PERFORMANCE QUALIFICATION

PROTOCOL

FOR

BLOW FILL & SEAL MACHINE-603

EQUIPMENT ID No.	
LOCATION	**Filling Room**
DATE OF QUALIFICATION	
SUPERSEDE PROTOCOL No.	**Nil**

PERFORMANCE QUALIFICATION PROTOCOL FOR BLOW FILL & SEAL MACHINE

PROTOCOL CONTENTS

PERFORMANCE QUALIFICATION PROTOCOL FOR BLOW FILL & SEAL MACHINE

1.0 PROTOCOL APPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER / EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

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

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			

PERFORMANCE QUALIFICATION PROTOCOL FOR BLOW FILL & SEAL MACHINE

2.0 OBJECTIVE:

The objective of this protocol is to establish documented evidence that the **BFS603** Filling Machine will produce the results consistently, within the specified acceptance limits, when operated as per the standard operating procedures.

3.0 SCOPE:

- The scope of this particular protocol is applicable for **BFS603** Filling Machine installed. This is producing Large Volume Parenterals using BFS technology in the capacity of 100 ml Bottle.

4.0 RESPONSIBILITY:

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

DEPARTMENTS	RESPONSIBILITIES
Quality Assurance	• Preparation, 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 of Performance Qualification Protocol. • To co-ordinate and support Performance qualification Activity.
Engineering	• Review of Performance Qualification Protocol. • To co-ordinate and support Validation Activity. • Responsible for Trouble shooting during execution (If Occurs).
Quality Control	• Review of Performance Qualification Protocol. • To co-ordinate and support Performance qualification Activity.

PERFORMANCE QUALIFICATION PROTOCOL FOR BLOW FILL & SEAL MACHINE

5.0 EQUIPMENT DETAILS:

Equipment Name	**Blow Fill & Seal Machine-603**
Equipment ID No.	
Model No.	**BFS-603**
Manufacturer's Name	**M/s Weiler Engineering Inc.**
Supplier's Name	**M/s SteriMax Engineering Pvt. Ltd.**
Place of Installation	**LVP Filling Area**

6.0 SYSTEM DESCRIPTION:

Bottle pack m/c 603 is a compactly built machine for processing of plastic containers in one single process. The feeder supplies plastic granulates to the granule hopper. From hopper the granules fall in to the extruder screw & here it is compressed, homogenized by heating, and forced through the extrusion head under pressure.

The hot melt plastic leaves the extrusion head in the shape of parison. The speed of the extruder screw controls the discharge speed. Adjustment of the ring- shape nozzle gap changes the parison wall thickness.

The parison clamp device clamps the end of the parison and thereby seals it & sterile support air inside the sack prevents sticking together of its walls.
The mould consists of two equal and symmetrical halves along with closing unit.

Each half consists of-
a) Supporting jaw (To hold the parison)
b) Head mould (Shaping the container's head)
c) Main mould (Shaping the container's body & bottom)

The supporting jaw holds the parison by vacuum. Incandescent cutting knife cut off the parison between the supporting jaw & parison clamp.
Vacuum channels leads to the mould. The plasticized material is attached to the mould cavity with the help of sterile support air and vacuum. The plastic material solidifies & forms the cavities to contain the product. The closing unit moves to the filling station. The tear off pins moves in to the bottom of containers.

The solution level is continuously maintained in the buffer tank through flow control regulating valve, which is supplied through SS 316 pipeline under constant sterile buffer air pressure.

The filling mandrels inside the sterile air move down into the containers, which are still open on top. The product dose flows into the containers. The air expelled from the containers escapes through the air outlet channel the mandrel unit moves up. Then head mould closes and seals the containers.

The hydraulically operated closing unit open and moves to the parison position. Punching press cuts off the waste. Then mould opens & pin leaves the containers to the conveyor.

All the critical components are steam sterilizable with the help of pure steam with an automatically controlled system.

7.0 REASON FOR QUALIFICATION:

- Installation of New System.
- Any major modification in the existing system.
- Change of Location.
- Periodic Qualification
- **(Specific Reason)**

8.0 SITE OF STUDY:

LVP Line.

9.0 FREQUENCY OF QUALIFICATION:

- Yearly as per Validation Master Plan.
- After any major modification.

PERFORMANCE QUALIFICATION PROTOCOL FOR BLOW FILL & SEAL MACHINE

10.0 PRE-QUALIFICATION REQUIREMENTS:

10.1 TEST EQUIPMENT:

S.No.	Test Instrument
1.	Anemometer
2.	Aerosol photometer and scanning port
3.	Active Air Sampler
4.	Non - Viable Particle Counter
5.	Weighing Balance
6.	Measuring Cylinder (Should be Calibrated on 100 ml, 101 ml,102 ml, 103 ml & 104 ml)
7.	Vernier Calipers
8.	Leak Test Apparatus

10.2 UTILITY:

S.No.	Parameter	Required	Actual
1.	Temperature of Cooling Water		
2.	Temperature of Barrel of Plastic Parrison		
3.	Cycle Time of Machine		
4.	Parrision Program of Machine		

10.3 TRAINING OF EXECUTION TEAM:

Provide the training to a team for the execution of protocol before execution of the same. Record of training shall be recorded in the Performance qualification Report.

11.0 TESTS & CHECKS:

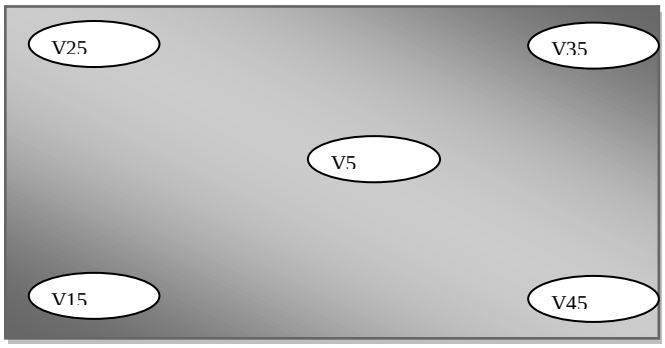
11.1 AIR VELOCITY TEST OF FILLING ZONE:

A) OBJECTIVE:

To demonstrate that the system is capable of delivering Air Velocities as per the requirement and to maintain continuous Laminarity under the Filter in the filling zone.

B) METHOD APPLIED:

Ensure that the filter blower is switch **"ON"** at least 30 minutes prior to the start of the observations. Measure the Air Velocity 6 inches below the grill, at 5 locations of each filters (Four Corners and Center shown in fig.) with the Digital Anemometer and record. Calculate the Average Velocity of air coming from Supply Grill.



Sampling Locations

C) ACCEPTANCE CRITERIA:

Average Velocity across the Filter should be within the range of 90± 20% FPM.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report

11.2 HEPA FILTER INTEGRITY TEST:

A) Objective :

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

B) Equipments & Instruments:

- Aerosol photometer and scanning port.

C) Procedure:

1. Before starting the test start the Machine before one hour.
2. Check PAO (Poly Alfa Olefin) solution level into aerosol generator tank.
3. Connect the compressed air to aerosol generator.
4. Orient the supply tube (PU tube) of aerosol toward the riser and orient the PU (for Down stream Concentration) tube on opening of supply aerosol tube - then check the upstream Concentration 100 % (20-80 mg/m^3) above the HEPA through port.
5. Scan the downstream side of the filter with an appropriate photometer probe.
6. The Probe Should be scan the entire face and frame at a position about 2 inch (5cm) from the face of the filter surface in overlapping strokes at a traverse rate of not more than 5-10 cm/sec so that the entire face is checked for any leakage.
7. Keep the aerosol supply tube near the riser grill.
8. Scan the Supply grill (HEPA Grill) for checking filter integrity test. Adjust the concentration of aerosol above HEPA 100%.

D) 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.

E) Observation:

- Record the observations in the performance qualification report.

11.3 NON - VIABLE PARTICLE COUNT TEST:

A) OBJECTIVE:

To establish that in critical work locations under Filter meet the requirement for desired cleanliness.

B) METHOD APPLIED:

Perform the test in static conditions i.e. in static condition Filling Operation shall not be carried out. Analyst shall stand away from the Working Zone.

C) ACCEPTANCE CRITERIA:

0.5µm particle is not more than 3520 and 5.0µm particle is not more than 20 in $1m^3$ of air at static condition.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.4 ACTIVE AIR SAMPLING METHOD:

A) OBJECTIVE:

To describe the procedure of Microbiological Monitoring in the air of filling zone by Sampling of air through the Air Sampler.

B) PROCEDURE:

- Media Plates shall be prepared with Soybean Casein Digest Agar (SCDA).
- Pre Incubated Plate shall be placed in Plate Holder of Air Sampler.
- Perform the Active Air Sampling under Filling zone at Working height.
- The Sampling shall be done for Single day.
- After the Air Sampling Operation, Plates shall be transferred for Incubation.
- Exposed Plate shall be incubated for 20 to 25^0C for 72 hrs followed by 30 to 35^0C for further 48 Hrs.
- Plates shall be observed 72 hours and five day for any Microbial Growth.
- Colony Forming Units shall be counted after the Incubation Period for each Location & calculate the CFU Per cubic Meter.

C) ACCEPTANCE CRITERIA:

<1 CFU / m^3 of Air.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.5 VERIFICATION OF SPEED OF THE MACHINE: (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the machine is capable of producing the containers at fix speed as mentioned by the manufacturer in the manual without affecting the quality of the product.

B) METHOD APPLIED:

- **MACHINE SPEED DESCRIPTION**

MACHINE SPEED		
100 ml	Fix Speed	3000 Bottles /hrs

- **PROCEDURE FOR SPEED VERIFICATION & SEALING QUALITY TEST OF 100 ML**

LDPE BOTTLE

- The test shall be carried out at 3000 Bottles / hrs speed in Triplicate for 100 ml size of LDPE Bottles.
- Switch "ON" the machine and operate as per SOP.
- Run the machine at a speed for 10 minutes
- Collect the LDPE bottle and check as per checklist.

C) ACCEPTANCE CRITERIA:

Rejection found should not be more than 1.0%.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report**.**

11.6 VERIFICATION OF VOLUME (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the filled volume in each container is constant within the acceptance criteria. Verification shall be done with the help of Calibrated Measuring Cylinder.

B) METHOD APPLIED:

Verification shall be done with the help of measuring cylinder.

C) ACCEPTANCE CRITERIA:

For 100 ml filling volume should be 102 ml ± 2 ml.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report

11.7 WEIGHT VERIFICATION OF EMPTY CONTAINERS: (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the empty weight of each individual container is consistent within the acceptance limit of 11.0 to 13.0 g.

B) METHOD APPLIED:

Verification shall be done with the help of weighing balance.

C) ACCEPTANCE CRITERIA:

Weight of individual bottle should be 11.0 to 13.0 g.

D) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.8 VERIFICATION OF LEAK TEST OF THE CONTAINERS: (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the pressure leak test of each cavity container is consistent within the acceptance limit.

B) EQUIPMENT/INSTRUMENT USED:

Leak Test Apparatus

C) METHOD APPLIED:

- Load the Vials in Leak test apparatus.
- Perform the Leak test Apparatus as per the respective SOP.

D) ACCEPTANCE CRITERIA:

No Leaked vials should not be found at pressure 0.75 to 1.0 kg/cm^2.

E) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.9 VERIFICATION OF PHYSICAL APPEARANCE OF BOTTLES: (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the physical appearance at any portion of each cavity vial is consistently within the acceptance limit.

B) ACCEPTANCE CRITERIA:

All the surfaces of bottle should be-

- Smooth with no scratches.
- No deformities should be observed.
- Joining lines and sealing should be smooth.
- No extra plastic should be observed.
- No particles should be observed either in the solution or on the surface.
- Marking and coding on the containers should be perfect.

C) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.10 VERIFICATION OF WALL THICKNESS: (3-Trial)

A) OBJECTIVE:

This study is carried out to ensure that the wall thickness at four portion (ie left side, right side, front & back side) of each cavity container is consistently within the acceptance limit.

B) ACCEPTANCE CRITERIA:

NLT 0.4 mm to 0.6 mm

C) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

11.11 STERILITY OF EMPTY CONTAINER, BLOW AIR & BLOWING AIR.

A) OBJECTIVE:

This study is carried out to ensure that the empty container, blow air & blowing air are sterile.

B) ACCEPTANCE CRITERIA:

Should be sterile

C) RESULT:

Recording of all the observations shall be done in Performance qualification Report.

12.0 CHECKLIST OF ALL TESTS AND CHECKS:

This checklist is provided to ensure that all tests or checks required for this protocol to be executed and consisting of following tests.

S.No.	TESTS OR CHECKS
1.	Air velocity (Filling zone verification)
2.	HEPA Filter Integrity Test:
3.	Non viable particle count test (Filling zone verification)
4.	Viable Particle Count (Filling zone verification) (By Active Air Sampling)
5.	Verification of Speed of The Machine
6.	Verification of volume
7.	Weight Verification of Empty Containers
8.	Verification of Leak Test of the Containers
9.	Verification of Physical Appearance of Bottles
10.	Verification of Wall Thickness
11.	Sterility of Empty Container

13.0 REFERENCES:

- Master Validation Plan.
- Schedule – M "Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products."
- SOP for "Cleaning, sterilization & Operation of Blow Fill & Seal System".
- SOP of "Operation of Non Viable Particle Counter".

14.0 DOCUMENTS TO BE ATTACHED:

- Raw data of Microbiological Analysis
- Calibration Certificates for Anemometer
- Calibration Certificates for Airborne particle counter
- Calibration Certificates for Measuring Cylinder.
- Calibration Certificates for Vernier Caliper

15.0 NON COMPLIANCE:

- All non-compliance, during the execution of protocol shall be handled as per current version of **Handling of General Non-Compliance Incidence"** and same shall be a part of Validation Report.

16.0 DEVIATION FROM PRE-DEFINED SPECIFICATION, IF ANY:

- All protocol deviation, non conformances and out of specification results obtained shall be investigated as per current version of **"Handling of Deviation"** and same shall be a part of Validation Report.

17.0 CHANGE CONTROL, IF ANY:

- All change control, during the execution of protocol shall be handled as per current version of **"Change Control"** and same shall be a part of Validation Report.

18.0 ABBREVIATIONS:

QA	:	Quality Assurance
QC	:	Quality Control
No.	:	Number
Ltd.	:	Limited
ID No.	:	Identification Number
ml	:	Milliliter
FPM	:	Feet per Minute
BFS	:	Blow Fill & Seal
LDPE	:	Low Density Polyethylene
PAO	:	Poly Alfa Olefin