VETERINARY SERVICES MEMORANDUM NO. 800.78

TO: Veterinary Services Leadership Team
    Directors, Center for Veterinary Biologics
    Biologics Licensees, Permittees, and Applicants

FROM: Jack A. Shere /s/ B. Healey for J. Shere August 18, 2017
      Deputy Administrator

SUBJECT: Preparation and Submission of Facilities Documents

I. PURPOSE

This memorandum provides guidance to firms on preparing and submitting facilities documents to the Animal and Plant Health Inspection Service (APHIS) in order to meet the intent of the regulations, as specified in title 9, Code of Federal Regulations (9 CFR), part 108. Facilities documents are one of the foundational requirements when applying for and maintaining a U.S. Veterinary Biologics Establishment License or U.S. Veterinary Biological Permit for Distribution and Sale.

II. CANCELLATION

This memorandum cancels Veterinary Services (VS) Memorandum No. 800.78 dated November 11, 2010.

III. BACKGROUND

Regulations in 9 CFR 108 provide instruction to licensees and permittees on preparing, revising, and submitting facilities documents. The documents should allow those familiar with veterinary biologics preparation to determine if the facilities’ arrangement/design, functions described, and processes listed are adequate to allow for consistent preparation of product in accordance with the regulations and filed Outline of Production.

The types of facilities used by licensees and permittees to prepare veterinary biological products range from firms with a single site and one building to firms having multiple sites with many buildings per site. Facilities documents include the plot plan, the corresponding plot plan legend, the blueprint(s) and the corresponding blueprint legend(s), and any applicable appendices/addenda to the plot plan and/or blueprint legends.

Through a thorough review, the Center for Veterinary Biologics (CVB)-Inspection and Compliance assesses each facilities document submission to ensure biological products are prepared in facilities that meet the intent of the regulations as outlined in...
IV. DEFINITIONS

A. Prepare or Preparation. Sometimes referred to as manufacture or produce; refers to the steps and procedures used in the manufacturing, processing, testing, packaging, labeling, and storing of a biological product.

B. Production Facility. A location on licensed premises or foreign manufacturing sites where any step in preparing veterinary biological products occurs.

C. Separate and Apart. A building or area on licensed premises that is physically and/or functionally distinct from the production facility to effectively mitigate the possibility of cross-contaminating product from known and unknown sources.

If a research facility/area is considered to be separate and apart by the CVB, then the CVB does not have to authorize the preparation of experimental biological products as described in 9 CFR 103.1.

The CVB is implementing a similar practice for Quality Control (QC) areas that are considered by the CVB to be separate and apart from the manufacturing area. For such QC areas, entities will be allowed to continue to conduct serial release testing but will not need CVB authorization to move experimental products, seeds, or cells into these areas for testing. The entity will be responsible for updating and submitting the list of fractions on an annual basis or as requested by the CVB for these QC areas. This should facilitate testing and may lead to a shorter submission time by the regulated entities in support of licensure.

D. Fraction. A specific antigen, its antibodies, or its antitoxin that constitutes a component of a biological product. For the purpose of facilities documents and 9 CFR 108, in addition to listing fractions, also list all live or inactivated organisms (whether or not they are used to prepare licensed product); DNA, RNA, or proteins prepared as a component of final product; and infected and non-infected cell lines. For the rest of this memorandum, all items listed above will be referred to as “fractions.” Completed product in sealed, final containers is not considered to be a fraction and does not need to be listed for labeling and packaging areas.

E. Stationary Equipment. Equipment used in the preparation of biological product (including testing) that is attached to the floor, wall, or ceiling of a room; that would require disassembly to remove from a room; and/or would require validation after it was moved and prior to use. Examples include, but are not limited to, autoclaves and lyophilizers built into a wall, hard-ducted biological safety cabinets, and equipment supporting air and water quality used in production areas, such as high-efficiency particulate air (HEPA) filter banks and water for injection (WFI) systems.
F. Compartments. A controlled environment that uses air handling systems or other methods (such as a clean room) or specialized equipment (such as a laminar flow biosafety cabinet) to ensure protection of product and personnel and/or maintenance of adequate environmental conditions.

V. GENERAL GUIDANCE ON PREPARING FACILITIES DOCUMENTS

A. Facilities documents should include the following:

1. The establishment/permittee name and number, as shown on the U.S. Veterinary Biologics Establishment license or the U.S. Veterinary Biological Product Permit, on each page of the submission.

2. The address of the facility or premises the document(s) pertain to clearly identified on each page of the submission. This is particularly important for establishments with multiple site locations.

3. Identification of the document on each page of the submission; e.g., ‘Blueprint for Building 1, 1st Floor’ or ‘Addendum A – List of Fractions.’

4. A page number on each legend page. Addendum pages should also be numbered. Plot plan and blueprint drawings do not require a page number. Cover pages and tables of contents are not required to be provided with your facilities document submissions.

5. The signature of a responsible firm official on plot plans and blueprints. This should be the liaison or an alternate liaison designated for the entity.

6. Assurance that adequate water, lighting, and drains exist in all areas. This can be accomplished by a single statement in the plot plan legend or blueprint legend.

7. Legible documents. Plot plans and blueprints must be decipherable without the use of a magnifying glass. If needed, the plot plan and blueprint drawings may be on paper larger than standard size to ensure legibility.

While we are moving to electronic submission of these documents, the requirements and ensuing processes have not yet been determined.

8. A 2-inch margin at the bottom of each document page to allow for the application of the VS file stamp.
B. Plot Plan and Plot Plan Legend

1. All buildings located on the licensed premises, even if they are not used in the preparation of biological products, must be identified and included on the plot plan.

2. If aerial photographs are used as a plot plan submission, they must meet all the requirements for a plot plan as described in 9 CFR 108.3.

3. The plot plan legend must list the function of each building shown on the plot plan. If a research or QC building is considered by the CVB as separate and apart, the date of this approval should be clearly noted in the plot plan legend as part of the description for the building function.

4. Addendums that may be associated with the plot plan legend:

   a. For entities with multiple sites, a description of the movement of biological material between licensed premises and the precautions taken to maintain proper storage conditions during transport. See VS Memorandum No. 800.87 for more information.

   b. A list of the location and condition of records storage at alternate locations (off-licensed premises) when authorized by the CVB. In accordance with 9 CFR 116.1(c), there is a requirement to also provide permission to allow the inspection of these records by the CVB. These records may be requested for review during an on-site inspection.

      Include reference to the CVB mail log number and the date of the authorization letter in the addendum.

   c. The name and address of the off-site storage for portions of master seeds and master cells must be listed. See VS Memorandum No. 800.113 for more information.

      Include reference to the CVB mail log number and the date of the authorization letter in the addendum.

C. Blueprint

1. Even if only a portion of the floor is used for biological production, the entire floor should show the same level of detail. In the spirit of regulatory flexibility, if a portion of the floor used for non-biological processes is considered separate and apart by the CVB, as described in the blueprint legend, the portion of the facility used for non-biological processes does not need to be shown with the same level of detail as the biological production areas. Stationary equipment, sinks, drains,
etc. do not need to be shown on the blueprint for these areas. The functions of the non-biological production areas should have a general description listed in the blueprint legend; e.g., preparation of veterinary pharmaceuticals.

2. All rooms shown on the blueprint must be identified by a letter or number and correlate with the identity of the room listed in the blueprint legend and at the establishment. This includes hallways, stairwells, closets, etc.

3. All symbols and shapes on the blueprint must be identified; e.g., using a key on the blueprint or listed in the blueprint legend. Be aware that symbols or shapes used for architectural purposes may not be appropriate for blueprints submitted in accordance with 9 CFR 108.

4. Stationary equipment must be shown on the blueprint.
   a. Firms may identify coded stationary equipment using the same identifier. For example, all autoclaves may be identified as “A” on the blueprints. The unique identification for each piece of equipment should not be included on the blueprint or listed in the blueprint legend.
   b. Note: The intended purpose of the equipment may impact the code given. For instance, a laminar flow clean bench is not considered to be the same equipment as a biological safety cabinet, since they function in different ways and are used for different purposes. They should be given two distinct identifiers on the blueprint.
   c. Only stationary equipment essential for the preparation of biological product is required to be shown. Displaying additional items (such as countertops, cabinets, shelves, etc.) may introduce unnecessary complexity to the submission.
   d. Equipment that is not considered stationary should not be shown on the blueprint.

5. Water outlets (e.g., sinks and floor drains) must be shown for rooms in which product is exposed to the surroundings.

6. An alternative to an addendum describing other precautions against cross-contamination is the use of a separate blueprint that would show clean room classification, air pressure differentials, and/or areas served by specific HVAC units. Personnel, equipment, and product movement may also be captured on a blueprint for the same purpose.
D. Blueprint Legend

1. Identify all rooms and clearly state the function(s) of these rooms. Avoid vague room function/use descriptions such as “laboratory,” “storage,” “production,” etc. For example, the description of a production room should identify what production steps occur there. Clearly identify the rooms used for both research and development (R&D) and licensed product preparation.

2. If research or QC areas within a building are considered by the CVB as separate and apart, the date of this approval and mail log number (if applicable) should be clearly noted in the blueprint legend as part of the description for the room functions.

3. If non-biological production areas are considered separate and apart from biological production by the CVB and described in the blueprint legend, the amount of detail required for the areas not used for biological production could be reduced, with only a description of the room functions being required.

An example would be the manufacturing of pharmaceuticals in the same building as biologics. The blueprint legend would list the general function of the pharmaceutical production area and applicable room numbers as shown on the blueprint. A description regarding the controls used to ensure biological product quality should also be included. See section V.C.1.

Note: Biological production and non-biological production is not the same as licensed biological production and unlicensed biological production. If FDA-Export Reform and Enhancement Act (FDA-EREA) and/or R&D biologics are prepared in the same building as licensed biologics, the same level of detail would be required for all areas.

4. Rooms in which product and raw materials are exposed to the surroundings should be clearly identified in the blueprint legend or on the blueprint itself in order to determine if the processes used to mitigate cross-contamination are adequate. This would include all rooms or compartments where product may be manipulated outside of a closed system.

5. Identify stationary equipment located in the room in the blueprint legend unless the items are sufficiently described on the blueprint. List other essential (non-stationary) equipment used for product preparation within the room. Equipment that produces aerosols, such as, but not limited to, sonicators and centrifuges, is of particular interest and should be noted as such.

6. Addendums associated with the blueprint legends should be clearly linked to a specific room. When the listing of fractions, equipment, other precautions against cross contamination of product, etc. is repetitive across several rooms, such
information may be listed at the end of the blueprint legend as an addendum. A reference to one or more of these addendums would be made for each applicable room listed in the blueprint legend. Do not list or include standard operating procedures.

Blueprint legend addendums may include:

a. *Methods used to Mitigate Contamination of Product.* Pay special attention to the processes used in rooms in which product or raw materials are exposed to the surroundings.

(1) Decontamination procedures. The cleaning and disinfection methods should be appropriate for the fractions used and the processes performed.

- Identify disinfectant by chemical type so that the antimicrobial properties can be determined. Do not only use the trade name of the disinfectant.

- Document frequency of the process in specific terms. For example, “as needed, but at least after every use” may be adequate; whereas, terms such as “as needed” or “on a routine basis” do not provide sufficient information to determine the appropriateness of the process.

(2) Other precautions against cross contamination. Essential processes beyond the decontamination procedures to mitigate contamination of the product. The following items may be included in this addendum:

- Entry and exit procedures for personnel, equipment, and materials. This may include gowing procedures that may occur in an area remotely located from a production room; e.g., changing into scrubs upon entry into a production building.
- Room/Area access
- Campaign manufacturing – working with only one fraction at a time within a production room
- Environmental monitoring
- Clean room classification, room air pressure differentials, and/or dedicated HVAC units with HEPA filtered air supply and/or exhaust shown on a blueprint drawing
- Personnel, equipment, and product movement (may be shown on a blueprint drawing)
- Drainage and plumbing systems - constructed to prevent effluent backflow into critical production rooms. Drainage lines can be decontaminated.
b. *Fractions List(s).* See section IV.D.

(1) Bacterial, viral, fungal, parasitic, prion agent fractions, etc. that are listed in the facility documents will be considered to be live agents, unless clearly stated otherwise.

(2) Only include fractions prepared at the facility for which the documents are being submitted. List only the fractions routinely prepared in the room. Refrain from listing any and all fractions that may ever possibly be used in a room. The fraction listing does not require immediate updating whenever a new fraction is obtained, but rather can be revised on a regular basis.

(3) QC and R&D rooms may have a broader list of fractions.

(4) Do not refer to fractions as “approved.” The purpose for listing fractions in the facilities document is to determine if the facilities, equipment, and processes are appropriate to mitigate contamination, not a confirmation of the CVB-Policy, Evaluation, and Licensing authorization to introduce an organism into the production facility.

(5) Listing fractions in the facilities documents is not the process used to request permission to prepare experimental biological product in a production facility in accordance with 9 CFR 103.1.

c. *Exemptions to 9 CFR 109, Sterilization of Equipment*

(1) Sterilization methods, other than those listed in 9 CFR 109.1, for containers, instruments, and equipment in contact with product must be exempted. The exemption listing should include the following:

- Listing of containers, instruments, and/or equipment
- Method of sterilization/sanitation used
  - Time
  - Temperatures
  - Exposure ranges – e.g., irradiation processes reported in kilograys or other validated assurance levels
  - Sanitation methods – e.g., fractionation columns
- Statement indicating records supporting verification/validation of the method are on file at the establishment. Depending on the proposed sterilization method, the CVB may request additional information.
- System of recordkeeping for the alternative method
(2) Steam and dry-heat sterilizers shall be equipped with automatic recording gauges. Some older equipment or smaller equipment does not have automatic recording gauges. In these instances, an exemption to 9 CFR 109.2 is required. The exemption listing should include the alternative method of recordkeeping for critical parameters required for sterilization.

A written request must be made to the CVB for any exemption to 9 CFR 109.1 or 109.2 that has not already been filed at the CVB. It is suggested that this request be included in the cover letter accompanying the facilities document submission. The exemption(s) also need to be described in the summary of changes for the documents.

7. When preparing the blueprint legends, it is preferable to avoid listing only one room per page, which will often result in half of the page remaining blank. Instead, maximize the information listed per page. Doing so will reduce the quantity of pages of the submission.

E. Revision of Facilities Documents

1. Facilities documents should be reviewed on a regular basis (e.g., annually) and revised when changes occur to the facilities and/or procedures described in the facilities documents that may impact the preparation of licensed product. This includes additions to or deletions from the ‘Fractions’ list.

2. A summary of changes is required with each revised submission of facilities documents. The summary should list the changes made and why. Placing a supersedes date on each page is no longer required, but is a good documentation practice.

F. Preliminary Documents

Licensees, permittees, and applicants may submit preliminary drawings for comment before construction of new facilities when the company anticipates renovation of existing facilities or other facility changes affecting workflow. The preliminary facilities documents are not approved (filed) but will be maintained for future reference. The CVB may require an inspection of new construction or renovation of facilities prior to product preparation in these areas.

G. Submission of Facilities Documents

1. Prior to submission, ensure personnel familiar with the regulations and guidance documents pertaining to facilities documents review the submission for adequacy and completion. This is a critical step in reducing the amount of preparation and review time required by both the firm and the CVB.
2. Acceptable submissions will be stamped as filed. The CVB will return one stamped copy to the submitter and file one copy. The CVB may return facilities document submissions requiring revision as unprocessed, with a request for the licensed, permitted, or applying establishment to resubmit the documents to the CVB after the necessary revisions have been made.

3. Licensees and permittees should submit two copies of the facilities documents to the Center for Veterinary Biologics-Inspection and Compliance, 1920 Dayton Avenue, P.O. Box 844, Ames, IA 50010.

4. If submitting more than two copies of the facilities documents, explain why this is necessary in a cover letter.

H. Examples of Facilities Documents

Examples for each type of facility document typically found in a complete facilities document submission are provided as appendices to this memorandum. These examples are not intended to address all of the requirements associated with preparing facilities documents. They are not intended to be templates; rather, they are examples to be used in conjunction with the regulations listed in 9 CFR 108 and guidance in VS Memorandum No. 800.78.

Appendices
Appendix I: Plot Plan (example)

Plot Plan
Establishment XYZ
Best Biologics
1234 Coastal Highway
Anywhere, Texas 92510

J.M. Liaison
Signature of Liaison
May 28, 2015
Date of Preparation

Boundary of Licensed Premises

Note: The content of this appendix does not constitute endorsement by APHIS of the facilities methods, or procedures represented in this example

Leave a 2-inch margin at the bottom of the page to allow for the Veterinary Services file stamp.
Appendix II: Plot Plan Legend (example)

Best Biologics                                       1234 Coastal Highway
Establishment 2468                                   Anywhere, Texas

Building 1
Function: Preparation of viral veterinary biological products.
Construction Materials: Steel frame with exterior walls composed of concrete panels with a metal roof. Interior walls are epoxy painted concrete block or drywall or fiberglass reinforced paneling. Ceilings are epoxy-painted drywall. Floors are poured epoxy over concrete.

Building 2
Function: Small animal building used for QC testing of veterinary biological products.
Construction Materials: Steel frame with exterior walls composed of concrete panels with a metal roof. Interior walls are epoxy paint over concrete block. Ceilings are epoxy-painted drywall. Floors are poured epoxy over concrete.

Note: This building is considered separate and apart from production. See the CVB authorization letter dated January 22, 2017 (ML 123456).

Building 3
Function: Administrative Offices (records regarding the preparation of licensed product are maintained here).

Building 4
Function: Preparation of bacterial veterinary biological products, QC testing, and R&D.
Construction Materials: Steel frame with exterior walls composed of concrete panels with a metal roof. Interior walls are epoxy-painted concrete block or drywall or fiberglass reinforced paneling. Ceilings are epoxy-painted drywall. Floors are poured epoxy over concrete.

Building 5
Function: Warehouse, packaging and labeling
Construction Materials: Steel frame with metal siding and a metal roof. Interior walls and ceilings are epoxy-painted drywall. Floors are sealed concrete.

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Appendix II (continued): Plot Plan Legend (example)

Best Biologics                                       1234 Coastal Highway
Establishment 2468                                   Anywhere, Texas

Building 6
Function: Maintenance Shop

Water, Drainage, and Lighting – Adequate water, drains, and lighting exist in all rooms*
used in the preparation of veterinary biological product.

*Some rooms do not require water and/or drains.

Examples of buildings requiring blueprints:
Manufacturing
Shipping – Distribution
Testing, including animal facilities

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Appendix III: Plot Plan Legend, Addendum 1
Storage of Master Seed Off Licensed Premises (example)

Best Biologics
Establishment 2468
1234 Coastal Highway
Anywhere, Texas

In addition to the master seed organisms stored on Best Biologics licensed premises, additional quantities of these master seed organisms will be stored at the following:

A-1 Cold Storage
5678 Mountain Top Road
Somewhere, Colorado
Telephone: 777-888-9999

The management at A-1 storage has provided Best Biologics with written assurance that this off-site location may be inspected by APHIS inspectors. See the CVB authorization letter dated January 22, 2017 (ML 654321).

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Appendix IV: Blueprint - Building 1, Viral Suite (example)*

* For illustration purposes, this example only shows a portion of the production area, not the entire Building 1 floorspace. The expectation would be to have the entire floor of the building shown on the blueprint.

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Appendix V: Blueprint Legend - Building 1, Viral Suite (example)*

* For illustration purposes this example only describes a portion of the production area, not the entire Building 1 floor. The expectation would be to have a description of the entire floor in the actual blueprint legend.

Best Biologics
Establishment 2468

Room 1
Function: Material & Supply Entry
Equipment:
Coded Stationary Equipment: Autoclave (A)
Fractions: NA
Room Management: Addendum B, Section I

Room 2
Function: Storage for Clean/Sterile Production Equipment & Supplies
Equipment:
Coded Stationary Equipment: Autoclave (A)
Non-stationary equipment: filling equipment, lyophilizer trays & racks
Fractions: NA
Room Management: NA

Room 3
Function: Production Equipment Cleaning and Preparation
Equipment:
Coded Stationary Equipment: Double bin sink (S)
Fractions: NA
Room Management: Addendum B, Section I

Room 4
Function: Walk-in Cooler – Storage of Completed Product in Bulk and Final Container
Equipment:
Non-stationary equipment: Fill tanks
Fractions: See Addendum A, Section A
Room Management: NA

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Appendix V (continued): Blueprint Legend - Building 1, Viral Suite (example)

Best Biologics
Establishment 2468
1234 Coastal Highway
Anywhere, Texas

Room 4a
Function: Storage of APHIS Retention & QC Samples
Equipment: NA
Fractions: NA
Room Management: Chain link enclosure with secure entry

Room 5
Function: Hallway
Equipment: NA
Fractions: NA
Room Management: NA

Room 5a
Function: Product, Equipment, Material Airlock
Equipment: NA
Fractions: NA
Room Management: NA

Room 6
Function: Capping, Packaging, and Labeling of Lyophilized Product
Equipment:
Coded stationary equipment – Packaging/Labeling Line (Z); Capping machine (CM)
Non-stationary equipment – Portable and secure label storage cages; product transfer carts
Fractions: NA
Room Management: Addendum B, Section I

Room 7
Function: Product Transfer Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Section I

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Appendix V (continued): Blueprint Legend - Building 1, Viral Suite (example)

Best Biologics
Establishment 2468
1234 Coastal Highway
Anywhere, Texas

Room 8
Function: Lyophilization of Viral Products
Equipment:
Coded stationary equipment – Freeze Dryers (C)
Non-stationary equipment – Trays and racks for loading and transporting vials to be freeze dried; hand seal crimper
Fractions: See Addendum A, Section A
Room Management: Addendum B, Sections II & III

Room 8a
Function: Personnel Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Section I; Addendum C, Section II

Room 9
Function: Product Transfer Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Sections II (a-c) & III

Room 10
Function: Fill Room for Lyophilized Viral Products
Equipment:
Coded Stationary Equipment – Fill machine (B), Clean room (…)
Non-stationary equipment – Table top scale, transport rack for vials, intermediate-fill tank
Fractions: See Addendum A, Section A
Room Management: See Addendum B, Sections II & III; Addendum C, Section III

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Appendix V (continued): Blueprint Legend - Building 1, Viral Suite (example)

Best Biologics
Establishment 2468

Room 11
Function: Fill Tank Room
Equipment:
Non-stationary equipment: Fill tank
Fractions: See Addendum A, Section A
Room Management: Addendum B, Section I

Room 12
Function: Equipment and Supply Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Section I

Room 13
Function: Personnel Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Section I; Addendum C, Section III.a

Room 14
Function: Viral Production Primary Personnel Airlock
Equipment: NA
Fractions: NA
Room Management: Addendum B, Section I

Room 15
Function: Women’s Locker Room/Rest Room
Equipment: NA
Fractions: NA
Room Management: Addendum C, Section I

Room 16
Function: Men’s Locker Room/Rest Room
Equipment: NA
Fractions: NA
Room Management: Addendum C, Section I

Leave a 2-inch margin at the bottom of the page to allow for the VS file stamp.
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## Appendix VI: Blueprint Legend - Building 1, Addendum A

### Listing of Fractions (example)

<table>
<thead>
<tr>
<th>A. Viral Fractions</th>
<th>B. Bacterial Fractions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine Rhinotracheitis Virus</td>
<td>Actinobacillus pleuropneumoniae</td>
</tr>
<tr>
<td>Bovine Respiratory Syncytial Virus</td>
<td>Bordetella bronchiseptica</td>
</tr>
<tr>
<td>Parainfluenza Virus</td>
<td>Mannheimia haemolytica</td>
</tr>
<tr>
<td>Canine Distemper Virus</td>
<td>Pasteurella multocida</td>
</tr>
<tr>
<td>Canine Parvovirus</td>
<td>Campylobacter fetus</td>
</tr>
<tr>
<td>Canine Coronavirus</td>
<td>Clostridium chauvoei</td>
</tr>
<tr>
<td>Equine Herpesvirus, Type 3</td>
<td>Clostridium septicum</td>
</tr>
<tr>
<td>Equine Herpesvirus, Type 4</td>
<td>Haemophilus somnus</td>
</tr>
<tr>
<td>Equine Influenza Virus</td>
<td>Haemophilus parasuis</td>
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<tr>
<td>West Nile Virus</td>
<td>Leptospira canicola</td>
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<td>Leptospira hardjo</td>
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<tr>
<td></td>
<td>Leptospira icterohaemorrhagiae</td>
</tr>
<tr>
<td></td>
<td>Leptospira pomona</td>
</tr>
</tbody>
</table>

### C. Production Cell Lines

- Madin-Darby Bovine Kidney
- Dog Kidney
- Vero

### D. Organisms for Quality Control Use Only

- Bacillus subtilis
- Candida albicans

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*Leave a 2-inch margin at the bottom of the page to allow for the VS file stamp.*

*Note: The content of this Appendix does not constitute endorsement by APHIS of the facilities, methods, or procedures represented in this example.*
Appendix VII: Blueprint Legend - Building 1, Addendum B
Viral Suite - Decontamination Procedures (example)

Best Biologics              1234 Coastal Highway
Est 2468                    Anywhere, Texas

Section I. Applicable to all production areas:
  a. Floors are mopped with a phenolic disinfectant solution at the end of each shift/daily.
  b. Walls are cleaned with a phenolic disinfectant solution weekly.
  c. Ceilings are cleaned with a phenolic disinfectant solution quarterly.
  d. Room 1 only - Items entering into Room 1 are steam sterilized or are sprayed with a phenolic disinfectant solution and held for 20 minutes prior to exiting the room.
  e. Room 6 only - The capping machine and packaging line are cleaned with sodium hypochlorite disinfectant wipes after each serial is sealed/packaged.

Section II. Applicable to production rooms in which product is exposed to the surroundings:
  a. All work surfaces, including biological safety cabinet, are cleaned after each operation with 70% Isopropyl alcohol.
  b. Floors are cleaned after each operation with a phenolic disinfectant solution.
  c. Walls and ceilings are cleaned with a phenolic disinfectant solution weekly.
  d. Equipment, containers, instruments, and materials are placed in the airlock for the room and sprayed with a phenolic disinfectant solution and held for 20 minutes prior to moving into and or out of the production room.

Section III. Movement of equipment and material from rooms where product is exposed to the surroundings:
  a. Removable equipment items are bagged and sprayed with 70% Isopropyl alcohol.
  b. Waste is double bagged and the outer bag is sprayed with 70% Isopropyl alcohol prior to exiting the room.
  c. Contaminated waste is chemically sterilized or disinfected prior to final disposal.
  d. Room 8 only: Lyophilizer – Vial trays and lyophilizer shelves are wiped with a phenolic disinfectant solution. A steam-in-place (SIP) procedure is performed on the inside of each lyophilizer unit after each serial is freeze dried.
  e. Room 10 only: Fill line – Removable parts are cleaned and steam sterilized. The rest of the line and associated clean room is wiped with a phenolic disinfectant solution prior to and after each serial is filled.

Disinfectants used include: sodium hypochlorite, phenolic agents, 70% Isopropyl alcohol, and peracetic/acetic acid hydrogen peroxide. Sodium hypochlorite disinfectant wipes may also be used for surfaces.

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Note: The content of this Appendix does not constitute endorsement by APHIS of the facilities, methods, or procedures represented in this example.
Appendix VIII: Blueprint Legend - Building 1, Addendum C
Viral Suite - Other Precautions Against Cross Contamination (example)

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1234 Coastal Highway
Anywhere, Texas

Section I. Applicable to Building 1 Entry:
   a. Access to the Viral Suite is limited to authorized personnel.
   b. Employees and visitors change into scrubs, put on a bouffant cap, beard cover (if applicable), safety glasses, and shoe covers. Hands are washed and a sanitizing foam is used.

Section II. Additional precautions taken for working in Lyophilization Room 8:
Secondary gowning occurs prior to entry into Room 8, which includes donning a lab coat, surgical mask, gloves, and shoe covers. Secondary gowning is removed and hands are washed and/or hand sanitizer is used prior to exiting the production room.

Section III. Additional precautions taken for working in Fill Room 10 and Clean Room 10a.
   a. Full body sterile suit including gown, hood, and booties; mask; two pairs of gloves, and safety glasses are donned prior to entry into Room 10. Secondary gowning is removed and hands are washed and/or hand sanitizer is used prior to exiting the Production Room.
   b. Open manipulation of product is performed inside a positive pressure HEPA-filtered Clean Room.
   c. Environmental monitoring is performed during filling with alert and alarm levels determined to demonstrate effectiveness of processes to mitigate cross-contamination of product. Media fills are performed quarterly.

Section IV. Additional precautions against cross contamination may be shown using a specialized blueprint drawing such as Appendix IX – Building 1 HVAC/Airflow Blueprint.

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Appendix IX: Building 1- HVAC/Airflow Blueprint (example)*

* For illustration purposes, this example only shows a portion of the production area, not the entire Building 1 floorspace. The expectation would be to have the entire floor of the building shown on the blueprint.
Appendix X: Blueprint Legend - Building 1, Addendum D
Viral Suite - Items Exempted from the Requirements of
9 CFR 109.1 and/or 109.2 (example)

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The following equipment is exempted from the sterilization requirements in 9 CFR 109.1:

I. Glass vials used for bottling final product
   A. Method of Sterilization
   Vaccine bottles are sterilized by gamma irradiation at 30 kGy by the supplier.
   B. Documentation
      1. Certificate of sterility provided by the supplier is maintained by Quality Assurance.
      2. Each production record contains the lot number for the bottles used in serial preparation.

II. Rubber stoppers for vials of product
   A. Method of Sterilization
   Rubber stoppers are sterilized by gamma irradiation at 30 kGy by the supplier.
   B. Documentation
      1. Certificate of sterility provided by the supplier is maintained by Quality Assurance.
      2. Each production record contains the lot number for the stoppers used in serial preparation.

Records supporting verification/validation of the sterilization method described above are on file.

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The following equipment is exempted from the sterilizer recordkeeping system requirements specified in 9 CFR 109.2:

**Stainless Steel Fill Tanks**

**A. Method of Sterilization**

Tanks are steam sterilized in place (SIP) through a steam line in Room 4 for a minimum of 90 minutes at 121 °C. Temperature is verified visually by using a calibrated in-tank thermometer. Once 121 °C is achieved, this is the start time. Temperature readings are taken every 15 minutes with a final reading taken at 90 minutes.

**B. Documentation**

All SIP time and temperature readings are recorded in the SIP log in Room 4. The operator confirms the run time and temperature of the SIP for the tank along with the SIP run number in the appropriate space on the tank tag. The tag is subsequently placed into the production record. All records are authenticated and dated.

Signed:

______________________________________________________

Date: ______________

Printed name and title: _______________________________

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