Issued Draft Guidance #230 Compounding Animal Drugs from Bulk Drug Substances
  - Guidance documents are non-binding descriptions of FDA's interpretation of or policy on a regulatory issue
  - Directed at state-licensed pharmacies, licensed veterinarians, and facilities that register with FDA as outsourcing facilities under 503B of the Federal Food, Drug and Cosmetic Act
  - Drafted to replace CPG 608.400
  - FDA attempted to provide limited circumstances where it will take no enforcement action for the compounding of bulk substances

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230 (cont'd)
  - Permits state-licensed pharmacy under the direct supervision of pharmacist to compound when
    - Valid Rx from veterinarian for individually-identified animal patient submitted by veterinarian or patient's owner/caretaker; advance quantities possible depending on state rules for patient-specific Rx's based on history of product over consecutive 14-day period within last 6 months
    - Not for food-producing animals (food animals include cattle, swine, chicken, turkey, sheep, goats, and non-ornamental fish) and includes such statement; irrelevant whether a particular animal is actually intended to be introduced into food chain

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230 (cont'd)
  - Permits state-licensed pharmacy under the direct supervision of pharmacist to compound when (cont'd)
    - If there is an approved human or animal drug with same active ingredient, prescribing veterinarian must document why the change would produce a "clinical difference" and cannot be compounded from FDA-approved human or animal drugs
    - The veterinarian must document on the prescription that the compound is not for a food producing animal, and that "[t]here are no FDA approved animal or human drugs that can be used as labeled or in an extralabel manner under section 512(a)(4) or (5) and 21 CRF part 30 to appropriately treat a disease, symptom, or condition for which this drug is being prescribed."

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230 (cont'd)
  - Permits state-licensed pharmacy under the direct supervision of pharmacist to compound when (cont'd)
    - Pharmacy must document why the compounded drug cannot be made from an approved FDA drug if there is an approved drug with the same active ingredient
    - Bulk substances must be manufactured by an establishment registered under Section 510 of the Act along with a certificate of analysis
    - Drug must be compounded according to chapters <795> and <797> of the *United States Pharmacopeia and National Formulary* including sterility

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230 (cont'd)
  - Permits state-licensed pharmacy under the direct supervision of pharmacist to compound when (cont'd)
    - Drug not sold or transferred by an entity other than the compounding entity with an exception for administration of the compounded drug by a veterinarian
    - Within 15 days of a pharmacy becoming aware of an product defect or serious adverse event associated with drug compounded from bulk drug, it will be reported on Form FDA 1932a
    - Label of compounded drug includes the species of intended patient, name of animal patient, and name of owner/caretaker of the animal patient

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230: Compounding Animal Drugs from Bulk Drug Substances (cont'd)
  - Permits state-licensed veterinarian to compound when (similar to animal pharmacy with the following modifications):
    - Drug compounded and dispensed by a veterinarian to treat an individually-identified animal patient under his care
    - Permitted only when no FDA-approved animal or human drugs can be used as labeled or extralabel to treat the disease, symptom, or condition for which prescribed
    - Veterinarian may administer or dispense the compounded drug
    - [Note: Does not appear to include same provisions regarding advance compounding as with animal compounding pharmacies.]

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230: Compounding Animal Drugs from Bulk Drug Substances (cont'd)
  - Compounding by outsourcing facility (similar to animal pharmacy with the following modifications):
    - Only permitted to compound from bulk substances that appear on a positive list—this list requires that no marketed or approved drug can be used on or off label to treat the condition and requires immediate treatment with the compounded drug is required to avoid animal suffering or death;
    - Creates a new category of animal drug compounding by an outsourcing facility, similar to provisions for human drug compounding (but no statutory authority for this in animals)

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230: Compounding Animal Drugs from Bulk Drug Substances (cont'd)
  - Compounding by outsourcing facility (similar to animal pharmacy with the following modifications):
    - Drug compounded by or under supervision of a licensed pharmacist
    - Drug compounded in accordance with cGMP requirements
    - Drugs compounded for animals by an outsourcing facility are included in the report required by 503B of the FD&C Act to be submitted to FDA each June and December identifying drugs made by the facility in the previous 6-month period, including active ingredients and their source(s), NDC number of the source ingredient(s), strength of the active ingredient(s) per unit, the dosage form and route of administration, package description, number of individual units produced, NDC number of the final product, if assigned, along with which reported drugs were intended for animal use

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230: Compounding Animal Drugs from Bulk Drug Substances (cont'd)
  - Compounding by outsourcing facility (similar to animal pharmacy with the following modifications): (cont'd)
    - Veterinarian's prescription or order states the drug is intended to treat the species and condition(s) for which the substance is listed in the appendix developed in conjunction with the Guidance
    - Certain product labeling including language such as "Not for resale," "Compounded by [name of outsourcing facility]" and "Adverse events associated with tis compounded drug should be reported to FDA on Form FDA 1932a"
    - Veterinarian is only allow to administer bulk drug compounded at an outsourcing facility
    - [Note: Does not appear to include same provisions regarding advance compounding as with animal compounding pharmacies.]

FDA Regulation and Oversight of Animal Drug Compounding (cont'd)

- FDA Draft Guidance #230: Compounding Animal Drugs from Bulk Drug Substances (cont'd)
  - Concurrently FDA was supposed to be developing a list of bulk drug substances for Appendix A that entities registered as outsourcing facilities under Section 503B of the FD&C Act are limited to for purposes of compounding.
    - Compounding of an Appendix A drug allowed for an individual animal patient or veterinarian office use when that drug is listed on Appendix A for that species and condition only
    - FDA solicited input for bulk drug substances should be on the list in Appendix A

Views Regarding Animal Drug Compounding & FDA's Guidance

- State – Compounding View
  - Practice of pharmacy v. FDA's potential authority (and DEA)
  - State-specific rules and practices
- Veterinarians View – Comments on FDA's Draft Guidance
  - Concerns about drug availability, enforcement, adverse event reporting and more
- Pharma View
  - Compounding undercuts FDA-regulated manufacturing
  - Compounding quality issues ?
- Other filed comments on FDA's Draft Guidance

Defining the Controversy: Areas of Agreement and Disagreement

- Many animal drug manufacturers and veterinary compounder agree on some general terms of what is appropriate compounding.
  - Some defined rules are desirable – Statute or properly promulgated regulations are preferred, but at a minimum final guidance
  - The Compounding Quality Act is only applicable to human drugs (this includes 503B outsourcing facilities)
  - Compounding from finished dosage forms where practicable does not generally represent a regulatory issue
  - There is a legitimate role for veterinary compounding from bulk ingredients (e.g., exotic species where compounding from finished drugs is impractical)
  - Compounders should not make drugs that are essentially copies of approved drugs
  - Compounders should not manufacture drugs under the guise of pharmacy compounding

Defining the Controversy: Areas of Agreement and Disagreement

- However, there are significant areas of disagreement within the broad areas of agreement, mostly involving determining when compounding from bulk ingredients is appropriate.
  - In the absence of statute/regulations/final guidance, what is FDA's role and authority?
  - What legal authority does final guidance actually have?
  - What is a copy of an approved drug?
  - How much product can be compounded in "reasonable anticipation" of an order?
  - What constitutes and appropriate VCP relationship?
  - What is patient specific?
  - What scale is appropriate for compounding, and what constitutes manufacturing?

Defining the Controversy: Areas of Agreement and Disagreement

- However, there are significant areas of disagreement within the broad areas of agreement, mostly involving determining when compounding from bulk ingredients is appropriate (cont'd)
  - Is compounding for office stock appropriate? If so, how much?
  - What restrictions on interstate sales are appropriate?
  - What role should compounders play in meeting drug shortages?
  - What restrictions should be places on use of compounded drugs in food producing animals?
  - Are FDA's proposed record-keeping requirements reasonable and/or beneficial?
  - What are appropriate marketing practices for compounding services?

Questions?

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