July 14, 2014

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

Dear Dr. Dunham,

On behalf of the AVMA’s more than 85,000 members involved in a myriad of areas within the veterinary medical profession, we appreciated the opportunity to participate in the July 8 roundtable discussion on animal drug compounding.

Veterinary medicine is unique in that we treat a multitude of species with an even greater number of diseases and conditions. Approval of new animal drugs is paramount to veterinary medicine and engaging with the Agency and Congress in facilitating that process remains a high priority for our Association. However, as we discussed in the meeting, compounding is still a necessary practice for veterinarians because there are, and always will be, a limited number of FDA-approved drugs for the many species and conditions that we treat. In addition, intermittent drug shortages and the commercial unavailability of FDA-approved drugs drive the need for compounded preparations within veterinary practice.

AVMA’s policy is very clear in that the use of a compounded drug, regardless of the source of the active ingredient, should be done within, and driven by, a Veterinarian-Client-Patient Relationship, or VCPR, and limited to three conditions:

- those drugs for which both the safety and efficacy have been demonstrated in the compounded form in the target species, such as using potassium bromide solution to treat epilepsy in dogs;
- disease conditions for which response to the therapy or drug concentration can be monitored, such as monitoring heart rates of cats being treated with an atenolol suspension; and
- those individual patients for which no other method or route of drug delivery is practical. For example, transdermal methimazole is used to treat feline hyperthyroidism when the veterinary or human-approved tablets cause persistent vomiting.

The use of a compounded drug should be accompanied by the same precautions followed when using an approved drug, such as counseling a client regarding potential adverse reactions. The AVMA believes clients should be informed that compounds have not been evaluated by the FDA for potency, purity, stability, efficacy or safety, and should obtain client consent prior to their use. When adverse events are suspected, the AVMA also believes that veterinarians should report those immediately to the compounding pharmacist, the State Board of Pharmacy and the FDA Center for Veterinary Medicine.
We advise our members that there are two types of compounding within veterinary medicine. The first uses FDA-approved drugs and is lawful within the confines of FDA’s extra-label drug use and state rules. The other uses active pharmaceutical, or “bulk” ingredients, and is not currently considered lawful per the FDA, but may be medically necessary in limited scenarios. In general, we believe that there are three sets of circumstances in which veterinarians may need to compound from bulk ingredients to address the medical needs of their non-food animal (such as dogs, cats, horses, exotic pets, and zoo and wildlife species) patients within a VCPR:

- when the approved product is not commercially available. For example, chloramphenicol, used to treat bacterial infections in small animals, is currently on the FDA’s drug shortage list.
- when the needed compounded preparation cannot be made from the approved product. For example, transdermal methimazole, needed to treat certain cats with hyperthyroidism, is difficult to prepare using the FDA-approved drug. Another example is the occasional need to prepare an oral suspension of metronidazole, an antibacterial/antiparasitic medication for companion animals, because using the FDA-approved human drug does not fully neutralize the highly unpalatable nature of the product making it difficult to use this product to treat cats.
- when there is no approved product from which to compound the needed preparation. Examples of this include cisapride, used to treat cats with megacolon, and ronidazole, an antiprotozoal treatment also used in cats.

We acknowledge that the use of compounded preparations in food animals, such as cows and pigs, may have food safety and public health concerns that preclude their use. In food producing animals, the use of FDA-approved products provides significantly greater capacity to protect public health. Compounded preparations simply lack the quality control and the regulatory oversight seen in FDA-approved drugs. Therefore, the AVMA, the American Association of Bovine Practitioners and the American Association of Swine Veterinarians recommend that there be a publically available, current list of unapproved bulk substances that can be used to legally prepare compounded medications within a VCPR for food animal species. These medications should be specific and limited to euthanasia, depopulation and providing poison antidotes. If adequate scientific information is not available to assure avoidance of violative drug residues, then we believe the compound cannot be used in a food animal or the treated animal cannot enter the food supply. If none of these medically necessary circumstances exists, then, as previously stated, we believe the preparations should only be compounded from FDA-approved drugs.

The AVMA advises its members that animal health and patient medication compliance are appropriate reasons for compounding from bulk ingredients whereas economic reasons are not. We are opposed to pharmacies manufacturing under the guise of compounding because such products can be deleterious to animal health. Such egregious manufacturing also drives demand away from the drugs that have been approved by the FDA, potentially diminishing incentives for the pharmaceutical industry to invest in the development of new animal drugs. The AVMA encourages federal and state authorities to actively enforce manufacturing under the guise of compounding.
We hear from our members that the need for compounding is substantial and that there are certain species and specialties which rely upon compounding from bulk ingredients more than others. These species include: canines, felines, equines, and minor species, such as exotic animal pets, and animals maintained in zoos, aquaria, wildlife rehabilitation, and conservational facilities. Although it is not legal for preparations to be compounded in large quantities and sold to third parties, including veterinarians, for resale to individual patients, we feel it is absolutely critical for veterinarians to be able to legally maintain sufficient quantities of compounded preparations in their offices for medical emergent needs. For example:

- Nitrate and cyanide toxicity in cattle and copper intoxication in sheep requires immediate treatment with antidotes that can only be compounded from bulk ingredients. These needs have previously been recognized by the FDA by including ingredients like methylene blue in Appendix A of the Agency’s Compliance Policy Guide on Compounding of Drugs for Use in Animals.
- Megacolon in cats requires treatment upon diagnosis and there is no commercially available FDA-approved cisapride product or alternative medication to use.
- Many immobilization agents needed by zoo and wildlife veterinarians must be on hand at all times and can only be prepared by compounding.

In closing, we want to underscore the critical role compounding plays in allowing veterinarians to provide the best care for their animal patients. Veterinarians must be prepared to address the urgent medical needs of their patients and we believe they should be able to maintain necessary compounded preparations in their offices. We also maintain that compounded preparations should only be used within the confines of a VCPR to ensure that our clients understand the risks involved with using compounded medications. We believe that compounding from bulk ingredients should only be allowed when medically necessary to treat non-food animal species, but for food animals, our commitment to protecting food safety and public health means that this type of compounding should only be allowed in the very specific, limited situations outlined above. To better promote the health of our animal patients, we also advise that veterinarians should report adverse events immediately and compounded preparations should not be manufactured under the guise of compounding.

We thank you again for extending an invitation to us to speak at the roundtable and look forward to continuing the dialogue on this critical topic with FDA and other stakeholders. If you have questions or concerns, please contact Dr. Ashley Morgan at amorgan@avma.org or 202-289-3210.

Best regards,

Mark T. Lutschaunig, VMD MBA
Director
Governmental Relations Division