IOPQ PROTOCOL APPROVAL

The signatures listed below indicate approval of this protocol and its attachments and certify that it may be executed. This approval is the responsibility of the listed functional areas of the National Cancer Institute at Frederick (NCI-Frederick).

Author	_____	Date	_____
Equipment Owner	_____	Date	_____
Director, Quality Control	_____	Date	_____
BQA Management	_____	Date	_____
NCI/BRB	_____	Date	_____

TABLE OF CONTENTS

1.0 General

1.1 Purpose

The purpose of this Installation/Operation/Performance Qualification protocol is to demonstrate that the modified HVAC system (BDP #nnnn) servicing Rooms nn, n, and nn of Building nnn (reference SAIC-Frederick, Inc./FME Work Order # nnnnnn, April 2005) was installed, and performs in accordance with design specifications, manufacturers' recommendations, Biopharmaceutical Development Program (BDP) specifications, and current Good Manufacturing Practices (CGMP). The performance qualification portion of the protocol will consist environmental monitoring by Quality Control for 20 working days.

1.2 Authority and Responsibilities

The Equipment Owner and Biopharmaceutical Quality Assurance (BQA) have the authority to establish and delegate this procedure.

A. BDP Engineering is responsible for:

- System installation, startup, pre-qualification inspection and ongoing operation.
- Maintaining the system as required for dependable operation.
- Providing and reviewing written SOPs and manufacturers' manuals.
- Identifying and tagging equipment and components.
- Development/implementation of a preventive maintenance program.

B. Equipment Owner is responsible for:

- Reviewing and approving the protocol and final reports.
- Reviewing and interpreting data for accuracy and completeness.

C. Quality Control is responsible for:

- Performing environmental monitoring tests and collection of samples.
- Timely reporting of results and trending data.

D. Biopharmaceutical Quality Assurance is responsible for:

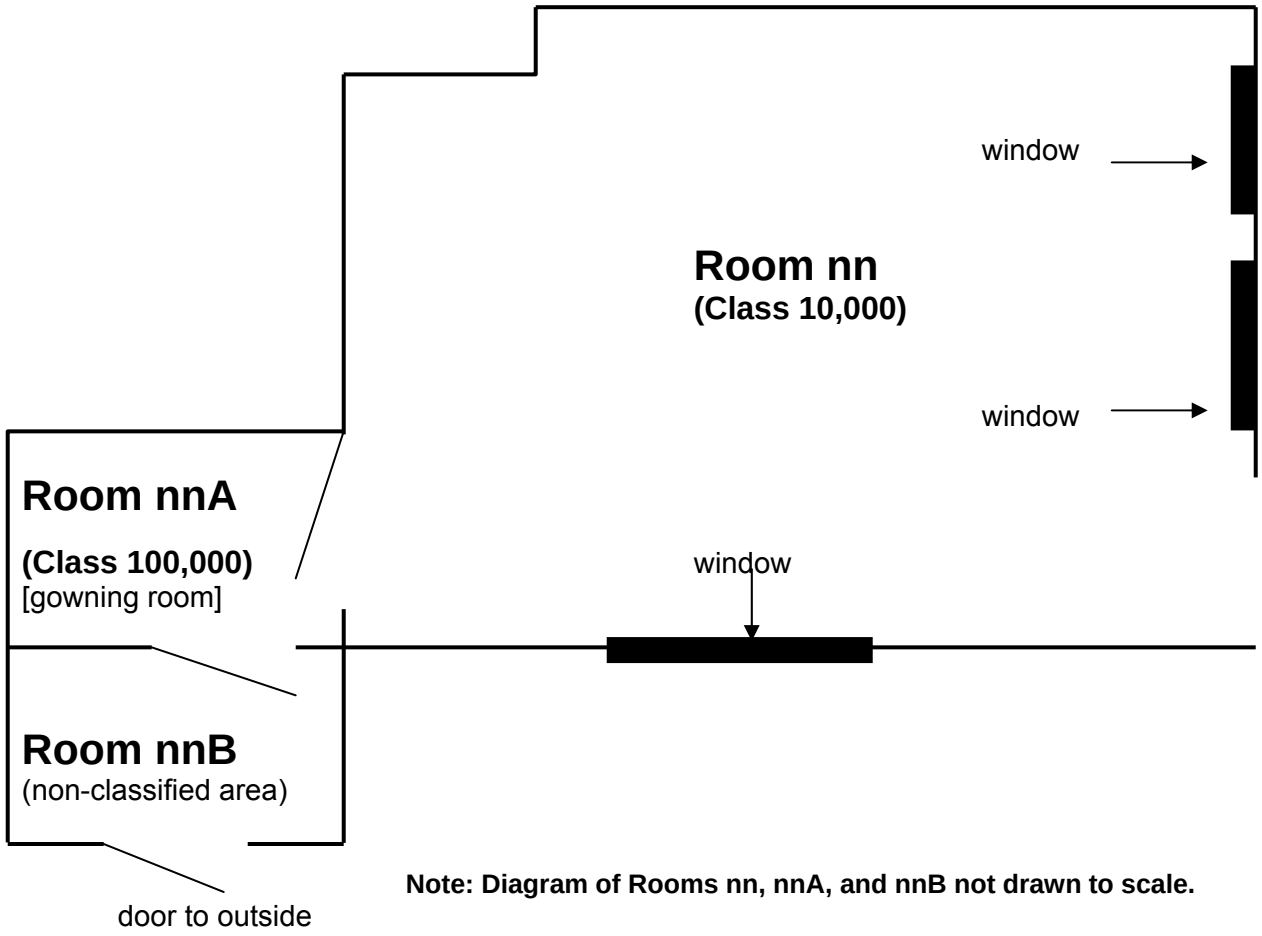
- Reviewing and approving qualification protocols.
- Reviewing and interpreting data for accuracy, completeness, and CGMP compliance.
- Reviewing and signing each attachment.
- Participating in the investigation of deviations and ensuring that corrective actions have been implemented.

2.0 System Description

The HVAC (Heating, Ventilation, and Air Conditioning) system functions to condition the air (heat/cool, humidify), pressurize spaces (containment and product protection), and provide a mechanism for cleaning the air entering and exiting the facility (filtration).

The central component of the HVAC system is a Carrier constant volume air-handling unit (nnnaaaannn) located in the north mechanical space of Building nnn. The sealed supply ducts feature durable, hard, non-particle generating, cleanable surfaces with access duct openings. The exterior of the ducts is covered with fiberglass insulation. Supply air to the duct is filtered through a 30% pre-filter and an 85% final filter installed at the discharge plenum. 99.997% ULPA filters are installed in Room nn. Preheat (steam), cooling (chilled water), and reheat coils in the AHU provide discharge air temperature control. The exhaust side of the system includes an American Air Filter exhaust fan (nnnaaaannn) with final filters prior to exhausting from the building.

As shown in the diagram below, Room nn will have an air particulate cleanliness level of ISO Class 7 (Class 10,000), Room nnA will have an air particulate cleanliness level of ISO Class 8 (Class 100,000) and Room nnB be non-classified. Classified areas will be pressurized for containment and airlocks exist where excessive pressure gradients occur.



Note: Diagram of Rooms nn, nnA, and nnB not drawn to scale.

3.0 General Protocol Execution

3.1 Safety

Follow safety precautions as recommended by the manufacturer and in the Environmental, Health, and Safety Compliance Program manual of NCI-Frederick.

3.2 Training

Personnel who engage in qualification activities will provide documentation that they are sufficiently trained, or have sufficient experience, to assure proper equipment usage and data collection.

3.3 Documentation

Document analyses, verifications, data and comments on the attachments provided as a part of this protocol in accordance with applicable Standard Operating Procedures (SOPs), current Good Manufacturing Practices (CGMP) guidelines, and Biopharmaceutical Development Program (BDP) practices.

Record all data in blue/black ink. Entries on attachments will be signed and dated by the person executing the protocol at the time of completion of the activity. BQA will review, sign, and date each completed attachment.

If entries are not required or information is not applicable complete the entry with the symbol N/A (Not Applicable). Do not leave blank entries on the attachments.

4.0 Procedures

4.1 General Protocol Functions

This section includes a summary of attachments and their acceptance criteria that apply for the entire IOQ Execution.

Attachment	Title	Acceptance Criteria
4.1 A	Signature Log	Individuals executing this protocol must provide their signature and initials.
4.1 B	Standard Operating Procedures	SOPs for CGMP procedures and the use and maintenance of the equipment are available.
4.1 C	Training Verification	Provide documentation that individuals executing this protocol are adequately trained.
4.1 D	Validation Test Equipment Identification and Calibration	Test equipment used for the validation is in current calibration.

4.2 Installation Qualification Test Functions

This portion of the protocol provides documented evidence that system components conform to design and user specifications and requirements. The table below offers a summary of the attachments to be completed for the Installation Qualification study. Specific instructions and requirements are provided on each attachment.

Attachment	Title	Acceptance Criteria
4.2 A	Purchase Order Inspection	Purchase Order for system is available.
4.2 B	Manufacturers' Documentation	Manufacturer's manual(s) is available and stored in the MEF room.
4.2 C	Drawing Verification	The engineering drawings accurately represent the installed HVAC system and its components.
4.2 D	Attributes	Manufacturer-related information on the HVAC system and its components is documented.
4.2 E	Utilities Verification	Actual utilities agree with specified ranges.
4.2 F	System Component Identification and Calibration	All components of the HVAC system are tagged and current in calibration.
4.2 G	IQ Completion and Acceptance	BQA must sign to authorize execution of the OQ.

4.3 Operation Qualification Test Functions

This portion of the qualification study consists of tests designed to prove that the HVAC performs as intended. The table below offers a summary of attachments to be completed for the qualification study. Specific instructions and requirements are provided on each attachment

Attachment	Title	Acceptance Criteria
4.3 A	Door Interlock Test	Door interlock system meets design and user specifications.
4.3 B	Air Volume and Change Rates	Air changes meet design and user specifications.
4.3 C	Directional Airflow	Directional airflow meets design and user specifications.
4.3 D	Differential Pressure	Differential pressure meets design and user specifications.
4.3 E	Temperature Study	Temperature is maintained within ± 5 °F of the setpoint temperature.
4.3 F	Relative Humidity Study	Humidity is maintained within 15 - 75% Relative Humidity.
4.3 G	Environmental Monitoring	
4.3 G-1	Classified Area Diagram	Diagram indicates sites where environmental monitoring samples are taken.
4.3 G-2	Activity Log	Activity in the classified areas is documented.
4.3 G-3	Non-Viables	Non-viable contaminants are maintained at sufficiently low levels to minimize risk of product contamination.
4.3 G-4	Airborne-Viables	Airborne viable contaminants are maintained at sufficiently low levels to minimize risk of product contamination.
4.3 G-5	Surface-Viables	Surface viable contaminants are maintained at sufficiently low levels to minimize risk of product contamination.

5.0 Protocol Deviations

Deviations from the protocol procedure or acceptance criteria must be documented on Attachment 5 and approved by the Equipment Owner and Biopharmaceutical Quality Assurance (BQA). Any deviation between installed equipment, utilities, controls, or identification labels and the specification or engineering drawings determined during execution of this protocol must also be documented.

If a deviation affects the remainder of the protocol, notify the Equipment Owner and Quality Assurance immediately. If a deviation affects a testing procedure, the Equipment Owner and Quality Assurance must approve the change in rationale prior to continuing.

6.0 Qualification Completion

Verify that test functions required by this protocol are completed, reconciled and supporting material attached to this protocol. Verify that deviations are documented, approved and attached to this protocol. The Equipment Owner, BQA, and NCI/BRB must review and approve the completed protocol before further validation protocols on the HVAC system are executed. The IOPQ is considered complete when signatures are entered in the Completion section on Attachment 6 of this document.

ATTACHMENT 4.1A

SIGNATURE LOG

(Copy as needed)

Page ____ of ____

Test Description: Individuals involved in executing this protocol shall complete the signature log below.

Acceptance Criteria: Individuals executing this protocol must provide the information below.

Print Name	Signature	Approved Initials	Date

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.1 B

STANDARD OPERATING PROCEDURES

Test Description: Document SOPs (or related SOPs) for CGMP procedures, operation of the HVAC system, and environmental monitoring testing procedures.

Acceptance Criteria: SOPs (or related SOPs) for CGMP procedures, operation of the HVAC system, and environmental monitoring testing are current and in an "Approved" status, except those which are indicated as being in "Draft" status.

SOP #	Title	Revision Level	Effective Date	Initial/Date
21600	Training and Qualification of Personnel in a CGMP Environment			
21409	Good Documentation Practices			
00110	Master Equipment Files			
17117	Gowning of Personnel in Building nnn, Rooms nn, nnA, and nnB (draft)			
17118	Flow of Personnel and Materials in Building nnn, Rooms nn, nnA, and nnB (draft)			
22309	Operation of the MAS-100 Air Sampler			
22929	Operation of the Met One Model 3315 Laser Particle Counter			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.1 C

TRAINING VERIFICATION

(Copy as needed)

Test Description: Provide documentation that individuals executing this protocol are adequately trained the use and maintenance of the equipment/system and in CGMP procedures in the procedures listed below.

Acceptance Criteria: Individuals executing this protocol are trained on the procedures listed. Include a copy of training records behind this attachment.

Procedure	Name of Trainee (print)	Date Training Completed	Initial/Date
SOP 21600: Training and Qualification of Personnel in a CGMP Environment			
SOP 21409: Good Documentation Practices			
SOP 00110: Master Equipment Files			
SOP 17117 (draft): Gowning of Personnel in Building nnn, Rooms nn, nnA, and nnB			
SOP 17118 (draft): Flow of Personnel and Materials in Building nnn, Rooms nn, nnA, and nnB			
SOP 22309: Operation of the MAS-100 Air Sampler			
SOP 22929: Operation of the MET-One Model 3315 Laser Particle Counter			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.1 C: _____

ATTACHMENT 4.1 D

VALIDATION TEST EQUIPMENT IDENTIFICATION AND CALIBRATION

(Copy as needed)

Page ___ of ___

Test Description: List validation equipment used for execution of this protocol below. Indicate the BDP number, manufacturer, model number, and calibration dates. Include copies of the calibration records behind this attachment.

Acceptance Criteria: Equipment used for validation must be in current calibration.

Instrument Description	BDP #	Manufacturer	Model #	Date Calibrated		Initial/ Date
				Done	Due	

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.1 D: _____

ATTACHMENT 4.2 A

PURCHASE ORDER INSPECTION

(Copy as needed)

Page ____ of ____

Test Description: Verify that the packaged equipment item(s) is supplied/installed. Packaged unit equipment items are those pieces of equipment formally designated with equipment numbers on the engineering drawings (if applicable).

Acceptance Criteria: Equipment specified on the respective purchase order(s) agrees with the installed packaged unit equipment. Attach a copy of the PO behind this attachment (if applicable).

PO #	Item(s) Description on PO	Installed item(s) agrees with PO?	Initial/Date

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.1 E: _____

ATTACHMENT 4.2 B

MANUFACTURER'S DOCUMENTATION

(Copy as needed)

Test Description: Record the title, revision number/date, and location of any manufacturers' manuals/documents in the table below.

Acceptance Criteria: The manufacturer's manual/document (if available) is documented and verified to exist in the Master Equipment File (MEF) room as the final storage location.

Title/Description	Revision/Date	In MEF Room?	Initial/Date

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.2 C

DRAWING VERIFICATION

(Copy as needed)

Page ____ of ____

Test Description: Locate the "as-built" drawings and compare them to the installed item(s) for accuracy. List and inspect specific design elements such as duct size, materials of construction, instrumentation types and locations, damper locations, piping and utilities supplied, etc. Document the results in the table below for each drawing.

Acceptance Criteria: Design elements and equipment systems are installed in accordance with the drawings.

Drawing #	
Title	
Date	
Revision	
Filename	
Originator	

Design Element	Installed in accordance with drawing? (Yes/No) (If No, reference Deviation)	Initial/Date

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.2 D

ATTRIBUTES

Test Description: Record the "As Found" attributes of the installed system.

Acceptance Criteria: Attributes of the installed system have been recorded.

Equipment	As Found	Initial/Date
Air Handling Unit		
Manufacturer		
Model Number		
Serial Number		
Supply Air Fan		
Manufacturer		
Model Number		
Serial Number		
Horsepower		
Motor (Supply Fan)		
Manufacturer		
Model Number		
Serial Number		
Horsepower		
Pre-filter		
Manufacturer		
Model Number		
Efficiency (30% ASHRAE)		
Size / Type / Quantity		
Final Filter		
Manufacturer		
Model Number		
Efficiency (85% ASHRAE)		
Size / Type / Quantity		

Equipment	As Found	Initial/Date
Terminal ULPA Filter		
Manufacturer		
Model Number		
Efficiency (>99.997%)		
Size / Type / Quantity		
Reheat Coil		
Manufacturer		
Model Number		
Serial Number		
Capacity (lb/hr)		
Material of Construction		
Room Exhaust Blower		
Manufacturer		
Model Number		
Serial Number		
Horsepower		
Motor Frame Designation		
Hood Exhaust Blower		
Manufacturer		
Model Number		
Serial Number		
Horsepower		
Motor Frame Designation		

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.2 E

UTILITIES VERIFICATION

Test Description: Confirm that the utilities listed below, and necessary for operation, have been installed in conformance with design and/or manufacturers' specifications and verify that electrical safety disconnects and circuit breakers are identified.

Acceptance Criteria: The actual utilities supplied to the components listed below meet the acceptable ranges and the electrical panel and circuit breaker are correctly identified.

Air Handling Unit (434SAHU001)						
System Component	**Utility**	**Specified**	**Acceptable Range**	**Actual**	**Pass/Fail**	**Initial/Date**
Chilled Water Cooling Coil	Temperature	42 °F	42 – 55°F			
Plant Steam Pre-heat Coil	Pressure	15 psig	12–20 psig			
Instrument Air	Pressure	20 psig	3–25 psig			
Fan Motor	Electrical Panel (location / label)	Record as found	Record as found			
	Circuit Breaker (breaker # / capacity)	Record as found	Record as found			
	Safety Disconnect (location / label)	Record as found	Record as found			
	Voltage	480 V	480 V ± 10%			
	Amperage	5.9 A	≤ 5.9 A			
	Phase	3	3			

Room Exhaust Blower (434HBLR001)						
System Component	**Utility**	**Specified**	**Acceptable Range**	**Actual**	**Pass/Fail**	**Initial/Date**
Fan Motor	Electrical Panel (location / label)	Record as found	Record as found			
	Circuit Breaker (breaker # / capacity)	Record as found	Record as found			
	Safety Disconnect (location / label)	Record as found	Record as found			
	Voltage	480 V	480 V ± 10%			
	Amperage	3.3 A	≤ 3.3 A			
	Phase	3	3			

BSC Exhaust Blower (434HBLR002)						
System Component	**Utility**	**Specified**	**Acceptable Range**	**Actual**	**Pass/Fail**	**Initial/Date**
Fan Motor	Electrical Panel (location / label)	Record as found	Record as found			
	Circuit Breaker (breaker # / capacity)	Record as found	Record as found			
	Safety Disconnect (location / label)	Record as found	Record as found			
	Voltage	480 V	480 V ± 10%			
	Amperage	3.3 A	≤ 3.3 A			
	Phase	3	3			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.2 F

SYSTEM COMPONENTS IDENTIFICATION AND CALIBRATION

Test Description: Verify that system components are identified and calibrated.

Acceptance Criteria: Components are identified and calibration information for the components is recorded. Attach calibration records behind this attachment.

Component Identification	Component tag # 0434X-HVAC-X-	Date Calibrated		Initial/Date
		Done	Due	
Air Handling Unit (434SAHU001)				
Outside air temperature gauge	HVTI-0001-X			
Supply air temperature gauge	HVTI-0002-X			
Chilled H_20, low limit, preheat gauge	HVTI-0003-X			
Discharge air temperature gauge	HVTI-0004-X			
Discharge relative humidity gauge	HVHP-0001-X			
Exhaust pre-filter magnehelic gauge	HVDP-0001-X			
Exhaust post-filter magnehelic gauge	HVDP-0002-X			
Magnehelic Gauge				
Room nn to nnA	BDP #80740			
Room nnA to nnB	BDP #80770			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.2 F: _____

ATTACHMENT 4.2 G

IQ COMPLETION AND ACCEPTANCE

Test Description: The Installation Qualification of the system meets the criteria outlined in Section 4.2 and expected results have been found, or deviations addressed except for the items listed below. BQA signature below allows the execution of the OQ to proceed.

Acceptance Criteria: BQA or designee must sign below to authorize execution of the OQ.

Item #	Description	Action

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.3 A

DOOR INTERLOCK AND EMERGENCY DISCONNECT SYSTEM

Test Description:

1) **Door Interlock Test**. The doors to Rooms nn, nnA, and nnB are unlocked when the doors are closed. However, when one door is opened, the other two doors will lock. Evaluate the door interlock system from each direction by opening one door and checking if the other two doors remain closed. Begin each step of the test with all doors closed.

2) **Emergency Disconnect Test**. Evaluate the emergency disconnect system by pressing the emergency disconnect button in one room and checking if all the doors will open. Begin each step of the test with all doors closed.

Acceptance Criteria:

1) **Door Interlock Test**. When one door is opened, the other two doors will be locked.

2) **Emergency Disconnect Test**. When the emergency disconnect button is pushed, all three doors will unlock and can be opened simultaneously.

Test Description	Expected Results	Actual Results	Pass/Fail	Initial/Date
DOOR INTERLOCK TEST				
Open door to Room nnB from outside.	Door to Room nnA from Room nnB and door to Room nn from Room nnA are locked.			
Open door to Room nnB from inside Room nnA.	Door to Room nn from Room nnA and door to outside from Room nnB are locked.			
Open door to Room nn from inside Room nnA.	Door to Room nnB from inside Room nnA and door to outside from Room nnB are locked.			
Open door to Room nnA from inside Room nn.	Door to Room nnB from Room nnA and door to outside from Room nnB are locked.			
Open door to Room nnB from Room nnA.	Door to Room nnA from Room nn and door to outside from Room nnB are locked.			

Test Description	Expected Results	Actual Results	Pass/Fail	Initial/Date
Open door to outside from Room nnB.	Door to Room nnA from Room nn and door to Room nnB from Room nnA are locked.			
EMERGENCY DISCONNECT TEST				
Press the emergency disconnect button in Room nnB.	Doors to Room nn, Room nnA, and Room nnB will be unlocked and can be opened simultaneously.			
Press the emergency disconnect button in Room nnA.	Doors to Room nn, Room nnA, and Room nnB will be unlocked and can be opened simultaneously.			
Press the emergency disconnect button in Room nn.	Doors to Room nn, Room nnA, and Room nnB will be unlocked and can be opened simultaneously.			
POWER FAILURE TEST				
Remove power to the door interlock system by flipping the circuit breaker (Panel A, breaker #18).	Doors to Room nn, Room nnA, and Room nnB will be unlocked and can be opened simultaneously.			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.3 B

AIR VOLUME AND CHANGE RATES

Test Description: Record the air volumes for all supply inlets and calculate the air change rate (ACH). Compare the result with the specified air change rate.

Acceptance Criteria: Air changes per hour are greater than or equal to the specified value.

A. Supply Air Volume (CFM)	**Room 12A**	**Room 12**
B. Total Supply Air Volume Per Minute (CFM) = $(A_1 + A_2 + A_3 + ... + A_n)$		
C. Room Volume (ft^3)		
D. Actual Air Change Rate (60*(B/C))		
E. Required Air Change Rate (ACH)	≥ 20	≥ 40
Pass/Fail (is D ≥ E?)		
Initial/Date		

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.3 B: _____

ATTACHMENT 4.3 C

DIRECTIONAL AIRFLOW

Test Procedure: Verify directional airflow using smoke visualization with the doors closed and with the doors open (1-2"). Record results in the tables below.

Acceptance Criteria: Direction of airflow is from the "positive" area to the "negative" area

Directional Air Flow with doors closed				
Positive Area	**Negative Area**	**Directional Air Flow**	**Pass/Fail**	**Initial/Date**
Vestibule nnA	Room nn			
Vestibule nnA	Vestibule nnB			

Directional Air Flow with doors open				
Positive Area	**Negative Area**	**Directional Air Flow**	**Pass/Fail**	**Initial/Date**
Vestibule nnA	Room nn			
Vestibule nnA	Vestibule nnB			

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.3 D

DIFFERENTIAL PRESSURE

Test Procedure: Record the differential pressure gauge reading for twenty (20) working days and compare the values to the design specifications indicated.

Acceptance Criteria: Differential pressure is greater than or equal to the design specifications. Include summary graphs behind this attachment.

Room nnA

Day #	Date	ΔP (inches H_20)		Pass/Fail	Initial/Date
		Specification	Differential Pressure		
Day 1					
Day 2					
Day 3					
Day 4					
Day 5					
Day 6					
Day 7					
Day 8					
Day 9					
Day 10					
Day 11					
Day 12					
Day 13					
Day 14					
Day 15					
Day 16					
Day 17					
Day 18					
Day 19					
Day 20					

Room nn

Day #	Date	ΔP (inches H_20)		Pass/Fail	Initial/Date
		Specification	Differential Pressure		
Day 1					
Day 2					
Day 3					
Day 4					
Day 5					
Day 6					
Day 7					
Day 8					
Day 9					
Day 10					
Day 11					
Day 12					
Day 13					
Day 14					
Day 15					
Day 16					
Day 17					
Day 18					
Day 19					
Day 20					

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.3 D: _____

ATTACHMENT 4.3 E

TEMPERATURE STUDY

Test Procedure: Record the daily maximum and minimum temperature in each classified area for 20 working days during Environmental Monitoring.

Acceptance Criteria: Each classified area maintains temperature within ± 5ºF of the setpoint.

Room nnA

Day #	Date	Temperature (°F)			Pass/Fail	Initial/Date
		Setpoint	Maximum	Minimum		
Day 1						
Day 2						
Day 3						
Day 4						
Day 5						
Day 6						
Day 7						
Day 8						
Day 9						
Day 10						
Day 11						
Day 12						
Day 13						
Day 14						
Day 15						
Day 16						
Day 17						
Day 18						
Day 19						
Day 20						

Room nn

Day #	Date	Temperature (^{o}F)			Pass/Fail	Initial/Date
		Setpoint	Maximum	Minimum		
Day 1						
Day 2						
Day 3						
Day 4						
Day 5						
Day 6						
Day 7						
Day 8						
Day 9						
Day 10						
Day 11						
Day 12						
Day 13						
Day 14						
Day 15						
Day 16						
Day 17						
Day 18						
Day 19						
Day 20						

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.3 E: _____

ATTACHMENT 4.3 F

RELATIVE HUMIDITY STUDY

Test Procedure: Obtain Relative Humidity readings for twenty (20) working days from the Met One particle counter during Environmental Monitoring. Record the daily minimum and maximum Relative Humidity. Include Met One particle counter data behind this Attachment.

Acceptance Criteria: Each classified area maintains 15% to 75% Relative Humidity (RH).

Room nnA

Day #	Date	Relative Humidity (%RH)		Pass/Fail	Initial/Date
		Maximum	Minimum		
Day 1					
Day 2					
Day 3					
Day 4					
Day 5					
Day 6					
Day 7					
Day 8					
Day 9					
Day 10					
Day 11					
Day 12					
Day 13					
Day 14					
Day 15					
Day 16					
Day 17					
Day 18					
Day 19					
Day 20					

Room nn

Day #	Date	Relative Humidity (%RH)		Pass/Fail	Initial/Date
		Maximum	Minimum		
Day 1					
Day 2					
Day 3					
Day 4					
Day 5					
Day 6					
Day 7					
Day 8					
Day 9					
Day 10					
Day 11					
Day 12					
Day 13					
Day 14					
Day 15					
Day 16					
Day 17					
Day 18					
Day 19					
Day 20					

Comments: _____

_____

_____

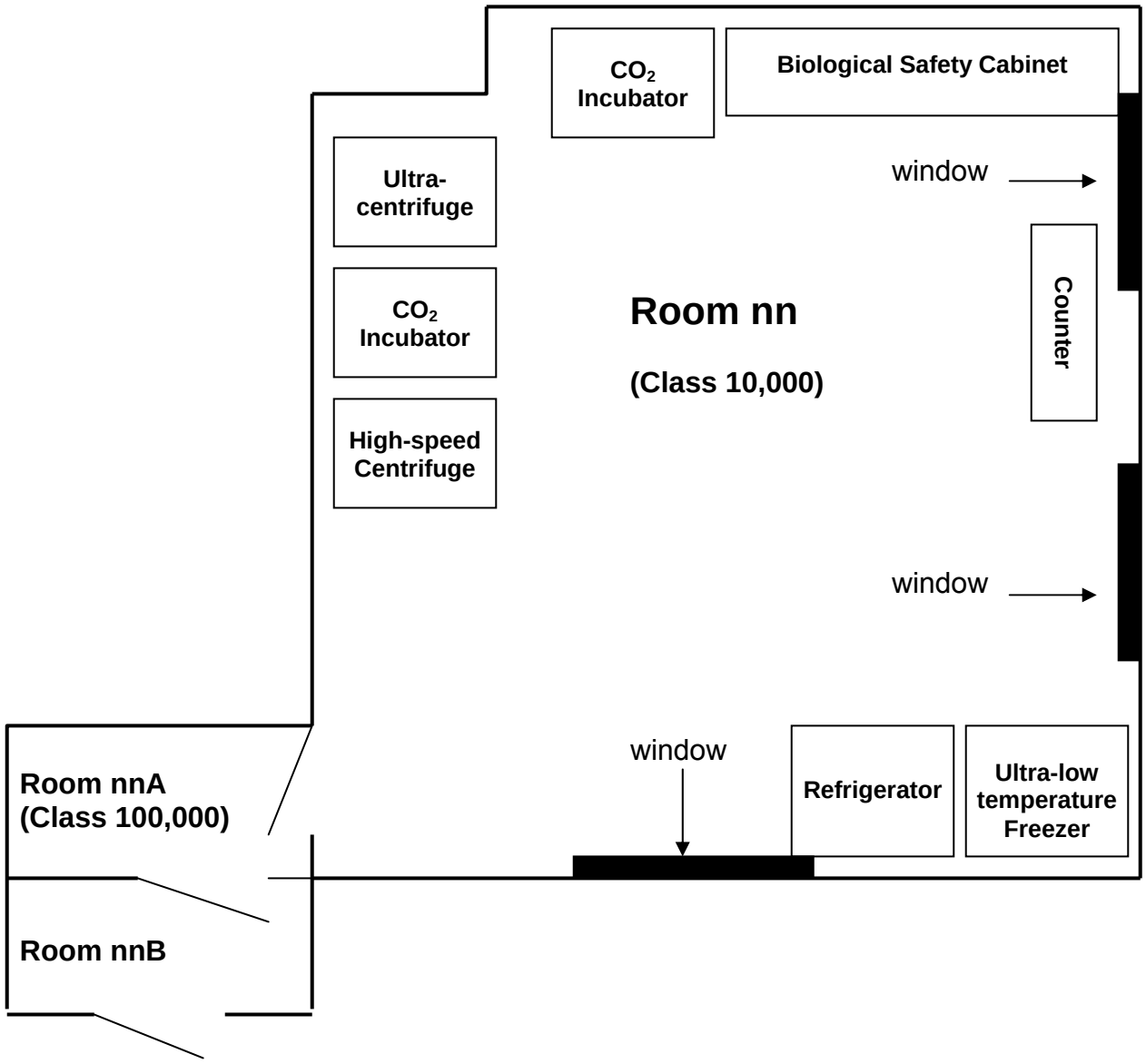
BQA Reviewed/Accepted: _____ **Date:** _____

Number of pages accompanying Attachment 4.3 F: _____

ATTACHMENT 4.3 G-1

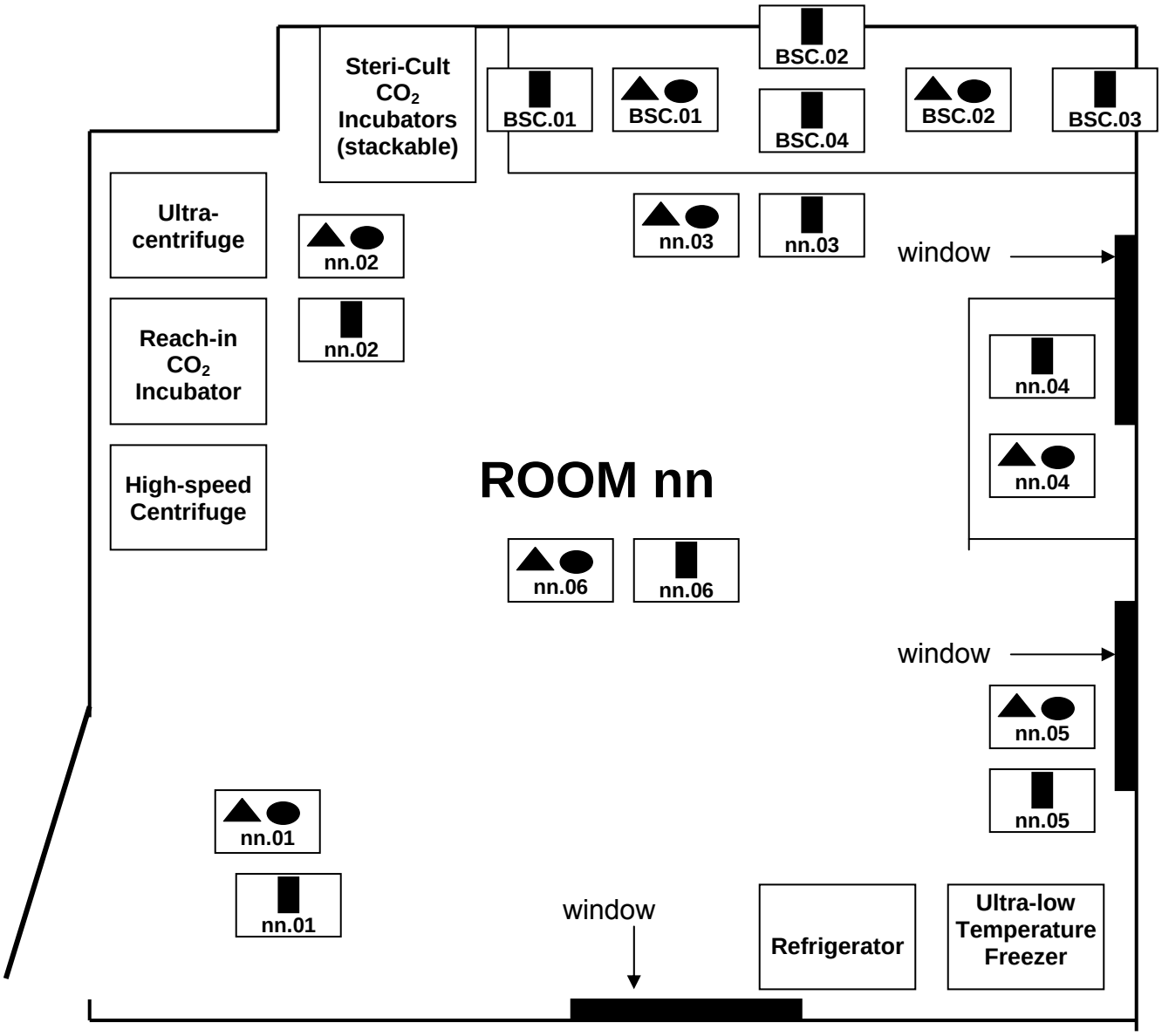
DIAGRAMS

ROOM nn, ROOM nnA, and ROOM nnB



Note: Diagram of Rooms nn, nnA, and nnB not drawn to scale.

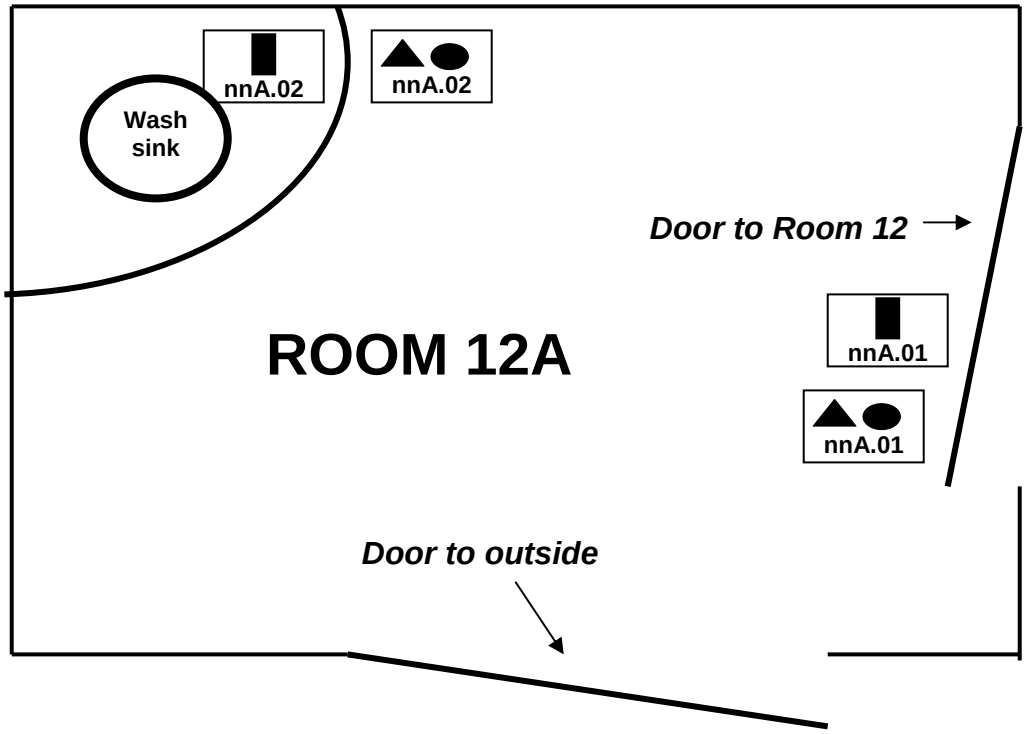
Room nn Environmental Monitoring Sites



Note: Diagram of Room nn not drawn to scale.

Environmental Monitoring	Symbol	Sampling Point	Location
Non-Viables	▲	nn.01	Near door
		nn.02	Near Reach-in CO_2 incubator
		nn.03	Near BSC
		nn.04	Top of counter
		nn.05	Near refrigerator and freezer
		nn.06	Floor (center of room)
		BSC.01	Left side bottom of BSC
		BSC.02	Right side bottom of BSC
Airborne Viables	●	nn.01	Near door
		nn.02	Near Reach-in CO_2 incubator
		nn.03	Near BSC
		nn.04	Top of counter
		nn.05	Near refrigerator and freezer
		nn.06	Floor (center of room)
		BSC.01	Left side bottom of BSC
		BSC.02	Right side bottom of BSC
Surface Viables	■	nn.01	Floor (by door)
		nn.02	Wall (above ultra-centrifuge)
		nn.03	Floor (by BSC)
		nn.04	Top of counter
		nn.05	Wall (under window)
		nn.06	Floor (center of room)
		BSC.01	Left wall of BSC
		BSC.02	Back wall of BSC
		BSC.03	Right wall of BSC
		BSC.04	Bottom center of BSC

Room nnA Environmental Monitoring Sites



Note: Diagram of Room nnA not drawn to scale.

Environmental Monitoring	Symbol	Sampling Point	Location
Non-Viables	▲	nnA.01	Door (entry to Room nn)
		nnA.02	Counter (near sink)
Airborne Viables	●	nnA.01	Door (entry to Room nn)
		nnA.02	Counter (near sink)
Surface Viables	■	nnA.01	Door (entry to Room nn)
		nnA.02	Wall (above sink)

ATTACHMENT 4.3 G-2

CLASSIFIED AREA ACTIVITY LOG

(Copy as needed)

Page ____ of ____

List all activities (including cleaning, maintenance, and operational activities) that occur in each classified area during Environmental Monitoring. Time can be entered as a range. The number of individuals in each area should also be listed. Post a copy of this form at the entry to each area.

Room nnA

Date	Time In	Time Out	# people	Description of Activity	Initial/Date

Comments: _____

_____

_____

BQA Reviewed/Accepted By: _____ **Date:** _____

ATTACHMENT 4.3 G-2

CLASSIFIED AREA ACTIVITY LOG

(Copy as needed)

Page ____ of ____

List all activities (including cleaning, maintenance, and operational activities) that occur in each classified area during Environmental Monitoring. Time can be entered as a range. The number of individuals in each area should also be listed. Post a copy of this form at the entry to each area.

Room nn

Date	Time In	Time Out	# people	Description of Activity	Initial/Date

Comments: _____

_____

_____

BQA Reviewed/Accepted By: _____ **Date:** _____

ATTACHMENT 4.3 G-3

NON-VIABLE ENVIRONMENTAL MONITORING

Test Description:

Each classified area will be tested for non-viable particulate contamination for 20 working days [5 days static monitoring and 15 days dynamic monitoring] at sample point locations denoted by a circle (●) on the floor plan provided in Attachment 4.3 G-1 (Diagram of Classified Areas). Environmental monitoring data collected is subject to the acceptance criteria listed below for demonstration of acceptable HVAC system operation and environmental control.

During testing, classified area doors will be kept closed. All operations of the particle counter will be in accordance with **SOP 22929, Operation of the Met One Model 3315 Laser Particle Counter**. Program the particle counter to perform three (3) cycles per day at each location. Place the particle counter at the first sample location in the classified area and begin counting. When all locations have been sampled, print the results from the particle counter. Calculate the average and Upper Confidence Limit (UCL) of the cycles after sampling (calculations are based on ISO 14644-1). The calculations will be reviewed for accuracy by the Quality Control (QC) Supervisor, or designee. Include copies of the printouts from the particle counter behind this Attachment.

Upper Confidence Limit (UCL) Factor for 95% Upper Confidence Limit

# of locations, N	2	3	4	5	6	7	8	9
95% of UCL Factor	6.31	2.92	2.35	2.13	2.02	1.94	1.90	1.86

Acceptance Criteria:

The 95% Upper Confidence Limit (UCL) is less than 100/ft^3 for particles ≥ 0.5 µm for ISO Class 5 (equivalent to Class 100) areas, 10,000 particles/ft^3 for particles ≥ 0.5 µm for ISO Class 7 (equivalent to Class 10,000) areas, and 100,000 particles/ft^3 for particles ≥ 0.5 µm for ISO Class 8 areas (equivalent to Class 100,000).

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO Class 8 (Class 100,000)	≤ 100,000 particles/ft^3
Room nn	ISO Class 7 (Class 10,000)	≤ 10,000 particles/ft^3
Biological Safety Cabinet (BSC)	ISO Class 5 (Class 100)	≤ 100 particles/ft^3

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO Class 8 (Class 100,000)	≤ 100,000 particles/ft^3

	Day #	Date	95% UCL	Pass/Fail	Initial/Date
Static	Day 1				
	Day 2				
	Day 3				
	Day 4				
	Day 5				
Dynamic	Day 6				
	Day 7				
	Day 8				
	Day 9				
	Day 10				
	Day 11				
	Day 12				
	Day 13				
	Day 14				
	Day 15				
	Day 16				
	Day 17				
	Day 18				
	Day 19				
	Day 20				

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
Room nn	ISO Class 7 (Class 10,000)	≤ 10,000 particles/ft^3

	Day #	Date	95% UCL	Pass/Fail	Initial/Date
Static	Day 1				
	Day 2				
	Day 3				
	Day 4				
	Day 5				
Dynamic	Day 6				
	Day 7				
	Day 8				
	Day 9				
	Day 10				
	Day 11				
	Day 12				
	Day 13				
	Day 14				
	Day 15				
	Day 16				
	Day 17				
	Day 18				
	Day 19				
	Day 20				

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
BSC	ISO Class 5 (Class 100)	≤ 100 particles/ft^3

	Day #	Date	95% UCL	Pass/Fail	Initial/Date
Static	Day 1				
	Day 2				
	Day 3				
	Day 4				
	Day 5				
Dynamic	Day 6				
	Day 7				
	Day 8				
	Day 9				
	Day 10				
	Day 11				
	Day 12				
	Day 13				
	Day 14				
	Day 15				
	Day 16				
	Day 17				
	Day 18				
	Day 19				
	Day 20				

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.3 G-4

AIRBORNE-VIABLE ENVIRONMENTAL MONITORING

Test Description:

Each classified area will be tested for viable particulate contamination for 20 working days [5 days static monitoring and 15 days dynamic monitoring] at sample point locations designated by a triangle (▼) on the floor plans provided in Attachment 4.3 G-1 (Diagram of Classified Areas). The first. Environmental monitoring data collected is subject to the acceptance criteria listed below for demonstration of acceptable HVAC system operation and environmental control.

During testing, all doors in the classified area will be closed. All operations of the air sampler will be in accordance with **SOP 22309, Operation of the MAS-100 Air Sampler.** Program the air sampler to perform one test cycle at each location. Record the results for each location in the table below.

Acceptance Criteria:

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO Class 8 (Class 100,000)	≤ 100 CFU/m^3
Room nn	ISO Class 7 (Class 10,000)	≤ 20 CFU/m^3
Biological Safety Cabinet (BSC)	ISO Class 5 (Class 100)	≤ 3 CFU/m^3

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO Class 8 (Class 100,000)	≤ 100 CFU/m^3

	Day #	Date	12A.01	12A.02	Pass/Fail	Initial/Date
Static	Day 1					
	Day 2					
	Day 3					
	Day 4					
	Day 5					
Dynamic	Day 6					
	Day 7					
	Day 8					
	Day 9					
	Day 10					
	Day 11					
	Day 12					
	Day 13					
	Day 14					
	Day 15					
	Day 16					
	Day 17					
	Day 18					
	Day 19					
	Day 20					

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
Room nn	ISO Class 7 (Class 10,000)	≤ 20 CFU/m^3

	Day #	Date	12.01	12.02	12.03	12.04	12.05	12.06	Pass/ Fail	Initial/Date
Static	Day 1									
	Day 2									
	Day 3									
	Day 4									
	Day 5									
Dynamic	Day 6									
	Day 7									
	Day 8									
	Day 9									
	Day 10									
	Day 11									
	Day 12									
	Day 13									
	Day 14									
	Day 15									
	Day 16									
	Day 17									
	Day 18									
	Day 19									
	Day 20									

Comments: _____

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BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
BSC	ISO Class 5 (Class 100)	≤ 3 CFU/m^3

	Day #	Date	BSC.01	BSC.02	Pass/Fail	Initial/Date
Static	Day 1					
	Day 2					
	Day 3					
	Day 4					
	Day 5					
Dynamic	Day 6					
	Day 7					
	Day 8					
	Day 9					
	Day 10					
	Day 11					
	Day 12					
	Day 13					
	Day 14					
	Day 15					
	Day 16					
	Day 17					
	Day 18					
	Day 19					
	Day 20					

Comments: _____

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_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 4.3 G-5

SURFACE-VIABLE ENVIRONMENTAL MONITORING

Test Description:

Each classified area will be tested for 20 working days [5 days static monitoring and 15 days dynamic monitoring] for surface viables at sample point locations denoted by a square (■) on the floor plan provided in Attachment 4.3 G-1 (Diagram of Classified Areas). Environmental Monitoring data collected is subject to the acceptance criteria listed below for demonstration of acceptable HVAC system operation and environmental control.

During testing, classified area doors will be kept closed. Record the number of colony forming units (CFU) on the RODAC plates at each location in the table below. The results will be reviewed for accuracy by the Quality Control (QC) Supervisor, or designee.

Acceptance Criteria:

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO Class 8 (Class 100,000)	≤ 100 CFU/plate
Room nn	ISO Class 7 (Class 10,000)	≤ 20 CFU/plate
Biological Safety Cabinet (BSC)	ISO Class 5 (Class 100)	≤ 3 CFU/plate

Classified Area	Classification	Acceptance Criteria
Room nnA	ISO CLASS 8 (Class 100,000)	≤ 100 CFU/plate

	Day #	Date	12A.01	12A.02	Pass/Fail	Initial/Date
Static	Day 1					
	Day 2					
	Day 3					
	Day 4					
	Day 5					
Dynamic	Day 6					
	Day 7					
	Day 8					
	Day 9					
	Day 10					
	Day 11					
	Day 12					
	Day 13					
	Day 14					
	Day 15					
	Day 16					
	Day 17					
	Day 18					
	Day 19					
	Day 20					

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
Room nn	ISO Class 7 (Class 10,000)	≤ 20 CFU/plate

	Day #	Date	12.01	12.02	12.03	12.04	12.05	12.06	Pass/ Fail	Initial/ Date
Static	Day 1									
	Day 2									
	Day 3									
	Day 4									
	Day 5									
Dynamic	Day 6									
	Day 7									
	Day 8									
	Day 9									
	Day 10									
	Day 11									
	Day 12									
	Day 13									
	Day 14									
	Day 15									
	Day 16									
	Day 17									
	Day 18									
	Day 19									
	Day 20									

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

Classified Area	Classification	Acceptance Criteria
BSC	ISO Class 5 (Class 100)	≤ 3 CFU/plate

	Day #	Date	BSC.01	BSC.02	BSC.03	BSC.04	Pass/Fail	Initial/Date
Static	Day 1							
	Day 2							
	Day 3							
	Day 4							
	Day 5							
Dynamic	Day 6							
	Day 7							
	Day 8							
	Day 9							
	Day 10							
	Day 11							
	Day 12							
	Day 13							
	Day 14							
	Day 15							
	Day 16							
	Day 17							
	Day 18							
	Day 19							
	Day 20							

Comments: _____

_____

_____

BQA Reviewed/Accepted: _____ **Date:** _____

ATTACHMENT 5

PROTOCOL DEVIATION RECORD
(Copy as needed)

DEVIATION #: _____

Explain the nature of non-conforming data and the acceptability or the action required to resolve the deviation. Use one form per deviation.

NATURE OF NON-CONFORMING DATA
DISPOSITION

REVIEW AND APPROVAL			
Originated By	_____	Date	_____
Equipment Owner	_____	Date	_____
BQA Management	_____	Date	_____

ATTACHMENT 6

IOPQ COMPLETION

By signing below, the following individuals acknowledge that the test functions and supporting documents, including deviations, required by this Installation/Operation/Performance Qualification protocol have been completed, reviewed, and are acceptable. Therefore, this HVAC system is approved for use.

Equipment Owner	_____	Date	_____
BQA Management	_____	Date	_____
NCI/BRB	_____	Date	_____