

May 23, 2002

VETERINARY SERVICES MEMORANDUM NO. 800.102

Subject: Exemption from *Leptospira* Bacterin Testing Under 9 CFR 113.101(c),
113.102(c), 113.103(c), and 113.104(c)

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

I. PURPOSE

This memorandum provides guidance for obtaining an exemption to the requirement for testing leptospiral bacterins for potency in hamsters.

II. BACKGROUND

APHIS has published Standard Requirement (SR) potency tests for leptospiral bacterins in 9 CFR 113.101(c), 113.102(c), 113.103(c), and 113.104(c). These regulations require that such bacterins be tested for potency using a vaccination-challenge test conducted in hamsters. However, the regulations under 9 CFR 113.4(a) provide for the granting of an exemption to this requirement if the replacement test is at least equivalent to the SR test, and the test methods and procedures are described in the filed Outline of Production for the product.

In keeping with its commitment to replace animal tests with in vitro tests, APHIS' Center for Veterinary Biologics-Laboratory, in collaboration with veterinary biologics manufacturers, developed and validated monoclonal antibody based antigen capture enzyme-linked immunoassays (ELISAs) for potency testing leptospiral bacterins containing *Leptospira interrogans* serovars *pomona*, *icterohaemorrhagiae*, *canicola*, and *grippityphosa*.

At this time, the Center for Veterinary Biologics (CVB) is reviewing the SRs for leptospiral bacterins. While the review is not yet complete, we anticipate that a future proposed amendment to these requirements will include replacing hamster potency tests with ELISA tests. In anticipation of that proposal, we encourage firms to begin using the ELISA tests developed by CVB-L for releasing serials of leptospira bacterins.

This memorandum clarifies CVB policy concerning the granting of an exemption allowing ELISAs developed by the CVB-L to be used for potency testing leptospiral bacterins containing *Leptospira interrogans* serovars *pomona*, *icterohaemorrhagiae*, *canicola*, and *grippityphosa* in place of the hamster tests specified in the regulations.

Firms that are not interested in obtaining an exemption may continue to perform the hamster potency test pending revision of the SRs.

III. POLICY

To obtain an exemption to use the ELISAs developed by CVB-L in place of the SR test(s) for serial release testing of *Leptospira Bacterin*:

A. Request an Exemption to the SR test

Under 9 CFR 113.4, the licensee or permittee must request an exemption to the applicable SR test for *Leptospira Bacterin* prescribed in the regulations in sections 113.101, 113.102, 113.103, and 113.104.

B. Submit Protocols

Simultaneous with the firms request for an exemption to use the CVB-L ELISAs, protocols for qualifying a reference bacterin(s) for use with each assay, should be submitted to CVB for review and comment. Protocols should address the following:

1. *Procedures for qualifying reference bacterins in host animals* - It is recommended that reference bacterins be monovalent, contain the minimum antigenic mass specified in the filed Outline of Production, and qualified using a vaccination-challenge study in each species of host animals for which the product is recommended. For not less than 4 weeks after challenge, animals used in the vaccination-challenge study should be monitored for:

a. Clinical signs including elevated temperature, behavioral changes, changes in appetite or water consumption, dehydration, icterus, oliguria, general condition, and

b. Complete blood count, circulating antibodies to the relevant serovars, urinalysis (pH, bloody urine, protein, urobilinogen, and microscopic examination of sediment), and blood and urine cultures for the presence or absence of leptospire.

2. *Procedures for correlating the host animal protective dose to its protective endpoint in hamsters* - This should be done by performing limiting dilution studies using the applicable codified test in 9 CFR sections 113.101-104.

C. Specify the CVB-L ELISA in the Outline of Production

The CVB-L ELISA procedure(s) for *Leptospira pomona*, *Leptospira icterohaemorrhagiae*, *Leptospira canicola*, or *Leptospira grippotyphosa*, as applicable, must be described in the Outline of Production.

D. Document Exemptions

If CVB grants an exemption from the Standard Requirement test, Part V of the Outline of Production must indicate the date the exemption was granted.

/s/ Andrea M. Morgan for

W. Ron DeHaven
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Veterinary Services

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