Items to Consider regarding Facility Documents for Autologous Therapeutic Biologics

Veterinary Services Memorandum 800.121

This memo was first written in 2017 in response to preparation of autologous vaccines for cancers and other diseases in animals. These products ARE NOT autogenous products and not regulated as such. They are prepared for an individual animal under a prescription written by a licensed veterinary practitioner. The product code will be 95XX.XX, similar to the allergenic extract codes.

Background

There is no one method of preparation for these products, but the products are injectable or infused into the animal. These animals may already have a weakened immune system so the facilities, equipment, personnel and processes used to prepare these products must mitigate possible contaminates (organic or inorganic) and extraneous agents (via ingredients of animal origin or cross contamination with other material).

We anticipate many of these licensed facilities will be one room or a suite of rooms in communal buildings, such as University Research Parks or New Business Incubator buildings. As such, the facilities may not meet the traditional control and quality standards required for the manufacturing of a veterinary biological product.

Acceptance of a facility for the preparation of autologous product DOES NOT mean the facility meets standards in place for any other veterinary biological product.

To determine acceptable facilities CVB-IC personnel will use:

- The outline of production/special outline submitted and reviewed by CVB-PEL.
- Discussions with the licensee regarding the methods used for preparation of media and solutions used in the manufacturing, formulation and filling of the product. The methods used for preparation and sterilization should be included in the outline of production or a special outline. We are determining if the facilities are adequate for these processes.
    - Are media and solutions made by a central media area (Central Services) for the entire facility?
        - Central Services may need to be licensed
        - Alternative – may need to have an addendum to the facility documents describing control mechanisms
    - Are they made and sterilized in the laboratory?
        - Determine if the equipment in the laboratory is appropriate

        - Ensure the processes used are adequate and meet the intent listed in the outline of production or special outline
    - Are they purchased pre-made and sterilized?
        - Ensure this is listed in the OP or Special Outline

- Discuss the sterile preparation of containers, flasks, pipettes, etc. used in the production of the product
    - Are they sterilized on-site but not in the "licensed" laboratory?
        - Central Services may need to be licensed
        - Alternative – may need to have an addendum to the facility documents describing control mechanisms
    - Are they sterilized in the laboratory?
        - Determine if the equipment in the laboratory is appropriate
        - Ensure the processes used are adequate and in compliance with 9 CFR 109
    - Are they purchased pre-sterilized?
        - Ensure the exemption to 9 CFR 109.1 is complete and listed in the facility documents

- Observe (either during on-site inspection or based on the facility documents) placement of essential equipment, such as centrifuges, incubators, cooler, etc. Much of the equipment used will not be stationary equipment. Laminar flow hood for aseptic manipulations would be expected in these licensed areas.

Facility Document Requirements 9 CFR 108

We will require a plot plan, plot plan legend, blueprint, blueprint legend, and any relevant addendums be submitted for review and filed with CVB prior to issuance of the establishment and product license. They must conform to the current regulations; such as they must be signed, a compass point and scale should be included, etc. Some considerations will be provided for.

1. Plot Plan

    a. If the "licensed" premises is one room or one suite of rooms in a building, the surrounding rooms on the floor may be considered the same as surrounding buildings and adjacent properties on a traditional plot plan. [Reference: 9 CFR 108.3(c) and (e)]

b. The boundary of the licensed premises may be considered the single room or suite of rooms and should be marked as such. [Reference: 9 CFR 108.3(b)]

2. Plot Plan Legend

a. For multi-story building – a brief description of the functions housed on each floor should be included [Reference: 9 CFR 108.5(a)(1)]

b. For other entities occupying space on the same floor as the licensee – a general description of functions or activities performed should be listed.

3. Blueprint

a. If only a portion of a floor is occupied by the licensed entity, only that portion of the floor must be illustrated in the same detail as the room or suite of rooms used for preparation of the autologous product.

i. Areas other than the "licensed" room or suite occupied by the licensed entity provide insight to possible issues that may impact production of the autologous product.

ii. An alternative would be to submit an addendum citing controls between the "licensed" and unlicensed facilities occupied by the licensed entity.

b. As noted above, functions or activities performed by other entities on the remainder of the floor can be listed in the plot plan legend.

4. Blueprint Legend

a. A room should not list "areas" within a room to show separation of functions. All functions within the room must be listed and impact to the product must considered during review of the facility documents.

b. Sanitation of the production area and equipment will be significant in order to provide a relatively pure product.

i. In general pre-sterilized materials should be traced back to a Certificate of Analysis from the manufacturer and a receiving lot number.

ii. While we have reduced the trace back of smaller pieces of equipment as noted in **ICWI0028**, *Exemptions to 9 CFR Parts 109.1 and 109.2*, this should not be applied to the preparation of autologous products. We do not have experience or a historical perspective with these types of manufacturing entities and as such the level of predictability regarding the processes they use is unknown. This may change as we gain more experience with these types of manufacturers.

c. Some of these processes require unique equipment for the production and/or testing of the autologous product. Ensure they are listed for the room.

i. Look for sharing of equipment between rooms and for different functions. Ensure controlled processes are in place.

ii. Determine impact of sharing equipment and place.

d. Be aware of other activities, especially diagnostic activities or enrichment functions in the licensed area.

9 CFR 109.2

Most of the sterilization equipment we observe on inspection today has automatic time and temperature recording charts and in some cases they are computerized.

If the firm does not have an automatic recording charts for their dry heat oven, depryogenation tunnel or autoclave, or the automatic recording chart is not operational, they must request an exemption to 9 CFR 109.2.