August 23, 1999

VETERINARY SERVICES MEMORANDUM NO. 800.88

Subject: Testing for Reticuloendotheliosis Virus Contamination

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

I. PURPOSE

This memorandum provides guidance for licensees, permittees, and applicants interested in testing Master Seed Viruses (MSVs) of poultry biological products for reticuloendotheliosis virus (REV) contamination.

II. CANCELLATION

This memorandum cancels Veterinary Biologics Memorandum No. 800.88 dated June 12, 1996.

III. BACKGROUND

REV is a retrovirus of poultry which can cause neoplasia and immunosuppression in infected birds. The MSV of a licensed Fowl Pox Vaccine was found to be contaminated with REV. The regulations in 9 CFR 102.3(b) require that the purity of a biological product be established prior to issuance of a U.S. Veterinary Biological Product License. However, the tests found in the current Standard Requirements for viral products in 9 CFR 113.200 and 113.300 are insufficient to detect REV contamination.

In order to prevent a recurrence of this problem, Center for Veterinary Biologics-Laboratory (CVB-L) now performs a polymerase chain reaction (PCR) test for REV contamination when conducting confirmatory testing of new poultry MSVs. Additionally, the use of specific pathogen free (SPF) substrates in the production of poultry biologics, as specified in Veterinary Services Memorandum No. 800.65, provides assurance that REV contamination will not occur during the production process.

The Center for Veterinary Biologics (CVB) is currently reviewing the purity regulations for poultry products. While this review is not yet complete, we have determined that a future Proposed Rule should include a Standard Requirement test for contamination of poultry MSVs with REV. In anticipation of that proposal, we encourage firms to begin REV testing now so that they may assist in the development of a mutually agreeable Standard Requirement.

Therefore, this memorandum describes procedures for testing poultry MSVs for REV contamination. While not mandatory until a Standard Requirement is in place, prospective licensees should test new poultry MSVs for REV contamination prior to the submission of MSV samples to CVB-L for confirmatory testing. Furthermore, we encourage firms to develop a program for testing previously approved poultry MSVs for REV contamination.

IV. TEST PROCEDURES

Until a standard assay can be established, any one of the following three options is acceptable for REV testing of MSVs. This section, however, serves only as a general guideline; the specifics of the tests must be developed by each individual firm.

A. PCR Test

Conduct this test directly on the MSV sample. Upon request, the CVB-L can make available the method they use to perform their PCR test, or individual firms may develop similar tests.[1,2]

B. In-vivo Virus Amplification

Inoculate 1-day-old SPF chicks with the MSV; 2 weeks later evaluate blood samples for the presence of REV using an enzyme immunoassay (ELISA), fluorescent antibody (FA), or PCR test.[3,4]

C. Serology

Inoculate SPF chicks twice (at 2 and 4 weeks of age) with the MSV; 3 to 4 weeks later evaluate blood samples for the presence of REV-specific antibodies using ELISA or FA tests.[4,5]

[General comment: Do not filter the MSV sample (e.g., to remove pox virus) prior to conducting tests for REV. Filtering could reduce the titer of any potentially contaminating REV.]

V. TEST REPORTING

A. New MSVs

Report the results of tests conducted on new MSVs to CVB on the APHIS Form 2008 submitted when requesting confirmatory testing of the MSV. Submit the test method(s) used by an individual firm, along with data defining the sensitivity and specificity of the method described, with the data package accompanying the APHIS Form 2008.

B. Previously Approved MSVs

Again, we encourage firms to also test previously approved MSVs for REV. Firms conducting such tests should immediately report any positive results to CVB-Inspection and Compliance.

/s/

Alfonso Torres
Deputy Administrator
Veterinary Services

REFERENCES

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[4]Witter R. Reticuloendotheliosis. In: A laboratory manual for the isolation and identification of avian pathogens, 3rd ed. Purchase HG, Arp LH, Domermuth CH, Pearson JE, eds. Kendall/Hunt Publishing Co., Dubuque, IA. pp. 143-148. 1989.

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