February 10, 2014

Dr. Bernadette Dunham, Director
FDA Center for Veterinary Medicine
7519 Standish Place
Rockville, MD 20855

Dear Dr. Dunham,

The American Veterinary Medical Association recognizes there are not enough available pharmaceutical products approved by the Food and Drug Administration (FDA) to treat all the medical needs of various animal patients. Given the dynamic flux of drug availability including shortages/back orders and conversely, new approvals, we are writing to you today to emphasize support for FDA’s enforcement against egregious compounding, while also underscoring the need for veterinarians’ ability to utilize professional discretion in certain veterinary compounding circumstances.

Recognizing that compounding is a key regulatory priority for FDA Center for Veterinary Medicine (CVM), we first wish to underscore the value of the FDA’s extralabel drug use rules and FDA’s Compliance Policy Guide (CPG) 608.400 in FDA’s facilitation of enforcement against egregious use of bulk ingredients, including mimics of commercially available FDA-approved drugs, as well as compounding for food-producing animals which is a food safety concern. We continue to support enforcement against such acts. We also recognize and support FDA’s enforcement discretion for very specific, limited circumstances of compounding in food animals. The AVMA continues to utilize various communication vehicles to educate veterinarians regarding the need for compliance with FDA’s rules, use of evidence-based medicine, reporting of suspected adverse events, and use of compounding limited to situations where no other method or route of drug delivery is practical, where safety, efficacy, and stability have been demonstrated in the specific compounded form in the target species, or, disease conditions for which a quantifiable response to therapy or drug concentration can be monitored.

However, the current regulations and guidances have a significant shortcoming. They do not offer enforcement discretion for the limited use of medically necessary preparations compounded from bulk ingredients for non-food animals. We therefore recommend incorporation of two new concepts for FDA’s consideration as it considers new ways forward with regard to regulation of compounding for use in animals:

- **Use of a set of circumstances, not a prescribed list, for compounding from bulk in non-food animals.** In lieu of what has been called a ‘positive list,’ AVMA instead asserts there should be three general sets of circumstances (see attachment), in which compounding from bulk pharmaceutical ingredients may be medically necessary and should be allowed within the context of a Veterinarian-Client-Patient Relationship (VCPR) in non-food animals.
• **Office stock provisions.** The AVMA asserts veterinarians should be able to legally maintain sufficient quantities of compounded preparations in their office for urgent administration needs or emergency situations. If current federal statute does not allow FDA CVM to identify its enforcement plan regarding office stock, we understand from state stakeholders that it would be helpful for FDA CVM to provide its interpretation of the current federal status on office stock and anticipatory veterinary prescribing.

While recognizing the current focus on compounding has been the creation of ‘lists’ of acceptable bulk drugs for use of compounding in animals, we contend that the FDA's regulations can be made stronger through a shift towards the opportunity for veterinarians to compound in accordance with our policies.

Thank you for your time and consideration. Should you have questions regarding this policy or need additional clarification, kindly contact Dr. Lynne White-Shim at 800-248-2862 ext. 6784 or lwhite@avma.org.

Sincerely,

David E. Granstrom, DVM, PhD, DACVM (parasitology)
Associate Executive Vice President and COO
American Veterinary Medical Association
Appendix

Three general sets of circumstances in which compounding from bulk pharmaceutical ingredients may be medically necessary in non-food animals within the context of a VCPR:

- the approved product is not commercially available, or
- the needed compounded preparation cannot be made from the approved product, or
- there is no approved product from which to compound the needed preparation

Approved drugs can be unavailable commercially for several reasons:

a) No drug containing the needed ingredient was ever approved (e.g., potassium bromide for the control of seizures),

b) Withdrawn human drugs whose use in animals presents great benefits and negligible risks to animal and public health (e.g., cisapride for treatment of feline megacolon rather than surgical removal of the entire colon or euthanasia),

c) The sponsor ceases sale of the approved drug for business (not safety) reasons, or

d) The approved drug is temporarily unavailable for reasons such as backorder or interruptions in manufacturing. The COBTA believes drugs that are commercially unavailable for a one-month timeframe or longer meets the definition for ‘temporary commercial unavailability.’

The approved product can be inadequate for compounding for several reasons:

a) The concentration of active ingredient in the approved drug is too low to produce a compounded preparation with the needed concentration in a practical dosing volume or size. The dose of compounded suspensions, capsules, or parenterals must be of a volume or size to be practically administered by mouth or injection, including injection by dart.

b) Compounding from the approved drug has negative effects on the quality of the preparation.

1. Sterile injectable drugs and eye drops may contain excipients, particulates, or pyrogens if approved drugs are used for compounding.

2. Gels, creams, or syrups may be gritty and active ingredients may be unevenly dispersed if approved drugs are used for compounding. The COBTA’s understanding is that any transdermal gel being prepared for medically necessary purposes must be done from use of raw, active ingredients.

3. Intravenous injections and preparations administered through subpalpebral catheters and feeding tubes may have particulate matter rather than being clear if approved drugs are used for compounding.

c) The approved product may contain an ingredient that the patient cannot tolerate (e.g., beef in allergic individuals).

d) Flavoring cannot mask the objectionable taste of some approved drugs. For example, some patients refuse flavored metronidazole hydrochloride because flavoring does not mask the metallic taste. Instead, tasteless metronidazole benzoate is flavored to enhance palatability. However, it is generally preferable to flavor approved drugs rather than bulk drugs because of the assurances of safety, efficacy, and quality that accompany approved drugs.