Title: Policies for Operation, Cleaning, and Routine Maintenance of Controlled Temperature Equipment

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1.0 Purpose

This procedure describes Biopharmaceutical Development Program (BOP) policies for operating and maintaining controlled-temperature equipment.

2.0 Scope

This procedure applies to BOP personnel who are responsible for any part of the operation, cleaning, and/or routine maintenance of controlled-temperature equipment. This Standard Operating Procedure (SOP) applies to free-standing and walk-in refrigerators, freezers, and controlled room temperature units. This SOP does not specify procedures for calibration or unplanned maintenance required on these units. Refer to ***SOP 21508 • Equipment Calibration***

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Program for those procedures. Refer to ***SOP 19102 - Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers, and Centrifuges*** for operation and maintenance requirements for incubators.

3.0 Authority and Responsibility

3.1 The Program and Technical Director, Biopharmaceutical Development Program, has the authority to define this procedure.

3.2 The Area Supervisor is responsible for training laboratory personnel in this procedure and for documenting this training.

3.3 Laboratory personnel are responsible for following this procedure.

3.4 Biopharmaceutical Quality Assurance (BQA) is responsible for quality oversight ofthis procedure.

4.0 Materials

4.1 Approved disinfectants:

4.1.1 70% Isopropyl Alcohol (Decon-Ahol), BDP PN 30129.

4.1.2 Dispatch, BDP PN 10167.

4.1.3 Cavicide, BDP PN 10168.

5.0 General Policies for Controlled-Temperature Equipment

5.1 Usage guidance.

5.1.1 Use protective gloves to protect hands when handling ultra-low frozen materials.

5.1.2 Material stored in cold rooms should be kept at least 6" from the walls and floors, and 12" from the ceiling. Floor restriction does not apply to drums which are to be placed on drum dollies. In freezers and refrigerators, do not store GMP materials on the base (floor) of the unit unless this location was specifically included in validation. Only shelf racks should be used.

5.2 Operating ranges and setpoints.

5.2.1 Refer to ***SOP 21902 - Requirements for Establishing Part Numbers and Specifications for BDP Components and Materials*** for the approved storage temperature ranges for BDP components and materials. The BDP does not specifically have controlled room temperature chambers, but most GMP rooms maintain a temperature of 16 to 22°C.

5.2.2 BDP has controlled temperature equipment for the following temperatures.

Name	Temperature Range in °C
Refrigerator or Cold Room	2-8
Freezer	-10 to -30
Freezer	-20 to -40
Ultra Low Freezer	-70 to -90
Liquid Nitrogen (LN_2) Vapor Phase	≤ -130

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract [redacted].

5.2.3 For controlled-temperature equipment that is considered part of a Good Manufacturing Practices (GMP) area or that stores GMP components or materials, the setpoints are established by the validation of that unit and stored as part of the validation protocol. Validated setpoint values may be reflected in the calibration system for single point calibration of the unit and may be posted on the unit itself. Setpoint changes are managed through the engineering change system.

5.2.4 For controlled-temperature equipment that is not considered part of a GMP area and does not store GMP components or materials, the following setpoints are recommended:

- To maintain +2 to +8°C, use a setpoint of +4°C
- To maintain -10 to -30°C, use a setpoint of -20°C
- To maintain ≤ -70°C, use a setpoint of -80°C
- Performance of individual controlled-temperature storage equipment will vary and depends on variables such as load and external ambient temperature. Thus, these setpoints are recommended starting points, but should be adjusted if alarms occur routinely indicating temperatures out of range or adjusted as part of the validation or revalidation process.

  Setpoints may be changed by equipment owners, but only after verifying that the change will not compromise the calibrated range of the unit. Contact Quality Engineering for this information.

5.2.5 Operating ranges for incubators should not exceed ±2°C from setpoint for GMP cell growth operations. Alternative ranges may be acceptable for specific operations as required by the process. If a tighter process tolerance is required, contact Quality Engineering.

5.3 Alarm setpoints (Local and SCADA).

5.3.1 Low temperature alarm setpoints should be 1 to 2 degrees above the low limits of the acceptable temperature ranges specified in ***SOP 21902 - Requirements for Establishing Part Numbers and Specifications for BDP Components and Materials***. For example, if the acceptable temperature range is 2 to 8°C, an effective low alarm setpoint is 3°C. The Supervisory Control and Data Acquisition (SCADA) system also uses a LO LO alarm in addition to the LO alarm. The LO LO should be the low point of the acceptable temperature range.

NOTE: It may not be possible to set the low temperature alarm above the lower limit of the range due to normal operation of the unit. In this case, the low temperature alarm setpoint must not be less than the lower limit of the range.

5.3.2 High temperature alarm setpoints should be 1 to 2 degrees below the high limits of the acceptable temperature ranges specified in ***SOP 21902 - Requirements for Establishing Part Numbers and Specifications for BDP Components and Materials***. For example, if the acceptable temperature range is 2 to 8°C, an

effective high alarm setpoint is 7°C. **The SCADA system also uses a HI HI alarm in addition to the HI alarm. The HI HI should be the high point of the acceptable temperature range.**

NOTE: It may not be possible to set the high temperature alarm below the upper limit of the range due to normal operation of the unit. In this case, the high temperature alarm setpoint must not exceed the upper limit of the range.

5.3.3 Probes controlling alarm response, both local and through SCADA, may be placed within a tube (typically a 15 or 50 mL centrifuge tube) containing air or liquid to dampen alarm response. Placing the probe in an air-filled tube should be the first option. If the delay is insufficient, a 50/50 mix of glycol and water may be used. The liquid volume should be minimized such that the delay only prevents the triggering of an alarm during typical opening durations needed for use. Excessive liquid volumes will mask critical alarms.

5.3.4 Alarm setpoints should take into account the tightness of the control range of the unit and should not be set so as to alarm routinely. If alarms setpoints cannot fall within the guidance above without nuisance alarms, consult with Quality Engineering.

5.3.5 For controlled-temperature equipment that is considered part of a GMP area, or that stores GMP components or materials, alarm setpoints are established by the validation of that unit and stored as part of the validation protocol. Alarm setpoint changes are managed through the engineering change system.

5.3.6 For controlled-temperature equipment that is not considered part of a GMP area and does not store GMP components or materials, alarm setpoints may be adjusted by the equipment owner. Record any adjustment to setpoints in the equipment logbook.

5.4 Temperature monitoring.

5.4.1 The following table illustrates temperature monitoring requirements and suggestions for various applications of controlled-temperature equipment.

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		Controlled-Temperature Equipment Application		
		Final product storage	Part of GMP area or storage of GMP components/materials	Not part of a GMP area and does not store GMP components/materials
Temperature Monitoring Method/Device	Local alarm or external temperature controller/alarm	R	R	S
	Alarm connection to Building Alarm System (SCADA)	R	R Any exceptions evaluated on a case-by-case basis	S
	Chart recorder	S Required if no SCADA connection	S Required if no SCADA connection	S

R = Required; **S** = Suggested.

5.4.2 Temperatures for GMP units must be monitored using at least two independent methods from SCADA, Chart Recorder, or Daily Check. Acceptable combinations include:

1. SCADA & Chart Recorder
2. SCADA & Daily Check.
3. Chart Recorder & Daily Check.

5.4.3 Refer to ***SOP 21507 - Monitoring Temperatures with Chart Recorders***, for instructions on how to maintain and annotate charts.

For controlled-temperature equipment that does not have an associated chart recorder, temperature should be monitored using the calibrated digital display on the unit at least daily when the equipment is in operation, excluding weekends, holidays, and facility closures. This information is recorded in the equipment logbook or Routine Plant Duties (RPD) form.

5.5 Safety

5.5.1 Do not store dry ice or packages which contain dry ice as the refrigerant in walk-in controlled-temperature equipment. This presents an oxygen depletion risk.

6.0 Routine Maintenance for Controlled-Temperature Equipment

6.1. The following routine maintenance items should be performed by the equipment owner or designee as a part of routine use and is general for most controlled-temperature equipment.

6.1.1. Check alarm back-up battery by looking for corresponding alarm or indicator.

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6.1.2. Check the area around the condenser screen/air filter for debris or objects that might block the air flow. There should be at least six inches of unobstructed air flow around the air inlet to the condenser.

6.1.3. Check the door gasket for leaks as indicated by ice buildup at the leak. Check the gasket for cuts, cracks, and holes. If the gasket is damaged, place a trouble call or call the proper technician.

6.1.4. Check the inside of the freezer for frost buildup.

6.1.4.1. If the frost buildup is one-inch thick or greater, defrosting is required.

6.1.4.2. Relocate the contents to another comparable freezer. The freezer must have the same range and validation status and alarm connections of equal or better. Record the relocation in each equipment logbook.

6.1.4.3. Defrost per manufacturer's recommendations. Once defrosted, wipe down the inside with an approved disinfectant listed in Section 4.1. After wipe-down, allow to dry, and then restore power to the unit.

6.1.4.4. Allow the freezer to return to proper operational range before returning contents.

6.1.4.5. Record activities in the equipment log.

6.1.4.6. Note that no change to Freezerworks inventory is required provided that the move is temporary while a unit is being defrosted, repaired, or validated, the move is captured in the equipment log, and items are returned to the original shelf location. The equipment log shall list the new temporary location and freezer MEF number, the dates and times of transfer to and from (returning contents to original freezer), and a statement that the entire contents had been transferred (and any exceptions).

6.1.5. Check condenser fan motor for unusual motor noise or vibration.

6.1.6. The listed checks, themselves, do not require documentation in the logbook. The fact that there was a routine maintenance check of the equipment and the actions taken as a result of the checks should be recorded in the equipment log.

6.2. The following routine maintenance tasks should be performed by the equipment owner or designee EVERY SIX MONTHS for units not in classified areas and EVERY TWELVE MONTHS / ANNUALLY for units in clean rooms as there is less load on the filters. The procedures are general for most controlled-temperature equipment. Refer to Section 6.3 for Cold Rooms.

6.2.1. Check the air filter and condenser screen. If the filter or screen is dirty or clogged, place a trouble call or call the proper service technician.

6.2.2. Check the inside of the freezer for frost buildup. Refer to Section 6.1.4.

6.2.3. Check condenser fan motor for unusual motor noise or vibration.

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6.3. Cold Rooms will be maintained by FME following an established Preventative Maintenance schedule managed by the Maximo program.

7.0 Cleaning of Controlled-Temperature Equipment

7.1 For routine cleaning, wipe down the interior and exterior of the controlled-temperature equipment with an approved disinfectant listed in Section 4.1, as necessary.

7.2 In the event of a biological spill inside or on the exterior of one of the units, follow ***SOP 22923, Procedures for Safe Handling and Decontamination of Viruses by BDP/BPA and Related Personnel*** or ***SOP 26106 - Spill Control and Clean-up in the BDP Production Areas of the*** [redacted] to disinfect and clean the spill**.**

8.0 Documentation

8.1 Document routine monitoring, maintenance, and cleaning of controlled-temperature units on **Form 21533-01** in the equipment logbook.

8.2 **Form 21533-01** will be populated with the logbook ID, the MEF number of the equipment, the equipment name or 'Description', and the page numbers. The fields for 'Range' (should match those established in Section 5.2 or a range approved by BQA), 'Building', and 'Room' may be customized at the time of request so that these fields are hard coded in the issued logbook.

8.3 Routine usage, the placement and withdrawal of materials, does not require a logbook entry in most cases. An entry should be made under the following conditions:

8.3.1 Placement or removal of high value materials or intermediate or final product.

8.3.2 When routine usage such as placing a large thermal mass results in a system alarm. The log entry can then be used to determine the reason for related SCADA alarms.

8.4 Facilities, Maintenance, and Engineering (FME) personnel will document maintenance in the equipment logbook for all GMP equipment and non-GMP equipment where a log was issued.

8.5 See ***SOP 21531 - Equipment Logs***, for instructions on keeping equipment logbooks.

9.0 References and Related Documents

9.1 **SOP 19102** *Routine Use and Disinfection of Biological Safety Cabinets, Incubators, Shakers, and Centrifuges.*

9.2 **SOP 21507** *Monitoring Temperatures with Chart Recorders.*

9.3 **SOP 21508** *Equipment Calibration Program.*

9.4 **SOP 21531** *Equipment Logs.*

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9.5 **SOP 21902** *Requirements for Establishing Part Numbers and Specifications for BDP Components and Materials*

9.6 **SOP 22923** *Procedures for Safe Handling and Decontamination of Viruses by BDP/BPA and Related Personnel.*

9.7 **SOP 26106** *Spill Control and Clean-up in the BDP Production Areas of the* [redacted].

10.0 Attachments

10.1 Attachment 1 Form 21533-01, Controlled-Temperature Equipment Logbook Template.

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Attachment 1

Controlled-Temperature Equipment Logbook Template

FNLCR, BDP
Form No.: 21533-01
SOP No.: 21533
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Biopharmaceutical Development Program
Equipment Logbook **EL-XXXX-XXXX,** MEF #XX.XX
Equipment Name or Description and Temperature Range °C_____
Bldg Room XXXXX

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Date	Time	Temperature in °C	Activity/Comments	Initials

Reviewed by:_____Date:_____

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