Animal and Plant Health Inspection Service

Veterinary Services

Center for Veterinary Biologics

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Inspection: Inspection Process Activities

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Notes:

The Inspection Proper

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1. Purpose and Scope

This document describes the Inspection Proper. The Inspection Team must determine that the products have been produced and tested by competent people using acceptable facilities, equipment and methods; that products being marketed are not worthless, contaminated, dangerous, or harmful; and that reports and records of production and testing of products are accurate and complete. Additional information can be found in **CVB-SOP-5113** *Virtual Inspections* and **CVB-SOP-5116** *Records Audits*.

2. Definitions

Audit - The inspector selects certain records for an in-depth review. Related records are reviewed to establish the validity of the entries on the master records selected. Exceptions are noted.

Observation - The inspector personally substantiates that the information provided to the Animal and Plant Health Inspection Service (APHIS) and records kept by the firm are in agreement with what was found at the actual situation or site at the establishment.

Perambulation - This is a special class of observations. The inspector unobtrusively watches ongoing operations for a sufficient time to observe unusual or uncharacteristic occurrences, especially regarding techniques of manufacture.

Internal Control - Well-managed enterprises have checks and balances built into their methods of operation to minimize and/or expose errors. The inspector, using experience and judgment, explores the adequacy of these controls. These findings may determine further inspection actions to accomplish a comprehensive inspection.

Inspection Notes - The inspector personally makes 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.

Formal Reports - The inspector communicates the findings in a written form that can be used later for discussions with supervisors, licensee representatives, other team members, subsequent teams, and others properly authorized to use the information gathered.

3. Rules of Conduct

The ideal relationship is one of mutual understanding, confidence, and respect. Although this ideal cannot always be reached, the inspector should observe these rules of conduct and procedure which will approach the ideal as nearly as possible. There are certain specific rules to be followed by all inspectors.

- The inspector is in the position of an observer and should in no way assume a note of supervision or enter into operational management. It is the inspector's responsibility

to note items which are not in compliance with the regulations. It is the firm's responsibility to determine how to meet the requirements.

- The inspector should be reasonable in demands on the time of manufacturing/laboratory personnel by limiting questions and conversation to that directly related and necessary to the inspection.

- The inspector should not discuss possible exceptions with sub-supervisory manufacturing/laboratory personnel or engage in conversations concerning controversial subjects.

- The inspector shall be aware that all information obtained is privileged and shall not be conveyed in any manner or form except to those officially authorized by the Center for Veterinary Biologics Inspection and Compliance (CVB-IC) Director.

- The inspector should observe all organisms and vector control requirements of the laboratory.

- Dress code should be business casual – closed toed shoes – jeans not acceptable – dress presentable. Be aware that jewelry and make-up may not be allowed in some production areas.

Following the assignments made during the pre-inspection meetings, each team member proceeds to obtain information and evaluate the information obtained from the various sources. Findings are reviewed with the team to assure a coordinated effort. If necessary, the team leader reassigns individual activities to maximize the effectiveness of the inspection. The team leader evaluates, coordinates, and finalizes the actions that are taken.

4. Conducting an Inspection

The inspection proper has three phases: 1) an initial meeting with the licensee representative(s) for making introductions, contacts and schedules, and explaining the purposes of the inspection; 2) the inspection activities themselves; and 3) a wrap-up meeting with the licensee to discuss the inspection findings.

4.1 Introductions

Upon arrival do the following so senior management officials will know what to expect:

4.1.1 The inspector should identify themselves to the licensee's receptionist. A printed card is useful.

4.1.2 Ask for the firm's official government liaison by name. If the liaison is not available, ask for the designated alternate. If none of the designated official

representatives are available, ask to see the individual in charge.

4.1.3 The inspector should identify themselves again to the official representative showing his/her official government badge and identification card. This should be a deliberate act even if the inspector is well known to the representative. Section 157 of Title 21, U.S. Code, gives authority to make the inspection only when it is shown that the inspector is duly authorized. The official identification may be delayed until the initial meeting with the management staff but must be done before any inspection activities. It should be documented in the inspection notes who in the management staff the badge is shown to.

- Do not trade the official government badge or identification card for a firm's identification badge.
- Do not allow the firm to copy the inspector's numbered badge or . the inspector's VS1-4 identification card.
- Do not provide the firm with any personal identification, such as a driver's license or Social Security card.
- Do not sign a confidentiality agreement connected in any way related to the duties as an inspector for the Center for Veterinary Biologics. The obligations under Veterinary Services Memorandum No. 800.2, *Confidential Information Concerning the Veterinary Biologics Program*, may be explained to the firm. If necessary, contact a IC Section Leader or the CVB-IC Director.

4.1.4 The licensee representative should be informed that the inspector is on the premises to conduct an inspection. Arrange a meeting with the representative, the individual in charge, and with as many of the supervisory or management staff as may be necessary to have present at the initial meeting. If this meeting cannot be done in a timely fashion (within the first 15 to 20 minutes upon arrival), then the inspector may request to forgo the meeting until a later time that day and begin the tour of the facilities.

4.2 Refusal of Entry

If, after proper identification (see **Section 5.1)**, the firm denies the inspector access to the licensed premises, areas of the premises, or documents that are germane to the inspection, then the inspector should proceed as described in the current version of **CVB-SOP-0043** *Refusal of Entry for Inspection, Assault, and Bribery Procedures* and **CVB-WI-0120** *Refusal of Entry Related to Inspections and Investigations*

4.3 Initial Meeting

Go over the following points in the initial meeting, being brief, businesslike, and courteous. **CVB-WI-5256** *Opening Meeting Brief* provides an example opening meeting discussion.

4.3.1 State the purpose. Explain what an inspection means. Go over the inspection categories in a general manner.

4.3.2 Develop a preliminary schedule with the licensee. Allocate time for:

- An orientation tour of the facilities
- License/blueprints/legends review
- A product review (Review of production records can include all records from the acquisition of seed material to the last container of product leaving the plant including operating procedures and records.)
- An equipment records and equipment operation review
- Review or experimental, field trial, and consumer complaint records
- Review of labels and packaging procedures and records and
- Wrap-up discussion session.
- **CVB-TEM-5117 and CVB-WI-5253** *Opening Meeting Request Template* is useful for providing initial requests to the firm

4.3.3 Discuss the APHIS Biologics Program Inspection Policy which is as follows:

- Will go anywhere it is felt is necessary but will respect licensee policy as nearly as possible and will not interfere with operations if it can be possibly avoided.
- Will accept individual to observe and accompany the inspector at any and all times. The firm may designate whomever they wish.
- Will discuss policy matters only with individuals specifically designated by the firm to do this.
- Will not instruct or admonish any employee.
- Will discuss findings only with employees that management designates. The items discussed will be repeated to management later.

4.3.4 Discuss what the inspectors need to help them in their inspection.

- How will inspectors move about the plant?
- Obtain the names of observers, if any, who will accompany inspectors. Establish the ground rules for observers.
- What are the working hours? Does the company work in shifts?
- Obtain a schedule of activities that will be occurring while inspectors are in the plant. This may include:

    - filling room schedules
    - test starting dates, animal challenge dates, observation times
    - inoculation or harvesting schedules
    - batching schedules

- Determine the locations where records are kept. This should include the following types of records:

- labels and label files
- animal acquisitions and disposals
- production and testing records
- sterilizer, lyophilizer and filling records
- outlines of production
- stock culture and master seed records--testing
- distribution records
- inventory records

- Where may inspectors work? Obtain working space in a location convenient to the records area and to production and testing facilities if possible.

4.3.5 Inform the firm that sampler training will be provided

4.3.5.1 Schedule a time for training with the firm
4.3.5.2 Provide training following **CVB-REF-5105** *On Site Sampler Training and Portal Submission* at the desired time

4.4 Documentation

The preliminary documentation, notes, or forms prepared during pre-inspection review (CVB-SOP-0034) are utilized during the inspection proper. Examples of typical documentation that may be used in the inspection are as follows:

- Daily Inspection Notes (**CVB-FRM-0084**)
- Inspection Product Check-Off Sheet (**CVB-FRM-0083**)
- Product Destruction Record (**APHIS Form 2045**)
- On-site Inspection Meeting Sign-in Sheet (**CVB-FRM-0085**)
- Requested Documents and Observations (**CVB-WI-0074**)
- Processes Observed Worksheet (**CVB-FRM-0095**)
- Requested Document Worksheet (**CVB-FRM-0096**)
- Opening Request Sheet (**CVB-TEM-5117**)
- Summary of Daily Observations for Wrap-Up Meeting (**CVB-FRM-5119**)

All documentation, forms, worksheets, other notes, schedules, copies of documents, exhibits, and employee statements become part of the notes. These must be usable as supporting evidence for all exceptions noted. – reference notes WI – (make copies of everything you sign)

- Make notes legible, clear, and indelible.
- Cross-index or number so sequences can be maintained, and any omissions made apparent.
- Identify by date or by person preparing.

4.5 How to Evaluate Exceptions

There are three types of exceptions: Minor, less serious, and serious

4.5.1 Minor exceptions. Are not apt to affect quality of product but indicate laxity or error that could become more serious if not corrected. If numerous minor exceptions are noted during the inspection, it is indicative of poor management and should be considered as having cumulative effect.

4.5.2 Less serious exceptions. By repetition or very nature, may affect quality of a product. They may require evaluation at the CVB-IC office before final action is taken.

Holding release of serials or products may be required.

4.5.3 Serious exceptions. Violations of this degree will probably affect the quality of the product or products or may be willful. This type of violation will require more thorough documentation and referral to higher authority. Either stop sale or temporary suspension of license should be considered.

Each exception must be related to the Virus-Serum-Toxin Act (VSTA) or to the regulations issued pursuant to the Act. An inspector must not go beyond this authority and should develop the habit of carefully determining what regulation might be violated when a possible exception is noted – see WI for Work Instruction – "phone a friend" as needed. This will ensure that the inspector has not exceeded the delegated authority and that the inspector will be continually increasing the effectiveness of work. A useful reference of violations with the related 9 CFR references can be found in **CVB-REF-5107** *Categories Cross Referenced with 9CFR*

4.5.4 Several other work instructions have been developed for use in evaluation of compliance – these include but are not limited to the following:

Inspection Techniques and Reporting Violations Related to 9 CFR 102.5(c)(1) and 114.8(d) - **CVB-WI-0140**

Findings related to 9 CFR Parts 109.1 and 109.2 exemptions - **CVB-WI-0070**

CVB Inspection and Compliance Policy Concerning Compliance with Title 9 CFR 114.11 and Out of Cooler Episodes - **CVB-WI-0081**

Evaluation of 9 CFR 116 related to Electronic Records and Digital Data - **CVB-WI-0135**

Evaluation of Electronic Record Keeping and Compliance with Title 9, Code of Federal Regulations, Part 116 - **CVB-SOP-0050**

Assessing Compliance with the Requirement of State Veterinarian Approval- **CVB-WI-5215**

Compliance Policy Regarding Exceptions and Exemptions to the Outline of Production and 9 CFR Regulations **CVB-SOP-5118**

Process for Evaluating Compliance with Requirements of VS Memo 800.210 and VS memo 800.57 – **CVB-WI-5218**

Investigation and Processing of Alleged Violations of the Virus Serum Toxin Act – **CVB-SOP-0037**

5. Inspection Notes

Inspection notes are the true inspection report. The typed report is just a summary. Everything in the summary report must be taken directly from notes or attachments. Nothing can appear in the summary that is not documented in notes or attachments. Remember, notes are confidential business information and must be kept secure or in the inspector's possession at all times.

5.1 Some of the uses of notes are:

- Writing the summary (formal) report
- Reference for the next inspection
- Reference to support action relating to special requests, complaints and testing
- Reference to support regulatory action
- Legal evidence for court proceedings (Notes will always accompany personnel to court.)
- Documenting what was done for supervisory or program review

5.2 See CVB-WI-5220 – *How to Take Inspection Notes* for reminders to assist in preparing notes.

6. Inspection Routines

Use of a planned routine to gather information on the compliance status of specific items or procedures is the best assurance that necessary information will be discovered. There is no way that all of the routines that are needed can be described. The following, however, are several routines of major importance covering the areas of records, products, production procedures, and controlled equipment. During the course of use of these planned routines, items may be

discovered that need further comprehensive investigation. The information that will subsequently develop as these "leads" are pursued will be dependent upon ingenuity and resourcefulness as an inspector. V.S. Memorandum lists numerous items which may be considered, reviewed or observed. **CVB-REF-5106** *14 Category Inspection Items Aid* is a memory jogging tool that has proven useful as aid to the memo.

6.1 Serial Record Audit

For a complete serial record review, start with the bulk/batch assembly record, following steps described in **CVB-SOP-5116** *Records Audits*

See Production Paperwork Review Process – **CVB-WI-5277** *Work Instruction for Paperwork Review Process*

6.2 Use of Outlines of Production

The inspectors complete their review of the products that were tentatively selected and of worksheets prepared during the pre-inspection review. Inspection techniques and reporting non-compliance with the Outlines of Production are described in **CVB-WI-0140** *Findings related to 9 CFR 102.5(c)(1) and 114.8(d). Process for Evaluating Compliance with Requirements of VS Memo 800.210 and VS memo 800.57* – **CVB-WI-5218** is useful for evaluating the firm's deviation investigations.

- Request to see the officially stamped copy of the product outline or special outline for the product, procedure, or equipment selected for examination.
- Request to see how the Firm downloads and saved documents - See USER Guide #2 on how a firm should save them) – evaluate system - is it available for employees to see the most current version for use.
- Outline Review Process - **CVB-WI-5282** *Pre-Inspection Tool to provide items to consider in evaluating compliance* provides information regarding review and understanding of an Outline of Production
- Check the page dates against the pre-inspection notes.
- Request completed detailed licensee records for the serial or other procedure selected.
- Review the records and compare with requirements in the outline.
- Observe procedures and compare with requirements in the outline.
- Make notes on the product check-off sheets. Record all exceptions.
- Check supporting records to substantiate the validity of the primary records.

6.3 Routines in the Observation of Production Procedures

The inspector will schedule their observations of production procedures from the production schedule provided by the firm and from pre-inspection notes.

- Consult pre-inspection notes to assist in selecting critical procedures to observe and make actual selection.
- Consign observation to one or more team members taking into consideration their field of specialization.
- Check with the firm for production schedules, schedule changes and request to observe procedures.
- Determine and follow specific restrictions necessary to enter limited access areas.
- Take the assigned product and physically follow the route of movement from room to room within the facility. Compare with the blueprint check-off sheet; note if each activity is where pre-inspection notes indicate.
- Spend enough time at each phase being observed to thoroughly understand exactly what movements are being made in what sequence. Mentally be able to do the complete sequence of movements. Return to the outline and recheck correct procedure. Record any deviations.
- Maintain an awareness of potential contamination; be aware of people's personal habits, environment factors affecting sterility, air movement, proximity to other organisms in use, etc.
- Watch if routines for strict sterility are being broken, particularly harvest, bulk mixing, and fill.
- Watch for deviations in proper lab procedure – placement of a sterile item on a non-sterile surface, then reusing.
- Observe if all surfaces of sterile rooms are being cleaned, walls and ceilings, as well as floors and lab tops.
- Notice if the line supervisor is aware of the conditions or restrictions of the outline. Often outlines are written and filed by management without line supervisor involvement.
- Watch measurement of ingredients – compare with allowed amounts in the outline.

- Watch the recording of each step as it is done, verifying it is concurrent with operations.

- Watch for evidence of reprocessing – watch steps taken post-incubation – compare with that allowed in the outline. Keep sufficient notes on the observation to enable proof as to whether or not a procedure is according to the outline.

- Call other inspectors to witness alleged exceptions. If procedure is dangerous to product or production people, call a team conference and request immediate review by firm personnel. TAKE ACTION.

- Go into coolers; check if unlabeled serials can be mixed up. Check if unreleased serials can be mistakenly sold or distributed.

- Recognize anything that is unlabeled or unidentified and require it be immediately identified and properly labeled, otherwise quarantine it and destroy under APHIS supervision.

- Be on the lookout for organisms in abnormal amounts or in abnormal places as signs of possible research or extra testing in production areas--maintain an awareness of what organisms are authorized where.

- Watch for activity in rooms where not so indicated in blueprints or legends.

- Watch if proper lab clothing and if safety equipment is in use or only present on a token basis.

- Watch for movement of people through a restricted area who are on official business but are not observing the restrictions (maintenance men, firm executives).

- Watch for nuisance things – food in coolers, lunching in laboratory rooms, desks and files in sterile rooms, lounging of idle employees in sterile rooms (often these are hidden and make good places to avoid the supervisor).

- Make notes on product check-off sheet. Record all exceptions and failures to follow good manufacturing practices.

6.4 Extraneous Agents – see **CVB-WI-0083** *CVB Inspection Compliance Policy Concerning Compliance to Title 9 CFR 113.53 - Ingredients of Animal Origin Testing*

6.5. Personnel – see **CVB-WI-5275** *Assessing Personnel during on-site inspections*

6.6 Inspection of Controlled Equipment - see **CVB-WI-5276** *Work Instruction for Assessing Equipment at Licensed Establishments*

6.7 Distribution - see **CVB-WI-5278** *Work Instruction for review of Distribution Records during on-site inspection*

7. Daily Team Review

Individual team members should review their notes at the end of each day. The team leader may assemble all members of the team daily.

- Meet at a location where privacy is assured. This permits free discussion and prevents disclosures of privileged information.
- Review the activities of each member of the team.
- Discuss each exception found.

While some firms may ask for a daily wrap up at the end of the day, this is not required, and in some instances takes time from the review time. A discussion with firm personnel during the inspection is often sufficient to keep the firm informed of findings during the inspection.

- Tentatively rate each exception as minor, less serious or serious. Look for guidelines in special circumstances. Contact IC Management if unable to mitigate.
- Check the documentation of each exception to be sure it can be substantiated. Have it ready for the wrap-up session.
- Discuss the next day's activities and modify assignments if indicated.
- Prepare a summary of findings and assemble a rough form of the inspection report as the inspection is winding up. Present findings logically. Usually use the general inspection category outline in presenting exceptions. Cite 9 CFR references, note these may change upon policy review by the Inspection Section Leader.
- A useful reference of violations with the related 9 CFR references can be found in **CVB-REF-5107** *Categories Cross Referenced with 9CFR*
- Note where dates must be set for corrections or where supervisors must be told of significant items. Have the rough form ready for verbal presentation at the plant wrap-up session.
- An example of summarizing daily observations is shown in **CVB-WI-5250** *Instructions for Daily Review and Closing Meeting Summary Form.*

8. Closing Meeting

Identification of an exception is only a beginning. Compliance with regulations is the desired end result. Many exceptions can be satisfactorily handled through meeting with representatives of management at the conclusion of the inspection. (**CVB-WI-5280** - *Suggestions for Closing Meeting Brief)*

- Record the names of the individuals attending the wrap-up session. (**CVB-FRM-0085**)
- Use the summary of exceptions prepared at the last team review session as the format for the verbal presentation.
- Allow each team member who worked on the category in which the exception was found to present the findings and exception(s) found. The team leader maintains responsibility for developing all actions to be taken as a result of the discussion on each category.
- Encourage an exchange of opinions with the representatives of the firm. Be sure any misconceptions or misunderstandings are resolved.
- 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.
- 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.
- 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 the three question in **CVB-SOP-0036** during all negotiations, discussions and actions:
    - Is the action consistent with regulations?
    - Is the action consistent with APHIS policy?
    - Is the action reasonable?
- Discourage tape recording the sessions. Taping tends to inhibit open and candid discussion. If a firm's secretary transcribes all or portions of the proceedings, insist that a copy be sent to the team leader.
- Make favorable, as well as unfavorable, comments.
- Do not use wording that allows the firm to continue to function out of compliance - such – " can continue for 30 days" should be " … agreed to document in accordance with the regulations beginning with the next process."

- Request the firm to provide confirmation of closing of all items in writing.

9. Guidelines for Actions in Special Circumstances

Document suspected or proven major violations using photocopies of records, employee statements and such other information as will stand legal scrutiny. See **CVB-SOP-0037,** *Investigation and Processing of Alleged Violations of the Virus-Serum-Toxin Act*, for more information. Consult with the CVB-IC Director to confirm action.

Impose a stop sale or hold release on products involved in a major violation(s). Do this only after exploring all aspects of the situation and with approval of CVB-IC Management. Do not use this option too quickly.

Do not rescind a stop sale or hold release until the alleged violation is disproved or the need for it is clearly removed by subsequent events or instructions. All regulatory actions require CVB-IC Management approval, including removal of holds.

Maintain security on evidence of willful violations so the results of the investigation will not be compromised. Discuss evidence only with those who need to know.

10. Verbal Abuse of Veterinary Biologics Inspectors

A question has arisen as to what recourse there is when an inspector is subjected to verbal abuse by the owner or manager of a licensed or permitted facility. Based on a case involving Animal Welfare inspectors, the Office of the General Counsel has determined that if the harassment is of a nature which compromises the inspector's ability to properly inspect the facility, the inspection should be terminated, and alleged violation initiated for failure to comply with the provisions of the VSTA. Consult the CVB- IC Director for advice.

11. APHIS Employees' Safety Responsibility While Conducting Inspections

In 1991, after a tragic loss of life to fire at a food processing plant in North Carolina, the Administrator issued a memorandum on employee responsibilities when safety violations are observed. Even though there is no regulatory authority for the safety of non-Federal employees at commercial facilities, there is a moral obligation to identify and report obvious unsafe conditions. If, during an inspection, conditions are observed that pose potentially disastrous consequences if not corrected, report safety hazards such as blocked fire exits or other workplace hazards to the owners or operators of the establishment.

12. Summary of Revisions

Version CVB-SOP-0035.02

- Information re-arranged to follow a better flow based on the actual inspection process
- Added newly created work instructions/forms based on outcome from Inspection Tool Kit Business Process Improvement project.
- Document number changed from ICSOP0013 to CVB-SOP-0035.

Version ICSOP0013.03

- **5.1**: Additions regarding parameters concerning identification of inspector at a firm (information received from Select Agent Program for Inspectors)

Version ICSOP0013.02

- The Contact information has been updated.
- **3.1/3.4:** These sections have been updated to use more common language.
- **5.3:** Batching schedules have been added.
- **8:** Batch has been added for clarification.
- **8.1:** The word "bulk" has been removed.
- **8.2:** Antigen production has been added for clarification.
- **9.** Noted that 9 CFR citations may be changed upon review.