Validation Exercise for Facility GMP HVAC System

Damilette De La Torre Vazquez

Advisor: Rafael Nieves Castro, Pharm.D. Graduate School Polytechnic Univerity of Puerto Rico

ABSTRACT

Technology Transfer Project requires the retrofit of the out of use facilities and utilities to provide adequate area for commercial manufacturing of new products. The facilities and utilities must be designed, retrofitted and validated. Project focus is to validate the Facility HVAC (Heating, Ventilation & Air Conditioning) System for this new facility. The HVAC System, including 5 Air Handling Units (AHUs), 2 Exhaust Fans (EF) and 1 Dust Collector (DC), was successfully validated. This validation process includes control systems to maintain the Facility HVAC System within specifications and environmental controls. Once this project was completed, the client will 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).

INTRODUCTION

The retrofit, refurbish and validation of existing facilities and utilities to provide a GMP manufacturing facility was the request. Since the area was out of service, no manufacturing or administrative activities were impacted. The purpose 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. This report will consider specifically the validation of the HVAC System including the impacted Air Handling Units, and Dust Collection System. The client's Critical Process Parameters (CPPs) and Critical Quality Attributes (CQAs) were established and converted into requirements for design.

This project completion established that the HVAC System is considered validated, suitable for its intended use, and released 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 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 term qualification is normally used for equipment, utilities, and systems; meanwhile, the term validation is typically used for processes.

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

OBJECTIVES

- Provide a validated and adequate Facility GMP HVAC System
- Comply with the GMP requirements as per 21 CFR and established client's standards and SOPs

METHODOLOGY

The Commissioning and Qualification (C&Q) Strategy was used to complete this project per clients Standard Operating Procedures (SOPs).

Table 1: C&Q Strategy Related Documents per Phases

Phases	Related Documents
Phase 1: Requirements Definition	• Change Control • User Requirements Specification (URS)
Phase 2: Specification & Design	• Critical Aspects Risk Assessment (CARA) • Critical Aspects Design Review (CADR) • Project Qualification Plan (PQP) • System Test Matrix (STM)
Phase 3: Commissioning & Qualification	• Commissioning Test Protocol • Installation / Operational Qualification Test Protocol • Performance Qualification Test Protocol • Test Protocols Summary Reports
Phase 4: Acceptance and Release	• Project Qualification Plan (PQP) Summary Report • Change Control Implementation/Closure

METHODOLOGY

The focus of this project will be to demonstrate that the Critical Aspects were tested and that identified Control and Detection Mechanisms (such as temperature, relative humidity and differential pressure sensors installation and calibration with their respective visual and audible alarms) 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

Since Facility GMP HVAC System CQAs and CPPs are related to the environmental conditions of the facilities served by these equipment, Figure 1 shows the Air Handling Units boundaries; it identifies the rooms served by each AHU.

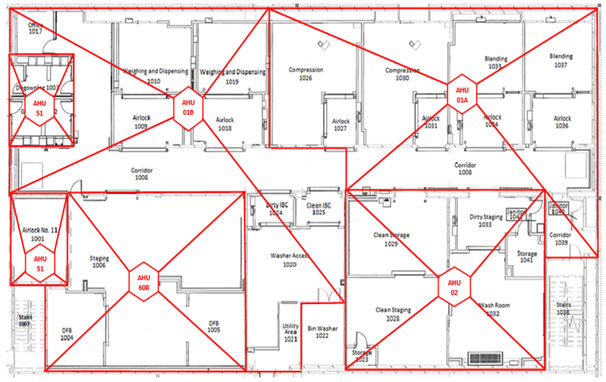

Figure 1. AHUs Boundaries

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.

RESULTS & DISCUSSION

Test Case 1 - HEPA Filters Integrity Testing

Objective: Verify integrity of HEPA Filters.

Acceptance Criteria / Results: HEPA filter integrity testing has been successfully completed for AHU-01A, AHU-01B, AHU-02, AHU-60 and AHU-51. HEPA Filter certifications for the AHUs equipment and Facilities Air Low Return Registers to the AHU were attached.

Test Case 2 - Preventive Maintenance Verification

Objective: Verify that preventive maintenance for the the Facility HVAC System has been included in the Plant Preventive Maintenance (PM) Program.

Acceptance Criteria / Results: The preventive maintenance for the Facility GMP HVAC System (AHU-01A, AHU-01B, AHU-02, AHU-60, AHU-51 and DC-33) has been included in the Plant Preventive Maintenance (PM) program. Print out of the computerized maintenance management system (CMMS) has been attached. A yearly HEPA Filters Certification was included to AHUs preventive maintenance job plans.

Test Case 3 – 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 / Results: Instruments requiring calibration were successfully calibrated against the National Institute of Standards and Technology (NIST) traceable standards 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 & DISCUSSION

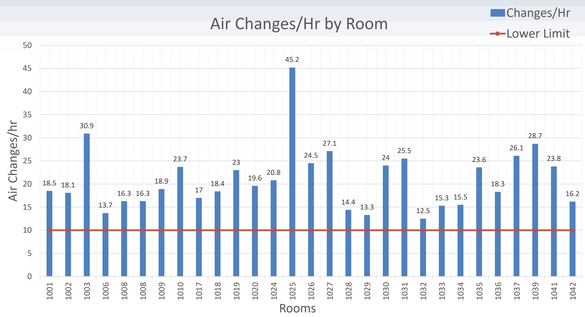

Figure 2. Testing, Adjusting & Balancing (TAB) Results - Air Changes Per Hour (ACPH)

Test Case 4 - 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 / Results: Facilities major cleaning was conducted prior to starting this test. For designated rooms in the GMP Facilities supplied by the Facility HVAC System, the airborne particulate cleanliness limits (≥ 0.5µm/m3) are less than 3,520,000 at rest. Facilities major cleaning, original Non-viable results and calibrations certificate of the instruments used were attached.

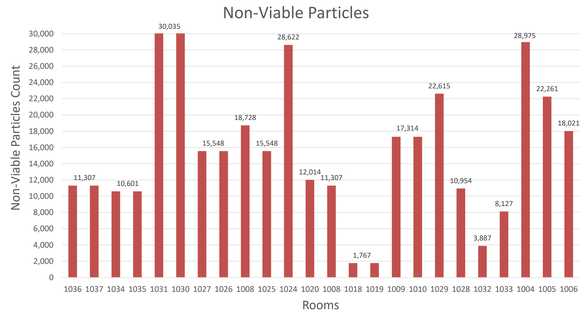

Figure 3. Airborne Particles (Non-Viable) Results

Test Case 5 - 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 / Results: 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 for the Viable results and calibrations certificate of the instruments used were attached. Rooms sharing airborne particulate (Viable) results mean that the test was performed with door open for sample to represent both rooms.

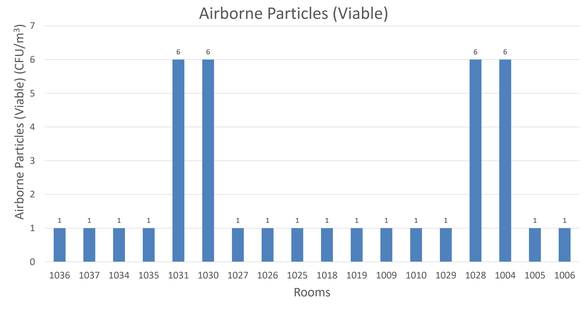

Figure 4. Airborne Particles (Viable) Results

RESULTS & DISCUSSION

Test Case 6 – 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 / Results: No Mechanical Failure occurred during this 24 hours monitored 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 (Temperature: 20-25°C (68-77°F) and Relative Humidity: 45-65%RH) as per Temperature and Relative Humidity SOP. Temperature and Relative Humidity Reports and Calibration Certificate(s) for instrument(s) used are attached. Temperature and relative humidity parameters readings were taken every 15 minutes during the 24 consecutive hours.

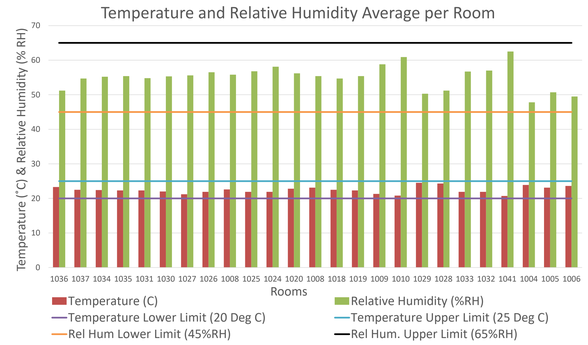

Figure 5. Temperature and Relative Humidity Results

Test Case 7 – Room Differential Pressure Verification – Dynamic Conditions

Objective: Verify that the applicable rooms served by the Facility HVAC system meet established Differential Pressure during Dynamic Conditions (people inside the area monitored) for a minimum of twenty four (24) consecutive hours monitoring (once per shift).

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 within SOP established ranges (≥ 0.03 in WG for Manufacturing Rooms, ≥ 0.06 in WG for Material Transfer, Gowning and Degowning Rooms and ≥ 0.015 in WG for Manufacturing Area Airlocks). Differential Pressure readings were copied from instruments display at the time of the reading; therefore, no differential pressure report was generated or attached. Copy of the calibration certificates of the instruments used and Pressurization Diagram/Drawing were attached.

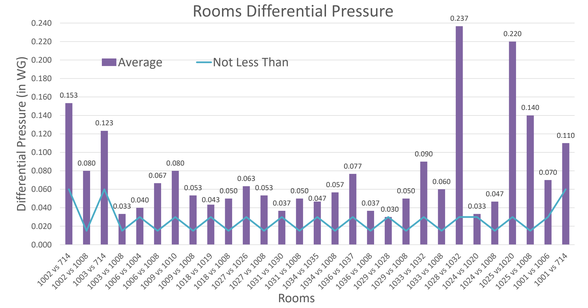

Figure 6. Rooms Differential Pressure Results

CONCLUSION

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.