Investigation Procedures Following a Report of a Disease Outbreak in an SPF Flock which Supplies SPF Eggs or Chickens for Use in Vaccine Production

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A. PURPOSE

Document information to support compliance with **Veterinary Services Memorandum No. 800.65**, for the listed agents of concern in suspect chickens or embryonated eggs.

- Notification procedures used to determine and share outbreak information and mitigate impact to veterinary biologic products.
- Investigation procedures used to coordinate official responses and testing.

B. INCOMING REPORT

Control Point: 2 hours of the report receipt to CVB

1. The CVB-IC Compliance Section Leader, Investigation Manager, or other member (or Acting member) of the Inspection and Compliance Management Team (ICMT) should be contacted within 2 hours of receipt of the report.

C. INITIAL NOTIFICATIONS

Control Point: **ACTIONS TO BE TAKEN WITHIN 1 FULL BUSINESS DAY OF THE REPORT**

1. A VBI will be opened, and a Biologics Specialist (Specialist) will be assigned.
    - CVB-SOP-0037, *Investigation and Processing of Alleged Violations of the Virus-Serum-Toxin Act*.
2. The Specialist will **contact the SUPPLIER** (source of the eggs or chickens) and ask for the following information:
    - Identification of source flock(s).
    - Identification of disqualifying disease or agent deemed inappropriate by APHIS, e.g., Chicken anemia virus (CAV).
    - The **date blood collected** of the last negative test result, or the onset of clinical signs.
    - The **date blood collected** of first positive test result.
    - List of licensed establishments that received suspect materials.

- Date the licensed establishments were notified.
- Number of eggs/chickens shipped to each establishment.
- Date of shipment(s) and associated invoice number(s) if available.
- Lay date for each shipment (more relevant than a shipping date).
    i. Use lay date to determine egg/chicken usage for producing product.
    ii. **Control Point**: The lay date must be prior to, or after, the suspect period in order to use eggs/chickens from a suspect flock for production without testing.

3. The Specialist will **determine the SUSPECT PERIOD**

- The suspect period will be determined case-by-case for notification to licensees and permittees.
    i. **Control Point**: The **blood collection date** from the flock frames the suspect period, not the test date.
- For CAV
    i. Suspect period for CAV begins 3 weeks prior to last negative test and ends the day after two weeks following the first positive test.
- Consider **VS Memo 800.65**
    i. In the event of a disease outbreak in a source flock used to produce embryonated eggs, set the date of initial seroconversion for the flock at 1 day after the collection of the last negative sera.
    ii. The period for suspect eggs should be
        1. For Newcastle disease virus (NDV), avian adenovirus, and *Salmonella spp.*
            a. 2 weeks prior to the seroconversion date
        2. For infectious bronchitis (IB) and *Mycoplasma spp.*
            a. 3 weeks prior to the seroconversion date
        3. For Avian encephalomyelitis virus (AE), Avian influenza virus (AI), Lymphoid leukosis virus (LL), Reticuloendotheliosis virus (REV) , and Avian reovirus (Reo)
            a. 4 weeks prior to the seroconversion date

iii. There is no suspect egg period for Laryngotracheitis virus (LT), Infectious bursal disease virus (IBD), Marek's disease virus (MD), or fowl pox.

iv. The suspect period for the production birds will be determined case by case.

- Contact the appropriate Poultry Disease Expert to determine or confirm the suspect period

4. The Specialist will **contact the APHIS official liaison(s)** of the licensed establishment(s).

Preparatory Steps and Talking Points:

- In order to communicate the suspect period dates established, obtain the test dates from the supplier prior to the call to the firm.

- Communicate eggs/chickens from the suspect period may not be used to produce licensed product if they were not inoculated prior to the time the supplier notified the firm of the outbreak.
    i. Eggs/chickens with a lay date at the beginning, within, or at the end of the suspect period must meet this criterion for use in production.

- Do not tell firm eggs/chickens need to be destroyed due to CAV outbreaks. Refer to **Veterinary Services Memorandum 800.89.**

- Form 2008s must not be submitted for final product prior to testing of bulk.

- Testing instructions will be provided through Official Correspondence citing a Veterinary Biologics Investigation (VBI) number.

Verbally verify:

- The date they were contacted by the egg/chicken supplier about the outbreak.

- Confirm the name of the supplier.

- Identification of disqualifying disease or other agents deemed inappropriate by APHIS, e.g., CAV.

- The flock number(s) involved.

- The determined suspect period.

- The disposition of all eggs/chickens received from suspect flock during suspect period.

- The list of bulks and serials produced with suspect eggs/chickens.
    i. In the case of bulks provide the bulk identification number and associated product code(s).

D. NOTIFICATION FOLLOW UP AND TESTING

1. The Specialist will send **Official Correspondence** to confirm verbal notification or faxed information provided the affected licensed establishments by **mailed letter or NCAH Portal submission.**
    - Email is not a suitable notification method.

    Control Point: The letter **must include** the following information:
    - Name of supplier.
    - Suspect flock identification
    - Identification of disease agent
    - Suspect period **as determined by CVB-IC**
    - The Veterinary Biologics Investigation (VBI) number to tag correspondence

2. The letter **should request** the following information:

    - Inventory of suspect eggs or chickens sourced from the identified flocks received during the suspect period. Firm may need to submit updates.

    - Date they were aware of the disqualifying disease or other agents deemed inappropriate by APHIS, e.g., CAV,
        i. This may be different than date informed by the supplier.

    - List of all serials produced from suspect eggs/chickens.

    - List of all bulk antigens produced from suspect material.

    - Disposition of all suspect material received during the suspect period including:
        i. The number of eggs/chickens used in biological products.
        ii. The number of eggs/chickens used for purposes other than production of biological products, e.g., QC testing, or R&D.

iii. The number of eggs/chickens discarded.

- The firm's policy for handling eggs or chickens suspected to be infected with a disqualifying disease agent/ or CAV.

- A time frame to respond with the requested information.

3. The letter **should include testing procedures and instructions** applicable to licensed products prepared during the suspect period.

    - Products prepared from eggs or chickens sourced during the suspect period are to be tested at the bulk stage (harvest) rather than final product prior to inactivation.

    - Testing must be performed exactly according to the testing protocol **provided with this letter**.
        i. If the protocol is not followed, the product is suspect and product may not be released.
        ii. If applicable: The PCR protocol is an uncontrolled copy which may be copied for internal use, but further distribution of this document outside of your firm is not authorized.

    - Provide a list of bulk lot numbers and associated product codes to be considered for Serial Release.

    - Provide testing results for review by CVB-IC. Bench records may be requested by CVB-IC. Bench records must be complete and include all associated gel photos, PCR results, HPLC results, etc.

    - A Special Test Request (STR) number will be assigned to samples requested for testing. CVB-IC will provide notification of the STR number assigned to initiate sample submissions and indicate the acceptable production stage for samples.

    - Samples must not be submitted without an STR number.

    - Prior to submitting samples for testing, confirm traceability across applicable production stages; source egg/flock, bulk, serial, and the product code under which it was prepared.

    - Prior to submitting samples, submit an APHIS Form 2008 (Form 2008) presenting the specific disease agent(s) test results, including results from additional tests requested by CVB-IC.

i. Follow VS Memo 800.65 for completing remarks on Form 2008.

ii. For Form 2008 portal submissions, use available tags and fields to complete remarks.

- An APHIS Form 2020 must be used to submit samples using the associated product code and bulk lot number along with a CVB assigned STR number.

E. ACTIONS TO BE TAKEN THROUGHOUT THE INVESTIGATION

1. **NCAH Notification.** The Specialist will provide timely courtesy outreach to notify as needed potential NCAH customers of the suspect eggs/birds:
   - The CVB Laboratory (Virology Section)
   - The NCAH Attending Veterinarian at the Animal Resources Unit (ARS)
   - The Diagnostic Virology Section (NVSL)

2. **Poultry Disease Expert.** The Specialist will contact the appropriate Poultry Disease Expert to collaborate on the testing protocol the firm will use to determine if the antigens prepared from the suspect material can be used in product, and for other matters as needed. The Specialist will be discrete regarding VBI information if an expert is not within CVB.

3. **Coordinate STR.** The Specialist will collaborate with the CVB laboratory (Lab) to coordinate resources for confirmatory testing, and sample receipt.
   - The Specialist provides the licensed establishment the official correspondence regarding notification of STR, testing protocols, testing results and determinations.
   - Either the Specialist or Lab may enter a STR into LSRTIS.
   - LSRTIS is used to track and process the Testing Plan, and Reagent List.
   - The Lab may contact the licensed establishment by email regarding the Testing Plan, Reagent List, or samples.
     i. The Specialist will be cc'd or provided the email for the VBI Folder.
   - The Specialist may provide a courtesy notice of incoming samples to NVSL Sample Processing.

4. **CAV Response**. If the veterinary biologics manufacturers are working with CAV, because CAV is environmentally stable, firms must make every effort to prevent CAV contamination of biological products within their establishment.

   - The Specialist will refer to **Veterinary Services Memorandum 800.89**.

5. **Hold Release.** The Specialist will place all serials (if known) prepared from the suspect material on hold release until testing has been completed satisfactorily using the supplied protocol.

6. **Establishment Follow Up.** The Specialist will routinely follow up with the licensed establishments to ensure timely progress.

    - The firm should submit quarterly summaries of antigen usage from suspect materials and a final report when all suspect material has been either destroyed of utilized in final product.

    - The Specialist will notify the licensed establishment that bulk antigens or serials produced from suspect materials that test negative to the disease agent by the supplied protocol may be considered eligible for release.

    - Follow up should include reference to the appropriate VBI number.

7. **Pre-inspection Preparation.** The Specialist may tag Mail Logs, such as; bulk antigen lots, material destroyed, serials produced, etc., to facilitate in-depth inspection preparation. The inspection Team Leader may audit records involved and may prepare a summary for the VBI folder.

    - Edit Mail Log item to add tag “Inspection Item to Consider”.

8. **Closing the VBI.** The Specialist will evaluate the suspect material shipment inventories provided by the supplier with the information provided by the licensed establishment. If all of the suspect material has been accounted for, and the establishment(s) have addressed items to satisfaction, then the Specialist may process the investigation for closure.