# PERFORMANCE QUALIFICATION

# PROTOCOL

# FOR

# VERTICAL LAMINAR AIR FLOW

| | |
|---|---|
| **EQUIPMENT ID. NO.** | |
| **LOCATION** | **Liquid Filling Area** |
| **DATE OF QUALIFICATION** | |
| **SUPERSEDES PROTOCOL No.** | **NIL** |

| PHARMA DEVILS | PERFORMANCE QUALIFICATION PROTOCOL FOR VERTICAL LAMINAR AIR FLOW | PROTOCOL No.: |
|---|---|---|

# PROTOCOL CONTENTS

|  PHARMA DEVILS | PERFORMANCE QUALIFICATION PROTOCOL FOR VERTICAL LAMINAR AIR FLOW | PROTOCOL No.: |
|---|---|---|

## 1.0 PROTOCOL PRE - APPROVAL:

**PREPARED BY:**

| DESIGNATION | NAME | SIGNATURE | DATE |
|---|---|---|---|
| OFFICER/EXECUTIVE (QUALITY ASSURANCE) | | | |

**REVIEWED BY:**

| DESIGNATION | NAME | SIGNATURE | DATE |
|---|---|---|---|
| OPERATING MANAGER (QUALITY ASSURANCE) | | | |
| HEAD (ENGINEERING) | | | |

**APPROVED BY:**

| DESIGNATION | NAME | SIGNATURE | DATE |
|---|---|---|---|
| HEAD (PRODUCTION) | | | |

## 2.0 OBJECTIVE:

- To provide documented evidence that the Equipment is performing consistently, repeatedly and reproducibly within its established operating range and the results of all the test parameters meet the pre-defined acceptance criteria.
- To confirm the suitability of the Standard Operating Procedures for all routine activities associated with the system.

## 3.0 SCOPE:

- The score of this report is limited for qualification of vertical Laminar Air Flow installed in the **Liquid Filling Area.**
- This report provides all the relevant information of the performance qualification activity, In-process observations and analytical data of testing of collected samples.

## 4.0 RESPONSIBILITY:

The Validation Group, comprising of a representative from each of the following departments, shall be responsible for the overall compliance of this Protocol:

| DEPARTMENTS | RESPONSIBILITIES |
|---|---|
| **Quality Assurance** | • Preparation, Review & Authorization of the Performance Qualification Protocol.<br>• Co-ordination with Quality Control, Production and Engineering to carryout Performance Qualification Activity.<br>• Monitoring of Performance Qualification. |
| **Production** | • Review of Performance Qualification Protocol.<br>• To co-ordinate and support Performance Qualification Activity. |
| **Quality Control** | • Analytical Support (Microbiological Testing/Analysis) |
| **Engineering** | • Review of Performance Qualification Protocol for correctness, completeness and technical excellence.<br>• Responsible for trouble shooting (if occurred during execution).<br>• Maintenance & preventive maintenance as per schedule. |
| **External Qualification Agency ( if Applicable)** | • Performance of qualification activity as per protocol |

## 5.0 EQUIPMENT DETAILS:

| | |
|---|---|
| **Equipment Name** | Vertical Laminar Air Flow |
| **Equipment** | |
| **Manufacturer's Name** | |
| **Model** | |
| **Sr.No.** | |
| **Supplier's Name** | |
| **Location of Installation** | Liquid Filling Area |

## 6.0 SYSTEM DESCRIPTION:

Vertical Laminar Air Flow in Disinfectant Preparation Area is used to control airborne contamination of sterile products during their extemporaneous preparation. Air is filtered through a High Efficiency Particulate Air (HEPA) filter removing 99.999% of all particles 0.3µ or larger. Parallel air streams bathe the work area with a velocity sufficient to provide the area free of Particles and microorganisms. The direction of air flow is vertical.

Hood does not produce sterilization, but merely prevents contaminants from settling onto the surface of the sterile product. Any movement of greater velocity and different direction than that of the hood's air flow will create a turbulence that reduces the hood's effectiveness. Contamination may be minimized by working at a smooth, steady place at least 6 inches into the hood.

## 7.0 REASON FOR QUALIFICATION:

- New equipment in **Liquid Filling Area 'I' Block**.
- After completion of the Operation Qualification of the Equipments, it is imperative to perform the Performance Qualification. The study will establish that the parameters are followed, critical variables are under control and the quality of the output is, as desired.

## 8.0 SITE OF STUDY:

- **Liquid Filling Area**.

## 9.0 FREQUENCY OF QUALIFICATION:

| S.No. | Tests | Performance Qualification Frequency |
|---|---|---|
| 1. | **Air Velocity Measurement** | • Initially<br>• Once in 6 months |
| 2. | **Filter Integrity Test (PAO test)** | • Initially<br>• Once in a year |
| 3. | **Differential pressure record** | • Daily for 3 days at every 4 hrs interval |
| 4. | **Non Viable Particle count** | • Initially<br>• Once in 6 months |
| 5. | **Viable Particulate Count Test** | • Settle plate – 3 days<br>• Air sampling - 3 days |
| 6. | **Air Flow Pattern Test** | • Initially<br>• Once in 2 year |

## 10.0 PRE – QUALIFICATION REQUIREMENTS:

Verification for availability, completeness and approval status of all the required relevant documents shall be done and observations shall be recorded in the performance qualification report.

### 10.1 Verification of Documents:

Record the observations for documents in the below mentioned table.

| S.No. | Document Name | Document / SOP No. | Completed (Yes/No) | Checked By (Engineering) Sign/Date | Verified By (QA) Sign/Date |
|---|---|---|---|---|---|
| 1. | Executed and approved Design Qualification document | | | | |
| 2. | Executed and approved Installation Qualification document | | | | |
| 3. | Executed and approved Operational Qualification document | | | | |
| 4. | SOP for operation & Cleaning of Laminar Air Flow | | | | |
| 5. | SOP for Preventive Maintenance of Laminar Air Flow | | | | |

### 10.2 Training Record of Validation Team:

- All the persons involved in the execution of Requalification Protocol must be trained in all aspects of the qualification activity including the test methodology, acceptance criteria and safety precautions to be followed during working at service floor.

### 10.3 Calibration of Test Instruments:

- Calibration of all the instruments used for qualification should be mentioned along with Calibration Certificates.

## 11.0 TESTS AND CHECKS:

## 11.1 EVALUATION OF AIR VELOCITY:

### 11.1.1 Objective:

- To verify the Average Air Flow Velocity across the HEPA filter in vertical laminar air flow.

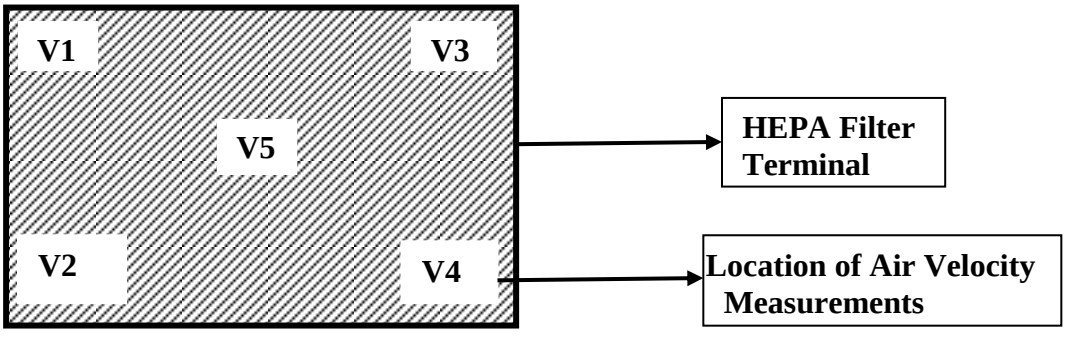
### 11.1.2 Equipment and Instruments

- Vane type Anemometer/Pitot Tube and Manometer/Hot wire anemometer

### 11.1.3 Procedure:

- Measure airflow velocities at the four corners and center of each terminal filter about 6 inches downstream of the filter.
- Measurement time at each location should be at least 10-second duration and the values should be recorded.

**Sampling point on the filter.**




### 11.1.4 Acceptance Criteria:

- An Average air flow rate of 90 ± 20 % feet per minute shall be maintained and measured at 6 inches below HEPA's.

### 11.1.5 Observation:

- Record the observations in the performance qualification report.

## 11.2 HEPA FILTER INTEGRITY TEST:

### 11.2.1 Objective :

- To demonstrate that HEPA Filter is capable of filtering above the 0.3 µ size particle.

**11.2.2 Equipments & Instruments:**

- Aerosol photometer and scanning port.

**11.2.3 Procedure:**

- Before starting the test start the Vertical Laminar Air Flow before one hour.
- Check PAO (Poly Alfa Olefin) solution level into aerosol photometer tank,
- Position the aerosol generator and introduce Aerosol into the upstream air, ahead of HEPA filters .at the concentration of 80-100 µg/liter of air at the filters designed airflow rating.
- Set the instrument at 100% concentration.
- Connect the compressed air to aerosol photometer.
- Orient the supply tube (PU tube) of aerosol toward the grill and orient the PU tube (for Down stream Concentration) on opening of supply aerosol tube - than check the upstream Concentration 100 % above the HEPA through port.
- Keep the aerosol supply tube near the grill.
- The probe should scan the filter face and frame at a position about 1to2 inches from the face of the filter.

**11.2.4 Acceptance criteria:**

- During scanning percentage of the PAO penetration shown by photometer should be less than 0.01% through the filter media and should be zero through mounting joints.

**11.2.5 Observation:**

- Record the observations in the performance qualification report.

**11.3 DIFFERENTIAL PRESSURE ACROSS HEPA FILTER:**

**11.3.1 Objective:**

- To demonstrate that the air system is capable to delivering sufficient air volume and maintain Pressure Differential across HEPA Filter & pre Filter in Laminar Air Flow.

**11.3.2 Equipment and Instrument:**

- Calibrated Magnehelic Gauge.

**11.3.3 Procedure:**

- Operate the Vertical Laminar Air Flow system about 15 mins. Prior to recording the Differential Pressure Across HEPA.
- Measure and record the Differential Pressure at every 4 hrs interval for up to 3 days.

**11.3.4 Acceptance Criteria:**

- Differential pressure of HEPA Filter should be in the range of (5-15 mm of water).
- Differential pressure of Pre Filter should be in the range of (2-8 mm of water).

**11.3.5 Observation:**

- Record the observations in the performance qualification report.

**11.4 NON -VIABLE PARTICULATE COUNT TEST:**

**11.4.1 Objective:**

- To demonstrate that the critical work locations/ stations within the clean rooms comply with their designed conditions and/or the cleanliness class with respect to the level of Non viable particle count and are in line with the regulatory requirements.

**11.4.2 Equipment & Instruments:** Particle counter

**11.4.3 Procedure:**

- Set particle counter at designated sampling location, & evaluate the particles of 0.5µ & 5.0 µ from the sampling location.

**11.4.4 Acceptance Criteria:**

**Acceptance Criteria for Non viable air borne particle count**

| S. No. | Grade | Limit for non viable particle count monitoring for clean room. | | |
|---|---|---|---|---|
| | | Particle size | Acceptance criteria (At Rest) | Acceptance criteria (In operation) |
| 1 | A | ≥ 0.5 µ Particle | 3500 | 3500 |
| | | ≥ 5.0 µ Particle | 00 | 00 |

**11.4.5 Observation:**

- Record the observations in the performance qualification report.

## 11.5 VIABLE AIR BORNE PARTICULATE COUNT TEST (By Settle Plate & Air Sampler):

### 11.5.1 Objective:

- To demonstrate that the critical work locations/stations within the clean rooms comply with their designed conditions and/or the cleanliness class with respect to the level of microbial contamination and are in line with the regulatory requirements.

### 11.5.2 Procedure For Settle Plate Method:

- Prepare the media plates with Soyabean casein digest agar (SCDA).
- Expose the plates in the areas at different locations for 4 hours.
  Incubate the exposed plates at 22.5 ± 2.5ºC for 72 hours initially followed by at 32.5ºC ±2.5ºC for 48 hours.
- Examine the plates visually after above mentioned period for any fungal and bacterial growth.
- Enter the results in the microbial test report.

### 11.5.3 Procedure For Air Sampling Method:

- Sanitize the air sampler with filtered 70% IPA.
- Transfer the air sampler in to concern area pass box and again sanitize with filtered 70% IPA.
- At the sampling location open the top lid of pre incubated SCDA plate and keeps the plate in cone of air sampler.
- After that immediately remove the aluminum foil or butter paper of perforated sieve and set it with head of air sampler over the SCDA plate. Vertically put the air sampler at the sampling location and carry out the air sampling of 1000 ltr.
- After air sampling, remove the plate (in the same area where it is exposed) from air sampler, close the lid immediately and place aside. Immediately clean the head cone of air sampler with lint free cloth previously wetted with filtered 70% IPA and carry out the air sampling for other specified locations.
- After air sampling collect, all the plates and wrap with same single aluminum foil. Place the plates in SS container and bring back the sampled plates in microbiology lab for incubation.
- Incubate all the plates first at 22.5 ± 2.5ºC for 72 hours and then at 32.5ºC ±2.5ºC for 48 hours in inverted position. For negative control incubate SCDA plate as it is without streaking.

### 11.5.4 Acceptance Criteria:

Performance Qualification shall be considered acceptable when all the conditions specified in within limit.

**Acceptance Criteria for viable air borne particle count**

| Grade | Recommended limits for microbial contamination. | |
|---|---|---|
| | Air Sample CFU/$m^3$ | Settle plate (Diameter 90 mm) CFU/4 Hours |
| A | <1 | <1 |

**11.5.5 Observation:**

- Record the observations in the performance qualification report.

## 11.6 AIR FLOW PATTERN TEST

**11.6.1 Objective:**

- The purpose of airflow direction test and visualization is to confirm that the airflow direction and its uniformity confirm to the design specifications.

**11.6.2 Equipment Used:**

- Video Camera & Aerosol Generator by Glycol base /Fogger/WFI or Distilled water

**11.6.3 Procedure:**

- Generate the aerosol with the help of Generator in the desired area where air flow direction test is being conduct.
- Supply of aerosol generator pipe should be placed typically 6 inches away from the HEPA filter face in downward position.
- After placing downward position, start the smoke remotely from the source and simultaneously shoot the video.
- Move the smoke generator pipe through the entire area to be tested, sliding the hands free stand slowly so that the whole clean zone area is observed and video recorded.

**11.6.4 Acceptance Criteria:**

- Airflow direction should be moving in a downward direction

**11.6.5 Observation:**

- Record the observations in the performance qualification report.

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## 12.0 CHECKLIST OF ALL TESTS & CHECKS

| S.No. | Name of Test or Check | | Acceptance Criteria | |
|---|---|---|---|---|
| 1. | Air Velocity Measurement | | Air flow rate of 90 ± 20 % feet per minute. | |
| 2. | HEPA Filter Integrity Test (PAO Test) Report | | HEPA filters should not be greater than 0.01% of the upstream PAO Concentration. | |
| 3. | Differential Pressure Record | Pre- Filter | 07-25 Pascal | |
| | | HEPA Filter | 05-15 mm of water | |
| 4. | Non - Viable Particle Count | ≥ 0.5 µ Particle | At rest | Operation |
| | | | 3500 | 3500 |
| | | ≥ 5.0 µ Particle | 00 | 00 |
| 5. | Air Flow Pattern | | Supply Air to Return Filter | |
| | | | Downward Direction | |
| 7. | Evaluation Of Viable Airborne Particulate testing – 1.Settle Plate Method<br>2. Air Sampling Method | | < 1 CFU/4 Hours<br>< 1 CFU/m3 | |

## 13.0 REFERENCES:

**The Principle Reference is the following:**

- Validation Master Plan
- Schedule-M – "Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products."
- WHO Technical Report Series 961, Annexure - 05.
- EU Guidelines to Good Manufacturing Practice Medicinal Products for Human and Veterinary Use Annex -1 Manufacture of Sterile Medicinal Products.- February 2008
- ISO 14644-1 of Clean Rooms and Associated Controlled Environments..

## 14.0 DOCUMENTS TO BE ATTACHED:

- Report of QC (Micro) Analysis
- Calibration Certificate of Test Instrument
- Any Other Relevant Document

## 15.0 NON COMPLIANCE:

- In case of any Non-Compliance observed during performance test, inform to head QA for required action.
- All the required action should be addressed in the report and justified.

## 16.0 DEVIATION FROM PREDEFINED SPECIFICATION IF, ANY:

- In case of any deviation observed during PQ, inform to Head QA for necessary action.
- Document the deviation detail in observed deviation section.
- The Head QA will study the impact of deviation. If deviation is acceptable and it does not have an Impact on properties of product & prepare final conclusion.

## 17.0 CHANGE CONTROL, IF ANY:

- If any change control is required during PQ, inform to Head QA for necessary action.
- Document the details observed.
- The Head QA will study the impact of change. If change is acceptable and it does not have an Impact on properties of product & prepare final conclusion.

## 18.0 ABBREVIATIONS:

| | | |
|---|---|---|
| % | : | Percent |
| & | : | And |
| µ | : | Micron |
| µg | : | micro gram |
| CFM | : | Cubic feet Meter |
| CFU | : | Colony forming unit |
| EU | : | European union |
| $ft^3$ | : | Cubic feet |
| GMP | : | Good Manufacturing practice |
| HEPA | : | High Efficiency Particulate Air Filter |
| ID. | : | Identification |
| ISO | : | International standard of organization |
| LAV | : | Vertical Laminar Air Flow |
| LTD | : | Limited |

| | | |
| --- | --- | --- |
| $m^3$ | : | meter cube |
| min | : | Minute |
| mm | : | Millimeter |
| No. | : | Number |
| SCDA | : | Soyabean casein digest agar |
| SOP | : | Standard operating procedure |
| WFI | : | Water for injection |
| WHO | : | World Health Organization |