



VETERINARY SERVICES MEMORANDUM NO. 800.101

Animal and Plant
Health Inspection
Service

Veterinary Services

1400 Independence
Ave, SW

Washington, DC
20250

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

FROM: Jack A. Shere
Deputy Administrator

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

I. PURPOSE

This memorandum provides guidance to persons wishing to import veterinary biological products for distribution and sale in the United States and applying for a U.S. Veterinary Biological Product Permit in accordance with Title 9, *Code of Federal Regulations* (9 CFR), Section 104.5.

II. REPLACEMENT

This memorandum replaces Veterinary Services (VS) Memorandum No. 800.101 dated June 6, 2013.

III. BACKGROUND

Persons wishing to import veterinary biological products for distribution and sale in the United States must apply for a U.S. Veterinary Biological Product Permit in accordance with 9 CFR 104.5. Permitted products must meet the standards of efficacy, potency, purity, and safety required under the Virus-Serum-Toxin Act, 21 U.S.C. 151-159 *et seq.* (as amended December 23, 1985 (99 Stat.1654)). Licensing requirements are discussed in VS Memorandum No. 800.50.

IV. POLICY

A. Obtaining a Permit for Distribution and Sale

1. Permit applicants must submit the same items required for issuance of a U.S. Veterinary Biological Product License, as described in VS Memorandum No. 800.50, except as follows:
 - a. Applicants must submit an "Application for a United States Veterinary Biological Product Permit" using APHIS Form 2005. Check "General Sale and Distribution" in box 2. To obtain the APHIS Form 2005, see section IV.A.3.b.(1).

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- b. Establishment licenses are not issued to manufacturers or importers of foreign-produced products.
 - c. Additional data concerning inactivation procedures on exotic disease agents may be requested by the Center for Veterinary Biologics (CVB).
 - d. The following studies must be based on data generated in the United States:
 - (1) adjuvant Safety to determine the appropriate slaughter withholding period;
 - (2) field safety; and
 - (3) diagnostic kit field evaluation.
2. In addition to those items described in section IV of VS Memorandum No. 800.50 and in VS Memorandum No. 800.109, the following items must also be submitted or addressed, as applicable, in support of a permit application:
- a. Applicants wishing to import veterinary biological products, Master Seed microorganisms, and Master Cell candidates into U.S. biologics facilities when they represent a risk of introducing foreign animal disease must complete a “Summary Information Format for the Importation of Veterinary Biological Products into the United States from Countries Where Foreign Animal Diseases Exist and Other Specified Countries.” This document enables the CVB to perform the required risk analysis and must provide a thorough evaluation of all potential sources of contamination during the development and manufacture of the item, identifying the information regarding the facilities, reagents, production procedures, and testing procedures that should be evaluated. Guidance for preparing this Summary Information Format (“SIF”) is available on the CVB Web site under Biologics Regulation and Guidance, Risk Analysis/Summary Information Formats.
 - (1) Countries from which importation of organisms, vectors, or biologics represents a risk include those where foreign animal diseases exist; those that supplement their meat supply by the importation of fresh, chilled, or frozen meat of ruminants or swine from countries where foreign animal diseases exist; and, those that have common land borders with countries where foreign animal diseases exist, as provided in 9 CFR part 94.

- (2) A separate SIF must be completed for each Master Seed microorganism, Master Cell, and final or finished product.
 - (3) The SIF is not required for bringing items into research and development facilities that are separate and apart from production facilities. In such a case, a National Import Export Services (NIES) permit allowing proposed Master Seeds and Master Cells into the United States is sufficient. If the facilities are not separate and apart, CVB permission for bringing the items into a facility is also required; the firm will contact its reviewer. See also section IV.A.3.b(2) regarding importing Master Seeds and Cells.
 - (4) A CVB Permit for Research and Evaluation is required for importation of a biological product for research and evaluation. See section IV.A.3.b(1) for information on submitting APHIS Form 2005 for research and evaluation through the Web-based e-Permits portal.
- b. Ingredients, including ingredients of animal origin, must comply with requirements in VS Memorandum No. 800.51, section IV.A.
 - c. The applicant must also provide a statement of organisms maintained at the manufacturing site that are etiological agents exotic to the United States. Also, a statement characterizing all ingredients of animal origin used in the production of the Master Seed and the final or finished product must be available on site for review during the pre-permit site inspection. The statement must include a country of origin for each ingredient, with supporting evidence (e.g., certification).
 - d. CVB must receive 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).
 - e. 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 information, it may not satisfy all requirements for the U.S. permit application. Portions of the dossier may be considered, as applicable, with other data, as required.
3. These additional requirements must be met before a Permit for Distribution and Sale may be issued:
 - a. The CVB-Inspection and Compliance (CVB-IC) section must conduct a pre-permit inspection of the facilities.

- (1) The CVB-IC requires a minimum of 3 months to schedule this inspection after the CVB-Policy, Evaluation, and Licensing (“CVB-PEL”) Directorate requests it. The CVB-PEL reviewer requests the pre-permit inspection when submissions indicate facility documents (e.g., the Outline of Production) and production processes will be acceptable and in place at the predicted time of inspection. The request is made according to CVB policy, with the assigned biologics specialist and the inspection section leader of the CVB-IC.
 - (2) The permit applicant must prepay all expenses (i.e., salary and travel) and arrange for a cooperative service agreement by contacting the CVB-IC.
 - (3) If 24 months elapse between a satisfactory pre-permit 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.
 - (4) If conditions change (e.g., a significant change in conditions that may affect products) at the manufacturing plant after a pre-permit CVB inspection, an additional inspection may be required at the prepaid expense of the permit applicant.
- b. Master Seeds and Cells imported pursuant to issuance of a Permit for Distribution and Sale must be accompanied by an import permit from NIES; see 9 CFR 122.2. NIES may require that certain Master Seeds and Cells be tested for exotic extraneous agents by the Foreign Animal Disease Diagnostic Laboratory, National Veterinary Services Laboratories, at Plum Island, New York, before entry into the U.S. mainland. The NIES permit applicant will bear the expense of the associated user fees.

A veterinary biological product (e.g., vaccine or test kits being imported to conduct required studies) must be accompanied by a CVB Permit for Research and Evaluation. Final or finished product imported for pre-permit evaluation (e.g., pre-license serials for confirmatory testing) is shipped with a copy of the Permit for Research and Evaluation directly from the manufacturer to the CVB-PEL laboratory.

- (1) To obtain a Permit for Research and Evaluation, submit a completed APHIS Form 2005 to the CVB-PEL Operational Support unit. This form can be accessed, completed, and submitted

by registering for Level 1 access through the e-Permits portal by visiting the Permits page within the Imports and Exports section of the APHIS Web site.

Additional instructions on registering and using e-Permits can be obtained by calling 301-851-3300, option 1, or via email AskNIES.Products@aphis.usda.gov.

- (2) To obtain the NIES permit, submit a VS Form 16-3, "Application for Permit to Import Controlled Material or Transport Organisms or Vectors," to NIES. This form can also be accessed and submitted through the e-Permits portal with a Level 2 eAuthentication access.

If the Master Seed was derived by recombinant methods, also submit a supplemental VS Form 16-7, "Application for Permit to Import Cell Cultures and Their Products (Supplemental to the VS 16-3)".

4. Eligibility for a U.S. Veterinary Biological Product Permit for Distribution and Sale
 - a. Permittees are limited to persons residing in the United States, or who operate a business establishment within the United States, or both. See 9 CFR 104.1(b).
 - b. One permittee number will be assigned to a permittee for all products imported from the same source (geographic location). The CVB will issue a separate permit for General Sale and Distribution for each imported product (see CVB Notice No. 13-03); the permittee number remains the same on each permit.
 - c. Separate permittee numbers will be assigned to permittees for product or products imported from different sources.
 - d. Eligibility may be adversely affected by the disease status of the manufacturing country, by U.S. State Department restrictions on Federal employee travel (i.e., inspectors cannot travel to the manufacturing country), or by trade embargos in effect.
5. Quarantine Facility. The permit applicant must establish a permanent U.S. site where the product will be received and held in quarantine until the product serial receives authorization from the CVB-IC to be distributed. The CVB-IC will conduct periodic unannounced inspections of the site.

6. Length of Permit

- a. A U.S. Veterinary Biological Product Permit for Distribution and Sale does not have an expiration date. However, the permittee must submit a written agreement for periodic re-inspection of the manufacturing site, at permittee expense.
- b. The permit may be revoked if the permittee violates, or fails to comply with, the Virus-Serum-Toxin Act.
- c. Conditional permits are not issued.

7. Restrictions on Permits. Restrictions, as applicable, may be listed on the Permit.

B. Importation of Product Under a Permit for Distribution and Sale. After the permit has been issued, the manufacturing firm may ship the product to the permittee's quarantine facility. Each shipment must be accompanied by a copy of the permit, plus an original and a copy of a completed APHIS Form 2008 (or equivalent). The Form 2008 is prepared in accordance with VS Memorandum No. 800.53. However, the entire inventory prepared must be listed in "Total Doses Manufactured" for marketing, as noted in block 11, "Remarks." Additionally, the portion of the inventory included in the current shipment to the United States is noted in block 10, "Inventory for Release." When a serial of product is imported in more than one shipment, each shipment must be accompanied by a separate Form 2008 (original and copy) or equivalent. When submitting the additional Form 2008 for a serial previously processed by the CVB, indicate in block 12 that it is a repeat (e.g., second, third) shipment of a previously-submitted serial by selecting "Firm Disposition of Other – Subsequent Shipment." The permittee receiving the shipment into quarantine shall:

1. Certify the inventory. A responsible individual at the U.S. permittee site (in the role of Liaison or Serial Release) must certify in block 10 of the original Form 2008 the total number of containers, doses and the date received by signing in block 11 and submitting the information to the CVB. If this information is entered in the Inventory for Release in the NCAH Portal in lieu of an APHIS Form 2008, the responsible individual at the permittee site will certify this information is correct by submitting the information. See the "Description of Portal Roles" user guide located within the NCAH Portal Guidance Web site at the CVB Veterinary Biologics home page for an explanation of roles.
2. Submit the certified original and one copy of the Form 2008 to the CVB-IC. Employees with the Liaison or Serial Release role and Level 2

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eAuthentication may submit the information to the CVB through the NCAH Portal in lieu of submitting the hard copy Form 2008.

3. Submit, as required, representative product samples to the CVB-PEL laboratory, as specified in 9 CFR 113.3. Final containers of product selected as APHIS samples by an authorized sampler must be shipped in the same shipment as the remaining inventory to the U.S. permittee site. The sampler at the U.S. Permittee site should submit the Form 2020 or submit the information through the NCAH Portal. See VS Memorandum No. 800.59 for further guidance.
 4. Maintain the product at proper storage conditions.
 5. Retain the shipment in quarantine until the shipment has been released by the CVB. A shipment which has been found unsatisfactory by a required test specified in a filed Outline of Production shall not be released for distribution or sale (9 CFR 113.6).
 6. Retain government reserve samples as specified in the filed Outline of Production.
 7. Maintain complete records of all approved labels, cartons, and inserts associated with the product.
 8. The use of labeling approved by the CVB is limited to the biological product imported by the permittee (i.e., limited to use in the United States). Permittees must add to the "Exceptions" section of the APHIS Form 2015, *"This label is to be used only on containers and packaging imported into the United States. Use of this label on serials (or portions thereof) not imported into the United States is prohibited."*
 9. The permittee must hold, in quarantine, all shipments with an APHIS unsatisfactory disposition for disposal under APHIS supervision.
- C. APHIS Release of Quarantined Product. Per the procedures outlined in VS Memorandum No. 800.53, the CVB-IC will review each Form 2008 or release information submitted through the NCAH Portal. The CVB-PEL laboratory may perform confirmatory testing. When the evaluation is complete, the permittee will be notified, by the return of a processed Form 2008 or Electronic Notification of Serial Release, of the APHIS disposition of the shipment.

IV IMPLEMENTATION/APPLICABILITY

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The NCAH Portal is the alternative to submission of APHIS Form 2020s with the release of this memorandum.