Table of Contents

1.0 Purpose

This document provides detailed instructions for the cleaning and disinfection of the Virus Production Facility (VPF) areas in the Advanced Technology Research Facility (ATRF.)

2.0 Scope

This procedure applies to the Biopharmaceutical Development Program (BDP) VPF. The adjoining locker room facilities are not covered by this Standard Operating Procedure (SOP) and are cleaned using general housekeeping methods. The manufacturing and support spaces on A1, A2, and B1 within the ATRF are covered in ***SOP 19408 - Cleaning and Disinfection of CGMP Areas in the ATRF***, and Cell Therapy Ares are covered in ***SOP 19504 - Cleaning and Disinfection of the ATRF Cell Therapy Areas***. Manufacturing process equipment is cleaned following separate procedures. This procedure does not apply to the surrounding areas within the ATRF.

3.0 Authority and Responsibility

3.1 The Director, Technical Operations, BDP has the authority to define this procedure.

3.2 BDP personnel and/or BDP-directed contract cleaning personnel are responsible for the implementation of this procedure.

3.3 The Director, Technical Operations, or designee is responsible for training the personnel who perform this procedure and for providing documentation of this training to Biopharmaceutical Quality Assurance (BQA).

3.4 Persons performing cleaning of the areas defined in this procedure are responsible for complying with the steps specified in this procedure.

3.5 It is the responsibility of Biopharmaceutical Quality Assurance (BQA) Engineering, (BQAE) or designee, to evaluate the effectiveness of this cleaning protocol by reviewing the environmental monitoring results for the VPF areas of the ATRF.

3.6 The Cleaning Coordinator (or designee) is responsible for review of completed cleaning logs.

3.7 BQA is responsible for quality oversight of this procedure.

4.0 Procedure

4.1 Safety

4.1.1 Avoid eye and skin contact with cleaning agents. Wear proper cleanroom gowning attire as described in ***SOP 19410 - Gowning Requirements for Personnel and Visitors for the ATRF Virus Production Facility***. Wear nitrile or other non-latex gloves that cover the wrist and hands to protect from exposure to disinfectant solution. Wear safety glasses or goggles when using disinfectants. Immediately rinse off the disinfectants using copious amounts of water from any exposed skin.

4.1.2 Post "Wet Floor" signs whenever the floor surface is wet due to cleaning activities. A wet floor can be slippery particularly when wearing disposable booties.

4.1.3 Refer to manufacturer's safety precautions and Safety Data Sheets (SDS) for appropriate protective equipment and safe handling procedures when using chemicals.

4.1.4 Use extreme caution around electrical outlets and Supervisory Control and Data Acquisition (SCADA) connection points. If moisture gets inside these fixtures, it can cause a short or electrical shock.

4.1.5 Use caution when cleaning near HEPA filters and HVAC air-intake ducts. They must never be exposed to any liquid. To avoid damage to the HVAC filters, **DO NOT mop or spray the HEPA filters, their protective grills or any air-intake ducts. To clean these areas, spray a wipe or pad style mop head with 70% IPA and carefully wipe the surfaces.**

4.1.6 Follow Environmental Health and Safety (EHS) Guidelines. These guidelines can be accessed online.

4.1.7 When using sporicidal concentrations of Decon-Spore (6.5 oz/190 mL per gallon of WFI) staff must use PAPR's equipped with a 3M GVP-443 cartridge, or a full face or half face respirator and goggles with cartridges 3M 60926 or 3M 60923. These cartridges are good for 40 hours of use or 6 months, whichever occurs first. Staff must be actively enrolled in the Respiratory Protection Program to use the equipment. Areas that have been cleaned using Decon-Spore must be posted with "Caution" signage (see attachment 20) for a minimum of 24 hours following cleaning. For additional safety, Decon-Spore is typically used from a 13-oz. bottle to facilitate easy batching in 2 gallons of WFI.

4.2 Materials

NOTE: Only equipment, materials, and supplies that have been specifically approved are to be used in the classified areas.

4.2.1 Approved Disinfectants and Diluents

4.2.1.1 Decon-Ahol® or equivalent, (70% IPA, sterile), BDP PN 30129

4.2.1.2 Decon-Cycle®, (Low pH Phenolic, sterile), BDP PN 30119

4.2.1.3 Simple Mix Decon-Cycle®, (sterile), BDP PN 31253

4.2.1.4 Decon-Spore® (Peracetic Acid & H_2O_2, sterile), BDP PN 30824

4.2.1.5 Simple Mix Decon-Spore® (sterile), BDP PN 30826

4.2.1.6 WFI - Water for Injection

NOTE: Water for Injection (WFI) does not need to be released for cleaning purposes.

4.2.1.7 Cavicide, BDP PN 10168

4.2.2 Approved Cleaners

4.2.2.1 Micro-90 (Concentrated Alkaline Cleaning Solution) – BDP PN 30393

4.2.2.2 Decon-Clean®, BDP PN 31326

4.2.3 Approved Cleaning Equipment

4.2.3.1 Step Ladder

4.2.3.2 Mop Systems

- Autoclavable double bucket with wheels dedicated to the VPF
- Stainless sieve
- Mop handle
- Mop head frame
- Other supplies with Manufacturing Manager approval

4.2.3.3 Volumetric Container for cleaning/disinfectant measurement

4.2.3.4 Sprayers – Hand Pump or Core 2 Clean System

4.2.3.5 PAPR Hood Assembly (3M PN S-655)

4.2.3.6 Belt Mounted PAPR Assembly (3M PN GVP-CB)

4.2.3.7 Air Purifying Cartridge (3M GVP-443)

4.2.3.8 Half face respirator with goggles or shield or full face using cartridge models (3M 60926 or 60923)

4.2.3.9 Other respiratory protection equipment as approved by EHS.

4.2.4 Consumables

4.2.4.1 Cleanroom Supplies

- Mop Head Pads, BDP PN 22116 or 22120.
- Short Loop Mop Head BDP PN 22150
- Biohazard Bags, Autoclavable, Red, 36” x 48” BDP PN 21827
- Biohazard Bags, Autoclavable, Clear, 30” x 36”, BDP PN 20728
- Wipes, sterile, BDP PN 20315
- Clean room wipes (9x9), BDP PN 21208

4.3 Cleaning

4.3.1 Preparation of Disinfectant Solution

4.3.1.1 Apply as indicated in Attachment 1.

4.3.1.2 Use Decon-Spore at sporicidal concentration for the first cleaning of each month on the floors before rotation of the next cleaning disinfectant.

4.3.1.3 Water must be brought into the VPF, as there is no WFI source within. **Use a carboy or bag to transport water as the cleaning bucket is not permitted within the adjoining A2 manufacturing areas. Disinfect the WFI container when moving either in or out of the VPF with Cavicide.**

4.3.1.4 Using the designated equipment for the area to be cleaned, fill the solution bucket with the proper amount of WFI.

4.3.1.5 Using a suitable volumetric container capable of measuring milliliters, add the appropriate amount of disinfectant concentrate to the buckets, as specified by the Disinfectant Dilution Chart in Attachment 1. Mix using the mop until the solution is visibly homogeneous, at least 30 seconds.

4.3.1.6 Document the disinfectant preparation on the Room Cleaning Log. (See Attachment 4.)

4.3.1.7 Disinfectant solutions will be prepared and disposed of daily.

4.3.2 Cleaning Techniques

NOTE: Short loop mop heads (BDP PN 22150) may only be used on floors.

4.3.2.1 Triple or Double-bucket wringer system for mopping ceilings walls, and floors.

- Submerge the mop in the first solution bucket.
- Fully wring the solution from the mop.
- Submerge the mop in the second rinse bucket.
- Partially wring solution from the mop leaving the mop wet.
- The wringer is placed on the third bucket when using a triple bucket.

4.3.2.2 Double-bucket with sieve pad-style mop technique for mopping ceilings, walls, and floors.

- Submerge the mop in the first solution bucket.
- Remove excess liquid using the sieve positioned over the second bucket.

4.3.2.3 Mop loading: Between submersions the mop must only be loaded in one direction and remain wet enough to ensure cleaning solution is applied on the entire surface the mop contacts. Avoid excess solution application to prevent pooling and long dry times. If at any point the mop is no longer sufficiently wet, it must be rewetted. Mop strokes should overlap by approximately 20% or 1/5th of the mop head length to ensure complete coverage.

4.3.2.4 **Ceilings**:Mop the ceilings, stroking from wall to wall in one direction.

NOTE: **DO NOT** mop, wipe, or spray HEPA filters. Wipe the protective grills of the HEPA filters with a cleanroom wipe or pad style mop head dampened with 70% IPA. Do not wet the HEPA filter.

4.3.2.5 **Walls**: Mop from the top down. Whenever cleaning around equipment and obstructions, walls may be mopped horizontally proceeding from top to bottom. Wipe the grills of the air returns with a cleanroom wipe dampened with 70% IPA.

NOTE: Ceilings and walls must be completed before floors. Once a mop head is used on the floor, it may not be used on ceilings or walls.

4.3.2.6 **Floors**: When mopping floors with a clean room mop, a modified technique may be used, where the mop handle is rotated 180° at each turn, so that a leading mop edge never reverses direction. **Remove excess cleaning solution while mopping to avoid residue build up and puddling of cleaning solution. Floors should remain wet for 5 to 10 minutes to allow proper contact time. Floors taking longer to dry are an indication that too much liquid is being applied which is not beneficial and leads to faster residue buildup.** Floors are to be done innermost to the exit.

NOTE: Change mop heads if they become heavily soiled. Solution should be changed more frequently if heavily soiled.

4.3.2.7 After mopping is complete, discard the used mop head(s).

NOTE: A maximum of 4 used mop heads may be placed in a single trash bag for subsequent autoclaving.

4.3.2.8 Empty the bucket into the drain in Room A2219 and wipe the buckets clean using wipes and 70% IPA.

NOTE: The bucket may exit via the Room A2218/A2223 airlock for non-BL3 campaigns. The bucket must exit via a liquid cycle in the autoclave during a BL3 campaign. Production staff will operate the autoclave.

4.3.2.9 **Sprayers**: Pump sprayers or sprayer sytems may be used for solution application on walls, floors, and ceilings provided no open work is in progress. Before spraying, cover any moisture sensitive equipment that may receive overspray with plastic. Excess cleaning solution may be removed by using the mopping techniques described previously in section 4.3.2.

4.3.3 Cleaning Sequence

4.3.3.1 Perform the following tasks, as required by the frequency chart, (Attachment 2) following the cleaning sequence for each area in

Attachment 3. The cleaning will be performed using cleaning techniques described in Section 4.3.2.

4.3.3.2 Waste removal

NOTE: Non-BDP cleaning staff will not be responsible for handling any waste in the VPF.

- BDP staff will seal and remove sharps, broken glass containers, and other trash as needed.
- All trash within the VPF is considered biohazardous and will be autoclaved out of the area.
- Non-biohazardous waste as marked by black bags is only within the Men's and Women's locker room and will be removed by cleaning staff.

4.3.3.3 Cleaning Sequence and Locations

- In general, clean ceilings, then walls and work surfaces, then clean the floors from the innermost areas toward the exit or the location where the solution is discarded, and supplies are stored.
- Walls include all vertical surfaces such as doors, door hardware, window frames, light and door activation switches, window, gowning mirrors, wall mounted phones, railings, and utility panels. (It is necessary to follow up cleaning of window glass with IPA to remove streaking and spotting caused by residual disinfectant).

  NOTE: When a wall is indicated on a cleaning form, it is implied that all the listed surfaces are included.

- Work surfaces include tables, carts, shelves, chairs, stools, gowning benches, trash cans, and other objects not classified as equipment or supplies.

  NOTE: When a wall is indicated on a cleaning form, it is implied that all work surfaces are also included.

- Document the tasks and rooms disinfected in the appropriate cleaning logbook after cleaning is completed**.**

4.3.3.4 Wash Down/Complete Cleaning

- When performing a complete cleaning that involves cleaning of the ceilings and walls, it is recommended and acceptable to apply disinfectant using a sprayer and use a pad style mop head as necessary to ensure even and total distribution.
- Clean work surfaces using Cavicide, BDP PN 10168, or batched disinfectant dispensed either by sprayer or wetted clean room wipes. Avoid getting liquid into sensitive equipment.

- The floors would then be done with a separate mop head and a bucket system. Staff may then move to the next sequential room, again using the sprayer and dedicated mop head on the ceilings and walls followed by the floor with the mop head previously used on the floor. This technique minimizes the number of solution preps and entries to an area.

4.3.3.5 Routine Floor and Surface Cleaning

- The cleaning type that occurs most often is for the floors and select surfaces. Floors are cleaned with the designated product and select surfaces are cleaned with Cavicide, BDP PN 10168. Select surfaces are to be cleaned prior to mopping floors.
- When floor cleaning is selected on the form as part of scheduled cleaning not involving the cleaning of walls, it is implied that all selected surfaces are also included.
- The select surfaces included in this cleaning are those that receive frequent contact or could otherwise impact the room environment. Surfaces may be sprayed directly or Cavicide may be sprayed first onto a clean room wipe to avoid overspray near instruments and telephones.

  Door activation hardware – This includes door handles or push plates or other activators.

  Tables – Staff should not move equipment to perform this activity. This does not include storage racks or carts which are the responsibility of production staff as part of production activities.

  Chairs – This includes chairs, stools, and gowning benches.

  Phones – Flat cleanroom units and the handset and keypad of traditional units. The traditional units are not waterproof and should have a protective cover in place.

4.3.4 Frequency of Cleaning (Attachment 2 – Frequency Chart)

NOTE: Attachment 2 lists the minimum cleanings required, but frequency is not limited to these minimums.

4.3.4.1 Area disinfection is to occur whenever an area status is “in service” following the frequency guidelines in Attachment 2. Cleaning frequency may be reduced for an area if its status is “limited use” or “shutdown”. See ***SOP 21554*** – ***GMP Area Status Management*** and the posted status sheets for status description details.

4.3.4.2 Campaign and production schedules will initiate special request cleanings.

4.3.4.3 A complete cleaning of product handling zones (as defined by the term “campaign” in Attachment 2) will occur as soon as possible after completion of the campaign. Completion includes the following tasks by manufacturing personnel prior to cleaning:

- The product removed from the area (or properly stored in Room A2217 for a BL3).
- Waste autoclaved and removed.
- Excess raw materials are discarded.
- VHP cycle is performed if required for the VPF.

4.3.4.4 Upon completion of the previous steps, a single wash-down of ceilings, walls, and floors will be performed using Decon-Cycle. The area will be deemed suitable for use the following day.

4.3.4.5 For the VPF fill area, Rooms [redacted], a single wash-down must have occurred within the previous 30 days to obtain clearance for a new campaign.

4.3.4.6 A rinse of floors is performed monthly prior to the application of Decon-Spore and documented. Additional rinses of surfaces including floors should be performed if a buildup of cleaning residue is observed.

- For rinsing purposes, WFI should be drawn from use point and used immediately. The rinsing procedure uses the same equipment, technique, and documentation as cleaning. Select “Other” for disinfectant and write in WFI.
- If WFI is insufficient to remove residue, other approved products may be used when directed by the BDP cleaning contact or BQA. Decon-Clean may be used to remove residue during shutdown periods prior to return to service disinfectant application. Decon-Clean is a non-sterile preparation and cannot be used without being followed by a disinfectant application as directed by the Quality Engineering and Validation Manager.

4.3.5 In-Process Cleaning

4.3.5.1 When work is in progress, the VPF manager will indicate on the cleaning coordination calendar or place signage on the entrance to the VPF updated daily to inform cleaning staff if they are permitted enter the area to clean and any special instructions such as: ***Cleaning Staff Entry Restricted*** which means there is no entry by cleaning staff at this time*,* ***Sprayer Use*** see step 4.3.5.2*,* ***Escort Required*** indicating that cleaning staff may enter only if accompanied by production personnel.

4.3.5.2 Mops are not permitted during production operations within 10 feet of Prodigy systems or other equipment with unprotected flow paths. Under these conditions, only sprayers shall be used within the boundary.

- If the VPF manager deems that mopping is necessary, the cleaning staff must be escorted and supervised by production staff. Alternatively, production staff shall perform the mopping.
- The monthly residue removal with WFI must be performed with a mop.

4.3.5.3 If cleaning staff are restricted from entry, it will become the responsibility of production personnel to perform the necessary cleaning. Arrangements may be made with the cleaning staff to make up deferred cleanings, however, the weekly frequency in attachment 2 must be adhered to.

4.3.6 Post-Renovation, Facility Shutdown/Failure Cleaning

4.3.6.1 For product changeover/area clearance see Section 4.3.4.3.

4.3.6.2 Standard requirements are described below and divided by classification. Depending on the conditions of the renovation / shutdown/failure, the number of cleanings required may be increased or decreased by the BQA Quality Engineering and Validation Manager or designee.

4.3.6.3 BQA Quality Engineering and Validation Manager or designee will indicate any rooms within the zone that first require detergent cleaning, including detailed wiping and a wash down with Micro 90 or approved equivalent. (This step is not required unless requested by BQA.)

4.3.6.4 A minimum of two cleanings (as described below) is standard procedure.

- The first required cleaning will include detailed wiping and a complete wash down of ceilings, walls, and floors with Decon-Spore at sporicidal concentration.
- The second required cleaning will be a complete wash down of ceilings, walls, and floors with ’ Decon-Cycle.

4.3.6.5 Cleaning status will be communicated by the Quality Engineering and Validation Manager or designee usually via ***SOP 21554 – GMP Area Status Management***.

4.4 Documentation

4.4.1 Log entries will follow documentation guidelines in ***SOP 21409 – Good Documentation Practices.***

4.4.2 Record disinfectant preparations at the bottom of the cleaning form as they are formulated. (See Attachment 4.)

4.4.3 Record all cleaning and disinfection activities on the zone-cleaning log form (Attachment 4). This will include the date, initials, time completed, rooms completed, tasks completed, and any comments.

4.4.4 Cleaning entries must be reviewed regularly by the Cleaning Coordinator or designee. Loose cleaning forms should be submitted for review weekly.

5.0 Definitions

5.1 **HEPA –** High Efficiency Particulate Air

5.2 **IPA –** Isopropyl Alcohol, sterile

5.3 **PPE –** Personal Protection Equipment

5.4 **CGMP Area –** Environmentally-controlled area with limited access

5.5 **WFI –** Water for Injection

5.6 **VPF –** Virus Production Facility

5.7 **Work Surfaces:** Work surfaces and horizontal surfaces including, but not limited to, shelves, transfer panels, tables, stools, door handles, and telephones.

5.8 **Cleaning Zones –** The facility is divided into "zones" to reduce cross contamination and allow for different cleaning schedules. Clean the rooms in the order indicated for each zone in **Attachment 3** unless ongoing production requires an adjusted order.

6.0 References and Related Documents

SOP 19407	*Flow of Personnel, Materials, Equipment, and Waste in the CGMP Areas of the ATRF*
SOP 19408	*Cleaning and Disinfection of CGMP Areas in the ATRF*
SOP 19410	*Gowning Requirements for Personnel and Visitor for the ATRF Virus Production Facility*
SOP 19504	*Cleaning and Disinfection of the ATRF Cell Therapy Areas*
SOP 21409	*Good Documentation Practices*
SOP 21526	*Engineering Event Management*
SOP 21554	*GMP Area Status Management*
Form 19409-01	**Cleaning Log Zone 1**

7.0 Attachments

7.1 **Attachment 1** Summary Sheet

7.2 **Attachment 2** Frequency Chart

7.3 **Attachment 3** Cleaning Zone Reference Sheet

		Simple mix products allow convenience as no WFI is required. Decon-Clean was added to have additional residue removal options.
4.2.3.4	Add reference to Core 2 Clean System	This is an advanced sprayer and application system using a stainless-steel reservoir using gas charged application, with a precision applicator. Use will be covered by a separate SOP.
4.3.1.5	Remove pre aliquoted containers.	They were never used in practice.
4.3.2.6	Added phrase about contact and drying time to limit product applied.	Excess product has no benefit for killing organisms and has several negatives including faster residue buildup and reduced slip safety.
Attachment 2	Increased cleaning frequency from 1 to 2 times per week and Decon-Spore application from 1 to 2 times per month.	The VPF has become more heavily used and the number of EM events suggests that cleaning frequency needs to be increased.

Attachment 1

Summary Sheet

DISINFECTANT DILUTION CHART			
Disinfectant	**BDP PN**	**Volume / Gallon**	**Volume / 5 Liter**
Decon-Cycle®	30119	15 mL	20 mL
Decon-Spore®	30824	6.5oz or 190ml	N/A

CLEANER DILUTION CHART			
Cleaner	**BDP PN**	**Volume / Gallon**	**Volume / 5 Liter**
Micro 90	30393	10 mL	13 mL
Decon-Clean	31326	30 mL	39 mL

PPLICATION CHART	
Disinfectant	**Month**
Decon-Spore®	The first cleaning of the month and mid-month on the floors. Special request, post-renovation, Post-facility shutdown, failure cleaning.
WFI	Used for cleaning agent residue removal. Used monthly prior to first application of Decon-Spore and additionally as needed.
Decon-Clean	Used for residue removal. Decon-Clean is a non-sterile preparation and should only be used during facility shutdown periods prior to return to service cleaning with disinfectants unless specifically directed by the Quality Engineering and Validation Manager.

Attachment 2

Frequency Chart

FREQUENCY CHART						
Zone	***Zone Name:***	**Ceilings**	**Walls**	**Curtains**	**Floors**	**Open Drains**
1	VPF	Campaign[1]	Campaign[1]	N/A	1 x Week (2 x month Decon-Spore)	N/A

[1] At the end of each campaign for product clearance. Will also be required as part of return to service.

NOTE: Cleaning frequency may be altered due to holidays, facility shutdown, inclement weather, or as directed by ***SOP 21526 - Engineering Event Management***.

Attachment 3

Cleaning Zone Reference Sheet

Whenever production concerns allow, clean the rooms in the order indicated for each zone. The primary equipment storage location, water source, and frequency are listed, but subject to change as production concerns require. The zone can only be cleaned with the designated equipment sets.

Zone 1 – VPF

Equipment Set: A Equipment Storage: A2217/A2225 Water source: A2404 via pass thru PT-01

Room #	Room Name	Classification	ISO Classification	Cleaning Order
A2214	Filling	10K	7	1
A2213	Filling Gown	10K	7	2
A2215	Filling Degown	10K	7	3
A2217	Storage	10K	7	4
A2216	Hall	10K	7	5
A2225	Decon	10K	7	6
PT-01	Pass-Thru (floor level)	NA	NA	7
A2211	Production area	10K	7	8
A2204, A2208	Overgown	10K	7	9
A2207, A2209	PAL	100K	8	10
A2203, A2205	PAL	100K	8	11
A2218	MAL	100K	8	12
A2223	MAL	NA	CNC	13