November 1, 2012

Please contact Ashley Morgan (amorgan@avma.org; 202-289-3210) if you have any questions or concerns.

**AVMA Responses to Senate HELP Committee**  
**Questions for Stakeholders Regarding Appropriate Regulation of Pharmacy Compounding**

To help us better understand current federal and state oversight of pharmacy compounding, any gaps that may exist, and the possibilities for and implications of any potential legislative solution, we invite you to provide written answers to the following questions. These questions should not be read to indicate intent to offer legislation addressing any particular issue discussed herein. We would appreciate feedback by **5pm on Wednesday, October 31st**. Please send written responses to Kathleen Laird in Chairman Harkin’s office (Kathleen_Laird@help.senate.gov) and Grace Stuntz in Ranking Member Enzi’s office (Grace_Stuntz@help.senate.gov).

- **Good Compounding Practices:** Should there be a federal requirement for compounding pharmacies to comply with USP standards for pharmaceutical compounding? Are there other standards that would be more appropriate? Should any good compounding practices requirement apply to all compounded products, or only a subset (e.g., sterile compounding, compounding in particular types of facilities?) How could federal good compounding standards be enforced?
  - FDA-approved products should be used to make compounded preparations. In cases where no approved drug or combination of approved drugs can adequately address a specific patient’s need, veterinarians and pharmacists must carefully assess whether the use of an unapproved substance in a compounded veterinary drug is consistent with state and federal law and FDA policy. If medical necessity dictates that a bulk active ingredient be used in the formulation, the pharmacist should ensure the integrity of all components used (e.g., certificates of analysis, USP National Formulary grade substance, or substances obtained from an FDA-registered supplier). The pharmacist can also identify the company from which products are purchased as well as the domestic or international location of the company. Formulas used for compounding should be obtained from a peer-reviewed source (e.g., published studies in primary literature, textbooks, or the USP) when possible.
• **Scale of Compounding:** Should any federal legislation distinguish between traditional compounding and large-scale compounding that more closely approximates manufacturing? If so, how should we define the two practices? Can criteria like volume, percentage of sales that are compounded product, standardization of drug products, or interstate sales inform that definition? If so, how? We would welcome proposed definitions drawing lines between practices that should and should not be encompassed.
  o Delineation between traditional compounding and large-scale compounding that approximates manufacturing would further clarify what is legal and what is not legal in the way of prescriptions for compounded preparations, which could be beneficial for veterinary practice. Specifically, if it’s determined that compounding from bulk ingredients is traditional compounding practice and not the manufacture of a “new animal drug,” then veterinarians who provide prescriptions for those compounds for reasons of medical necessity would be in compliance with the rules. The AVMA has not specifically advocated that compounding from bulk ingredients be considered traditional compounding practice due, in part, to concerns that, in the absence of adequate enforcement, large scale compounding that approximates manufacturing would be enabled, with potentially negative impacts to animal and human health.

• **Type of Compounding:** Should any federal legislation differentiate between types of compounded products, for example as sterile or non-sterile, products used for particular applications, or by some other measure? What other measures might be appropriate? If divisions by product type are appropriate, should facilities producing different types of products be subject to different federal requirements?
  o Clarity and consistency of rules across various types of compounded preparations would be helpful for veterinarians who would be prescribing these treatments for their patients.

• **Ingredients in Compounded Products:** What, if any, federal regulations should there be around the bulk ingredients used in compounding? Should pharmacies be limited to using FDA-approved ingredients and/or ingredients from FDA-registered facilities in compounded products? Should the use of marketed unapproved drugs be permitted in compounding?
  o Ideally, there would be FDA-approved drug products for each and every clinical scenario a veterinarian is faced with in practice, particularly given the many species and conditions veterinarians treat. While we support increased availability and expedited approvals of FDA-approved animal drugs, the AVMA believes it is medically necessary for veterinarians or pharmacists to compound from bulk ingredients in limited circumstances. There are two general sets of
circumstances in which the AVMA believes compounding from bulk ingredients may be necessary:
- the approved drug is not commercially available, or
- the needed compounded preparation cannot be made from the approved drug.

- **The Prescription:** Should there be a federal requirement that compounded products be made only in response to a prescription? Or in anticipation of a prescription based on previous sales? If so, should there be a federal requirement that the prescription or notation ordering a compounded drug product explicitly call for the drug to be compounded?
  - Compounding that is consistent with the FDA Extra-Label Drug Use regulations is the customized manipulation of an approved drug(s) by a veterinarian, or by a pharmacist upon the prescription of a veterinarian, to meet the needs of a particular patient. At the same time, some states, such as California, provide the opportunity for veterinarians to dispense previously-compounded preparations (prepared by external pharmacies) for individual patients so the medical condition can start to be treated while an external compounding pharmacy simultaneously starts developing a preparation. We understand this flexibility afforded to veterinarians in California can be particularly helpful during weekends after an animal is discharged from an emergency clinic (when compounding pharmacies may be closed), or for individual animals with a rare need (such as an exotic animal species) for a particular compound requiring a particularly unique preparation for the clinical scenario at hand.

- **Office Stock:** Should there be federal restrictions on compounding for office use? If so, what should the requirements or restrictions be?
  - Should the compounder be required to receive and/or reconcile prescriptions from the physician once the compounded product has been dispensed in the physician’s office?
  - Should the amount of product compounded for office stock be limited or capped in any way?
  - Should there be specific labeling requirements for compounded product for office use?
  - Should there be an allowance for compounding for research, teaching, or chemical analysis and not for sale or dispensing?
    - In-office use, and any subsequent allowance for dispensing to go home with the patient, should be limited to an individual patient’s current medical condition. Any purposeful procurement of compounds prepared from bulk ingredients that are mimics (slight variations from commercially available FDA-approved drugs) is not appropriate and should be actively enforced. In-
office use and dispensing of compounded preparations should be allowed only when the patient’s life is threatened, or suffering or death may result from failure to treat, and a commercially available, FDA-approved drug cannot be used in its original, manufactured form to treat the medical condition at hand.

- We do not have a definitive answer on possible limitation or “cap” of office stock of compounded preparations, but we caution that a severely limited volume may not provide the needed flexibility for practitioners to adequately treat a patient’s condition when there might be a legitimate need for a previously-compounded “stock” preparation to be used in-office or to be dispensed (for example, in-house stock of phenoxybenzamine for immediate treatment of cats with urethral blockage).

- **Compounded Product Labeling:** Should there be a required disclaimer on the labeling of compounded drugs that notifies practitioners and consumers that the product at issue is compounded? If so, what should this disclaimer look like?
  - FDA-approved animal drug products can be identified by the six-digit New Animal Drug Application (NADA) number for brand-name drug products or the six-digit ANADA number for generic drug products. The NADA or ANADA number and the statement “Approved by FDA” can usually be found on the drug product’s label, including the package insert. If all FDA-approved drugs contained an “Approved by FDA” statement, there would be an immediate distinction to end-users between FDA-approved drugs and compounded preparations. We do not have specific recommendations on whether a labeled disclaimer should be incorporated and/or what the disclaimer should look like.

- **Adverse Event Reporting:** What, if any, adverse event reporting requirements currently apply with respect to compounded drug products? Should compounding pharmacies be required to report all or a subset of adverse events to FDA? Should such a requirement be limited to only certain pharmacies that engage in compounding?
  - Veterinarians should report suspected adverse events or product failures involving compounded preparations to the compounding pharmacist, the State Board of Pharmacy and the FDA Center for Veterinary Medicine. Instructions for reporting adverse events to FDA can be found at the FDA website: [http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm](http://www.fda.gov/AnimalVeterinary/SafetyHealth/ReportaProblem/ucm055305.htm). Pharmacists should instruct pet owners to contact both the prescribing veterinarian and pharmacist immediately if a compounded preparation has caused an adverse event.
  - Being committed to the continuing availability of medicinal products that are pure, safe, potent and efficacious for animals, the AVMA encourages continued development and strengthening of adverse event reporting systems. This includes continued collaboration with constituent professional organizations, industry organizations, government entities and other stakeholders.
**Federal and State Coordination and Communication:** How well do federal and state officials coordinate existing authorities? Are adequate mechanisms in place to ensure appropriate communication between state and federal regulators with respect to oversight of compounding pharmacies? If not, how could such communication be improved? Should there be a specific federal requirement to coordinate enforcement and regulatory activities with respect to compounding pharmacy with state officials?

- Compounding from bulk for non-food animals in certain circumstances should be allowed only if effective regulatory mechanisms are in place and implemented to assure that such compounding is patient-specific and is performed only in the context of a veterinarian-client-patient relationship.

Please also comment on any other issues or buckets of issues that you think the Committee should consider when examining this topic.

**Additional comments:**

- We ask that you recognize the unique circumstances in which veterinarians practice every day. The species veterinarians treat that have regular compounding needs include household pets, such dogs, cats, ferrets, and birds; horses; exotic animals; and wildlife. Although many medical conditions are found across species, there are also species-specific exceptions that lend themselves to the need for compounded preparations (for example, very small pet birds being treated by syringe with a lower-strength pain medication).

- We ask that you also recognize that the term “compounding” comprises both compounding from FDA-approved drugs and from unapproved, bulk active pharmaceutical ingredients (API). Science-based evidence should be utilized to determine whether compounding a particular preparation should be done using a bulk API or an FDA-approved product with excipients. We understand that the knowledge base is growing and that some expert groups, such as the USP Compounding Committee, continue work to develop standards for the preparation of commonly used compounds.