United States Department of Agriculture

Marketing and Regulatory Programs

Animal and Plant Health Inspection Service

Veterinary Services

Center for Veterinary Biologics
Suite 104
510 South 17th Street
Ames, IA 50010
(515) 232-5785
FAX (515) 232-7120

August 1, 2001

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 01-10

Subject: Stability Testing of New Biotechnological/Biological Veterinary Medicinal Products

To: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics

I. PURPOSE

The purpose of this notice is to inform all interested parties of the disposition of the comments that we received in response to the *Federal Register* notice of availability and request for comments on a draft guideline titled "Stability Testing of New Biotechnological/Biological Veterinary Medicinal Products" (VICH Topic GL 17) developed by the International Cooperation on Harmonization of Technical Requirements for Veterinary Medicinal Products (VICH).

II. BACKGROUND

The guideline was published in the *Federal Register* (65 FR 5305-5306, Docket No. 99-068-1) on February 3, 2000. Because the topic of the draft guideline concerns veterinary biological products, we requested comments on its provisions so that we could include any relevant input on the draft to the VICH for its consideration to support the expertise available to the working group preparing the final guideline.

III. COMMENTS AND DISPOSITION

We received two sets of comments on the draft guideline. In one set of comments the commenter recommended three changes for incorporation into the final guideline. First, the commenter recommended that the term "drug or biologic" be used in the guideline in place of the terms "drug substance" and "drug product." The commenter stated that using the term "drug or biologic" would make it clear that the guideline applies to biologics as defined by APHIS. The working group considered the comment but decided that the reference to vaccine and conventional vaccine in the scope of the annex to the guideline was adequate to convey the applicability to biologics. The guideline was not changed in response to this recommendation.

ARCHIVED

Second, the commenter stated that the last sentence of the third paragraph in section V.B. of the guideline is presumptive and should be deleted. Section V.B. provides guidance for using potency tests to measure stability. The commenter disagreed with the concept presented in V.B. that states that current *in vitro* potency tests for biological activity and physiochemical characterization are impractical and provide inaccurate results when they are used to assess the stability of biotechnological/biological products where dissociation of the active ingredient from a carrier used in conjugates or adjuvants must be accomplished before potency can be measured. The concept presented in the guideline states that, in many cases, a validated *in vivo* potency test will indicate that there has been no significant dissociation of the active ingredient from the carrier. Therefore, by inference, if dissociation of the active ingredient from the carrier moiety or adjuvant was not successful, the stability measurement as determined by an *in vitro* potency test would not be meaningful. The working group acknowledged the difference of opinion concerning the efficacy of current treatments to effect the dissociation of active ingredients from carriers used in conjugates or adjuvants; however, the guidance presented in the guideline was not changed in response to this comment.

The third comment by this commenter concerned the wording of the second paragraph under Section VIII, Testing Frequency. The commenter said that the draft wording did not provide guidance concerning the testing frequency for products with an expected shelf life of one year. The wording of the second sentence provides guidance for products with an expected shelf life of greater than one year. The working group believed that the regimen for testing products with an expected shelf life of greater than one year was adequate to cover products with an expected shelf life of exactly one year since one of the quarterly testing intervals recommended for products with an expected shelf life of greater than one year would also apply to products with an expected shelf life of exactly one year. Thus, the product would be tested at one year whether the dating of the product is "greater than one year," or "one year or greater." The wording of the guidance presented in the guideline was not changed in response to this comment.

In the second set of comments, the commenter requested clarification of the scope of the guideline. The commenter asked if the guideline would apply to antigen stock (vaccine) that is not well characterized, highly purified, derived from r-DNA technology, or conjugated to carrier proteins. As specified in the Scope of the Annex, the guideline applies to vaccines that consist of well-characterized proteins or polypeptides. This would include well-characterized vaccines that are prepared using r-DNA technology and vaccines that consist of well-characterized proteins or polypeptides that may also be adjuvanted. The guideline does not apply to conventional vaccines prepared using antigens that are not well characterized. The guidance presented in the guideline was not changed in response to this comment.

ARCHIVED

IV. ACTION

Veterinary Services has issued the final guideline for Stability Testing of New Biotechnological/Biological Veterinary Medicinal Products as Veterinary Services Memorandum No. 800.300 which accompanies this notice.

/s/ James E. Tanner for

Richard E. Hill, Jr.
Director
Center for Veterinary Biologics

Enclosure

ARCHIVED