Validation Exercise for Facility GMP HVAC System

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***Abstract* —** *The client developed Technology Transfer Project to retrofit out of use manufacturing existing facilities and utilities to provide adequate area for the commercial manufacturing of new products. To achieve the Technology Transfer Project goals for new products manufacturing, the facilities and utilities must be designed, retrofitted, and validated successfully. The focus of this project is the design, retrofit, and validation of the Facility HVAC System (Heating, Ventilation, and Air Conditioning System) for the retrofitted manufacturing Facility. After the design and retrofit activities, the Facility HVAC System—which includes five Air Handling Units (AHUs), two Exhaust Fans (EF), and one Dust Collector (DC)—was successfully validated. This validation process includes control systems to maintain the Facility HVAC System within specifications and environmental controls. By providing this controlled Facility HVAC System, the client can perform Good Manufacturing Practices (GMP) and controlled manufacturing processes complying with the Food and Drug Administration (FDA) requirements as per 21 Code of Federal Regulations (CFR).*

Key Terms *— Air Handling Unit, Critical Process Parameter, HVAC System, Validation.*

PROBLEM STATEMENT

The client established their need to retrofit, refurbish, and validate existing facilities and utilities to provide a complete new GMP manufacturing facility. Since this area was out of service, no manufacturing or administrative activities were impacted at the time of the project. The purpose of the implementation of the project was to provide adequate facilities, needed utilities, and a continued environmental monitoring to an area that will be used for commercial manufacturing of new products in order to comply with GMP requirements. This report will consider specifically the validation of the Facility GMP HVAC System serving the retrofitted facility, including the impacted Air Handling Units, and Dust Collection System after their retrofit process. The client's Critical Process Parameters (CPPs) and Critical Quality Attributes (CQAs) were established and converted into requirements.

With the implementations of this project, the Facility GMP HVAC System can be considered validated, suitable for its intended use, and ready to be released to production. Therefore, the facilities to which this HVAC System supplies air, in combination with the facilities qualification, can be also considered GMP and an area that can be used for commercial production. This validation will represent a manufacturing improvement, since the client counts with more space to manufacture new and/or transferred products.

VALIDATION OVERVIEW

Validation has become one of the pharmaceutical industry's most recognized and discussed subjects. It is a critical success factor in product approval and ongoing commercialization [1]. Validation is the process of demonstrating by documented evidence that a system, process, equipment or facility meets a defined set of requirements and the desired level of compliance consistently. The validation process is important since it is an FDA and regulatory agencies requirement. In addition, the validation process is an essential part of the cGMPs (current Good Manufacturing Practices) and prove that critical aspects of the manufacturing processes are in control.

The term *qualification* is normally used for equipment, utilities, and systems; the term *validation* is typically used for processes. The validation process can be explained by three phases: design, qualification and continued verification.

Table 1
Three Phases of the Validation Process [2]

Phase	Description
Phase 1: Design	The manufacturing equipment, product and process are defined during this stage, based on knowledge acquired through development and scale-up activities.
Phase 2: Qualification	Equipment, facilities, utilities and process design are evaluated to determine if they are capable of reproducible commercial manufacturing.
Phase 3: Continued Verification	The ongoing assurance during manufacturing that the process remains in a state of control and the outcome is predictable.

There are four different types of validation: prospective, retrospective, concurrent and revalidation.

Table 2
Types of Validation [3]

Type	Description
Prospective	Carried out during the development stage of a product (prior to product production). Helps limit risks and errors that may occur on production scale.
Retrospective	Based on a review of historical manufacturing and testing data, and the analysis of accumulated results from past production.
Concurrent	Carried out during normal production.
Revalidation	Exploratory review of the current performance of the validation effect to confirm the validated status. Changes made are reasons to perform a revalidation.

HVAC SYSTEM

An HVAC System (Heating, Ventilation and Air Conditioning System) is used to control the environmental conditions of a space (facility). The HVAC System performs four basic functions:

- Control Airborne Particles, dust and microorganisms
- Maintain Room Pressure (delta P)
- Maintain Room Relative Humidity (% RH)
- Maintain Room Temperature

These four basic functions define the Critical Quality Attributes (CQAs) and the Critical Process Parameters (CPPs). The CQAs are the physical, chemical, biological, or microbiological properties or characteristic that should be within an appropriate limit, range, or distribution to ensure the desired product quality. The CPPs are the process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure the process's desired quality.

An HVAC System can be composed by Air Handling Units (AHUs), Exhaust Fans (EF), Dust Collectors (DC), etc. An AHU is used to regulate and circulate/move the air through the system processes to the served and controlled rooms. It takes fresh air from the outside or return air from the rooms served and filters it through 30% and 90-95% efficiency filters to collect any dust and particulates. Then the air passes through the cooling coil and reheat coils to decrease and increase the air temperature as required to achieve the desired air temperature by modulating their respective chilled water and reheat water valves and air flow. The air then is pumped by the AHU fan through the High Efficiency Particulate Air (HEPA) Filter, which has an efficiency of 99.97% supplying sterile air (free of microorganisms) to the clean rooms.

Figure 1
Air Handling Unit Example

Exhaust Fans and Dust Collectors provide additional air extraction in the GMP Facility; therefore, they are part of the air balancing of the served rooms. They are usually used in washrooms or rooms where steam and high temperatures are

registered due to the cleaning and/or manufacturing processes. These fans help to faster extract air with high temperatures within the room while the Air Handling Unit continues to supply cooled air; therefore, room temperature decreases faster to return the temperature to operational ranges. The incoming dust-laden air enters the inlet plenum, where a baffle forces large or heavy particles to drop out of the air stream and fall into the hopper. The clean air passes through the filter media from the outside to the inside of the filter cartridge and exits through the open top of each filter cartridge. The air then flows from the filters into the clean-air plenum, where it enters the dust collector's fan inlet and is exhausted to the atmosphere. The dust is captured on the outside of the filter media. Figure 2 shows an example of a centrifugal roof exhaust fan and a dust collector.

(a) **(b)**

Figure 2
(a) Centrifugal Exhaust Fan (b) Dust Collector

REGULATIONS

Validation is an integrated process in the pharmaceutical industry, as it is mandatory to comply with national and international standards of FDA and European Medicines Agency (EMA). Validation ensures that all the processes are in compliance with the established Current Good Manufacturing Practices (cGMPs) standards [4].

As per Title 21 of the Code of Federal Regulations for Food and Drugs, Part 211, Current Good Manufacturing Practice for Finished Pharmaceuticals, Subpart C, Buildings and Facilities, 211.46 Ventilation, air filtration, air heating and cooling requires the following [5]:

(a) Adequate ventilation shall be provided.

(b) Equipment for adequate control over air pressure, micro-organisms, dust, humidity, and temperature shall be provided when appropriate for the manufacture, processing, packing, or holding of a drug product.

(c) Air filtration systems, including prefilters and particulate matter air filters, shall be used when appropriate on air supplies to production areas. If air is recirculated to production areas, measures shall be taken to control recirculation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants.

(d) Air-handling systems for the manufacture, processing, and packing of penicillin shall be completely separate from those for other drug products for human use.

C&Q STRATEGY

The Commissioning and Qualification (C&Q) Strategy was used to complete this project as per clients Standard Operating Procedures (SOPs). The C&Q Strategy consider the following phases and documents:

Phase 1: Requirements Definition

- **Change Control:** Controls any addition, deletion, or modification to material, equipment, facilities, process, method, product, test method, specification, or procedures that may impact the identity, strength, safety, potency, quality, stability, purity, or validated state of products.
- **User Requirements Specification (URS):** Establishes product(s) and processes quality requirements used to define the equipment or systems fitness for use and owners/users general (non-quality) requirements based on the CQAs and CPPs. Table 3 presents all user requirements to be tested.

Table 3

HVAC System Requirements Specifications

Requirement Description	Specification	
Airborne Particles (Viable)	Alert Leve: 80 cfu/m^2	Action Level: 273 cfu/m^2
Airborne Particles (Non-Viable)	Less than 3,520,000 particles of size 0.5µm / m^3 at rest	
Room Temperature	68˚F - 77 ˚F with allowed excursions from 59 ˚F - 86 ˚F	
Room Relative Humidity	45% - 65% RH with allowed excursions from 30% - 80% RH	
Room Differential Pressure	Manufacturing Area	Negative from Manufacturing room to hallways
	Wash Rooms and Dirty Rooms	Negative from room to adjacent area/room
Air Changes Per Hour (ACPH)	No less than 10 ACPH	
Dust and Particulate Control	Use HEPA Filters (99.97% of efficiency)	

Phase 2: Specification and Design

- **Critical Aspects Risk Assessment (CARA):** The focus is to identify risks/hazards and failure mode to mitigate them by establishing control and detection mechanisms and reduce their occurrence. For this project the identified hazards are: Temperature and/or Relative Humidity Out of Specifications (OOS) due to mechanical and/or power failures. These hazards and failure modes can be controlled by installing and calibrating sensors for these parameters and by adding the equipment into the Preventive Maintenance (PM) Program. The detection mechanism can be a visible and audible alarm. Another Hazard can be the air flow in opposite direction due to mechanical and/or power failure or due to doors malfunction or inadequate sealing. Hazards and failure modes can be controlled by installing and calibrating differential pressure sensors and by controlling the Differential Pressure parameters by SOP. Detection mechanism can also be a visible and audible alarm. In addition, the last identified hazard is to have particulate in the air entering through the AHU. The control is the installation of HEPA filters and the detection is to establish this HEPA filter requirement by SOP and PM for filter Change.
- **Critical Aspects Design Review (CADR):** Captures the final risk assessment and confirms that each critical aspect is integrated in the design.
- **Project Qualification Plan (PQP):** Outlines the project overall specification, design, verification, and acceptance and release approach to be employed.
- **System Test Matrix (STM):** Lists all appropriate qualification tests to be performed; it also defines the testing methodology and acceptance criteria used for qualification testing. This document lists all the executed testing required by the STM as per client's SOPs. The focus of this project will be to demonstrate that the Critical Aspects with risks as per the CARA document were tested and that identified Control and Detection Mechanisms are sufficient to maintain the Facility GMP HVAC System validated and in control. Therefore, only the following tests were taken into consideration for this project.
  - HEPA Filter Integrity Testing
  - Preventive Maintenance Verification
  - Air Balancing
  - Airborne Particulate (Non-Viable)
  - Airborne Particles (Viable)
  - Environmental Monitoring – Dynamic Conditions
  - Room Differential Pressure Verification – Dynamic Conditions

Phase 3: Commissioning & Qualification

- **Commissioning Test Protocol:** Documented series of inspections, adjustments, and tests.
- **Installation / Operational Qualification (IOQ) Test Protocol:** Documented verification that all aspects that can affect product quality adhere to approved specifications and are correctly installed and operate as intended throughout all anticipate operating ranges.

- **Performance Qualification (PQ) Test Protocol:** Documented verification that all aspects perform as intended and consistently meet predetermined acceptance criteria under manufacturing conditions.
- **Test Protocols Summary Reports:** All testing performed during the protocol's execution are summarized. It confirms that the equipment/system can pass to the next validation step.

Phase 4: Acceptance and Release

- **PQP Summary Report:** Generated to confirm that all required test cases for each aspect have been completed as required by the PQP.
- **Change Control Implementation/Closure:** Shows successful completion of all qualification and validation activities. Indicates that the equipment/system will be considered suitable for its intended use and release to production.

IMPACTED HVAC SYSTEM

Table 4 presents an overview of the activities or modifications performed to each of the impacted system component:

Table 4
Impacted HVAC System and Its Modifications

System	Modifications
AHU-01A	• Ductwork Modifications • New Airflow • New and modified components • New stand-alone control system
AHU-01B	
AHU-02	
AHU-60	
AHU-51	
DC-33	• Mechanical Modifications • Airflow Modifications

Additional impacted components are the EF-02 and EF-03. The EF-02 is part of the AHU-02 components, and EF-03 is part of the AHU-01A components.

Since Facility GMP HVAC System CQAs and CPPs are related to the environmental conditions of the facilities served by this equipment, table 5 shows the Air Handling Units boundaries; it identifies the rooms served by each AHU.

Table 5
Air Handling Units Boundaries

Air Handling Units Distribution		
AHU	**Room #**	**Room Description**
AHU-01A	1008	Production Corridor
	1026	Compression Room
	1027	Air Lock for Room 1026
	1030	Compression Room
	1031	Air Lock for Room1030
	1034	Air Lock for Room 1035
	1035	Blending Room
	1036	Air Lock for Room1037
	1037	Blending Room
	1039	Corridor
	1040	Janitor Area
AHU-01B	1008	Production Corridor
	1009	Air Lock for Room 1010
	1010	Weighing/Dispensing Room
	1017	Office Area
	1018	Air Lock for Room 1019
	1019	Weighing/Dispensing Room
	1020	Washer Area
	1021	Bin Washer Area
	1024	Dirty Room
	1025	Clean Room
AHU-02	1023	Storage Closet
	1028	Clean Staging Room
	1029	Clean Storage Room
	1032	Washroom
	1033	Dirty Staging Room
	1041	Storage Closet
	1042	Janitor Area
AHU-060R	1004	Down Flow Booth Area
	1005	Down Flow Booth Area
	1006	Material Staging Room
AHU-51	1001	Air Lock No.11 (Material Transfer)
	1002	Gowning
	1003	De-Gowning

RESULTS

As established in the C&Q Strategy, the test cases presented in tables 6 and 7 were completed under the scope of this Design Project.

HEPA Filters Integrity Testing

- Objective: Verify integrity of HEPA Filters.
- Acceptance Criteria: HEPA filter integrity testing has been successfully completed. HEPA Filter certification is attached.
- Results: Acceptance Criteria was met with no deviations reported to AHU-01A, AHU-01B, AHU-02, AHU-60 and AHU-51. HEPA Filters Certifications for the AHUs equipment and Facilities Air Low Return Registers to the

AHU were attached to this test case execution in the IOQ Test Protocol.

Preventive Maintenance Verification

- **Objective:** Verify that preventive maintenance for the equipment of the Facility HVAC System has been included in the Plant Preventive Maintenance (PM) Program.
- **Acceptance Criteria:** The preventive maintenance for the equipment of the Facility GMP HVAC System has been included in the Plant Preventive Maintenance (PM) program. A printout of the maintenance management system has been attached.
- **Results:** Acceptance Criteria was met with no deviations reported to AHU-01A, AHU-01B, AHU-02, AHU-60, AHU-51, EF-02, EF-03 and DC-33. Print out from the Computerized Maintenance Management System (CMMS) was attached to this test case execution in the IOQ Test Protocol. A yearly HEPA Filters Certification was included to AHUs preventive maintenance job plans.

Air Balancing

- **Objective:** Verify that air adjusting and balancing for the Facility HVAC System that supplies the GMP Facility has been successfully completed.
- **Acceptance Criteria:** Calibration was completed prior to performing this test. Air Changes per Hour (ACPH) meet requirement specifications of no less than 10 ACPH. Approved Testing Adjusting and Balancing (TAB) report and evidence of calibration certificate for instruments used was attached.
- **Results:** Instruments requiring calibration were successfully calibrated to the National Institute of Standards and Technology (NIST) traceable standards. Acceptance Criteria was met with no deviations reported to AHU-01A, AHU-01B, AHU-02, AHU-60, AHU-51 and DC-33. Approved TAB report and evidence of calibration certificate of the instruments used were attached to this test case execution in the IOQ Test Protocol. Actual results are presented in table 6.

Table 6: Tab Results of ACPH

Expected Result: No less than 10 ACPH			**Pass/ Fail**
AHU	**Room No.**	**Actual Result**	
AHU-01A	1036	18.3 ACPH	PASS
	1037	26.1 ACPH	PASS
	1034	15.5 ACPH	PASS
	1035	23.6 ACPH	PASS
	1031	25.5 ACPH	PASS
	1030	24.0 ACPH	PASS
	1027	27.1 ACPH	PASS
	1026	24.5 ACPH	PASS
	1008 (South)	16.3 ACPH	PASS
	1039	28.7 ACPH	PASS
AHU-01B	1025	45.2 ACPH	PASS
	1024	20.8 ACPH	PASS
	1020	19.6 ACPH	PASS
	1008 (North)	16.3 ACPH	PASS
	1017	17.0 ACPH	PASS
	1018	18.4 ACPH	PASS
	1019	23.0 ACPH	PASS
	1009	18.9 ACPH	PASS
	1010	23.7 ACPH	PASS
AHU-02	1029	13.3 ACPH	PASS
	1028	14.4 ACPH	PASS
	1033	15.3 ACPH	PASS
	1032	12.5 ACPH	PASS
	1042	16.2 ACPH	PASS
	1041	23.8 ACPH	PASS
AHU-60	1006	13.7 ACPH	PASS
AHU-51	1001	18.5 ACPH	PASS
	1002	18.1 ACPH	PASS
	1003	30.9 ACPH	PASS

The values of the differential pressure required to achieve air flow directions are specified by Differential Pressure SOP and were verified during the Room Differential Pressure Verification – Dynamic Conditions Test Case.

Airborne Particles (Non-Viable)

- **Objective:** Verify that the GMP Facilities supplied by the Facility HVAC system meet specification requirements of Airborne Particles (Non-Viable).
- **Acceptance Criteria:** Major cleaning of the facilities was done prior to starting this test. For designated rooms in the GMP Facilities supplied by the Facility HVAC System, the airborne particulate cleanliness limits ($\geq 0.5\mu m/m^3$) are less than 3,520,000 at rest. Evidence is attached.

- **Results:** Acceptance Criteria was met with no deviations reported to all rooms served by AHU-01A, AHU-01B, AHU-02 and AHU-60. Facilities major cleaning, original Non-viable results (actual results are presented in table 7) and calibrations certificate of the instruments used were attached to this test case execution in the IOQ Test Protocol.

Table 7
Airborne Particles (Non-Viable) Results

Expected Result: (≥ 0.5µm/m³) are less than 3,520,000 at rest			
AHU	**Room No.**	**Actual Result**	**Pass/Fail**
AHU-01A	1036	11,307 particles	PASS
	1037		PASS
	1034	10,601 particles	PASS
	1035		PASS
	1031	30,035 particles	PASS
	1030		PASS
	1027	15,548 particles	PASS
	1026		PASS
	1008 (South)	18,728 particles	PASS
AHU-01B	1025	15,548 particles	PASS
	1024	28,622 particles	PASS
	1020	12,014 particles	PASS
	1008 (North)	11,307 particles	PASS
	1018	1,767 particles	PASS
	1019		PASS
	1009	17,314 particles	PASS
	1010		PASS
AHU-02	1029	22,615 particles	PASS
	1028	10,954 particles	PASS
	1032	3,887 particles	PASS
	1033	8,127 particles	PASS
AHU-60	1004	28,975 particles	PASS
	1005	22,261 particles	PASS
	1006	18,021 particles	PASS

Rooms sharing airborne particulate (Non-Viable) results mean that the test was performed with door open for sample to represent both rooms. This test does not apply to rooms not mentioned in table 6, including those served by AHU-51.

Airborne Particles (Viable)

- **Objective:** Verify that the applicable rooms served by the Facility HVAC system meet specification requirements of Airborne Particulate (Viable) as per applicable Microbiology Laboratory SOP.
- **Acceptance Criteria:** Airborne Particles (Viable) met specification of no more than 273 CFU/m^3 (Action Level) (CFU = Colony Forming Unit) at the applicable rooms served by the Facility HVAC system as per applicable Microbiology Laboratory SOP. Microbiology Laboratory Sampling Report and Calibration certificate of the instrument(s) used are attached.
- **Results:** Acceptance Criteria was met with no deviations reported to all rooms served by AHU-01A, AHU-01B, AHU-02, AHU-60 and DC-33. Copy of the Microbiology Laboratory Sampling Report for the Viable results (actual results are presented in table 8) and calibrations certificate of the instruments used were attached to this test case execution in the PQ Test Protocol.

Table 8
Airborne Particles (Viable) Results

Expected Result: Total Combined Counts Alert Level = 80 CFU/m^3 Total Combined Counts Action Level = 273 CFU/m^3			
AHU	**Room No.**	**Actual Result**	**Pass/Fail**
AHU-01A	1036	< 1 CFU/m^3	PASS
	1037		PASS
	1034	< 1 CFU/m^3	PASS
	1035		PASS
	1031	6 CFU/m^3	PASS
	1030		PASS
	1027	< 1 CFU/m^3	PASS
	1026		PASS
AHU-01B	1025	< 1 CFU/m^3	PASS
	1018	< 1 CFU/m^3	PASS
	1019		PASS
	1009	< 1 CFU/m^3	PASS
	1010		PASS
AHU-02	1029	< 1 CFU/m^3	PASS
	1028	6 CFU/m^3	PASS
AHU-60	1004	6 CFU/m^3	PASS
	1005	< 1 CFU/m^3	PASS
	1006		PASS

Rooms sharing airborne particulate (Viable) results mean that the test was performed with door open for sample to represent both rooms. This test does not apply to rooms not mentioned in table 8, including those served by AHU-51.

Environmental Monitoring – Dynamic Conditions

- **Objective:** Verify and confirm that the Facility HVAC system will maintain the temperature and relative humidity as required, as per SOP, during Dynamic Conditions (people inside the

area monitored) for a minimum of twenty-four (24) consecutive hours monitoring in the rooms served by the Facility HVAC system.

- **Acceptance Criteria:** No Mechanical Failures occurred during this 24-hour monitoring period. Temperature and Relative Humidity can be maintained in the applicable rooms served by the Facility HVAC system during Dynamic Conditions within the established ranges as per Temperature and Relative Humidity SOP. Temperature and Relative Humidity Reports and Calibration Certificate(s) for instrument(s) used are attached.
- **Results:** Acceptance Criteria was met with no deviations reported to all rooms served by AHU-01A, AHU-01B, AHU-02, AHU-60 and DC-33. Temperature and Relative Humidity Report and calibration certificates of the instruments used were attached to this test case execution in the PQ Test Protocol.

Temperature and relative humidity parameters readings were taken every 15 minutes during 24 consecutive hours. Table 9 presents the Temperature and Relative Humidity average results demonstrating that they were maintained within SOP established ranges (refer to table 10).

Table 9
Temperature and Relative Humidity Results

Expected Results: Temperature: 20-25°C (68-77°F) and Relative Humidity: 45-65%				
AHU	**Room**	**Temperature (°C)**	**Rel. Hum. (% RH)**	**Pass/Fail**
AHU-01A	1036	23.3 °C	51.2 % RH	PASS
	1037	22.5 °C	54.7 % RH	PASS
	1034	22.4 °C	55.2 % RH	PASS
	1035	22.3 °C	55.4 % RH	PASS
	1031	22.3 °C	54.8 % RH	PASS
	1030	22.0 °C	55.3 % RH	PASS
	1027	21.2 °C	55.6 % RH	PASS
	1026	21.9 °C	56.5 % RH	PASS
	1008 (South)	22.6 °C	55.8 % RH	PASS
AHU-01B	1025	21.9 °C	56.8 % RH	PASS
	1024	21.9 °C	58.1 % RH	PASS
	1020	22.8 °C	56.2 % RH	PASS
	1008 (North)	23.1 °C	55.4 % RH	PASS
	1018	22.5 °C	54.7 % RH	PASS
	1019	22.3 °C	55.4 % RH	PASS
	1009	21.3 °C	58.8 % RH	PASS
	1010	20.8 °C	60.9 % RH	PASS
AHU-02	1029	24.5 °C	50.3 % RH	PASS
	1028	24.3 °C	51.2 % RH	PASS
	1033	21.9 °C	56.7 % RH	PASS
	1032	21.9 °C	57.0 % RH	PASS
	1041	20.7 °C	62.5 % RH	PASS
AHU-60	1004	23.9 °C	47.8 % RH	PASS
	1005	23.1 °C	50.7 % RH	PASS
	1006	23.6 °C	49.5 % RH	PASS

Table 10
Temperature and Relative Humidity Parameters Ranges as per Clients SOP

TEMPERATURE				
Major Deviation (Alarm Condition)	Minor Deviation (Alarm Condition)	Operational Range	Minor Deviation (Alarm Condition)	Major Deviation (Alarm Condition)
RED	YELLOW	GREEN	YELLOW	RED
Manufacturing				
< 59°F (15°C)	< 68°F (20°C)	68-77°F (20-25°C)	> 77°F (25°C)	> 86°F (30°C)

RELATIVE HUMIDITY				
Major Deviation (Alarm Condition)	Minor Deviation (Alarm Condition)	Operational Range	Minor Deviation (Alarm Condition)	Major Deviation (Alarm Condition)
RED	YELLOW	GREEN	YELLOW	RED
Manufacturing				
< 30 %RH	< 45 %RH	45-65 %RH	> 65 %RH	> 80 %RH

- Acceptance Criteria: The applicable rooms served by the Facility HVAC system meet the Differential Pressure criteria (airflow direction pattern), as per applicable Engineering drawings and applicable SOP. Differential Pressure Report, Calibration Certificates and Pressurization Diagram/Drawing are attached.
- Results: Acceptance Criteria was met with no deviations reported to all rooms served by AHU-01A, AHU-01B, AHU-02, AHU-60, AHU-51 and DC-33. Copy of the calibration certificates of the instruments used were attached to this test case execution in the PQ Test Protocol.

Differential Pressure readings were copied from instruments display at the time of the reading; therefore, no differential pressure report was generated or attached. Table 11 presents the differential pressure results demonstrating that they were maintained within SOP established ranges (refer to table 12).

Table 11
Differential Pressure Parameters Ranges as per Client SOP

DIFFERENTIAL PRESSURE		
Rooms	Major Deviation [1] (Out of Parameters for more than 10 min)	Operational Range
	RED	GREEN
For Manufacturing Rooms	< 0.03 in WG	≥ 0.03 in WG
For Airlock No. 11, Gowning and Degowning Rooms [2]	< 0.06 in WG	≥ 0.06 in WG
Manufacturing Area Airlocks[3]	< 0.015 in WG	≥ 0.015 in WG

1 Major deviation alarm will change to an Urgent Alarm after 1 hr period.
2 Airlock No. 11, Gowning and De-Gowning areas against outside corridor.
3 Manufacturing Area Airlocks against Production Corridor (Room 1008).

Table 12

Differential Pressure Results per Room (Room Diff. Press. Verification – Dynamic Conditions)

Expected Results: As per Figure 5				
Room vs Room	**1st Shift**	**2nd Shift**	**3rd Shift**	**Pass/Fail**
1002 vs 714	0.15 in WG	0.15 in WG	0.15 in WG	PASS
1002 vs 1008	0.08 in WG	0.08 in WG	0.08 in WG	PASS
1003 vs 714	0.03 in WG	0.04 in WG	0.03 in WG	PASS
1003 vs 1008	0.12 in WG	0.13 in WG	0.12 in WG	PASS
1006 vs 1004	0.04 in WG	0.04 in WG	0.04 in WG	PASS
1006 vs 1008	0.06 in WG	0.07 in WG	0.07 in WG	PASS
1009 vs 1010	0.08 in WG	0.08 in WG	0.08 in WG	PASS
1009 vs 1008	0.05 in WG	0.06 in WG	0.05 in WG	PASS
1018 vs 1019	0.05 in WG	0.04 in WG	0.04 in WG	PASS
1018 vs 1008	0.05 in WG	0.05 in WG	0.05 in WG	PASS
1027 vs 1026	0.07 in WG	0.06 in WG	0.06 in WG	PASS
1027 vs 1008	0.06 in WG	0.05 in WG	0.05 in WG	PASS
1031 vs 1030	0.03 in WG	0.04 in WG	0.04 in WG	PASS
1031 vs 1008	0.05 in WG	0.05 in WG	0.05 in WG	PASS
1034 vs 1035	0.04 in WG	0.05 in WG	0.05 in WG	PASS
1034 vs 1008	0.07 in WG	0.05 in WG	0.05 in WG	PASS
1036 vs 1037	0.07 in WG	0.08 in WG	0.08 in WG	PASS
1036 vs 1008	0.03 in WG	0.04 in WG	0.04 in WG	PASS
1029 vs 1028	0.03 in WG	0.03 in WG	0.03 in WG	PASS
1029 vs 1008	0.05 in WG	0.05 in WG	0.05 in WG	PASS
1033 vs 1032	0.09 in WG	0.09 in WG	0.09 in WG	PASS
1033 vs 1008	0.06 in WG	0.05 in WG	0.07 in WG	PASS
1028 vs 1032	0.24 in WG	0.23 in WG	0.24 in WG	PASS
1024 vs 1020	0.03 in WG	0.04 in WG	0.03 in WG	PASS
1024 vs 1008	0.05 in WG	0.05 in WG	0.04 in WG	PASS
1025 vs1020	0.22 in WG	0.22 in WG	0.22 in WG	PASS
1025 vs 1008	0.14 in WG	0.14 in WG	0.14 in WG	PASS
1001 vs 1006	0.07 in WG	0.07 in WG	0.07 in WG	PASS
1001 vs 714	0.11 in WG	0.11 in WG	0.11 in WG	PASS

CONCLUSION

Table 13 is a summary of all critical process parameters with identification of the qualified operating ranges for the project.

Table 13

Qualified Operational Ranged to comply with CPPs

CPP	Qualified Range	Applicable Rooms
Room Temperature	68°F - 77°F (20°C – 25°C)	Manufacturing Rooms
Room Relative Humidity	45% to 65% RH	Manufacturing Rooms
Room Differential Pressure	≥0.03 in WG	Manufacturing Rooms
	≥0.06 in WG	For Airlock #11, Gowning and De-Gowning Rooms against outside Corridor
	≥0.015 in WG	Manufacturing Area Airlocks

All test cases related to the Facility GMP HVAC System related to the critical aspects were successfully completed through the commissioning and qualification documents in alignment with the established qualification plan and project objectives. The outcome of this project demonstrates that the Facility GMP HVAC System operates in accordance with all established specifications, parameters, and procedures and it met the established acceptance criteria; therefore, can be considered qualified, fit for its intended use and released to production.

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