



June 16, 2010

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 10-05

**United States
Department of
Agriculture**

Animal and Plant
Health Inspection
Service

Veterinary Services

Center for Veterinary
Biologics

1920 Dayton Avenue
PO Box 844
Ames, IA 50010
(515) 337-6100

TO: Biologics Licensees, Permittees, and Applicants
Directors, Center for Veterinary Biologics
Veterinary Services Management Team

FROM: Richard E. Hill, Jr. /s/ *Richard E. Hill, Jr.*
Director
Center for Veterinary Biologics

SUBJECT: International Cooperation on Harmonization of Technical Requirements
for the Registration of Veterinary Medicinal Products (VICH): Final
Guidelines for Target Animal Safety for Veterinary Live and Inactivated
Vaccines

I. PURPOSE

The purpose of this notice is to inform interested parties of the disposition of the comments received in response to the *Federal Register* notice of availability and request for comments on a draft guideline titled, "VICH: Target Animal Safety Guidelines for Veterinary Live and Inactivated Vaccines," (VICH GL44) developed by the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH).

II. BACKGROUND

The guideline was published in the *Federal Register* (Federal Register Vol. 73, No. 32, Docket No. APHIS-2008-0024) on February 15, 2008. Since the topic of the draft guideline concerns veterinary biological products, comments on its provisions were requested so that any relevant input regarding the draft could be forwarded to the VICH for its consideration to support the expertise available to the working group preparing the final guideline.

III. COMMENTS AND DISPOSITION

The agency received one general comment. The comment included concerns regarding revaccination intervals, use of adjuvants, the role of the agency, and the motives of the veterinary biologics industry. The draft guideline is intended to provide guidance for designing and executing studies to evaluate the safety of the final formulation of veterinary live and inactivated vaccines, prior to approval for licensing/registration.



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The comment did not refute the reasoning outlined in the proposed guideline, nor provide a technical evaluation of the proposed guideline, so no revisions to the guideline were forwarded.

The agency received a comment regarding Sections 2.1.1, Overdose Test for Live Vaccines. The need to use seronegative animals for the overdose test for live vaccines was questioned. The working group reviewed the comment and decided that no revisions to the document were necessary. The guideline states that generally, for each target species, the most sensitive class, age, and sex proposed on the label should be used. The guideline currently states that in cases where seronegative animals are not reasonably available, alternatives should be justified. Since the guideline already allows for the use of seropositive animals, when justified appropriately, no changes were made to the document. Clarification was requested regarding the use of control animals for the overdose test for live vaccines, described in Section 2.1.1. This section does not refer to control animal. Therefore, no control animals are required for the overdose test for live vaccines.

Clarification was requested for Section 2.2, the reproductive safety test. The observations to be collected were not specified. The working group reviewed this comment and decided no revisions to the document were necessary. This section does indicate that the design and extent of the laboratory and field safety studies will be based upon the type of organism(s) involved, the type of vaccine, the timing and route of delivery, and the animal species involved. Safety observations to be taken are included in Section 2.1.3. Section 2.2 indicates that vaccines recommended for use in pregnant animals should include an observation period that must be extended to parturition, to examine any harmful effects during gestation or on progeny. When scientifically warranted, additional studies may be required to determine the effects of investigational veterinary vaccines on semen, including shedding of live organisms in the semen. The observation period should be appropriate for the purpose of the study. For investigational veterinary vaccines recommended for use in future laying hens or layers, the study design should include an evaluation of parameters that are appropriate for the class of hens vaccinated.

The need for the use of seronegative animals for the field safety test described in Section 2.3 was also questioned. The working group reviewed this comment and decided no revisions to the document were necessary. Section 2.3.1 states that the animals should be in the age range/class intended for treatment as indicated in the proposed labeling. This section also indicates that serological status may be considered; therefore, the guideline already allows for the use of seropositive animals when justified appropriately. Clarification was also requested for Section 2.3, the field safety test, regarding the numbers of animals required, if a specified proportion should be of minimum age, and the requirements for the formulation of the product. With regard to the number of animals required and the proportion of animals that should be of minimum age, Section 2.3

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indicates that consultation with regional regulatory authorities regarding study design prior to the conduct of studies is recommended. The guidance included in Veterinary Services Memorandum No. 800.204 should also be considered for studies conducted in the United States. With regard to the requirement for formulation of the product, Section 2.3 indicates that studies should be conducted using representative batch(es) of the investigational veterinary vaccines. Some regions may require that the field safety study be performed using more than one batch of product. The guidance included in Veterinary Services Memorandum No. 800.204 should also be considered for studies conducted in the United States.