



United States
Department of
Agriculture

Animal and Plant
Health Inspection
Service

Veterinary Services

Washington, DC
20250

VETERINARY SERVICES MEMORANDUM NO. 800.65

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

FROM: Jack A. Shere
for Deputy Administrator

SUBJECT: Eggs and Chickens for Production of Veterinary Biological Products

I. PURPOSE

This memorandum provides guidance on preparing veterinary biological products that use embryonated chicken eggs or chicken tissue as an ingredient. It is meant to assist licensees, permittees, and applicants in meeting the purity and quality requirements in title 9, *Code of Federal Regulations* (9 CFR), part 113.50.

II. CANCELLATION

This memorandum cancels Veterinary Services Memorandum No. 800.65 dated September 20, 2002.

III. BACKGROUND

Purity and quality requirements for ingredients of veterinary biological products are specified in 9 CFR 113.50. Specific ingredient requirements for each licensed product are found in the applicable Outline of Production or Special Outline. This memorandum defines the infectious agents that should be excluded from domestic specific pathogen free (SPF) eggs and chickens used to produce veterinary biological products without specifying the methods by which a source flock should be established or maintained. It also recommends procedures for the management and disposition of eggs and chickens after a disqualifying disease outbreak in a source flock. Information is also provided on interpretations of a specific test for reporting results on an APHIS Form 2008.

IV. PURITY AND QUALITY RECOMMENDATIONS

A. Source Flock

For the purposes of this memorandum, the term “source flock” will be defined as the flock maintained for the production of embryonated SPF eggs. Domestic source flocks shall be used to prepare products. If the embryonated eggs are hatched to produce SPF birds for the production of infectious bursal disease or coccidiosis vaccines, these birds are considered part of the source flock and should be free of any clinical signs of infectious disease.



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B. Agents of Concern

The licensee or permittee should maintain records to demonstrate that each lot of embryonated chicken eggs or chickens used to produce veterinary biological products has been derived from an unvaccinated flock free of the following infectious agents, as demonstrated by negative serology:

1. Avian adenoviruses; groups I (serotypes 1-12), II, and III
2. Avian encephalomyelitis virus (AE)
3. Avian influenza virus (AI), type A
4. Avian reovirus (Reo)
5. Infectious bronchitis virus (IB); Massachusetts, Connecticut, Arkansas, and JMK strains
6. Infectious bursal disease virus (IBD)
7. Laryngotracheitis virus (LT)
8. Lymphoid leukosis virus (LL); subgroups A, B, and J
9. Marek's disease virus (MD); serotypes 1, 2, and 3
10. Newcastle disease virus (NDV)
11. Reticuloendotheliosis virus (REV)
12. *Mycoplasma gallisepticum*
13. *Mycoplasma synoviae*
14. *Salmonella gallinarum*
15. *Salmonella pullorum*
16. Other agents deemed inappropriate by APHIS

C. Clinical Signs in a Source Flock

In the case of eggs or tissue culture derived from eggs, the licensee or permittee should document that the source flock is negative for lymphoid leukosis antigen (subgroups A, B, and J), negative for clinical signs of fowlpox, and negative on environmental culture for *Salmonella spp.* Birds used for production should be free of clinical signs of any infectious disease. An agent causing clinical signs or seroconversion in production birds is referred to as a disease agent. Disqualifying agents or disease agents are to be treated in a similar fashion as for disease outbreaks.

D. Source Flock Monitoring

The licensee or permittee shall describe, in a filed Outline of Production or Special Outline, the methods and frequency of source flock monitoring and the test methods used.

E. Procedures for Handling Eggs and Chickens

Once introduced into the licensed establishment, licensees and permittees should handle eggs and chickens for the production of veterinary biological products in a manner that maintains their pathogen-free status. The licensee or permittee should describe such handling procedures in the facility blueprint legend.

V. DISEASE OUTBREAKS

A. Notification of Disease Outbreaks

The licensee or permittee should require notification from the source flock owner within 24 hours of a positive test indicating the presence of a disqualifying disease or any disease agent causing clinical signs in a source flock (including birds used to produce infectious bursal disease virus and coccidia fractions). If a disqualifying disease or disease agent is confirmed in a source flock, the licensee or permittee shall notify the Center for Veterinary Biologics-Inspection and Compliance (CVB-IC) within 24 hours.

B. Determining the Period of Suspect Eggs and Birds

In the event of a disease outbreak in a source flock used to produce embryonated eggs, CVB-IC will set the date of initial seroconversion for the flock at 1 day after the collection of the last negative sera. CVB will notify licensees and permittees of that date. If clinical signs appear in production birds, CVB-IC will set the date of initial infection case by case and notify licensees and permittees of the date.

A Veterinary Biologics Investigation (VBI) number is assigned to each outbreak. Each firm is required to account for all suspect eggs and chickens it receives. The period for suspect eggs should be the 2 weeks prior to the seroconversion date for NDV, avian adenovirus, and Salmonella; the 3 weeks prior to the seroconversion date for IB and Mycoplasma; and the 4 weeks prior to the seroconversion date for AE, AI, LL, REV, and Reo. There is no suspect egg period for LT, IBD, MD, or fowlpox. The suspect period for the production birds will be determined case by case.

C. Disposition of Suspect Materials

When a disease outbreak is confirmed within a source flock, licensees and permittees should take the following actions:

1. *Uninoculated Eggs, Chickens, and Cell Cultures.* Discard all suspect eggs, chickens, and cell cultures derived from suspect eggs if they have not yet been inoculated with production seed.

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2. *Inoculated Eggs, Chickens, and Cell Cultures.* If already inoculated with production seed, discard suspect eggs, chickens, and cell cultures derived from suspect eggs, or continue in production, provided the product is appropriately tested and the presence of the disqualifying or disease agent cannot be demonstrated. (See E below for testing information.)

D. Eggs from Recovered Source Flocks

Licensees and permittees may be permitted to use eggs from a source flock which has recovered from a disqualifying disease outbreak for the production of inactivated products if the product is appropriately tested and the presence of the disqualifying agent cannot be demonstrated. (See E below for testing information.)

E. Testing for Disqualifying or Disease Agents

Appropriate testing depends on the disqualifying or disease agent. CVB will provide a testing protocol to licensees and permittees.

1. *Test Methods.* Testing for disqualifying or disease agents could include, but would not be limited to, the following methods:
 - a. For live products, licensees and permittees should attempt to isolate the disqualifying or disease organism from bulk or final container samples of the completed product.
 - b. For killed products, licensees and permittees should attempt to isolate the disqualifying or disease organism from samples of the bulk harvest material prior to inactivation.
 - c. For both live and killed products, licensees and permittees should attempt to detect seroconversion to the disqualifying or disease agent in chickens inoculated with bulk or final container samples of the completed product.
2. For a test result to be considered valid, the appropriate positive and negative controls should be used.
3. *Reporting Test Results.* Licensees or permittees should report results of tests for disqualifying or disease agents conducted on bulks or serials of product produced from suspect eggs or chickens to CVB-IC on the APHIS Form 2008.
 - a. Reference VBI number assigned to the disease outbreak in the remarks (section 11).
 - b. Report test data and results in test data section (section 9).

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- c. Depending on the test results, mark the appropriate disposition (section 12).
 - (1) For bulk material, mark “Other” and type “File for Information.”
 - (2) For final serials in which the test results were satisfactory, mark “Eligible for Release.”
 - (3) For final serials in which test results were reported unsatisfactory, mark “Destroyed by Firm” as a confirmation the serial has been destroyed.
- d. The CVB will process the APHIS Form 2008 and provide a disposition in accordance with VS Memorandum No. 800.53.
- e. For serials prepared with bulks that have been deemed acceptable for use, note the bulk lot in the remarks (section 11).

VI. IMPLEMENTATION/APPLICABILITY

All Outlines of Production and Special Outlines for products that use embryonated eggs or chicken tissue as an ingredient shall conform to this memorandum.