



VETERINARY SERVICES MEMORANDUM NO. 800.116

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 /s/ B. Healey for J. Shere, August 14, 2017
Deputy Administrator

SUBJECT: Target Animal Safety Testing Exemption

I. PURPOSE

This memorandum provides guidance to licensed firms on requesting an exemption under title 9, *Code of Federal Regulations* (9 CFR), part 113.4, to target animal safety testing as required in section V.B. of the Outline of Production and 9 CFR 113.64, 113.100, and 113.300. The Center for Veterinary Biologics (CVB) will consider granting an exemption to target animal safety testing for specific products with a documented history of acceptable safety results and controlled manufacturing processes that have ensured batch-to-batch consistency and sterility.

II. REPLACEMENT

This memorandum replaces Veterinary Services Memorandum No. 800.116 dated July 31, 2013.

III. BACKGROUND

Safety testing in animals has been a component of the approval process for each serial of product released for marketing by the CVB since the program's inception. This release testing provides assurance that each serial of product will not have unfavorable results in the target animal. General safety requirements for live bacterial vaccines are described in 9 CFR 113.64, inactivated bacterial products in 9 CFR 113.100, killed virus vaccines in 9 CFR 113.200, live virus vaccines in 9 CFR 113.300, and antibody products in 9 CFR 113.450.

Depending on the type of product, target animal safety testing may be conducted in the cat (9 CFR 113.39), dog (9 CFR 113.40), calf (9 CFR 113.41), pig (9 CFR 113.44), sheep (9 CFR 113.45), poultry (9 CFR 113.100(b)(2)), or aquatic species or reptiles (9 CFR 113.100(b)(3)). If the Standard Requirement (stipulated in 9 CFR) for a product does not specify the animal safety test method, section V.B. in the Outline of Production must indicate a method and state the animal species to be used in safety testing. With the number of serials produced by all licensed manufacturers, the number of target animals used for safety testing can be substantial.

Some products may have established historical data documenting product safety and consistency in manufacturing processes, precluding the need for continued target animal safety testing. Therefore, a process by which firms could obtain an exemption from target animal safety testing is presented below.

USDA's consideration of an exemption to target animal safety testing is consistent with the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Products (VICH) Steering Committee's recommendations described in "*Harmonization of Criteria to Waive Target Animal Batch Safety Testing (TABST) for Inactivated Vaccines* (TABST; [GL50](#)) and "*Harmonisation of Criteria to Waive Target Animal Batch Safety Testing for Live Vaccines for Veterinary Use*" (TABST; [GL55](#)), aimed to minimize the use of target animal safety tests and the principles of reducing, refining, and replacing the use of animals in testing.

IV. POLICY

- A. The CVB will consider exemption requests for all products with documented consistency in manufacturing processes and product safety with the exception of safety tests associated as precursors to potency tests.
 1. A submitted report should provide an overall assessment of all aspects of the product's safety performance, including serial release and pharmacovigilance data (number of years on the market, number of doses sold, frequency and severity of adverse event reports). Specific data for 10 serials, or a minimum of 5 serials if 10 serials are not manufactured within 3 years, should be submitted. The serials should be consecutive and from different vaccine bulks. Fallout products of larger combinations may be supported by these data. Information on any serials failing animal safety testing or deviating from the Outline of Production during this time period should be disclosed.
 2. To ensure that products exempt from safety testing in animals perform in the field as expected, the licensee or permittee must maintain detailed pharmacovigilance records for all adverse event reports received for the respective products they produce or distribute. For products receiving this exemption, summaries of adverse events should be provided to the CVB annually per license restriction.
 3. Outlines of Production containing inadequate production details must be revised and submitted for review before the CVB can consider the exemption. Adequate details include the maximum antigen content based on safety test information, historical antigen input, etc. Changes to the Outline of Production open up the exemption for reexamination.

B. Suspension of Safety Testing Exemption and Reissuance

1. If a serial is manufactured with a nonconformance to the Outline of Production, the exemption may be suspended. The serial must be tested according to the applicable requirements. Reissuance of the exemption will require adequate information demonstrating that the production process is controlled, including provision of satisfactory safety test results for 10 consecutive serials, or 5 if made infrequently. In the event of unfavorable pharmacovigilance report updates, an exemption may be suspended. If changes are made to the Outline of Production, additional serial safety testing may be requested to continue the exemption.
2. An exemption may be suspended if production nonconformities discovered during onsite inspection could have a material effect on the product as determined by the Inspection and Compliance staff.

V. IMPLEMENTATION/APPLICABILITY

This change will be effective 30 days from the date of this memorandum.