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United States  
Department of  
Agriculture

**VETERINARY SERVICES MEMORANDUM NO. 800.85**

Animal and Plant  
Health Inspection  
Service

**SUBJECT:** Avian Influenza Vaccines

Veterinary Services

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

Washington, DC  
20250

**I. PURPOSE**

This memorandum informs all interested parties of the conditions under which the Center for Veterinary Biologics will consider license applications for Avian influenza Vaccines. This information supplements the applicable Standard Requirements found in 9 CFR 113.200 and 113.300.

**II. CANCELLATION**

This memorandum cancels Veterinary Biologics Memorandum No. 800.85 dated July 23, 1999.

**111. BACKGROUND**

USDA, APHIS, Veterinary Services (VS) considers avian influenza (AI) in chickens an exotic disease and regulates the production of vaccine according to guidelines specified in VS Memorandum No. 565.12. The importation and/or interstate shipment of AI viruses is regulated by permit issued pursuant to 9 CFR 122.2.

**IV. PRODUCT MASTER SEED VIRUSES (MSVs)**

Licensees and applicants (firms) must meet all applicable Standard Requirements for MSVs, prescribed in 9 CFR 113.200 and 113.300, with the following additional considerations:

- A. Interstate Movement – VS will continue to regulate all importations or interstate movements of AI viruses by permit, under 9 CFR 122.2.
- B. Conventional Killed Vaccines – APHIS will consider licensing conventional killed AI vaccines provided that firms obtain and use the MSVs under the following conditions:



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1. *Acceptable MSVs* – Firms must only use AI viruses of low pathogenicity obtained from the Diagnostic Virology Laboratory of the National Veterinary Services Laboratories (NVSL), to produce MSVs for conventional killed vaccines. Firms may obtain any hemagglutinin (H) type from this source.
  2. *VS National Center for Import and Export (NCIE) Permit Required* – Firms must apply for a NCIE permit to obtain AI isolates; typically, a biosecurity inspection is required before issuing such permit. NCIE will issue permits for AI isolates with the restriction that the isolate be used only for in vitro studies. AI isolates may be used for the production and testing of vaccines only when authorized by APHIS.
- C. *Recombinant Derived Vaccines* – APHIS will consider licensing live or inactivated recombinant vaccines, subunit vaccines, or other biotechnology-derived AI vaccines produced from recombinant-derived MSVs. Firms must obtain a NCIE permit to acquire the AI viruses necessary to construct such MSVs.
- D. *Conventional Modified Live Vaccines* – Due to the high rate of mutation documented for AI viruses, APHIS will not consider license applications for conventional modified live AI vaccines.

## **V. PRODUCT DEVELOPMENT**

All applicable Standard Requirements for licensure must be met, including but not limited to 9 CFR 113.200 and 113.300, with the following additional considerations:

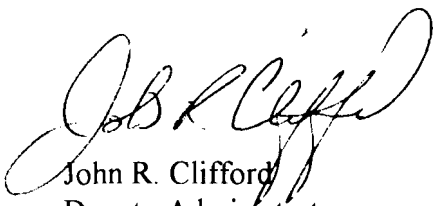
- A. *Product Claims* – Firms may develop products with a claim for use in either chickens or turkeys for any H type. Firms must support all claims for each species, each H type, and each age and route of administration with appropriate data.
- B. *Challenge Studies Involving Licensed Product* – Firms must support applications for regularly licensed products with appropriate vaccination-challenge efficacy data. Challenge studies which utilize highly pathogenic avian influenza virus in support of an application for licensure must be conducted under biosafety level 3 (BSL 3) containment conditions. Regardless of the challenge strain used, firms must obtain CVB approval of the laboratory, study protocol, and challenge virus prior to the initiation of the study.
- C. *Conditional Licensing* – APHIS will only consider applications for conditionally licensed products if the conditions found in 9 CFR 102.6 are met. Furthermore, all applicants or licensees seeking or holding conditional licenses for AI vaccines must work toward eventual regular licensure of these products.

## VI. PRODUCT LICENSE RESTRICTIONS

- A. General License Restrictions – APHIS will add the following restrictions to all licenses issued for AI vaccines:
1. *Distribution in Each State* – "Distribution in each State shall be limited to authorized recipients designated by proper State officials--under such additional conditions as these authorities may require."
  2. *Distribution for Export* – "Export distribution shall be limited to authorized recipients designated by proper animal health regulatory officials--under such additional conditions as these authorities may require."
- B. Additional License Restrictions – APHIS will add the following additional restrictions to licenses issued for all AI vaccines for use in chickens, as well as for all H5 and H7 AI vaccines for use in turkeys: "Domestic distribution and use shall be under the supervision or control of USDA, APHIS, Veterinary Services, as part of an official USDA animal disease control program."

## VII. PRODUCT LABELING

- A. Limited Species Recommendations – Because of the license restrictions on distribution and use, individual product labels may recommend use of the product in chickens or turkeys but not both.
- B. Distribution Statement – For licenses carrying the restriction listed in VI-B above, the domestic product labels must carry the following statement: "This product may only be distributed and used as part of an official USDA animal disease control program."
- C. Indication of Types – Product labels must indicate the H and N type of the AI virus used to produce the product.



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