May 28, 2002

VETERINARY SERVICES MEMORANDUM NO. 800.101

Subject: U.S. Veterinary Biological Product Permits for Distribution and Sale

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

I. PURPOSE

Persons wishing to import biological products for distribution and sale in the United States must apply for a U.S. Veterinary Biological Product Permit, in accordance with Title 9, Code of Federal Regulations (9 CFR), Section 104.5. Permitted products must meet the same standards of efficacy, purity, and safety under the Virus-Serum-Toxin Act (Act of Congress, approved March 4, 1913 (37 Stat. 832) as amended December 23, 1985 (99 Stat.1654)), as those products produced domestically ("licensed" products). Licensing requirements are discussed in Veterinary Services (VS) Memorandum No. 800.50, and permit applicants should refer to that memorandum for general guidance. The purpose of this memorandum is to provide additional guidelines specific to the acquisition and maintenance of a Permit for Distribution and Sale.

II. OBTAINING A PERMIT FOR DISTRIBUTION AND SALE

A. *Permit applicants must submit the same items required for issuance of a U.S. Veterinary Biological Product License, as described in Sections IV.B and IV.C of VS Memorandum No. 800.50, except as follows:*

1. Submit an Application for a United States Veterinary Biological Product Permit, APHIS Form 2005, instead of APHIS Form 2003.

2. Establishment licenses are not issued to manufacturers or importers of foreign-produced (permitted) products.

3. The Outline of Production must include, in addition to those items required for products manufactured in the United States, the following:

a. Section I of the Outline must certify the country of origin for all materials of animal origin used in production.

b. Section VI of the Outline must state the port of entry into the United States. The port of entry will also appear on issued permits.

4. Additional data concerning the effect of inactivation procedures on exotic disease agents may be requested, as deemed necessary, by the Center for Veterinary Biologics (CVB).

5. The following studies must be based on data generated in the United States, unless specific permission is obtained from the CVB to perform them elsewhere:

a. Adjuvant Safety (to determine the appropriate slaughter withholding period)
b. Field Safety
c. Diagnostic Kit Field Evaluation

B. *In addition to those items described in Sections IV.B and IV.C of VS Memorandum No. 800.50, the following items also must be submitted in support of a permit application:*

1. Applicants wishing to import biological products into the U.S. from countries that represent a risk for the introduction of foreign animal disease must complete a Summary Information Format (SIF) for the Importation of Veterinary Biologics. This document is available on the CVB website at www.aphis.usda.gov/vs/cvb/LPD/sifs/vbimp.html. Completion of the SIF allows the CVB to perform a scientifically valid and credible risk analysis.

This SIF must be submitted with proposals to import Master Seed microorganisms or veterinary biological products from:

a. Countries where foreign animal diseases exist, or

b. Other specified countries that supplement their national meat supply by the importation of fresh, chilled, or frozen meat of ruminants or swine from, or have common land borders with, countries where foreign animal diseases exist, as provided in 9 CFR Part 94.

For proposals to import veterinary biological products containing more than one antigenic fraction, a separate SIF must be completed for each Master Seed microorganism. The SIF(s) must be approved by the CVB prior to importing Master Seeds and/or biological product and prior to conducting field trials with such products.

2. Statement of organism(s) maintained at the manufacturing site that are etiological agents of List "A" Diseases of the Office International des Epizooties (OIE) and/or are exotic to the United States. Also, a statement characterizing all ingredients of animals origin that are used in the production of the Master Seed or finished product must be available on-site for review during the pre-permit site inspection. The statement must include a validated country of origin for each ingredient.

3. Written permission to inspect all parts of the foreign manufacturing facility in which biological products are prepared, in accordance with 9 CFR 104.5(a)(2).

4. Although an official dossier, submitted to foreign regulatory officials for registration in other countries, may be submitted to the CVB in addition to the above, it may not satisfy all requirements for the U.S. application. Portions of the dossier may be considered, as applicable, in addition to other data required.

C. *Additional requirements that must be met before a Permit for Distribution and Sale may be issued:*

1. The Center for Veterinary Biologics-Inspection and Compliance (CVB-IC) must conduct a pre-permit inspection of the facilities.

a. A minimum of six weeks is needed by CVB-IC to schedule a foreign inspection after it has been requested by the Center for Veterinary Biologics-Licensing and Policy Development (CVB-LPD).

b. All expenses must be prepaid by the permit applicant. A cooperative agreement must be arranged in advance by contacting CVB-LPD.

c . If 24 months elapse between a satisfactory inspection and issuance of a Permit for Distribution and Sale, a repeat inspection may be required, at the prepaid expense of the permit applicant, before the permit is issued.

d. If conditions change at the manufacturing plant after a CVB inspection, an additional inspection will be required at the prepaid expense of the permit applicant.

2. Master Seeds or biological product imported prior to issuance of a Permit for Distribution and Sale must be accompanied by a U.S. Veterinary Permit for Importation and Transportation of Controlled Materials and Organisms and Vectors (9 CFR 122.2) or a U.S. Veterinary Biological Permit for Research and Evaluation (9 CFR 104.4), respectively.

a. To obtain a Permit for Research and Evaluation, submit a completed APHIS Form 2005, and a VS Form 16-3 (Application for Permit to Import Controlled Material/Import or Transport Organisms or Vectors) to CVB-LPD. If the Master Seed was derived by recombinant methods, also submit VS Form 16-7, Additional Information for Cell Cultures and their Products (Monoclonal Antibodies, Recombinant Products, Extracts, Viruses, etc.). CVB-LPD will forward the documents to the appropriate authorities for consideration of the Permit for Research and Evaluation.

VS Form 16-3 is available at www.aphis.usda.gov/forms/vs16-3.pdf
VS Form 16-7 is available at www.aphis.usda.gov/forms/vs16-7.pdf

b. The CVB may require that certain Master Seeds be tested for exotic extraneous agents by the Foreign Animal Disease Diagnostic Laboratory, National Veterinary Services Laboratories, USDA-APHIS, at Plum Island, New York, before entry into the U.S. mainland. The permit applicant will bear the expense of the associated user fees.

c. Final product for pre-permit evaluation is shipped with a copy of the Permit for Research and Evaluation directly from the manufacturer to the Center for Veterinary Biologics-Laboratory (CVB-L).

D. *Eligibility for a U.S. Veterinary Biological Product Permit for Distribution and Sale*

1. Permittees are limited to persons residing in the United States, or who operate a business establishment within the United States, or both (9 CFR 104.1(b)).

2. One permittee number will be assigned to a permittee for all products imported from the same source.

3. Separate permittee numbers will be assigned to permittees for product(s) imported from different sources.

E. Quarantine Facility

The permit applicant must establish a permanent site where product will be received and held in quarantine until the product serial receives authorization from the CVB-IC to be distributed. Periodic inspections of the site will be conducted by the CVB-IC.

F. Length of Permit

1. A United States Veterinary Biological Product Permit does not have an expiration date. However, the permittee must furnish a written agreement to periodic re-inspection of the manufacturing site at permittee expense.

2. The permit may be revoked if the permittee violates, or fails to comply with, the Virus-Serum-Toxin Act.

III. IMPORTATION OF PRODUCT UNDER A PERMIT FOR DISTRIBUTION AND SALE

After a permit has been issued, the manufacturing firm ships the product to the quarantine facility. Each shipment must be accompanied by a copy of the permit, plus two copies of APHIS Form 2008 (2008). The 2008 is prepared in accordance with VS Memorandum No. 800.53, except that the entire inventory prepared for marketing is noted in Block 10 and the portion of the inventory included in the current shipment to the U.S. is noted in Block 11 .

A. *The permittee receiving the shipment into quarantine shall do the following:*

1. Certify the inventory. An authorized sampler at the U.S. permittee site must record in Block 11, "Remarks," of each 2008 the total number of containers and doses received, the date received, and sign the statement.

2. Submit the original and one copy of the 2008 to CVB-IC.

3. Maintain the product at proper storage conditions.

4. Retain the shipment in quarantine until the shipment has been released by APHIS. A shipment which has been found unsatisfactory by a required test prescribed in a filed Outline of Production shall not be released for distribution or sale (9 CFR 113.6.).

5. Submit, as applicable, representative product samples to the CVB-L, per 9 CFR 113.3. Containers of product that are selected as APHIS samples by an authorized sampler must be shipped in the same shipment as the remaining inventory.

6. Retain government reserve samples.

7. Maintain complete records of all approved labels, cartons, and inserts associated with the product.

8. Maintain responsibility for all shipments found unsatisfactory by APHIS. The permittee must hold, in quarantine, all shipments with an APHIS unsatisfactory disposition, for disposal under APHIS supervision.

IV. APHIS RELEASE OF QUARANTINED PRODUCT

Per the procedures outlined in VS Memorandum No. 800.53, CVB-IC will review each 2008. The CVB-L may perform confirmatory testing. When evaluation by the CVB is complete, the permittee will be notified, by return of a processed 2008, of the APHIS disposition of the shipment.

When a serial of product is imported in more than one shipment, each shipment must be accompanied by a separate 2008. Each 2008, and representative samples from each shipment, must be submitted to the CVB-IC and CVB-L, respectively. Each shipment shall be released independently by APHIS for distribution and sale. When submitting additional 2008s for a serial previously processed by the CVB, indicate in Block 11, Remarks, of the 2008 that it is a repeat (e.g., second, third) shipment of a previously submitted serial.

/s/ W. Ron DeHaven

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Deputy Administrator
Veterinary Services