United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

Washington, DC 20250

VETERINARY SERVICES MEMORANDUM NO. 800.115

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

FROM: Jack A. Shere
Deputy Administrator
for ROSEMARY SIFFORD
Digitally signed by ROSEMARY SIFFORD
Date: 2019.04.11 14:54:33 -04'00'

SUBJECT: Potency and Safety Testing by Unlicensed Facilities

I. PURPOSE

This memorandum provides guidance to licensees, permittees, and applicants for engaging unlicensed facilities to conduct potency and safety testing of biological products.

II. REPLACEMENT

This memorandum replaces Veterinary Services (VS) Memorandum No. 800.115 dated June 21, 2013.

III. BACKGROUND

Manufacturers must maintain testing expertise to assess their products properly, as described in title 9, *Code of Federal Regulations* (9 CFR), part 113.5(b). Also, per 9 CFR, part 114.3(a), licensed establishments must be separate from any other establishments used for biological products. Consequently, potency and safety testing of a product by an unlicensed facility under contract has not routinely been permitted.

Methods for potency testing have become increasingly sophisticated, often requiring specialized laboratory equipment with specially trained operators. It may be impractical for manufacturers to acquire and maintain this equipment and operating expertise, althoughthe associated potency methods may be superior to available alternatives. In other circumstances, manufacturers may not require animal facilities for any tests other than final product safety testing. Thus, the Center for Veterinary Biologics (CVB) considers it permissible and prudent to allow manufacturers to contract with unlicensed facilities to perform certain testing under specific circumstances.

V. POLICY

The appendix of this memorandum provides guidance for engaging unlicensed facilities to perform potency and animal safety testing.

VI. IMPLEMENTATION/APPLICABILITY

This guidance is effective immediately.

Appendix

Appendix

Guidelines for Implementation of Testing by Unlicensed Facilities

1. *Scope of Testing*

Manufacturers may contract with unlicensed facilities to perform serial release safety and potency testing, but not for other serial release testing. Potency testing by unlicensed laboratories is restricted largely to bioanalytical methods. Classical culture and titration methods will not be considered unless there is a specialized requirement associated with the test. Potency tests which require animals will not be considered without extenuating circumstances.

Serial release animal testing by unlicensed contractors is limited to target animal and non-target animal safety tests when the need to conduct those tests is the only reason the licensed establishment maintains animal facilities.

2. *Location of Unlicensed Facility*

The facility must be located in the United States, District of Columbia, the Territories, or any other place under the regulatory jurisdiction of the United States.

3. *Authority to Inspect*

The unlicensed facility must agree to submit to periodic inspections of the facility by CVB. It is the responsibility of the licensee to obtain this permission. A letter of consent must be on file at CVB. The mail log number of the consent letter must be documented in section V of the Outline of Production for the product being tested.

4. *Procedure to Obtain CVB Approval of Testing by Unlicensed Facility*

   a. *Submission requirements*. Submit the following information to CVB-Policy, Evaluation, and Licensing (CVB-PEL):

      1. *Proposal.* Include the name, address, and phone number of the facility; the primary and alternate site contact at the unlicensed facility; and, the type of testing performed, by product code.

      2. *Audit*. Licensees must perform an on-site audit of the unlicensed facility, provide the audit report and an audit plan to CVB. The audit report must include descriptions of the facility, testing capability, quality assurance program, sample quarantine, sample tracking system, sample disposal procedure, and qualifications of personnel. The audit plan must describe the plan for subsequent audits and identify who will perform the audits as part of ongoing quality management at the unlicensed facility. If the audit has not been conducted by the time the proposal is

submitted, it must be submitted and approved before commencing testing at the facility.

3. *Authorization to Inspect*. Provide a letter from the unlicensed facility authorizing Animal Plant and Health Inspection Services (APHIS) to inspect the facility and review all records relevant to the testing of veterinary biologic products. CVB may elect to conduct an inspection prior to approving use of the facility.

4. *Verification of Test Method Transfer*. If the licensee developed and validated the test method, then provide a report verifying that the test method has been satisfactorily transferred from the licensee to the unlicensed facility. Material tested by the licensee and the unlicensed facility should produce equivalent results. CVB may also require confirmatory testing.

   If the unlicensed facility developed and validated a potency test method, then provide an assay validation report to CVB for review, approval, and possible confirmatory testing. This section does not apply to animal safety tests.

5. *Outline of Production*. Submit a revised Outline of Production containing the following information in section V.C:

   - Facility name, address.
   - Identification of the test.
   - Conditions for shipment of product to the testing site, including the number of samples per test, volume, mode of transportation, and temperature/packaging requirements.
   - The mail log number and date of the CVB approval for the contract testing (for each test).
   - Detailed description of test method or reference to a Special Outline for each test.

b. *Notification of Approval by CVB*. CVB will notify the licensee by letter that testing by the unlicensed facility is approved. CVB will reissue the product license with the restriction described above and approve the revised Outline of Production.

   Once the licensee receives the letter of approval, product license, and updated Outline of Production naming the unlicensed facility, the licensee may begin using the unlicensed facility for testing.

5. *Licensee Responsibilities*

Regardless of the site where serial release testing is performed, the licensee retains responsibility for ensuring testing is conducted according to the approved Outline of Production and for maintaining records as described in 9 CFR, parts 113.5(c), 115.1(a), and 116.

As described in 9 CFR 113, 114, 115, and 116, the licensee is responsible for compliance with the regulations for all steps in the preparation of the product. The licensee must maintain records of all written, electronic, and oral communication with the unlicensed facility pertaining to testing of prelicense and licensed product. The licensee must have procedures for shipping, tracking, and disposing of samples shipped to the unlicensed facility.

The licensee must report unsatisfactory test results (per 9 CFR, part 116.5 and VS Memorandum No. 800.57). Changes in the testing procedure, or changes at the unlicensed facility affecting testing, must be submitted for review to CVB-PEL prior to implementation of the changes.

6. *Unlicensed Facility Responsibilities*

The unlicensed facility must provide the licensee with a letter, signed by an officer of the facility, indicating the unlicensed facility agrees to inspection under the Virus Serum Toxin Act.

Personnel at the facility must store samples and perform testing according to the procedure described in the licensee's filed Outlines of Production and Special Outlines. They must inform the licensee of any proposed changes in testing methodology. These changes must be approved by CVB prior to implementation (9 CFR, part 114.8).

Unlicensed facilities must maintain original testing and sample storage records on site and have these documents available for inspection by CVB. They should provide exact copies of these records to the licensee.

7. *Animal facilities*

Facilities conducting animal tests must have a functional Animal Care and Use Committee and operate in compliance with all applicable animal welfare regulations.

8. *Revoking unlicensed facility authorization*

If either the licensee and/or the unlicensed facility fails to meet their responsibilities, the approval related to the contract testing may be revoked.