

## **Evaluation of Autogenous Biologics Manufacturer's Adherence to Policy During the Inspection Proper**

### **Background:**

Under the provisions of the Code of Federal Regulations, Title 9 (9 CFR):

1. §113.113 states "Autogenous biologics shall be prepared from cultures of microorganisms which have been inactivated and are nontoxic. Such products shall be prepared only for use by or under the direction of a veterinarian under a veterinarian-client-patient relationship, *Provided*, That, such products may be prepared for use under the direction of a person of appropriate expertise in specialized situations such as aquaculture, if approved by the Administrator."
2. §113.113(a)(2) and (3) allows for the the Administrator to authorize preparation of an autogenous biologic for use in herds adjacent and nonadjacent to the herd of origin.
3. §113.113(a)(4) allows for the the Administrator to authorize extended use of an isolate beyond 15 months from the date of isolation.
4. Veterinary Services Memorandum No. 800.69, dated August 7, 2009, informed licensees:
  - a. Shipments to adjacent and nonadjacent herds will be permitted, provided the information cited in §113.113(a)(2) and (3) is on file with the licensee prior to the shipment of an autogenous product for use in a herd other than the herd of origin.
  - b. Autogenous isolates may be used for 24 months without requesting permission from CVB, provided the information cited in §113.113(a)(4) is on file with the licensee.
5. Center for Veterinary Biologics Notice No. 09-15 restricts the use of Autogenous Biologics containing Porcine Circovirus (PCV) to the herd of origin unless the the killing agent (including inactivation kinetics) and tests to assure complete inactivation are included in the approved Outline of Production, and were approved specifically for PCV.

### **Evaluation of Documentation during the Inspection Proper:**

A sampling of the firm's adjacent/nonadjacent and isolate extension documentation should be reviewed for completeness and consistency with shipment and production records.

§113.113(a)(2) requires the following documentation to support adjacent usage of an autogenous biologic:

1. Name, address, and phone number of the owner of the herd of origin.
2. Attending veterinarian's name, address, and phone number, including a Veterinarian/Client/Patient Relationship.
3. Animal species and number in herd of origin.
4. Identification of microorganism(s), at least to genus.
5. Diagnosis or clinical signs of the disease observed.
6. Name and address of the person who isolated the microorganism(s) and the date of isolation.
7. Number of doses of autogenous biologic requested and vaccination schedule.
8. Each adjacent herd owner's name, address, and phone number.
9. Number of animals and species in each adjacent herd.

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10. The attending veterinarian's or approved specialist's assessment of the involvement of the adjacent herd(s) with the disease observed.
  - a. While §113.113 allows “for use under the direction of a person of appropriate expertise in specialized situations such as aquaculture, if approved by the Administrator”, such approval is rarely, if ever, requested. If a specialist is requesting the autogenous biologic, verify Administrator approval of the specialist is documented.
11. The licensee shall give notice to the State Veterinarian or other appropriate State Official in writing when an autogenous biologic is to be used in adjacent herds and provide written approval/acknowledgement from the State Veterinarian or other appropriate State Official in the State in which the autogenous biologic is to be used in nonadjacent herds.
  - a. As a condition of State approval, e.g., California, the firm may be required to submit adverse event reports and/or be subject to an expiration date for the approval. The firm should be evaluated for compliance to the State's conditions.

§113.113(a)(3) requires, except as provided below, the same information which is required for preparation of such product for use in herds adjacent to the herd of origin to prepare a product for use in herds not adjacent to the herd of origin. Because the recipient herd involved may not be known when autogenous biologics are to be used in other geographic areas, the following data may be used in place of the data required in items 8 and 9 above:

1. Names and addresses of practitioners in the area in place of the name, address, and phone number of the adjacent herd owner.
2. The geographic designations of the area involved.
3. A summary of the epidemiology of the disease situation that links the designated geographic areas with the herd of origin.

In addition, an applicant shall provide written approval from the State Veterinarian or other appropriate State Official in the State in which the autogenous biologic is to be used in nonadjacent herds.

§113.113(a)(4) requires the following documentation to support extended use of an isolate up to 24 months from the date of isolation:

1. Identification of the Microorganism
2. Assessment of Continued Involvement
3. Documentation of Satisfactory Performance
4. Any other information the Administrator may require in order to determine the need to use the microorganism to make additional serials.

§113.113(b)(1) states that microorganisms used to prepare autogenous biologics shall not be maintained in the licensed establishment beyond the time authorized for use in production.

1. Unless the requirements outlined above have been met, microorganism(s) used for the production of autogenous biologics may not be older than 15 months from the date of isolation, or 12 months from the date of harvest of the first serial of product produced

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from the microorganism(s), whichever comes first, and such microorganisms must not be maintained in the licensed establishment.

2. No serials of autogenous biologics shall be made from microorganisms that are older than 24 months from the date of isolation, without prior approval by the Center for Veterinary Biologics-Policy, Evaluation, and Licensing, per §113.113(c)(2)(iv).

Center for Veterinary Biologics Notice No. 09-15 restricts the use of Autogenous Biologics containing PCV to the herd of origin unless the CVB:

1. Has approved an inactivation procedure, including inactivation kinetics, specifically for PCV which is included in the filed Outline of Production.
2. Has approved tests to assure complete inactivation specifically for PCV which is included in the filed Outline of Production.

**Note:** *If the firm is producing PCV containing autogenous biologics, determine if adequate procedures are in place to prevent cross contamination. Facilities which are separate and apart are optimal for containment of Circoviruses, e.g., Chicken Anemia Virus. [Reference: 9 CFR 103.1 and 102.5, VS Memorandum No. 800.89]*

### Exceptions:

**Minor exceptions:** Such violations 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 a cumulative effect.

**Less serious exceptions:** These violations, by repetition or very nature, may indicate a disregard for compliance. They may require evaluation at the IC office before final action is taken.

**Serious exceptions:** Violations of this degree may be willful. This type of violation will require more thorough documentation and referral to higher authority. Temporary or permanent suspension of the firm's autogenous oversight without prior Administrator approval should be considered.