May 17, 2010

Environmental Protection Agency
Office of Pesticide Programs (OPP)
Regulatory Public Docket (7502P)
1200 Pennsylvania Ave., NW
Washington, D.C. 20460-0001

Re: Docket No. EPA-HQ-OPP-2010-0229; FRL-8816-8 – Pet Spot-On Analysis and Mitigation Plan Available for Public Comment; Notice of Availability

Dear Sir or Madam:

I am writing on behalf of the American Veterinary Medical Association (AVMA), established in 1863 and the largest veterinary medical association in the world. As a not-for-profit association established to advance the science and art of veterinary medicine, the AVMA is the recognized national voice for the veterinary profession. The association’s more than 80,000 members comprise approximately 83% of U.S. veterinarians, all of whom are involved in a myriad of areas of veterinary medical practice including private, corporate, academic, industrial, governmental, military, and public health services.

The U.S. Environmental Protection Agency (EPA) asserts that due to a significant increase in adverse incidents, it is taking a series of actions to increase the safety of spot-on pesticide products for flea and tick control for cats and dogs. Immediately, EPA will begin reviewing labels to determine which ones need stronger and clearer labeling statements. Next, EPA will develop more stringent testing and evaluation requirements for both existing and new products. EPA expects these steps will help prevent adverse reactions. In dogs and cats that can include skin effects, such as irritation, redness, or gastrointestinal problems that include vomiting or diarrhea, or effects to the nervous system, such as trembling, appearing depressed or seizures— from pet spot-on products.

The EPA’s specific mitigation plan includes the following:

- Requiring manufacturers of spot-on pesticide products to improve labeling, making instructions clearer to prevent product misuse.
- Requiring more precise label instructions to ensure proper dosage per pet weight.
- Requiring clear markings to differentiate between dog and cat products, and disallowing similar brand names for dog and cat products. Similar names may have led to misuse.
- Requiring additional changes for specific products, as needed, based on product-specific evaluations.
- When new products are registered, granting only conditional, time-limited registrations to allow for post-marketing product surveillance. If there are incidents of concern associated with the product, EPA will take appropriate regulatory action.
Restricting the use of certain inert ingredients that EPA finds may contribute to the incidents.

Launching a consumer information campaign to explain new label directions and to help users avoid making medication errors.

The AVMA applauds the EPA for its continued efforts to ensure the safety of pesticides used to relieve animal pain and suffering. We appreciate the EPA's recent initiative to examine the reasons for which adverse event incidents associated with pet spot-on products have risen, and to help minimize any safety concerns by ensuring clear label directions, effective pre-marketing testing, and strong post-marketing surveillance. While we find the intent laudable, the AVMA shares its recommended ways forward as the EPA considers various mitigation steps affecting pet spot-on products.

**Adverse Events**

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.

The AVMA understands that the EPA plans to pursue standardized adverse event reporting, including standard formatting and content, which will allow for more efficient analysis of data and for more efficient post-marketing surveillance of these products. We recommend that the EPA coordinate with the Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA) to incorporate adverse events reports associated with pesticides for animals, into the FDA's new web portal, MedWatch, for harmonization of adverse event reporting of products used in animals. This would be particularly helpful considering that while most pesticides are regulated by the EPA, some are regulated by the FDA as new animal drugs.

Moreover, we believe that there must be a strong, science-based, transparent and systematic post-market surveillance system, especially considering the wide scope of species and disease conditions that veterinarians treat. It is critical that the surveillance system provides for early and clear detection of associations between products and adverse events while maintaining adequate specificity to reduce spurious, false associations. Sufficient and meaningful data inputs (adverse event reports) are imperative for a strong reporting system foundation. In addition to those data needs, a strong system also requires that only statistically significant findings be utilized in the identification of adverse event causality. Subjective assessments are insufficient and may in fact be detrimental to analysis since bias could be introduced. We underscore the need for quantitative statistical analyses of adverse event data prior to implementation of mitigation steps.

Finally, although transparency must be ensured, identity of individual patients and clients must be maintained as confidential. The AVMA recommends that also EPA gain and retain contact information from all individuals who submit adverse event reports. We contend that false reports could be submitted to EPA more readily if individual contact information is not required for report submission. We assert that such contact information is essential, so that the EPA, attending veterinarian, and product manufacturer are able to follow up with reporting individuals for needed verification and confirmation toward appropriate action and resolution.

**Veterinary access to safe and effective pesticide products**

During the course of professional practice, veterinarians must treat and support a variety of animal species under numerous clinical scenarios. We ask that the EPA pursue specific understandings of veterinary clinical medicine as it develops specific mitigation steps to ensure safety of pet spot-on products.

In addition to ensuring the safety of pet spot-on products, the AVMA asserts that both the safety and efficacy of these products must be maintained. We understand the EPA's current adverse event analyses showed that
small breed dogs were adversely affected by some of these products more frequently than larger dogs and the EPA therefore plans to pursue packaging or labeling changes to narrow the weight ranges of products. The AVMA contends that a close evaluation of the current data (and, if necessary, additional study data) is necessary to ensure both efficacy and safety of products that could ultimately have a dosage labeled for a narrowed weight range.

Communication
The AVMA appreciates the EPA’s plan to enhance communication efforts with the public on proper use of pesticides. As the EPA determines how to clarify labels to limit misuse, toxicoses in nontarget species, and any other safety concerns, we welcome the opportunity to share feedback on any potential label language the EPA develops. We also ask that as EPA evaluates how to clarify the label, it consider including the following on pet spot-on labels:
- Recommended consultation with a veterinarian pre-administration, and post-administration if adverse effects are observed
- Applicable federal agency contact information as well as company contact information, to facilitate adverse event reporting

The AVMA also offers itself as a communication vehicle for EPA’s communication plan as it develops any label changes and restrictions the EPA places on spot-on products. Because veterinarians are the gateway distribution channel for many spot-on products, it is important that the AVMA participate in EPA communication efforts in any way permissible.

In conclusion, the AVMA lauds the EPA’s effort to ensure the safety of pet spot-on products. However, we offer the following as EPA determines how to proceed with its next steps:
- A robust adverse event reporting system is critical for effective post-marketing surveillance. We recommend harmonization of EPA’s adverse event reporting with FDA’s through the FDA MedWatch program.
- We assert that both safety and efficacy of pet spot-on products is important as the EPA determines if and how to narrow the targeted weight ranges for various dosages of spot-on products.
- The AVMA welcomes the opportunity to serve as a resource to the EPA as it clarifies pet spot-on product label language, and as the EPA rolls out a communication plan with the public on how to safely use spot-on products.

The AVMA appreciates the opportunity to comment and would like to continue the dialog on this and other important matters. We also would welcome the opportunity to further provide our insights and feedback. For further clarification on the AVMA’s comments, please contact Dr. Lynne White-Shim at 800-248-2862 ext. 6784, or at lwhite@avma.org.

Respectfully,

[Signature]
W. Ron DeHaven, DVM, MBA
Executive Vice President
American Veterinary Medical Association

cc: Dr. Kit Farwell, DVM, DABT; Health Effects Division