November 16, 2015

Dr. Neal Bataller
Center for Veterinary Medicine
Director, Division of Surveillance
FDA Center for Veterinary Medicine
7519 Standish Pl
Rockville, MD 20852

Re: Docket No. FDA-2015-N-1196 - List of Bulk Drug Substances That May Be Used by an Outsourcing Facility To Compound Drugs for Use in Animals: Request for Nominations

Dear Dr. Bataller:

The American Veterinary Medical Association recognizes that the List of Bulk Drug Substances That May Be Used by an Outsourcing Facility To Compound Drugs for Use in Animals [Docket No. FDA-2015-N-1196] proposes that outsourcing facilities compound animal drugs only from bulk drug substances that will be listed in Appendix A of the final guidance, either pursuant to a veterinarian’s order or pursuant to a patient-specific prescription. We understand that when a facility registered as an outsourcing facility under section 503B of the Federal Food, Drug, & Cosmetic Act uses the listed bulk drug substances to make the specified drug products pursuant to an order from a licensed veterinarian without a prescription for an individually identified animal, the FDA does not intend to take action under sections 512(a), 501(a)(5) (21 U.S.C. 351(a)(5)), 502(f), and 501(a)(2)(B) as long as such compounding is done in accordance with any associated conditions described in GFI #230.

We continue to have reservations related to creation of a “list” of bulk drug substances, even considering that the Appendix A list is focused upon in-office use, which is a subset of wider needs to compound from bulk drug substances. In lieu of a list, the AVMA continues to believe that there are three circumstances wherein compounding from bulk drug substances may be medically necessary in nonfood animals and should be allowable within the confines of a Veterinarian-Client-Patient Relationship, specifically when:

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

We have a number of concerns related to the use of a list of bulk drug substances that can be used to create compounded preparations for in-office emergent needs:

- In species including, but not limited to zoo animals, laboratory animals, exotic pets, wildlife, aquaria animals, and nonfood aquacultural animals, the use of compounded preparations is unquestionably
necessary. Although significant time and resources went into the development of our nominations, the bibliographies required for each submission are lacking because of the sometimes limited numbers of studies showing safety and efficacy of the needed dosage forms across the various species and conditions seen by veterinarians. Many of the compounding needs in these species are due to requirements to limit stress in the animals, promote worker safety, and diminish the need for lethal methods of wildlife and zoo immobilization in a dangerous public setting. For example, a zoo and wildlife veterinarian’s use of a consistently produced compounded immobilization preparation to dart an escaped animal is more desirable in the eyes of the public than the use of a firearm, even if the substance used to prepare the medication has been subject to only limited research studies illustrating safety and efficacy.

- How will the list be maintained in an up-to-date, clinically relevant way? We contend that the FDA should provide for an immediate, nimble mechanism to consider and allow for changes to the list. Patients in need of emergency care cannot afford to wait for a response to a citizen’s petition each time a new need arises. To preserve the FDA’s drug approval process, we ask that the FDA also ensure the immediate removal of a bulk drug substance when it is no longer necessary.

- The FDA’s request for information on “safety concerns” of nominated bulk drug substances is difficult, if not impossible, to fulfill. Any substance can be toxic in certain scenarios (e.g., used at a toxic dose or used in a patient with an idiosyncratic response). Substances that have known, serious safety concerns in the target species have not been included in our nominations.

- We understand the FDA seeks to mirror veterinary compounding enforcement to that of human compounding. However, veterinary bulk drug substance nominations are required to illustrate needs above and beyond those required for human compounding. Specifically, veterinary compounding nominations must illustrate why immediate treatment with the compounded preparation is necessary to avoid animal suffering or death. Why is there this discrepancy? Any delay in treatment of an animal’s medical condition inherently endangers animal health and welfare. We again contend that the FDA should instead use the AVMA’s three circumstances for compounding from bulk drug substances, as bulleted above.

Despite our reservations related to the feasibility of a list of bulk drug substances for outsourcing facilities to prepare compounded preparations for in-office use, we are submitting nominations for the list on behalf of our members. We wish to help ensure the list is fitting with the needs of our patients as much as possible; see our attachment.

Extensive consideration was given to preparations that are compounded from bulk drug substances and needed for in-office use for emergent and urgent situations. Our list of nominations is based on existing availability of FDA-approved drug products. As we have stressed in previous communications, backorders and shortages of FDA-approved drug products make access to compounded preparations even more important. Some of these medications are needed for in-office use. How will the FDA address access to these substances during the short- and long-term breaks in availability? If the FDA mirrors the human framework by allowing outsourcing facilities to compound using substances on a shortage list, will outsourcing facilities be able to respond appropriately and in a timely fashion during these periods? As stated in our letter dated August 14, 2015, we appreciate that the use of outsourcing facilities in the preparation of office stock is intended to increase safety of compounded preparations, yet we caution that use of outsourcing facilities might have the unintended consequence that some preparations of critical importance to animal health may no longer be available because of economic or other business considerations. We contend that before any list is finalized, the FDA must engage in further discussions.
with the pharmacy, veterinary, and drug manufacturing communities to determine how the Agency will address this issue.

Additionally, we recognize that food-animal compounding is not permissible within the draft Guidance For Industry #230 nor its Appendix A. We reiterate our previous request that the FDA develop a separate guidance document specific to compounding from bulk drug substances in food animals and limited to euthanasia, depopulation, and poison antidote preparations.

The AVMA, founded in 1863, is one of the oldest and largest veterinary medical organizations in the world, with more than 86,500 member veterinarians worldwide engaged in a wide variety of professional activities and dedicated to the art and science of veterinary medicine. Thank you for your time and consideration of our comments and nominations. For questions or concerns regarding the AVMA’s request, please contact Dr. Lynne White-Shim at (800) 248-2862 ext. 6784 or at lwhite@avma.org and Dr. Ashley Morgan at (202) 289-3210 or at amorgan@avma.org.

Respectfully,

W. Ron DeHaven, DVM, MBA
Executive Vice President and CEO