COMPOUNDING – Are you following the rules?

Dr. Lynne White-Shim
MS, DVM
Assistant Director, Scientific Activities
American Veterinary Medical Association

Common Questions

- What is compounding?
- What can I legally compound?
- Can I keep compounds to use in my clinic?
- Can I keep compounds to dispense from my clinic?
- What's AVMA doing to protect compounding needs?

"What is Compounding?"

- Intended as individually mixed drugs for specific patients with special needs not met by FDA approved drugs
- *Any* manipulation of drug product
- Two types of compounding
  - From FDA-approved drug: legal*
  - From unapproved drug: not legal in animals per FDA

* If following federal and state rules

"What is 'Bulk' Compounding?"

- Not a volume of drug – it is a type of drug.
- It is compounding from a raw, active ingredient.

"What is 'Bulk' Compounding?"

- It is the active pharmaceutical ingredient (API) that …
  - can be used in the manufacture of an FDA-approved drug, and/or
  - can be used by a pharmacist to prepare a compound.

"But I heard it's actually not illegal, that FDA just interprets it that way?"

- Here is what we know:
  - FDA is the lead federal authority over drugs.
  - FDA incorporates in its rules that compounding from FDA-approved drugs is the legal type of compounding.

"But I heard it's actually not illegal, that FDA just interprets it that way?"

- Here is what we know:
  - Some groups say compounding is a traditional pharmacy practice that Congress never meant FDA to regulate.
  - FDA asserts it attained the authority to regulate compounding through the Federal Food Drug and Cosmetic Act.

"But I heard it's actually not illegal, that FDA just interprets it that way?"

- Here is what we know:
  - 3 of 3 appellate courts have said compounded drugs are New Animal Drugs and, as such, are regulated by FDA under the FFD&C Act:
    - 7th Circuit: *9/1Kg. Containers*, 854 F.2d 173 (7th Cir 1988), *cert. denied*, 489 U.S. 1010 (1989)
    - 9th Circuit: *Medical Center Pharmacy*, 536 F.3d 383
    - 3rd Circuit: *United States v. Algon Chem. Inc.*, 879 F.2d 1154 (3d Cir. 1989).

"But I heard FDA doesn't have a rule on this, just a 'CPG'?"

- 21 CFR 530 – a federal rule – says compounding from bulk is not permitted.
- FDA also has a Compliance Policy Guide (CPG)
  - Defers day-to-day authority to states
  - But FDA can enforce the preparation of even one compound from bulk.

"But I heard FDA doesn't have a rule on this, just a 'CPG'?"

- FDA CPG
  - Indicates it is more likely to use enforcement in especially egregious activities like manufacturing mimics of FDA-approved drugs.
  - It has an Appendix A which is a list of compounds FDA would not normally object to having prepared.

"Where are the rules?"

- Federal Food Drug and Cosmetic Act
- 21 CFR 530
- State pharmacy rules
- State veterinary medical rules (prescription drugs)

FDA Extralabel Drug Use Rules

- Veterinarian-Client-Patient Relationship (VCPR)
- Animal health/life threatened
- Labeling and recordkeeping requirements

FDA Extralabel Drug Use Rules

- Compounding allowed…
  - If done by licensed vet or pharmacist
  - When no approved drug can be used per label or extralabel
  - Using FDA-approved drug
  - Safety/effectiveness processes in place

"How do I decide what to use in my non-food animal patient?"

- Top legal option: use an FDA-approved drug labeled for the species you are treating, and use it per label, or (per ELDU rules) can use human equivalent.
- Next legal option: use another FDA-approved drug labeled for another species of animal (per ELDU rules).

"How do I decide what to use in my non-food animal patient?"

- Third legal option: somehow modify a human or animal FDA-approved drug (per ELDU rules)
  - Ex: crush tablets and add a flavor.
- If you compound:
  - It should be based on good evidence showing safety/efficacy,
  - You should monitor therapeutic effect, or
  - It should be done if no other viable choice.

Compounding preparations

- Nonfood animal examples
  - Injectable antibiotic + glycerin: otic prep
  - Liquid amoxicillin + tuna flavor for cat
  - Mixing pre-meds into one syringe

Compounding preparations

- Food animal example
  - Mixing 50% dextrose, b-vitamins, dexamethasone for prompt IV ketosis tx
- Additional requirements
  - Extended withdrawal period
  - None from prohibited list

"How do I decide what to use in my non-food animal patient?"

- Compounding from "bulk"
  - Currently not legal per the FDA
  - We think it's medically necessary in nonfood animals in some circumstances – but know it's currently illegal.
  - Economic reasons are not a justification for compounding from bulk

"How do I know if a drug is FDA-approved or not?"

- Animal drugs that are approved almost always have one of two possible numbers on the package:
  - NADA number (New Animal Drug Application for pioneer drugs)
  - ANADA Number (Abbreviated New Animal Drug Application for generic/non-proprietary drugs)
  - Many FDA-approved drugs have "Approved by FDA" on the label

"How do I know if a drug is FDA-approved or not?"

- Human approval numbers:
  - A New Drug Application number (NDA) and Abbreviated New Drug Application (ANDA) are associated with FDA-approved human drugs.

Challenging clinical scenarios

- Status epilepticus
  - IV Diazepam
  - Alternative benzodiazepines
  - When backorders occur: options?

Challenging clinical scenarios

- Perioperative analgesia
  - Robenacoxib approved
    - only available as tablets
    - may not be appropriate in immediate postoperative period
  - Other NSAIDs: do not have safety & efficacy information in cats
  - Options during backorders?

Challenging clinical scenarios: Wildlife immobilization need

- Medetomidine
  - High potency alpha-2 agonist
  - Indications:
    - Capture and immobilization of wildlife such as deer, bison, bear, etc.

Challenging clinical scenarios: Wildlife immobilization need

- Dose for 550kg brown bear = 0.075 mg/kg
- Total dose = 37.5 mg
  - Approved formula (1mg/ml): 37.5 mL
  - Compounded formula (20 mg/mL): 1.9 mL

"Can I keep compounds in my office to administer?"

- In most states (unclear in 14 states).
  - Some states specify that compounds must always be ordered for a specific patient.
  - Some states have decreased the allowances for in-office use due to recent fungal meningitis outbreak from compounds.

"Can I keep compounds in my office to dispense?"

- In Arizona – yes, veterinary dispensing is defined to include compounding (new law passed in 2013).
- In California – yes, to a limited extent.
  - It's legal to dispense 72-hours worth of a previously prepared compound for a patient.

"Can I keep compounds in my office to dispense?"

- In 22 other states – no, not based on our knowledge of current rules.
  - In these states it is not legal to have a pharmacy send you a compound, to put your clinic label on it, and dispense it.
- In remaining states – unclear.

"Can I keep compounds in my office to dispense?"

- Be familiar with the statutes and regulations governing compounding in your state.
- Check with your state boards of veterinary medicine and pharmacy on how the compounding laws and regulations in your state are interpreted and enforced.

"Can I keep compounds in my office to dispense?"

- In states with no laws specifically addressing compounding, or where the laws are vague, veterinarians may be at risk in administering or dispensing such products and are urged to use caution.

"But I'm an exotic animal veterinarian and need to keep a stock in my clinic?"

- Your current legal options we are aware of:
  - Script out the compound for a pharmacy to prepare for the owner to pick up.
  - Prepare the compound from an FDA-approved drug on your own to dispense.
  - Have a pharmacy prepare a compound from FDA-approved drug for you to administer in the clinic (if the state allows).

"The patient will not be treated if the client cannot get a cheaper compound. Options?"

- FDA has not identified cost as a legitimate reason for compounding.
- Recognize benefits/risks of selecting a compound because it is cheaper.
  - Potential for liability
  - Potential for lack of safety/efficacy of a compound when the FDA-approved version is known.

"What's AVMA doing to protect compounding needs?" *AVMA is trying to identify good solutions*

- Congress is going to consider compounding legislation.
- We need to be prepared to help shape any legislation appropriately.
- Our *current* policies do not advocate for legalization of compounding.

Three-step approach to revising compounding policies

- Volunteer groups prepared revisions.
- Member feedback sought through April 22, 2013.
- Volunteer groups will consider feedback, make any changes and submit revisions to the Executive Board.

"Who are the volunteers working on the policies?"

- Volunteer veterinarians on councils and committees – many working in practice – identify best ways forward.
- AVMA staff facilitate their work.
- Volunteer veterinarians on the Executive Board will ultimately consider the proposed revisions.

Current AVMA Policies & Statements

- Compounding
- Compounding from Bulk (Unapproved) Substances
- AVMA Letter to FDA – *Compliance Policy Guide Sec. 608.400: Compounding of Drugs for Use in Animals*

What we currently say… Compounding – AVMA Policy

- Veterinarian-driven, not pharmacist-driven
- Based on a Veterinarian-Client-Patient Relationship (VCPR)
- Compliance with the Animal Medicinal Drug Use Clarification Act (AMDUCA) and the FDA Compliance Policy Guide

What we currently say… Compounding – AVMA Policy

- Drugs for which both safety and efficacy have been demonstrated
  - in the compounded form
  - in the target species

or…

What we currently say… Compounding – AVMA Policy

- Disease conditions for which response to therapy or drug concentration can be monitored

or…

What we currently say… Compounding – AVMA Policy

- Patients for which no other method or route of drug delivery is practical

What we currently say… Compounding – AVMA Policy

- Used with same precautions as an approved drug, including:
  - Counseling regarding potential adverse reactions; and
  - Attention to the potential for unintended human or animal exposure

What we currently say… Compounding from Bulk (Unapproved) Substances - AVMA Policy

- Non-food animals
- Medically necessary in certain situations
- Should be allowed through enforcement discretion

IF…

What we currently say… Compounding from Bulk (Unapproved) Substances - AVMA Policy

- Used under the conditions for extra-label (AMDUCA)
- Effective regulatory mechanisms in place
- Patient-specific
- Performed only in the context of a VCPR

What we currently say… Compounding from Bulk

- Drugs should be compounded only from approved drugs unless:
  - Approved drug is not commercially available; or
  - Needed compounded preparation cannot be made from the approved drug
- Cost is not an appropriate reason

New concepts AVMA volunteer groups are proposing…

- Underscoring that potency/purity/safety cannot be guaranteed with drugs compounded from bulk
- Medically necessary when:
  - FDA-approved product not commercially available, or
  - FDA-approved drug is available but the needed compound cannot be prepared from it, or
  - The needed drug is not in an FDA-approved, commercially available form

New concepts AVMA volunteer groups are proposing…

- For dogs, cats and horses:
  - A list of compounds that are legal to prepare
- For nonfood minor species:
  - Wide compounding ability if no FDA-approved or indexed drug can be used
- For food animals:
  - A list of poison antidotes, depopulation, and euthanasia compounds

New concepts AVMA volunteer groups are proposing…

- The need to inform clients that drugs compounded from bulk are not evaluated by FDA
- Labeling compounded drugs that they are not FDA approved

New concepts AVMA volunteer groups are proposing…

- Advocating legalization of compounds in-office for urgent/emergency needs
- Advocating for quality assurance oversight of compound preparation

We need your feedback…

- Proposed revisions on AVMA NOAH Discussion Groups ("AVMA Seeks Feedback on Compounding")
  - Will need to login as an AVMA member.
- Feedback opportunity through April 22, 2013.

AVMA Resources

- Compounding website
  - Includes policies, compounding brochure, FDA letters

Other Resources

- State veterinary medical associations
- State veterinary licensing boards

Other Resources

- State boards of pharmacy
- Society of Veterinary Hospital Pharmacists

Other Resources

- United States Pharmacopeia
- International Academy of Compounding Pharmacists
- FDA Center for Veterinary Medicine

Contact

Dr. Lynne White-Shim
AVMA – Scientific Activities
lwhite@avma.org