**USDA**

**Animal and Plant Health Inspection Service**

**Veterinary Services**

**Center for Veterinary Biologics**

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# Record Audit Inspections

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**Notes:** *Process for Special Inspection - Bench Record Review done remotely*

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## 1.        Purpose and Scope

This document describes the policy related to preparing for, conducting, and reporting Record Audit Inspections. These are considered Special inspections and coded as such in LSRTIS, Inspection Dashboard. The Inspection Special Type is "Bench Record Review". Establishments with multiple sites, the Record Audit will be specific to one site, if possible. This was communicated to the industry in CVB Public Notice 21-02, Record Audit Inspections.

The use of the remote Record Audit has been expanded to include review of serials and placebos prepared for use in efficacy studies and serials (pivotal efficacy and/or consistency) used to support licensure of a product.

While this type of inspection has always been available to CVB, conducting a record audit using the current tools, such as LSRTIS - Mail Log Module and video conferencing, allows CVB-IC to supplement the compliance strategy. A Record Audit Inspection includes conducting a pre-inspection review, selecting specific serials, performing a record audit of these serials and reporting out the findings.

Record audits are one facet of the on-site inspection and some parts of recordkeeping for serial preparation and testing lend themselves to be done remotely. These audits can be used to determine if the veterinary biologics establishments have the appropriate checks and balances built into their methods of operation that minimize, expose or preferably eliminate non-compliant actions. While this is only a snapshot in time for a small sampling of the entirety of the manufacturing process, documentation of all production and testing steps is required and used to measure compliance to the regulations cited in 9 CFR and the outlines of production on file with CVB.

This SOP specifically defines additional or different requirements for the Record Audit Inspection from the traditional on-site inspections. Unless specified in this SOP, policies listed in **CVB-SOP-0034**, *Inspection: Pre-Inspection Activities,* **CVB-SOP-0035**, *Inspection: The Inspection Proper*, and **CVB-SOP-0036**, *Inspection: Post-Inspection Activities* should be followed.

## 2.        Responsibilities

### 2.1        Biologics Specialist – Inspection Team Leader

Responsible for pre-inspection review of material, requesting documents to be audited, reviewing documents for compliance with the regulations and outlines of production and reporting results of audit.

### 2.2        Section Leader, Inspection

Responsible for providing a list of establishments for the Record Audit Inspection process in LSRTIS-Inspections Dashboard-Recommended Inspections Tab-Special. Approves Record Audit requests from PEL. Consults with Biologics Specialist concerning Record Audits not on the Recommended Tab but may be needed. Reviews outgoing inspection

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report for policy. Acts as a resource for the Biologics Specialist regarding the inspection process.

**2.3    Biologics Compliance Assistant (BCA) – including Lead BCA**

Reviews incoming information in accordance with **CVB-SOP-0049,** *Inspection and Compliance Correspondence (LSRTIS, Mail Log Procedures).*

Aids on background documentation as requested by the Specialist.

Responsible for the Finalization of correspondence and inspection reports in accordance with **CVB-SOP-0046,** *General Inspection and Compliance Correspondence Guidance* and **CVB-WI-0121,** *Inspection: BCA process for Finalization of Inspection Report.*

**3.    Pre-inspection Activities**

The Record Audit Inspection priorities will be set by the Inspection Section Leader. These inspections are posted on the Recommended Tab as Special, Bench Record Review. The Specialist assigned to the establishment should either perform the inspection or find another Specialist to conduct the inspection.

Prior to scheduling the inspection, pre-inspection will need to be performed. **CVB-WI-0076,** *Inspection: Pre-Inspection Packet Checklist– LSRTIS Information and Preparation* can be referenced for many of the pre-inspection records to be reviewed. This review is done by the responsible Specialist. This will help determine which products and serials are to be audited. Review documents, submissions and reports from LSRTIS for past issues, patterns in non-compliance and current situations.

**3.1** For inspections requested by PEL regarding efficacy or support of licensure, the Specialist will audit the serial(s) in question and the placebo if applicable.

**3.2** Review the last two in-depth inspection reports for that site. Review all special/follow-up inspections that were performed since the last in-depth inspection. Review any follow up submissions related to the inspection and review Inspection Action Items.

3.2.1    For Inspection Reports – Use LSRTIS-Inspections-Inspection Search. Enter Establishment number and click on Filter out Cancelled/Denied. This will provide a listing of inspections. If it is for a specific location, type the location in the search box at the top right corner of results, this will filter out the other locations. Click on Info for the inspection and then click on Inspection Report Mail Item #.

3.2.2.   Inspection Action Items – See **CVB-WI-0076** #15

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**3.3** Review the most recent Administrative Inspection Review (AIR) response from the establishment. Advanced Search (IC) – Establishment # - AIR Correspondence. This will get a listing of AIRs for the firm.

**3.4** Review ML submissions

    3.4.1 Inspection Items to Consider -See **CVB-WI-0076** #16

    3.4.2 Regulatory Actions – Go to IC Search and enter Establishment Number and the tag "Regulatory Action". This should give you a history of the regulatory actions for the establishment.

    3.4.3 Outline Submissions – Go to PEL Search and enter Establishment Number and Type "Outlines". You may also specify a timeframe the date received field, usually the date used is from the last in-depth inspection. You can sort the list based on product code. Clicking on the specific ML also provide additional information.

==**At this point in time you should have enough information to narrow down which products you will select for auditing. The next list of information will assist in choosing specific serials to audit.**==

**3.5** Review Investigations - See **CVB-WI-0076** #17. This is to see if there are specific issues with a product or serial, not to close or confirm an outcome of an investigation.

**3.6** Review Internal Doses Report - See **CVB-WI-0076** #11

**3.7** APHIS Form 2008s Reviewed - See **CVB-WI-0076** #9

**3.8** Samples - See **CVB-WI-0076** #14

**3.9** Export Documents Certified - See **CVB-WI-0076** #18a – search on 2017 as they are serial specific. This is not required but may be helpful in determining a serial to review though distribution.

**3.10** Select up to three serials. They may be for the same product or for different products. Review the Outlines of Production associated with the products selected.

**4.** **Scheduling and Notification of Inspections**

**4.1** When the Specialist has determined products and serials to audit, the Specialist will start the Record Audit Inspection by creating a ML for the initial request, using the current version of **CVB-TEM-0040**, *Request for Records*.

    4.1.1 The letter will list the product codes and serials to be audited.

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4.1.1.1 This initial request will be for serial assembly records (information usually found in Section IV.E. of the outline of production). Request:
Minimum # of serials – One
Maximum # of serials – Three

4.1.1.2 Product deviation summaries for one, two or all three products selected may also be requested. The summary can cover a specific timeframe, but suggest it not be longer than the past 2 years. The suggestion is to select only one product for submission of a deviation summary.

4.1.1.3 Each serial and process deviation should be submitted in a separate ML.

4.1.1.4 The establishment should submit the first set of records within 3 working days of receipt of the request.

4.1.1.5 The firm should not make any changes or corrections to the records being requested prior to submission.

4.1.1.6 The Specialist may determine there is another area of concern that can be reviewed during the audit, such as adverse event reports. Consult with a Section Leader or Manager to determine relevancy to the Record Audit.

4.1.2 Create Mail Item: Enter Establishment Number, Product Codes/Serials being audited, Product Code for List of Process Deviation, Date Submitted, Submission Type (Inspection), Submission Subtype (Record Audit), Tag (Return Action Required by Firm), Establishment Site and a Brief Description: Initial Request for Record Audit Inspection.

4.1.3 Attach letter to the ML and move to the responsible BCA for Finalization.

**4.2** Go to Recommended Inspection listed in LSRTIS under Special and click on "Request" for the establishment you are inspecting.

4.2.1 Add the Products and Serials listed in CVB-TEM-0040 under Product/Serial Info.

4.2.2 All Travel and Start Dates are required fields. Suggested dates to use for each (these can be edited at a later date). Do not list any of these dates on a weekend or government holiday.
Travel Out Date - date the ML was created for initial record request
Travel Back Date – 30 days from travel out date
Start Date – 3 working days from the date the ML was created
End Date – same as travel back date

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4.2.3. The inspection will now be located under Pending Approval. While in this queue, Specialist can edit inspection information as needed.

4.2.4 Upon approval of the letter requesting records, the Section Leader for Inspections will approve the inspection. This will move the inspection activity to Pending Report.

## 5.    Batch Record Review and Audit Path Selection

**5.1**      In response to the initial records request, Mail Log Items should be submitted by the Establishment as Submission Type: Inspection and Submission Subtype: Record Audit. The product code should be entered and if related to a specific serial, the serial number should be entered. Process Deviation lists will not have a specific serial listed but should be in a separate Mail Log Item. A specific establishment contact person for each Mail Log Item can be designated in the Brief Description. The contact person must have an APHIS Form 2007 on file with CVB and be authorized for this specific communication by the Liaison. The BCA will review the incoming ML to ensure it is correct and complete. They will move the ML forward to the responsible specialist, Review (Specialist).

**5.2**      Review each of the batch records for the serials selected against the Outlines of Production and the regulations. See Section 7 for information on inspection notes. **This is considered the first day of the inspection for the inspection notes.** Determine which audit path you will choose for each serial.

    5.2.1    Production Record Audit: This is a review of records from inoculation through batching. It can include tracing a fraction bulk back to its master seed. For products with multiple fractions, only one antigen bulk needs to be audited.

    5.2.2    Final Production Record Audit: This is a review of records from batching through filling, packaging, and distribution.

    5.2.3    Testing and Sampling Record Audit: This is a review of records related to Section V. testing and sample selection, submission and retention.

**5.3**      Using the assembly record, **request additional documents as needed** that substantiate specific steps in the Outline of Production, based on the audit path chosen below. Stress the need for accountability throughout the process and identification of materials used and steps performed. The firm must determine which records fulfill the audit needs.

    5.3.1    Initiate Child Workflow for the specific Mail Item. Choose "Request Info from Submitter" activity and provide a routing comment. Click on button, Initiate Child Workflow to move request to the firm. See **CVB-REF-5101**, *Quick Reference Guide – Specialist Functions for Mail Log.* If the request cannot be captured in a child-loop a reference slip may be used (see Section 6.3 below).

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5.3.2 **Production Record Audit** is related to VSM 800.91, Section C.7). Seeds and Cells and Section C.8). Production (inoculation through batching). This covers inoculation through batching and can include traceback to master seed and use/testing of ingredients of animal origin.

5.3.2.1 The request for records should include the product code, serial number, antigen lot number and sections of the outline or special outline you want to audit against.

5.3.2.2 Using VSM 800.206, General Licensing Considerations: Preparing Outlines of Production for Vaccines, Bacterins, Antigens, Toxoids, and Diagnostic Test Kits; parts of the outline that would be related to this type of records audit include
- Sections II.F through IV.A – inoculation through harvest and inactivation (if applicable)
- Section IV.B – adjuvant and stabilizer, may also reference special outlines
- Section IV.C – concentration of antigen bulks

5.3.2.3 An example routing comment would be "Provide copies of records that substantiate Code(x), Serial (y), Antigen Lot (z), related to Outline of Production, Section (fill in applicable sections).

5.3.3 **Final Production Record Audit** is related to VSM 800.91, Section C.90. Final Production (filling to labeling and packaging), Section C.10). Labels and Packaging, and Section C.13). Distribution. This covers filling through distribution (except for final product testing and sampling).

5.3.3.1 The request for records should include the product code, serial number, and sections of the outline or special outline you want to audit against.

5.3.3.2 Using VSM 800.206 and the regulations, type of records audits would include
- Sections IV.F through IV.H – filling and lyophilization or controlled freezing (if applicable)
- 9 CFR 116.3 and 112.1, Labels
- 9 CFR 116.2, Distribution

5.3.3.3 An example routing comment would be "Provide copies of records that substantiate Code(x), Serial (y), related to Outline of Production, Section (fill in applicable sections and regulations (fill in applicable regulation).

5.3.4 **Testing and Sampling Record Audit** is related to VSM 800.91, Section C.9) Final Production (filling to labeling and packaging), Section C.11) Testing (Quality Control), Section C.12) Animals (if applicable) and Section C.14) Miscellaneous. This covers final product testing and APHIS Sample Selection, Submission and Retention.

> 5.3.4.1 The request for records should include the product code, serial number, and sections of the outline or special outline you want to audit against.

> 5.3.4.2 Using VSM 800.206 and the regulations, type of records audits would include
> - Sections V. and applicable Special Outlines/standard requirements - testing
>   9 CFR 113.3 and VSM 800.59, Veterinary Biological Product Samples – samples

> 5.3.4.3 An example routing comment would be "Provide copies of records that substantiate Code(x), Serial (y), related to Outline of Production, Section (fill in applicable sections and regulations).

**5.4** The Record Audit process is in lieu of on-site inspections, therefore the turnaround time for submitting record requests to CVB should be within 3 days. If the firm does not respond this may be a violation of title 9, *Code of Federal Regulations,* section 116.5(a). However, care should be taken to not request more records than needed for each review step.

**5.5** Informal means of communication, such as emails and phone calls, may be used to answer clarifying questions about the intended submission. But in the end the establishment must provide documentation to substantiate the product was made in compliance with the Outline of Production and the regulations.

**6.      Record Audit**

**6.1** The establishment attaches the records to be audited to the specific Mail Log Item and closes the Child-Loop. The Specialist will receive an email with the subject "Submitter has appended documents to Mail Item XXXXXX". When the Specialist receives this notification, they must go into ML, Pending Other Input tab and complete the child workflow. See **CVB-REF-5101**, *Quick Reference Guide – Specialist Functions for Mail Log.*

**6.2** The specialist reviews the records. **CVB-WI-5277,** Work Instruction for Paperwork Review Process can be used as a guide for the audit. See Section 7 for information on inspection notes.

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**6.3**    Once the record(s) has been reviewed, ensuing questions or issues should be addressed by a firm representative. Questions can be submitted to the firm representative. This can be done prior to setting up a phone conference or video conference.

If using a phone call to provide the questions, attach the phone log to the appropriate ML. If you want the questions to be in writing use the comment field in Request Info from Submitter for the appropriate ML, but space is limited.

If more space is needed the following process can be used in conjunction with the Request Info from Submitter ML (Record Audit ML), or a stand-alone in preparation for a conference call or video conference.

> 1. Use Reference Slip CVB-TEM-0024 to provide a list of questions, pdf the document and digitally sign the reference slip.
>
> 2. Create Reference Slip ML – Submission Type "Inspection" and Submission Subtype "Record Audit". Add a brief summary and include "Please submit response under ML XXXXXX (Record Audit ML).
>
> 3. Informationally link Reference Slip ML to the related Record Audit ML.
>
> 4. Attach the reference slip to the Reference Slip ML as "Outgoing Enclosure"
>
> 5. Move Reference Slip ML to the "Workflow Completed – No Records Management". This action sends the ML to the firm. NOTE – there is no quality check by the BCAs, SL or Record Management, so make sure the information is clear and complete.

<u>DO NOT USE EMAIL</u>.

If you need additional records, such as testing of ingredients of animal origin for a specific lot used, validation of a specific piece of equipment used, or accountability of labels, materials, or final inventory, use the Request Info from Submitter for the appropriate ML.

REMINDER – **Video conferences used to discuss records are not meant to be live video stream of on-going procedures. The focus of the inspection is record audit. If it isn't documented, it didn't happen.**

> 6.3.1    Video conferences are the preferred method to communicate issues as it allows screens to be shared and can help with communication.
>
> 6.3.2    Suggest each video meeting be for a specific product and be limited to 2 hours or less.

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6.3.3    There is no limit to the number of video meetings and there can be 2-3 video meetings per day if needed.

6.3.4    See Section 7 for information on inspection notes.

**6.4**    Additional records can be requested by Initiate Child Workflow for the specific Mail Item and choosing Request Info from Submitter. Provide a routing comment. It is important to maintain all related records in a single ML. See **CVB-REF-5101**, *Quick Reference Guide – Specialist Functions for Mail Log.*

6.4.1    While this process of requesting additional records does not have a finite number of requests, be aware that it is easy to "over ask" for all information, relevant and irrelevant, and hard to determine an appropriate stopping point to determine compliance. As a rule of thumb, each product/serial audit should not take more than one to three days.

6.4.2    Requested documents should be readily available and submitted within 3 working days of the request.

6.4.3    If significant information regarding compliance is not submitted for review after one or two rounds of requests, consider this to be a violation and should be cited as such in the inspection report.

**7.        Inspection Notes**

**7.1**    Inspection notes should be taken each time records are reviewed, or information is discussed with establishment personnel. Ensure to concurrently document your review for EACH day.

**7.2**    Use the current version of CVB-WI-5220, How to Take Notes, with the following exceptions:

**7.2.1** The inspection notes do not need to be handwritten. The Specialist can use the pdf fillable form CVB-FRM-0084 and document audit results electronically.

**7.2.2** The Specialist does not need to us a "Page 1" of the notes each day they review the records. The notes can be continuous as long as each date of review is recorded and all conversations with the firm are accurately documented.

**7.3**    Make a record of the findings in such a logical and systematic manner that this record may be later admissible as evidence of the audit and findings in a court of law.

**7.4**    The official inspection notes will be printed, a cover sheet added, and filed in the same fashion as all other inspection notes, including initial and dating of the hardcopy when we return to the office. They are NOT to be included in ML submissions.

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## 8. Closing Meeting – this is the last day of the inspection

**8.1** Check the documentation of each violation to be sure it can be substantiated.

**8.2** Prepare a summary of findings and assemble a draft outline of the inspection report as a list for inspection findings to be discussed.

**8.3** Schedule a wrap-up meeting by phone or video conference with the Liaison to go over the findings.

**8.4** Present findings logically. Note where dates must be set for corrections.

**8.5** Encourage an exchange of opinions with the representatives of the firm. Be sure any misconceptions or misunderstandings are resolved.

**8.6** Record the important points that are brought out in the discussion. If some differences cannot be reconciled, tell the firm representatives that final actions will be determined after consultations with the appropriate APHIS personnel.

**8.7** Ask the firm representatives to suggest a date by which each exception will be corrected. If a date is not reasonable, try to set one by negotiation. If these approaches fail, assign a date by which corrections must be made. No product should be prepared outside of the OP and submitted for consideration for release.

**8.8** Attempt to have written confirmation of all agreements made at the meeting returned to the licensee within 15 days of the conclusion of the inspection. Keep three questions in mind during all negotiations, discussions, and actions:

> Is the action consistent with regulations?
> Is the action consistent with APHIS policy?
> Is the action reasonable?

## 9. Inspection Report

Inspection Report – follow the applicable policies listed in the current version of **CVB-SOP-0036**. The current version of **CVB-TEM-0037** (short form) is use for the report. Follow guidance listed in **CVB-WI-0136**, *Inspection: Specialist Routing of Inspection Reports*. This includes entering action items into LSRTIS.

When the Inspection Report ML is routed to the Inspection SL, they will "approve" the inspection in LSRTIS and it will move the inspection record to Pending Report.

The Inspection Report ML should be informationally lined to the Record Audit MLs (the MLs that contained the records audited). The Record Audit MLs can be moved to "Workflow Completed,

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No Records Management" to close the MLs after the Inspection Report has been reviewed and approved by the Section Leader.