PERFORMANCE QUALIFICATION PROTOCOL FOR AMPOULE FILLING AND SEALING MACHINE

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EQUIPMENT ID. No.	
LOCATION	**AMPOULE FILLING & SEALING ROOM**
DATE OF QUALIFICATION	
SUPERSEDE PROTOCOL No.	**NIL**

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PROTOCOL CONTENTS

PERFORMANCE QUALIFICATION PROTOCOL FOR AMPOULE FILLING AND SEALING MACHINE

1.0 PROTOCOL PRE – APPROVAL:

INITIATED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (PRODUCTION)			
HEAD (ENGINEERING)			

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			

PERFORMANCE QUALIFICATION PROTOCOL FOR AMPOULE FILLING AND SEALING MACHINE

2.0 OBJECTIVE:

To carry out the Performance Qualification of **Ampoule Filling and Sealing Machine** being used for filling and sealing of ampoules.

To Provide Documented Verification that the Equipment as connected with ancillary system is suitable for indented purpose and produced product as per pre defined Acceptance Criteria

3.0 SCOPE:

The scope of this qualification protocol is limited to qualification of **Ampoule Filling and Sealing Machine (Make: Truking Technology Limited)** installed in the **Ampoule Filling and Sealing Room**.

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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 cum Report:

DEPARTMENTS	RESPONSIBILITIES
Quality Assurance	• Preparation, Review, Approval and Compilation of the Performance Qualification Protocol. • Protocol Training. • Co-ordination with Quality Control, Production and Engineering to carryout Performance Qualification Activity. • Monitoring of Performance Qualification.
Production	• Review & Approval of Protocol. • To co-ordinate and support Performance Qualification Activity.
Quality Control	• Analytical Support (Microbiological Testing / Analysis).
Engineering	• Review & Approval of Protocol. • Co-ordination, Execution and technical support in Qualification activity. • Calibration of Process Instruments. • Responsible for Trouble shooting (if occurs during execution).

PERFORMANCE QUALIFICATION PROTOCOL FOR AMPOULE FILLING AND SEALING MACHINE

5.0 EQUIPMENT DETAILS:

Equipment Name	Ampoule Filling and Sealing Machine
Equipment ID.	……..
Model	AGF12
Manufacturer's Name	Truking Technology Limited
Supplier's Name	Truking Technology Limited
Location of Installation	Ampoule Filling and Sealing Room

6.0 EQUIPEMENT DESCRIPTION:

Ampoule Filling & Sealing Machine adopts linear intermittent for filling and sealing. The ampoules which come from sterilization and drying tunnel access to infeed Conveying Belt No. 1 via the connection board, move to scroll No.2. The scroll will arrange out of order ampoules in separation status, it pushes the ampoules individually to the infeed star wheel No. 4,infeed star wheel No. 4 continuously conveys the ampoules to the walking beam No.5, front walking beam No. 5 can change the continuous movement of ampoules to intermittent movement. The middle walking beam No. 6 can convey the ampoules in a stepping mode to the next station. Ampoule leaning part No. 7 is used for orientation in the static station. The 5 intermittent stations are listed below:

1) **Front Charging Station**
2) **Filling Station**
3) **Rear Charging Station**
4) **Preheating Station**
5) **Sealing Station**

Front Charging Station:. The front charging station is set with nitrogen gas purging.

Filling Station: At the filling station, rotary piston pump consists of a piece of to-and fro rotary valve, a piece of movable piston rod and a piece of pump cylinder The rotary valve is on the upper side of pump cylinder, and it connects with drive group of rotary valve via a stand- alone servo motor via ball screw pair, lifting rod and connection rod. By to and fro movement, the liquid medicine is filled into ampoules by the filling pump.

Rear Charging Station: The rear charging station can be set as inert gas charging.

Preheating & Sealing Station: At the preheating station, ampoules are preheated by the nozzle of LPG and Oxygen, and they spin automatically by the idler wheel. At the station of sealing, ampoules are softened by heat and sealed. The sealed ampoules are conveyed through out feed star wheel to ampoule receiving tray.

7.0 REASON FOR QUALIFICATION:

- New equipment installed in Ampoule filling & Sealing room**.**
- 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:

Ampoule Filling & Sealing Machine **installed in Ampoule Filling & Sealing room.**

9.0 FREQUENCY OF QUALIFICATION

- Yearly ± 1 month as per Validation Master Plan for Filling Machine.
- After any major breakdown or after major modification

For Laminar Air Flow

S.No.	Tests	Performance Qualification Frequency
1.	**Air Velocity Measurement**	• Once in a 6 months
2.	**Filter Integrity Test (PAO test)**	• Once in a year
3.	**Differential pressure record**	• Daily
4.	**Non Viable Particle count**	• Once in 6 months
5.	**Viable Particulate Count Test**	• Settle plate – Daily & 7 days for qualification • Air sampling – Daily & 7 days for qualification
6.	**Air Flow Pattern Test**	• Once in 2 year

PERFORMANCE QUALIFICATION PROTOCOL FOR AMPOULE FILLING AND SEALING MACHINE

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 cum report				
2.	Executed and approved Installation Qualification cum report				
3.	Executed and approved Operational Qualification cum report				
4.	SOP for Operation & Cleaning of Ampoule Filling & Sealing Machine				
5.	SOP for Preventive Maintenance of Ampoule Filling & Sealing Machine				

Checked By
(Production)
Sign/Date: ……

Verified By
(Quality Assurance)
Sign/Date: ……

Inference:

……

……

……

Reviewed By
(Manager QA)
Sign/Date: ……

10.2 Training Record of Validation Team:

- All the persons involved in the execution of qualification activity must be trained in all aspects of the qualification activity including the test methodology, acceptance criteria and safety precautions to be followed during working.
- Verify the training records and record the details in table mentioned in performance qualification report.

10.3 Calibration of Test Instruments:

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

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11.0 TESTS AND CHECKS:

The following performance test have been carried out in order to demonstrate the Performance in Conformance.

- Speed Optimization
- Fill Weight Variation
- Damage rate
- Sealing Qualified Rate

11.1 EVALUATION OF AIR VELOCITY:

1.1.1 Objective:

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

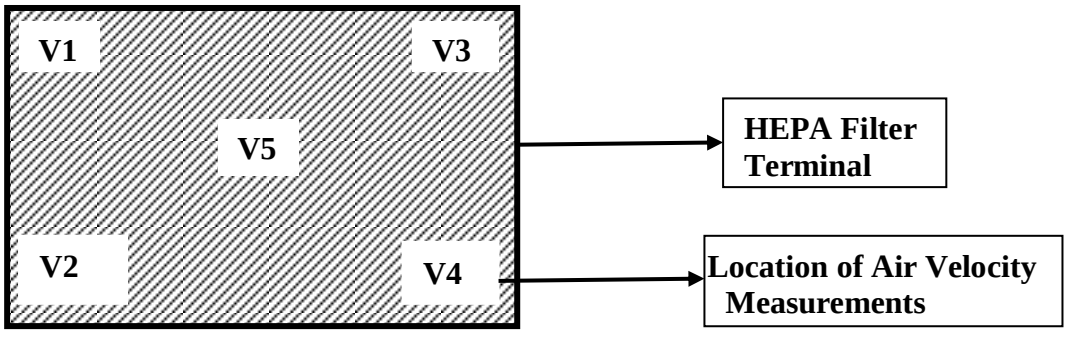
1.1.2 Equipment and Instruments

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

1.1.3 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.



1.1.4 Acceptance Criteria:

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

1.1.5 Observation:

- Record the observations in the performance qualification report.

1.2 HEPA FILTER INTEGRITY TEST:

1.2.1 Objective :

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

1.2.2 Equipments & Instruments:

- Aerosol photometer and scanning port.

1.2.3 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 20-80 mg/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.

1.2.4 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.

1.2.5 Observation:

- Record the observations in the Performance Qualification Report.

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1.3 DIFFERENTIAL PRESSURE ACROSS HEPA FILTER:

1.3.1 Objective:

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

1.3.2 Equipment and Instrument:

- Calibrated Magnehelic Gauge.

1.3.3 Procedure:

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

1.3.4 Acceptance Criteria:

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

1.3.5 Observation:

- Record the observations in the Performance Qualification Report.

1.4 NON -VIABLE PARTICULATE COUNT TEST:

1.4.1 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.

1.4.2 Equipment & Instruments: Particle counter

1.4.3 Procedure:

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

1.4.4 Acceptance Criteria:

Acceptance Criteria for Non viable air borne particle count

S.No.	Maximum number of permitted particles per cubic meter equal to or above as tabulated.	
	Particle size	Acceptance criteria
1.	≥ 0.5 µ Particle	NMT 3,520 particles/m^3 of 0.5µ or above at rest condition should be observed in Grade- A
2.	≥ 5.0 µ Particle	NMT 20/m^3 Particles of 5.0µ or above at rest /in operation condition should be observed in Grade-A

1.4.5 Observation:

- Record the observations in the Performance Qualification Report.

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

1.5.1 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.

1.5.2 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.

1.5.3 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.

1.5.4 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
B	10	05
C	100	50
D	200	100

1.5.5 Observation:

- Record the observations in the Performance Qualification Report.

1.6 AIR FLOW PATTERN TEST

1.6.1 Objective:

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

1.6.2 Equipment Used:

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

1.6.3 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.

1.6.4 Acceptance Criteria:

- Airflow direction should be moving in a downward direction

1.6.5 Observation:

- Record the observations in the Performance Qualification Report.

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11.2 PERFORMANCE EVALUATION FOR SPEED OPTMIZATION

A) OBJECTIVE:

To establish machine speed optimization by the different sets of Filling nozzles on different volumes.

B) EQUIPMENT/INSTRUMENT USED:

NA

C) METHOD APPLIED:

- The test should be carried out on each size of ampoule.
- Load the Ampoules in Ampoule filling & Sealing Machine.
- Switch "ON" the machine & Operate as per **SOP .**
- Set the machine speed (Ampoule /Minute) through HMI as per below table.

Ampoule Size	Machine Speed (100%)	Machine Speed (80%)	Machine Speed (50%)
1 ml	450 Amp./min	400 Amp./min	350 Amp./min
2 ml	410 Amp./min	375 Amp./min	350 Amp./min
3 ml	400 Amp./min	360 Amp./min	320 Amp./min
5 ml	350 Amp./min	330 Amp./min	300 Amp./min

- Start the machine with individual speed & count the ampoules after 30 minute for each speed.
- Repeat it three times at each speed.
- Final machine output shall be decided & verified after performing the test.

11.3 TEST FOR DAMAGE RATE

A) OBJECTIVE:

To evaluate the Damage rate in the ampoules.

B) METHOD APPLIED:

- This test evaluate with speed optimization.
- Check whether the ampoules break in the process of infeed, filling, sealing and outfeed.
- Perform it three times at individual speed and calculate the average damage rate.
- Perform the test for each size of ampoule by filling WFI.

C) ACCEPTANCE CRITERIA:

Damage rate should not be more than 0.3 %.

D) RESULT RECORDING:

Record the results in Performance Qualification Report.

11.4 TEST FOR VOLUME VERIFICATION:

A) OBJECTIVE: To establish that the filling volume variation in the ampoules filled by the different sets of Filling nozzles.

B) EQUIPMENT/INSTRUMENT USED:

Measuring Cylinder/Syringe

C) METHOD APPLIED:

- The test should be carried out in triplicate for each size of ampoules.
- Load the Liquid filling & Sealing Machine with the ampoules.
- Switch "ON" the machine & Operate as per SOP.
- Collect Filled ampoules from the machine at initial, middle and End stage. Measure Filled Volume through calibrated measuring cylinder/Syrings.
- Perform the test for 1,2,3 ml & 5 ml size Ampoules.
- Perform the test by filling WFI.

D) **ACCEPTANCE CRITERIA:**

S.No.	Ampoule Size	Filled Volume Limit
1.	1ml -1.5 ml	1.5 %
2.	More than 1.5 ml	1 %

E) RESULT RECORDING:

Record the results in Performance Qualification Report.

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11.5 TEST FOR SEALING QUALITY:

A) OBJECTIVE: To qualify for the Sealing Quality.

B) EQUIPMENT/INSTRUMENT USED:

NA

C) METHOD APPLIED:

- The test should be carried out in triplicate for each size of ampoules.
- Collect sealed ampoules and calculate for sealing qualified rate.
- Perform the test for 1, 2, 3 ml & 5 ml size Ampoules.

D) ACCEPTANCE CRITERIA:

Sealing Ampoules should be round and smooth and qualified rate should be not less than 98%.

E) RESULT RECORDING:

Record the results in Performance Qualification Report.

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12.0 CHECKLIST OF ALL TESTS & CHECKS

S.No.	Name of Test or Check	Execution (Yes/No.)	Remark	Verified By (Sign & Date)
1.	Performance Evaluation for Machine Speed Optimization			
2.	Test for volume verification			
3.	Test for Damage rate			
4.	Test For Sealing Quality			
5.	Test For Leak Test			

13.0 REFERENCES:

- Vendor Documents
- As Per VMP

14.0 DOCUMENTS TO BE ATTACHED:

- Operation and Maintenance Manual.
- Any other Relevant Documents.

15.0 NON COMPLIANCE:

- In case of any Non compliance observed during PQ, inform to Head QA for necessary action.
- Document the details observed.
- The Head QA will study the impact of Non compliance. If Non compliance is acceptable and it does not have an impact on performance of the Qualification, prepare final conclusion.

16.0 DEVIATION FROM PRE-DEFINED 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 performance of the Qualification, prepare final conclusion & 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 performance of the Qualification, prepare final conclusion & prepare final conclusion.

18.0 ABBREVIATIONS:

No.	:	Number
WHO	:	World Health Organization
AFM	:	Ampoule Filling Machine
DQ	:	Design Qualification
IQ	:	Installation Qualification
OQ	:	Operational Qualification
SOP	:	Standard Operating Procedure
ID.	:	Identification
IB	:	Injection block
No.	:	Number
PPQ	:	Performance qualification protocol
%	:	Percentage