



Animal and Plant
Health Inspection
Service

Veterinary Services

1400 Independence
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Washington, DC
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VETERINARY SERVICES MEMORANDUM NO. 800.210

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

FROM: Jack A. Shere
Deputy Administrator

SUBJECT: Manufacturing Deviations Identified Prior to Marketing Release

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Date: 2018.05.31
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I. PURPOSE

This memorandum provides guidance to licensees and permittees regarding processes to follow prior to marketing release when product preparation does not agree with a filed Outline of Production or the regulations. This document does not cover non-compliance with any statutory requirements of the Virus-Serum-Toxin Act. These procedures do not apply to contamination events or to products containing rabies virus or derived from select agents.

II. CANCELLATION

This memorandum replaces Veterinary Services Memorandum No. 800.210, dated December 22, 2010.

III. BACKGROUND

The Virus-Serum-Toxin Act protects veterinary biologics users from worthless, contaminated, dangerous, or harmful products. Title 9, *Code of Federal Regulations* (9 CFR), [part 102.5\(c\)\(1\)](#) requires producers of licensed biological products prepare them as required by the regulations and in accordance with a filed Outline of Production. Producers must conform to the Outline of Production to consistently prepare quality products. Products may be considered worthless, contaminated, dangerous, or harmful when not prepared in accordance with the filed Outline of Production or the regulations.

The Center for Veterinary Biologics (CVB) acknowledges that deviations may occur during the manufacturing of biological products. The CVB may consider products manufactured with inadvertent deviations eligible for marketing release if the licensee or permittee discovers and thoroughly investigates and analyzes the deviations before marketing release. Products not evaluated appropriately may be considered worthless, contaminated, dangerous, or harmful.

The CVB may also need to determine whether certain deviations would cause harm to the public interest; and, if the licensee or permittee releases the product to the market, if the public should be aware of the circumstances. Evaluation of the product by the

VETERINARY SERVICES MEMORANDUM NO. 800.210

Page 2

Outline of Production testing alone will not satisfy the criteria for the evaluation and risk assessment. The evaluation should provide scientific justification for the conclusion. The licensee or permittee keeps the documentation and must provide it for CVB review upon request.

If the licensee or permittee discovers it did not prepare the product in accordance with the Outline of Production or the regulations after submitting APHIS Form 2008 or the CVB marketing release, it must follow the procedures in 9 CFR [116.5\(b\)](#), as defined in Veterinary Services Memorandum No. [800.57](#).

IV. PROCEDURES

- A. If a licensee or permittee discovers a manufacturing deviation before submitting APHIS Form 2008, it can evaluate whether the deviation has adversely affected the product, the testing of the product, and the shelf life of the product. The licensee or permittee must have a systematic, documented procedure in place to address deviations.
- B. Documentation of the investigation by the licensee or permittee shall include:
 - 1. A detailed systematic process-driven investigation of the incident, including a root cause and risk analysis, possible previous occurrences, the effect on the product, and similar incidence in other products or processes.
 - 2. If the licensee or permittee has several manufacturing sites, an analysis to address the impact of licensed/permited products at the different licensed/permited sites, as well as the communication of the deviation and investigation to other sites.
 - 3. All associated copies of testing or other materials to support the disposition of the product.
 - 4. Corrective and preventive actions, including a review process for effectiveness.
- C. The results of an investigation supporting that the product performs as intended throughout shelf life, despite not being prepared in accordance with the Outline of Production or the regulations may be considered eligible for consideration for market release.
- D. The licensee or permittee must dispose of product determined to be unsatisfactory according to 9 CFR [114.15](#).
- E. CVB may consider the licensee or permittee's failure to adequately investigate, document, or institute appropriate corrective or preventive actions when the licensee or permittee produces a product not in accordance with the Outline of Production or the regulations and releases it to the market willful or harmful and not in the public

VETERINARY SERVICES MEMORANDUM NO. 800.210

Page 3

interest. The CVB may take regulatory action against the licensee/permittee in accordance with 9 CFR [105.1](#), [105.2](#), or [105.3](#).

- F. APHIS may revoke without prior review a licensee or permittee's privilege to determine a product's eligibility for consideration for marketing release.

V. IMPLEMENTATION/APPLICABILITY

This change is effective immediately.