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1.0 Purpose

This document provides detailed instructions for the cleaning and disinfection of the current Good Manufacturing Practices (CGMP) manufacturing and support areas [redacted]

2.0 Scope

This procedure applies to Biopharmaceutical Development Program (BDP) manufacturing and support spaces on floors A1, A2, and B1 [redacted]. The Virus Production Facility (VPF) is covered in ***SOP 19409 - Cleaning and Disinfection of the [redacted] Virus Production Facility***. Cell Therapy Production Suites in B wing are covered by SOP 19504 – Cleaning and Disinfection of the [redacted] Cell Therapy Areas. Manufacturing process equipment is cleaned following separate procedures. This procedure does not apply to the surrounding areas [redacted].

3.0 Authority and Responsibility

3.1 The Director, Technical Operations, Biopharmaceutical Development Program (BDP) has the authority to define this procedure.

3.2 The Director, Technical Operations, BDP, or designee, is responsible for the implementation of this procedure.

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

3.4 The Cleaning Coordinator (or designee) is responsible for review of the cleaning logs.

3.5 It is the responsibility of Biopharmaceutical Quality Assurance (BQA) or designee, to evaluate the effectiveness of this cleaning protocol by reviewing the environmental monitoring results for the CGMP areas [redacted].

3.6 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 19406*** - ***Gowning Requirements for Personnel and Visitors:*** [redacted] ***Manufacturing and Support Areas***. Wear nitrile or other non-latex gloves that cover the wrist and hands to protect from exposure to disinfectant solution even when not part of the gowning requirement for the area. 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 Material Safety Data Sheets (MSDS) for appropriate protective equipment and safe handling procedures when using chemicals.

4.1.4 When damp mopping or spraying the walls, 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. Cleanroom tape may be placed securely over these fixtures to reduce (but not eliminate) the risk. Remove tape after cleaning, if applicable.

4.1.5 Use caution when working around steam lines. Steam and exposed steam lines can cause severe burns.

4.1.6 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 grilles, or any air-intake ducts or the grills. Regular cleaning is not required for these surfaces. If needed they can be done as part of a requested cleaning. Spray a wipe with 70% IPA and carefully wipe the surfaces.**

4.1.7 Follow Environmental Health and Safety (EHS) Guidelines. These guidelines can be accessed by going to the NCI-Frederick Home Page on the Internet; go to Campus Resources, EHS, Useful Documents and Information, and choose which information is desired.

4.1.8 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. Ceilings are not routinely cleaned with Decon-Spore as a matter of risk versus benefit. Overspray or dripping solution from the ceiling poses a potential personnel safety risk while the likelihood of contamination to the ceiling is historically low. QA or the cleaning supervisor reserves the right to request Decon Spore use on the ceilings at sporicidal concentrations if warranted by EM data or other circumstances. If cleaning of the ceiling is performed with Decon-Spore the area should be posted with a "CAUTION" sign (see **Attachment 4**) for a minimum of 24 hours. 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

- Decon-Ahol® or equivalent, (70% IPA, sterile), BDP PN 30129
- Decon-Cycle®, (Low pH Phenolic, sterile), BDP PN 30119
- Simple Mix Decon-Cycle®, BDP PN 31253
- Decon-Spore® (Peracetic Acid & H_2O_2, sterile), BDP PN 30824
- Simple Mix Decon-Spore®, BDP PN 30826
- WFI - Water for Injection

NOTE: WFI does not need to be released for cleaning purposes.

- Steri-Perox® 6%, sterile, BDP PN 10665

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

- Triple Bucket System
- Double Bucket System

- Mop Handles
- Mop Head Frames

4.2.3.3 Volumetric container for cleaning/disinfectant measurement.

4.2.3.4 Sprayers – Hand Pump.

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 Other respiratory protection equipment as approved by EHS.

4.2.4 Consumables

4.2.4.1 Cleanroom Supplies

- Mop Head Pads, BDP PN 22116
- Mop Head Pads, BDP PN 22120
- Mop Head (Short Loop), BDP PN 22150
- Biohazard Bags, Autoclavable Red, 36" x 48," BDP PN 21827
- Biohazard Bags, Autoclavable Clear for autoclaving, 30” x 36” BDP PN 20728.
- Black Trash bags for non-biohazard waste.
- Wipes, sterile (for Sterile Core and BSC’s), BDP PN 20315
- Clean room wipes (9x9), BDP PN 21208

4.3 Cleaning

4.3.1 Cleaning Requests

4.3.1.1 Cleaning outside of the routine scheduled cleaning may be requested by BQA or by manufacturing staff due to EM results, utility service interruptions, or production campaign (between product) needs.

4.3.1.2 Requests should include the Zone(s) to be cleaned, the agent(s) to be used and the date range when cleaning should occur i.e. after 1/26/22 but before 2/2/22.

4.3.1.3 Requests may be sent via email and should include the cleaning supervisor. Note: Some form of written request for non-routine cleaning is required. Verbal requests are not sufficient.

4.3.2 Preparation of Disinfectant Solution

4.3.2.1 Apply as indicated in **Attachment 1**.

4.3.2.2 Use Decon-Spore at sporicidal concentration for the first cleaning of each month on the floors. **NOTE**: This requirement is not applicable to first floor areas with the exception of [redacted] due to the buildup of peroxyacetic acid vapors. The use of Decon-Spore does not occur for all other first floor areas unless specifically indicated by the Quality Engineering and Validation Manager with detailed instructions for application.

4.3.2.3 Using equipment dedicated for the areas defined by this SOP, fill the rinse and solution buckets with the proper amount of WFI.

4.3.2.4 Using a volumetric container capable of measuring milliliters and wearing applicable PPE, 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.

NOTE: The mixing of Decon-Spore should be performed by carefully dispensing one 13oz bottle of Decon-Spore into a bucket/sprayer already filled with 2 gallons of WFI.

SimpleMix® solutions do not require measuring of components or the need for WFI. The operator simply pushes the plunger on the container completely down and swirls to allow the concentrate to mix with the water and the solution is then ready to use.

4.3.2.5 Document the disinfectant preparation on the Room Cleaning Log. See section 6.0.

4.3.2.6 Disinfectant solutions will be prepared and disposed of daily.

4.3.3 Cleaning Techniques

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

4.3.3.1 Double bucket wringer system for mopping ceilings, walls, and floors.

- Submerge the mop in the first solution bucket.
- Partially wring solution from the mop leaving the mop wet.
- The wringer is placed over the second bucket.

4.3.3.2 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.

4.3.3.3 Mop loading: Between rinses the mop must maintain the same leading-edge during application and remain wetted enough to ensure cleaning solution is applied on the entire surface the mop contacts. If at any point the mop is no longer sufficiently wetted, it must be rewetted following the procedure for the mopping system. Mop strokes should overlap, by approximately 20% or 1/5th of the mop head length to ensure complete coverage.

4.3.3.4 **Ceilings**: Spray or mop the ceilings, stroking from wall to wall in one direction.

NOTE: **DO NOT** mop, wipe, or spray HEPA filters. The protective grills of the HEPA filters may be wiped with a cleanroom wipe dampened with 70% IPA if needed. Do not wet the HEPA filter.

4.3.3.5 **Walls:** Spray or Mop from the top down. 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 or Steri-Perox 6%.

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

4.3.3.6 **Curtain Panels:** Clean curtain panels by spraying with Steri-Perox 6%. Use wipes as needed to assist with removal of any residue. Do not use other products on curtains as they will both dry and yellow the curtains.

4.3.3.7 **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 are to be done from the furthest point of the room and work toward the exit or toward the janitor's closet. 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.

NOTE: Change mops heads and cleaning solution after completing each zone or if either becomes heavily soiled.

4.3.3.8 After mopping is complete, discard the used mop head and empty the buckets. Clean the buckets after use by removing debris using 70% IPA and wipes. Equipment may also be rinsed with WFI if needed.

4.3.3.9 Sprayers: Pump sprayers may be used for solution application on walls, floors, and ceilings provided no open work is in progress. Stay clear of moisture sensitive equipment or cover with plastic any that may receive overspray before spraying. Use as fine a mist as possible and do not apply excess such that material runs down the wall.

4.3.3.10 **Non-cleanroom Spaces:** Zones 19, 20, and 22 differ from the facilities otherwise cleaned per this SOP. These are uncontrolled, non-classified GMP spaces and should be cleaned as indicated. Zone 19 requires a once monthly sweeping or vacuuming of the floors. Zone 20 requires a once monthly mopping of the floors using Decon-Cycle. The cold room of Zone 20 [redacted] may require washing of the ceilings and walls upon request in response to environmental monitoring and may utilize Decon-Spore. Zone 22 is done 2x per week with Decon-Cycle and may utilize Decon-Spore for a special request. Additional cleaning beyond these requirements may be requested.

4.3.4 Cleaning Sequence

4.3.4.1 Perform the following tasks, as required by the frequency chart (**Attachment 2**) and following the cleaning sequence for each area in **Attachment 3**. The cleaning will be performed using cleaning techniques described in Section 4.3.3.

4.3.4.2 Waste removal

NOTE: The [redacted] has multiple waste streams. Refer to ***SOP 19407 – Flow Personnel, Materials, Equipment, and Waste in the CGMP Areas*** [redacted] for a detailed waste flow procedure.

4.3.4.2.1 BDP staff will seal and remove sharps and broken glass containers as needed and deposit them in the appropriate waste bin.

4.3.4.2.2 Trash receptacles will be emptied as needed.

4.3.4.2.3 All biohazardous trash as marked by a red trash receptacle and biohazard bag will be placed in the biohazardous waste collection bin near the autoclaves [redacted] to be autoclaved by manufacturing staff.

4.3.4.2.4 All non-biohazardous waste as marked by a black bag or by a bag indicating that it has been autoclaved will be placed in the non-biohazardous waste collection bin [redacted] for waste generated on A2. Non-biohazardous waste generated on the first floor will exit out [redacted] and into the common corridor.

4.3.4.2.5 The contents of the non-biohazardous waste bin should be taken to the dumpsters daily during non-production hours by the cleaning staff.

4.3.4.3 Cleaning Sequence and Locations

4.3.4.3.1 In general, clean ceilings, then walls and work surfaces, then clean the floors from the innermost area toward the exit or the location where the solution is discarded, and supplies are stored.

4.3.4.3.2 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 recommended 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.

4.3.4.3.3 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 the work surfaces are also included.

4.3.4.3.4 Drains – Disinfect open drains by pouring a minimum of one (1) liter of disinfectant solution down the drain. Ensure the solution encounters the entire drain area. If necessary, use a spraying apparatus to accomplish this.

4.3.4.3.5 Document the tasks and rooms disinfected on the appropriate room cleaning log form after cleaning is completed for each zone.

4.3.4.4 Wash Down/Complete Cleaning

4.3.4.4.1 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 to ensure even and total distribution.

4.3.4.4.2 Clean work surfaces using Steri-Perox 6%, BDP PN 10665 or batched disinfectant dispensed either by sprayer or wetted clean room wipes. Avoid getting liquid into sensitive equipment.

4.3.4.4.3 The floors would then be done with a separate mop head and a bucket system. Staff may then move to the next sequential room in the cleaning zone, 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.

4.3.4.5 Routine Floor and Surface Cleaning

4.3.3.5.1 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 Steri-Perox 6%, BDP PN 10665. Select surfaces are to be cleaned prior to mopping floors.

4.3.3.5.2 When floor cleaning is selected on the form as part of scheduled cleaning not involving the cleaning of walls, it is implied that all select surfaces are also included.

4.3.3.5.3 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 Steri-Perox 6% 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 that <u>are not</u> touch free (i.e., wave to open is excluded).
- **Tables –** Staff should not move equipment to perform this activity. This <u>does not</u> 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 –** This includes the 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.

4.3.5 Frequency of Cleaning (**Attachment 2** – Frequency Chart)

<u>NOTE</u>: **Attachment 2** lists the minimum cleanings required, but frequency is not limited to these minimums.

4.3.5.1 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***.***

4.3.5.2 Campaign and production schedules will initiate special request cleanings.

4.3.5.3 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 for the specified zones:

- Fill Area: Zone 2
  - The product is removed from the area.
  - Product contact equipment must be cleaned and product changeover completed.
  - Waste removed.
- All other areas
  - The product removed from the area.
  - Product contact equipment must be cleaned.
  - Waste removed.

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

4.3.4.3.2 For Fill/Finish area (Zone 2) a single wash-down must have occurred **within the previous 30 days** to obtain clearance for a new campaign.

4.3.5.4 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. **This procedure is not applicable to first floor B1 areas (see note in section 4.3.1.2).**

- 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.
  Note: Decon-Clean may be used to remove residue during shutdown periods prior to return to service disinfectant cleaning. Decon-Clean is a non-sterile preparation and cannot be used without being followed by a disinfectant cleaning as directed by the Quality Engineer and Validation Manager.

4.3.6 In-Process Cleaning

4.3.6.1 When work is in progress, seek authorization from the Area Supervisor before cleaning. Should work in progress prevent the cleaning staff from performing scheduled cleaning, arrangements may be made with the cleaning staff to make up deferred cleanings. However, the frequency in **Attachment 2** must be adhered to. It will become the responsibility of production personnel for the affected area to perform the necessary cleaning if arrangements with cleaning staff cannot be made to comply with the frequency.

4.3.7 Post-Renovation, Facility Shutdown/Failure Cleaning

4.3.7.1 For product changeover/area clearance see Section 4.3.4.3.

4.3.7.2 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.

4.3.7.3 BQA Quality Engineering and Validation Manager or designee will indicate any zones 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.)

4.3.7.4 For CNC and ISO 8 classified areas.

- The first required cleaning will include detailed wiping and a wash down of floors with Decon-Spore at sporicidal concentration. **(See section 4.3.1.2).**
- The second required cleaning will be a wash down of the ceiling, walls, and floors with Decon-Cycle).

4.3.7.5 For ISO 7 and ISO 5 classified areas.

- The first required cleaning will include detailed wiping and a wash down of walls, and floors with Decon-Spore at sporicidal concentration. **(See section 4.3.1.2).**
- The second required cleaning will be a complete wash down of ceilings, walls, and floors with Decon-Cycle).

4.3.7.6 When a Single Wash Down is required per return to service guidance, use ’Decon-Cycle.

4.3.7.7 Cleaning status will be communicated by the BQA 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 each cleaning form as they are formulated or as soon after formulation as possible. See section 6.0 for forms.

4.4.3 Record all cleaning and disinfection activities on the appropriate zone cleaning log form as each area is completed or as soon after completion as possible. 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. 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, tables, carts, shelves, chairs, stools, gowning benches, trash cans, and other objects not classified as equipment or supplies.

5.8 **Select Surfaces –** Surfaces that receive frequent contact and include door activation hardware, tables, chairs and phones.

5.9 **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

6.1	**SOP 19406**	*Gowning Requirements for Personnel and Visitors:* [redacted] *Manufacturing and Support Areas*
6.2	**SOP 19407**	*Flow of Personnel, Materials, Equipment, and Waste in the CGMP Areas* [redacted]
6.3	**SOP 19409**	*Cleaning and Disinfection of the* [redacted] *Virus Production Facility*
6.4	**SOP 19504**	*Cleaning and Disinfection of the* [redacted] *Cell Therapy Areas*
6.5	**SOP 21409**	*Good Documentation Practices*
6.6	**SOP 21526**	*Engineering Event Management*
6.7	**SOP 21554**	*GMP Area Status Management*
6.8	**Form 19408-01**	Room Cleaning Log Zone 2, Filling Suite
6.9	**Form 19408-02**	Room Cleaning Log Zone 3, Component Prep
6.10	**Form 19408-03**	Room Cleaning Log Zone 4, Purification Pre-Virus Removal
6.11	**Form 19408-04**	Room Cleaning Log Zone 5, Purification Post-Virus Removal
6.12	**Form 19408-05**	Room Cleaning Log Zone 6, Bacterial Purification
6.13	**Form 19408-06**	Room Cleaning Log Zone 7, Upstream Cell Culture
6.14	**Form 19408-07**	Room Cleaning Log Zone 8, Upstream Fermentation
6.15	**Form 19408-08**	Room Cleaning Log Zone 9, Entry Corridor and Return Corridor
6.16	**Form 19408-09**	Room Cleaning Log Zone 10, Buffer Prep and Storage
6.17	**Form 19408-10**	Room Cleaning Log Zone 11, Entry Corridor and Storage
6.18	**Form 19408-11**	Room Cleaning Log Zone 12, Labeling and Clean Staging
6.19	**Form 19408-12**	Room Cleaning Log Zone 13, Second Floor CNC Areas
6.20	**Form 19408-13**	Room Cleaning Log Zone 14, First Floor CNC Areas
6.21	**Form 19408-14**	Room Cleaning Log Zone 15, Material Weigh Out and Sampling
6.22	**Form 19408-15**	Room Cleaning Log Zone 16, First Floor Sampling
6.23	**Form 19408-16**	Room Cleaning Log Zone 17, Cell Banking
6.24	**Form 19408-17**	Room Cleaning Log Zone 18, Media Prep
6.25	**Form 19408-18**	Room Cleaning Log Zone 19, Warehouse
6.26	**Form 19408-19**	Room Cleaning Log Zone 20, MMIC Freezer Farm and Coldroom
6.27	**Form 19408-20**	Room Cleaning Log Zone 22, Locker Rooms

7.0 Attachments

7.1	**Attachment 1**	Preparation and Application Timing of Disinfectant Solution for Room Cleaning / Disinfection
7.2	**Attachment 2**	Frequency Chart
7.3	**Attachment 3**	Cleaning Zone Reference Sheet
7.4	**Attachment 4**	Sterilizing Agent Caution Sign

8.0 Change Summary

[redacted]

Attachment 1

Preparation and Application Timing of Disinfectant Solution for Room Cleaning/Disinfection

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

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

APPLICATION CHART	
Disinfectant	**Month**
Decon-Spore®	At the start of the month on the floors . Special Request, post-renovation, post-facility shutdown, failure cleaning.
WFI	Used for residue removal. Used monthly prior to 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 (Including Select Surfaces)**	**Open Drains**
2	Filling Suite	Campaign[1]	Campaign[1]	Campaign[1]	1 x week	N/A
3	Component Prep	Quarterly	Quarterly	N/A	2 x week	1 x week
4	Purification Pre-Virus Removal	Campaign[1]	Campaign[1]	N/A	2 x week	1 x week
5	Purification Post-Virus Removal	Campaign[1]	Campaign[1]	N/A	2 x week	1 x week
6	Bacterial Purification	Campaign[1]	Campaign[1]	N/A	2 x week	1 x week
7	Upstream Cell Culture	Campaign[1]	Campaign[1]	N/A	2 x week	1 x week
8	Upstream Fermentation	Campaign[1]	Campaign[1]	N/A	2 x week	1 x week
9	Clean Corridor and Return Corridor	2 Times Per Year	2 Times Per Year	N/A	3 x week	N/A
10	Clean Corridor, Storage, and Buffer Prep	2 Times Per Year	2 Times Per Year	N/A	2 x week	N/A

[1] At the end of each campaign for product clearance. Also 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 2 (continued)
Frequency Chart

Zone	Zone Name	Ceilings	Walls	Curtains	Floors (Including Select Surfaces)	Open Drains
11	Entry Corridor and Storage	2 Times Per Year	2 Times Per Year	N/A	3 x week (2 x month Decon-Spore)	N/A
12	Labeling, and Clean Staging	2 Times Per Year	2 Times Per Year	N/A	2 x week	N/A
13	CNC Areas	Annually	Annually	N/A	1 x week	1 x week
14	First Floor CNC Areas	By Request	By Request	N/A	1 x week	N/A
15	First Floor Weighout and Staging	By Request	By Request	N/A	1 x week	N/A
16	First Floor Sampling	2 Times Per Year	2 Times Per Year	N/A	1 x week	N/A
17	Cell Banking	Campaign[1]	Campaign[1]	N/A	1 x week	N/A
18	Media Prep	Campaign[1]	Campaign[1]	N/A	2 x week	N/A
19	Warehouse	N/A	N/A	N/A	1 x month	N/A
20	MMIC Freezer Farm and Coldroom	N/A	N/A	N/A	1 x month	N/A
22	Locker Rooms	N/A	N/A	N/A	2 x week	N/A

[1] At the end of each campaign for product clearance. Also 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

Cleaning Zones – The facility is divided into "zones" to reduce cross contamination. 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. Zones should be cleaned with the designated equipment sets (the exception to this would be the first of two cleanings following a shutdown/out of service period).

Zone 1 – VPF

See **SOP 19409, *Cleaning and Disinfection of the*** [redacted] ***Virus Production Facility***

Zone 2 – Filling Suite

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Large filling (clean within curtain ISO5 first)	100/1000	5/7	1
	Small filling	100/1000	5/7	2
	Clean staging	10K	7	3
	Fill Corridor	10K	7	4
	MAL/PAL	10K	7	5
	Pass through	NA	NA	6
	Formulation	10K	7	7
	MAL/PAL	10K	7	8
	MAL/PAL	100K	8	9
	MAL/PAL	100K	8	10

Zone 3 – Component Prep

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	PAL	10K	7	1
	MAL	10K	7	2
	Component Prep	10K	7	3
	Exit MAL/PAL	100K	8	4

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 4 – Purification Pre-Virus Removal

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Purification	10K	7	1
[redacted]	Entry PAL	10K	7	2
[redacted]	Entry MAL	10K	7	3
[redacted]	Exit PAL/MAL	100K	8	4

Zone 5 – Purification Post-Virus Removal

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Purification	10K	7	1
[redacted]	Entry PAL	10K	7	2
[redacted]	Entry MAL	10K	7	3
[redacted]	Exit PAL/MAL	100K	8	4

Zone 6 – Bacterial Purification

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Purification	10K	7	1
[redacted]	Entry PAL	10K	7	2
[redacted]	Entry MAL	10K	7	3
[redacted]	Exit PAL/MAL	100K	8	4

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 7 – Upstream Cell Culture

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Inoculum	10K	7	1
	Cell Culture	100K	8	2
	Entry PAL	100K	8	3
	Entry MAL	100K	8	4
	Cold Room	NA	NA	5
	Exit PAL/MAL	100K	8	6

Zone 8 – Upstream Fermentation

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Inoculum	10K	7	1
	Fermentation	100K	8	2
	Entry PAL	100K	8	3
	Entry MAL	100K	8	4
	Cold Room	NA	NA	5
	Exit PAL/MAL	100K	8	6

Zone 9 – Clean Corridor and Return Corridor

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	PAL	100K	8	1
	Clean Corridor	100K	8	2
	Tool	100K	8	3
	PAL/MAL	100K	8	4
	PAL/MAL	100K	8	5
	Storage	100K	8	6
	CL	100K	8	7
	Return Corridor	100K	8	8
	PAL/MAL	100K	8	9

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 10 – Buffer Prep and Storage

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Buffer Prep	100K	8	1
	PAL/MAL	100K	8	2
	Column Packing	100K	8	3
	Buffer Storage	100K	8	4
	Cold Room	NA	NA	5
	Freezer	100K	8	6
	Clean Storage	100K	8	7
	Clean Corridor Closet	100K	8	8

Zone 11 – Entry Corridor and Storage

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	PAL/MAL	100K	8	1
	Clean Corridor	100K	8	2
	PAL/MAL	100K	8	3
	Men's Gowning	100K	8	4
	Women's Gowning	100K	8	5
	Cold Room	100K	NA	6
	Corridor	100K	8	7
	CGMP Supply	100K	8	8
	MAL	100K	8	9
	Corridor	100K	8	8
	Corridor	100K	8	5
	CGMP Supply	100K	8	9
	MAL	100K	8	10
(clean side only)	Elevator Lobby	NA	CNC	11

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 12 – Labeling and Clean Staging

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Vial Pass-Through	NA	NA	1
	Sample Pass-Through	NA	NA	2
	Labeling	100K	8	3
	Inspection	100K	8	4
	MAL	100K	8	6
	Clean Staging	100K	8	7

Zone 13 – Second Floor CNC Areas

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Wash	NA	CNC	1
[redacted]	Pre-wash	NA	CNC	2
[redacted]	CIP	NA	CNC	3
[redacted]	GMP Equipment Storage	NA	CNC	4
[redacted]	Degown PAL/MAL	NA	CNC	5
[redacted]	Corridor	NA	CNC	6
[redacted]	Corridor	NA	CNC	7

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 14 – First Floor CNC Areas

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Elevator Lobby ("dirty" side only)	NA	CNC	1
	GMP Elevator	NA	NA	2
	Dispensing Booth Non-Growth	NA	LAF (used as CNC)	3
	Non-Growth	100K	8 (used as CNC)	4
	Raw Material Staging	100K	8 (used as CNC)	5
	Entry PAL/MAL	100K	8 (used as CNC)	6
	PAL/MAL	NA	CNC	7
	Staging	100K	8 (used as CNC)	8
	MAL/Degown	100K	8 (used as CNC)	9
	Hall	NA	CNC	10
	PAL/MAL	NA	CNC	11
	A/L	NA	CNC	12

Zone 15 – Material Weigh Out and Sampling

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Dispensing Booth Growth	NA	LAF	1
[redacted]	Growth	100K	8	2

Zone 16 – First floor sampling

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Sample	100K	8	1
	Gown/Degown	100K	8	2
	A/L	NA	CNC	3

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Zone 17 – Cell Banking

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Cell Bank	10K	7	1
[redacted]	PAL/MAL	100K	8	2

Zone 18 – Media Prep

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Media Prep	100K	8	1
[redacted]	PAL/MAL	100K	8	2

Zone 19 – Warehouse**

Equipment Set: NA Equipment Storage: NA Water source: NA
Routine cleaning uses brooms or vacuum maintained by cleaning staff.

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Released	NA	NA	1
[redacted]	Quarantine	NA	NA	2

Zone 20 – MMIC Freezer Farm and Coldroom

Equipment Storage: [redacted] Water source: [redacted]

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Freezer Farm	NA	NA	NA
[redacted]	Coldroom	NA	NA	NA

Zone 21 – Cell Therapy Areas

See **SOP 19504, *Cleaning and Disinfection of the*** [redacted] ***Cell Therapy Areas***

Zone 22 – Locker Rooms

Equipment Set: Generic/non-Cleanroom Equipment Storage: [redacted] Water source: [redacted] (Tap)

Room #	Room Name	Classification	ISO Classification	Cleaning Order
[redacted]	Shower	NA	NA	NA
[redacted]	Women's toilet	NA	NA	NA
[redacted]	Women's locker	NA	NA	NA
[redacted]	Shower	NA	NA	NA
[redacted]	Men's toilet	NA	NA	NA
[redacted]	Men's locker	NA	NA	NA

Decon-Spore use by request only.

Attachment 3 (Continued)
Cleaning Zone Reference Sheet

Equipment Summary

Zone	Description	Equipment Storage	Primary Water Source
2	Filling Suite	[redacted]	
3	Component Prep		
4	Purification Pre-Virus Removal		
5	Purification Post-Virus Removal		
6	Bacterial Purification		
7	Upstream Cell Culture		
8	Upstream Fermentation		
9	Clean Corridor, Media Prep, and Return Corridor		
10	Clean Corridor, Storage, and Buffer Prep		
11	Entry Corridor and Storage		
12	Labeling and Clean Staging		
13	Second Floor CNC Areas		
14	First Floor CNC Areas		
15	Material Weigh Out and Staging		
16	First Floor Sampling		
17	Cell Banking		
18	Media Prep		
19**	Warehouse		
20	MMIC Freezer Farm and Coldroom		
22	Locker Rooms		

** Mopping is not part of routine scheduled cleaning. If mopping is requested standard mops and buckets and tap water may be used.

Attachment 4
Sterilizing Agent Caution Sign