

**United States Department of Agriculture
Center for Veterinary Biologics**

Standard Operating Policy/Procedure

Product Sampling

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Product Sampling

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1. Purpose and Scope

This document covers the procedures of sample collection, identification, and submission of biological samples for testing by the Center of Veterinary Biologics (CVB), and the handling and storage of Animal and Plant Health Inspection Service (APHIS) reserve samples at licensed establishments.

The current Laboratory Resources Unit Customer Service Plan and **SOP-SP-001**, *Processing Biologic Sample Submissions*, covers the receipt, tracking, storage, distribution, and disposal of samples, kits, seeds, and cells submitted to CVB for testing. The current version of **ICSOP0035**, *Processing of the APHIS Form 2007 by the Center for Veterinary Biologics-Inspection and Compliance*, addresses the processing of APHIS Form 2007 for Authorized Samplers.

2. Authority

Title 9, *Code of Federal Regulations* (9 CFR), section 113.3, states “each licensee and permittee shall furnish representative samples of each serial or subserial of a biological product manufactured in the United States or imported into the United States as prescribed in this section.” Veterinary Services (VS) Memorandum No. 800.59 established the policies and procedures for selecting, authenticating, and submitting veterinary biological product samples for testing by the CVB or for retention for APHIS.

3. Roles and Responsibilities

3.1 Authorized Samplers

Collection of biologics samples is performed either by an employee of the United States Department of Agriculture (USDA), VS, or by an employee of the licensee or permittee who has been authorized by CVB to collect and handle biologics samples.

- The employee must be trained by a person familiar with sampling procedures according to 9 CFR 113.3 and VS Memorandum No. 800.59 in order to be an authorized sampler.
- Firms must submit an APHIS Form 2007, *Qualifications of Veterinary Biologics Personnel*, to the CVB for each person the firm requests to become an authorized sampler. In addition, the firm must request sampler authorization in writing (formal correspondence) or via the NCAH Portal.
- Negligent or deliberate disregard for proper sampling procedures is a violation of the regulations and grounds for revocation or suspension of product and/or establishment licenses or permits.

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3.2 The Specialist

- Confirm by official correspondence the authorization for a licensee or permittee employee to be a sampler for APHIS. The Specialist must use the most recent version of template **ICTEM0023**, *Sampler Authorization Letter*, or authorize via the Mail Log, see **ICWI0055**, Appendix I.
- Required to train samplers during the prelicensing inspection, regardless of past experience by the employees.
- Arrange to train new and current samplers, as necessary, during inspections.
- Verify that a firm is using proper product sampling techniques during inspection. The Specialist should observe that:
 - only authorized samplers are selecting samples for APHIS testing
 - samples collected must be representative (see **Section 4**)
 - the correct number of samples is retained as reserve samples
 - reserve samples are properly authenticated, labeled, rendered tamper-evident, stored, and secured (see **Section 7**)
 - samples are packed appropriately for shipment (see **Section 6**)
 - the firm is correctly preparing and submitting the APHIS Form 2020 (see **Section 5**)

4. Sample Selection

The authorized sampler should select representative containers from each market serial or subserial according to 9 CFR 113.3 or an approved Outline of Production. This includes samples for outline revision, samples for Master Seeds, Master Cell Stocks and serials submitted in support of an application for a product license or permit.

Prelicensing establishments may submit samples for Master Seeds and Master Cell Stocks and serials presented in support of an application for license or permit prior to authorization of a sampler. In these cases, CVB-Policy, Evaluation, and Licensing may authorize a designated employee to submit those samples. These samples may not be submitted via the NCAH Portal, unless the manufacturer has been enabled for use.

The sampler should review 9 CFR 113.3, VS Memorandum No. 800.59, and the approved Outline of Production to ensure the correct number of samples are submitted to the Sample

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Processing Section or retained by the licensee or permittee for each serial of licensed product. The sampler should ensure that each container is correctly identified.

Note: Please note that biologics sampling should be representative sampling in which selection is made using a plan involving judgment factors. Random sampling, by contrast, is a statistical technique in which each and every container in the serial would have a specified probability of being selected. (Industrial sampling plans often incorporate both random and systematic elements.) Biologics sampling does not usually include random selection methods.

After sampling, the sampler must keep the samples in their possession until transferring to another authorized sampler; placing in a secured storage area with limited access; or sealing them in packaging for submission to the Sample Processing Section. Reserve samples should be rendered tamper-evident and placed in a secured storage area at the recommended temperature.

4.1 Final Container Samples

The entire serial or subserial should be presented for sampling.

- Sampling should include all container sizes of the same serial in representative proportions.
- Samples should be selected from several containers or trays in order to obtain samples that represent different time periods of the filling process or different locations in the lyophilizer.
- Samples from each serial or subserial should be properly identified and secured at all times.
- Bulk samples of completed product may be selected for testing as prescribed in 9 CFR 113.3 (a)(1) and (3).

4.2 Bulk Samples

The entire serial should be presented for sampling.

The identity of the bulk should be verified by checking tags, labels, or other markings on the tank or container in which the bulk product is held.

Agitators or mixers in the tanks or containers should be in operation for enough time to ensure the product is completely mixed and uniform.

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4.3 Serum Samples

Samplers should select, authenticate, and submit serum samples from host animal potency tests intended for confirmatory testing according to VS Memorandum No. 800.79.

5. Proper Identification and Documentation

Each sample must be properly labeled and correspond with the accompanying paperwork. Approved printed labels or other labels with the essential information can be used. For a prelicensing sample, all essential information must appear on a label. All labels should be legible and durable.

5.1 Sample Labels

Firms should properly identify each sample from a market serial or subserial with a legible and indelible label showing:

- Producer's name
- License or permit number
- True name of product (may be abbreviated)
- Serial or subserial number
- Volume of contents (in cc's, mL's, or units)
- Number of doses
- Expiration date, if available
- The Product Code
- A red check mark using permanent ink if the contents contain thimerosal

Firms should identify samples of Master Seeds and Master Cell Stocks by a unique number or other identification which reflects the identity of material stored at the establishment and as specified in the Outline(s) of Production.

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5.2 APHIS Form 2020 (Form 2020) – See NCAH Portal Guidance, User Guide 6, Submitting Routine Biologics Samples, for portal submission.

- A completed Form 2020, *Shipment and Receipt of Biologics Samples*, must accompany each shipment for each type of sample submitted to the Sample Processing Section. The licensee completes all portions of the form except Blocks 9 and 17-19.
- Block 4 of the form must be clearly marked as to which group is being submitted. Only one type of sample group may be listed on each Form 2020. For example, if a firm submits routine concurrent samples and master seeds on the same day, two Form 2020s are required.
 - Routine Concurrent Samples – includes both bulk and final container samples
 - Retention Samples
 - Resubmissions – for additional samples submitted in response to CVB requests or other circumstances, including outline changes or technology transfers special test requests.
 - Prelicensing Samples – samples submitted in support of a product license or permit.
 - Master Seed
 - Cell Line
 - Other – for stock cultures, serums, reagents, or other type not specified above. The sample type to be specified in Block 16, Remarks.
- The data appearing on the label and on Form 2020 should agree.
- An asterisk is to be placed in front of the product name on Form 2020 for products containing thimerosal.
- Block 14 must be signed by an Authorized Sampler.

6. Sample Submission

- Samples are to be packaged to withstand leakage of contents, shocks, pressure changes, and other conditions incident to ordinary handling in transportation. Special care should be taken to prevent breakage of glass containers. All vials, glass or

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plastic, should be packed in nested cartons or by other methods commonly used when shipping to distributors or consumers.

- Leakage of liquid from a carton may mean refusal by a common carrier to handle it. Damaged shipments may be destroyed by Sample Processing Section personnel upon receipt.
- The licensee is responsible for actual shipment of samples to the Sample Processing Section.

7. Reserve Samples

Reserve samples for each serial or subserial are to “be held in a special compartment set aside by the licensee or permittee for holding these samples under refrigeration at the storage temperature recommended on the labels for 6 months after the expiration date.” These samples may be requested by the government at any time (9 CFR 113.3(e)(4)). They should be tamper-evident and held separately from the other serials or subserials in an approved secure storage area.

Rendering samples tamper-evident involves placing samples in cartons (or other containers) and subsequently sealing the cartons so they cannot be opened or the contents disturbed without it being obvious to the Sample Processing Section at receipt, or to a VS employee during an inspection at the facility.

- Samples not placed in a second container must be individually rendered tamper-evident and the identification maintained.
- Containers should be sealed with tape surrounding the container or by other acceptable methods.
- Initials or signature should be applied across the tape surrounding the containers or nesting cartons. Inked stamps are unacceptable.

8. Sampler Roster

Authorized samplers are listed in LSRTIS, Licensing, Establishment Employees, for a particular firm. The Sample Processing Section should use the listing to determine if samples have been submitted by an authorized sampler. If the firm uses the NCAH Portal for sample submission, only those with the role of Sampler can submit via the portal.

9. Summary of Revisions

Version .05

- **1:** Updated references to other documents.
- **2:** Simplified authorities, removed information that can be found in the regulation and VS Memorandum 800.59.
- **3.1:** Added NCAH Portal.
- **3.2:** Added requirement for sampler training on prelicensing inspections.
- **4:** Clarified designated employee for the prelicensing establishments, as noted in VS Memorandum 800.59.
- **4.1 and 4.2:** Removed references about “entire” serial. Have not seen these types of issues in the last 25 years of inspection. Uncertain what it was meant to do.
- **4.1:** Removed “set patterns” as this may be an appropriate method to select samples based on risk factors.
- **5:** Product Codes should be on the sample label.
- **5.2:** Added NCAH Portal information and updated types of samples.
- **8:** Updated method of notification of samplers for Sample Processing staff.

Version .04

- **3.2:** Updated to read, “The Specialist must use the most recent version of template ICTEM0023, *Sampler Authorization Letter*.”

Version .03

- Inserted updated policy under 2. Authorities
- **3.2:** replaced old template letter with current QM template

Version .02

- The Contact information has been updated.
- References to BMPS have been changed to the Sample Processing Section throughout the document.

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