AVMA® American Veterinary Medical Association

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February 27, 2006

USDA-APHIS-VS-Center for Veterinary Biologics
510 South 17th Street
Suite 104
Ames, IA 50010

Re: Proposed changes to Veterinary Services Memorandum No. 800.203, General Licensing Considerations: Compatibility of Components

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, AVMA is the recognized national voice for the veterinary profession. The association's more than 73,000 members represent approximately 86% of U.S. veterinarians, all of whom are involved in myriad areas of veterinary medical practice including private, corporate, academic, industrial, governmental, military, and public health services.

The AVMA applauds the USDA Center for Veterinary Biologics efforts to post draft notices and memoranda for comments prior to publication. Thank you for your willingness to address the specific needs and concerns of the veterinary medical profession.

We appreciate the CVB attempts to strengthen the efficacy parameters for veterinary vaccines. The AVMA values clinically relevant enhancements to vaccine efficacy and safety. Nonetheless, we are concerned the proposed changes could limit the availability of polyvalent vaccines. Polyvalent vaccines may be the product of choice for various species groups—especially livestock veterinarians. We are somewhat concerned these changes could impact the ability of vaccine manufacturers to develop such products and/or it might limit their ability to routinely replace older antigens with newer strains in order to meet the ever-changing vaccination needs in the field.

We encourage the CVB to continue discussion with stakeholders prior to finalizing this memo. A summary of CVB's concerns did not accompany the proposed changes to VS Memo No. 800.203. Consequently, the AVMA has a number of questions regarding the basis for the proposed changes.

- Were repeat failures in product efficacy observed based on the current antigen interference guidelines? If so, were such failures observed in all species and product categories? Will these changes increase product efficacy or will they only result in higher hurdles toward obtaining and maintaining product licenses?

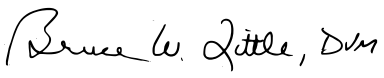
- What is the benefit of demonstrating serologic equivalence rather than non-inferiority when confirming a lack of interference—especially when serological correlation to efficacy has already been supported by approved host animal vaccination-challenge studies?

- Have the immunological principles regarding the expressed concerns over an elevated antibody response been commonly recognized and accepted for all antigens, i.e., in many instances, an increased humoral response may indeed reflect increased protection?

- What is the basis for the 70 percent criterion for determining a non-inferiority margin and is this number realistic? The 70 percent criterion limits the response to a rather narrow margin that approximates one-half of a two-fold titer dilution and thus requires an identical antibody response between two vaccinated groups. Will this guidance apply to all animals and animal pathogens? Can this margin appropriately account for the natural variability in response from animal to animal, which can be impacted significantly by multiple factors, e.g., species, family, genetics, antigen(s), environment, and etcetera? Will these provisions force vaccine developers to increase the number of animals needed to support such variations? Do such variations in response indicate that efficacy has been impacted?

Again, the AVMA values clinically relevant enhancements to vaccine efficacy and safety. However, until the above questions have been appropriately resolved, the AVMA recommends that CVB further engage all of the stakeholders involved in this issue prior to implementation.

Sincerely,



Bruce W. Little, DVM
Executive Vice President

BWL/ECG