



Animal and Plant
Health Inspection
Service

Veterinary Services

Center for Veterinary
Biologics

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CENTER FOR VETERINARY BIOLOGICS NOTICE 20-11

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

FROM: Byron Rippke
Director

SUBJECT: Documenting Appropriate Details for Potency Tests

I. PURPOSE

The purpose of this Notice is to request that all Outlines of Production (OPs) and Special Outlines (SOs) be updated to include complete information regarding how to conduct the serial release potency test. These documents must include all necessary details for testing a single vial and in instances when more than one vial has been used historically to conduct serial release potency tests, indicate the number of vials that are used and state the procedure for combining results across vials. It may be necessary, in some instances, to add additional criteria related to the individual vials (see Section III.3. for example).

The intent of this Notice is to clearly specify the current potency test and not to update potency tests to include additional vials or to reduce the number of vials that are used in the assay. The Notice applies to all products licensed by CVB.

II. BACKGROUND

Title 9, *Code of Federal Regulations*, part 113.5 (a) requires satisfactory completion of potency testing of all serials of biological products before they are released for marketing. Part 114.9 (c) – (f) lists the OP requirements for different types of products and all state that tests must be described in detail within Section V. Testing. Veterinary Services Memorandum No. 800.206 states that OPs or related SOs should “Include stepwise procedures in sufficient detail so a laboratory technician experienced in general laboratory techniques could perform the assay.” Descriptions will vary based on what is being tested, but the expected level of detail includes the lot controlled specific reagents required, the number of vials or samples tested, the testing performed on each, objective decision making steps for selecting subsets of wells/dilutions/plates/etc. used in later steps, validity criteria and calculations required to determine potency in a way that the reader could reproduce the results from the licensee or permittee.

III. ACTION (or POLICY)

At the next annual review of applicable Outlines of Production, review the description of the potency test in Section V.C., as well as associated SOs, and update to include details to the level that make the test fully reproducible, including any validity criteria or calculations, by an independent laboratory technician.

The following provide examples of the level of detail expected for serial release potency tests. These have been written to apply to all assay types, so not all information will be applicable to a given assay, but analogous information should be provided for all potency tests at a similar level of detail:

1. The number of vials or the number of samples, if taken from bulk, used for conducting the potency test for the test serials, controls, reference and any other preparation used in the assay. If more than one vial has been used historically, indicate that to avoid confusion between historic practices and new policy. Previously submitted APHIS Form 2008s could be used to demonstrate the number of vials that have historically been used for serial release.
2. Specify all level of detail for a given vial for each preparation. Examples include dilution factors, number of dilution series created, number of plates per dilution, countable range, etc. Include decision processes for selecting dilutions within the series or plates within a set, where applicable. Specify all calculation methods for each vial.
3. If a single potency measurement is derived from multiple vials, update the OP or SO to indicate the method for combining results across vials (i.e. arithmetic or geometric mean) and specify that value is used for serial release using the existing potency specifications. Do not alter current release or expiration potency specifications. Include an additional specification to apply to each individual vial such that the individual vials cannot differ by more than $0.7 \log_{10}$ from the mean potency specification for a viral titer and 2X from the mean potency specification for bacterial plate count assays.
4. If a test control is used, identify the control. Include validity requirements related to the test control in the Outline.
5. Clearly and objectively state any other validity criteria or inclusion criteria, such as methods for selecting a single dilution or determining countable ranges.
6. A sample calculation would be helpful for inclusion in the filed documentation.

IV. IMPLEMENTATION/ APPLICABILITY

Report results for each test on the APHIS Forms 2008, including validity and control requirements for each test needed to determine the test conclusion and compliance with the Outline. Update each Outline and include this pertinent information within 18 months of the date of this Notice.