



STANDARD OPERATING PROCEDURE

Title: Operating and Cleaning of Automatic High Speed Injectable Powder Filling and Stoppering Machine

SOP No.:		Department:	Production	
		Effective Date:		
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1.0 OBJECTIVE:

To lay down a procedure for Operation and cleaning of Automatic High Speed Injectable powder Filling and Stoppering Machine.

2.0 SCOPE:

This SOP is applicable for Operation and cleaning of Automatic High Speed Injectable powder filling and Stoppering Machine at production area in Dry Powder Injectable Section.

3.0 RESPONSIBILITY:

Operating Person – Production

4.0 ACCOUNTABILITY:

Head – Production.

5.0 ABBREVIATIONS:

DPI	Dry Powder Injection
IPQA	In Process Quality Assurance
ID No.	Identification Number
IPA	Isopropyl Alcohol
NMT	Not More Than
Ltd.	Limited
No.	Number
NLT	Not Less Than
mm	Milli Meter
PSI	Pound per Square Inch
QA	Quality Assurance
QC	Quality Control
WFI	Water for Injection
SOP	Standard operating procedure
LAF	Laminar Air flow
°C	Degree Celsius
RH	Relative humidity

6.0 PROCEDURE:

6.1 Precautions:

6.1.1 Production Operator will check and ensure that:

6.1.1.1 The availability of Power supply, check the power indicator available on electric panel of vial filling machine.

6.1.1.2 Filling and stoppering machine and surrounding area is cleaned and sanitized.



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- 6.1.1.3** All the machine parts (hopper, pistons, piston tips, “O” Rings, Doctor Blade, Wheel Guard, Powder Collector, and Port Wheel etc.) are clean and sterilized. In case, any machine parts found damaged /any other discrepancy observed, then repeat the cleaning and sterilization procedure (as per the requirement).
- 6.1.1.4** Transfer the sterilized machine parts and accessories to vial filling and stoppering machine with help of Mobile LAF.
- 6.1.1.5** Whenever the machine door opened for transfer of sterilized machine parts, machine parts assembly or any other reason, ensure that the door should be sanitized with 70% IPA before closure.
- 6.1.1.6** On completion of filling activity transfer the dismantled machine parts and accessories to equipment wash area through dynamic pass box for washing and sterilization.
- 6.1.1.7** Do not use damaged nylon scrubber for cleaning, if found damaged then discard the same and perform cleaning with new nylon scrubber.
- 6.1.1.8** Temperature of filling area is NMT 25°C and Relative Humidity of filling area is as per respective batch manufacturing record.
- 6.1.1.9** Laminar Air Flow – pressure on magnehelic Gauge is between 10-15 mm of water.
- 6.1.1.10** Nitrogen and vacuum is available in below mentioned range:
 - Nitrogen - 0.5-1.5 kg /cm²
 - Vacuum - 400-760 mm of Hg.

6.2 Machine Setting:

6.2.1 Machine parts assembling:

- 6.2.1.1** Laminar air flow should be in continues operation. In case LAF are switched off for cleaning or any other reason, then switch ON the LAF and start of the activity under LAF after 20 minutes.
- 6.2.1.2** Ensure that all the machine parts should be dry before assembling.
- 6.2.1.3** Set the railing guard and assemble the piston, piston tips, “O” ring, doctor blade, star wheel, vial separator and fix the port wheel with screw on filling head.
- 6.2.1.4** Set the powder collector on both side of port wheel and assemble the powder hopper on filling head with universal joint.
- 6.2.1.5** Adjust the nitrogen pressure of port wheel between 0.5 to 1.5 kg/cm². Set limit for pre and post purging of nitrogen (pre 0.5 Psi & post 0.2 Psi).
- 6.2.1.6** Switch “ON” power supply.



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- 6.2.1.7** Before start of batch filling, run the machine trial in inching mode with empty vials and adjust the vial guide rails as per the vial pack size by loosening left/right rail support mounting screw.
- 6.2.1.8** Discard the empty vials (used for machine trial) and record the quantity of discarded vials as rejection in respective BMR.
- 6.2.1.9** Adjust the “Filling Head” as per vial size by loosening head support column screw.
- 6.2.1.10** Take sterilized dosing piston as per requirement and position it with piston tips in the filing port of feed wheel.

S.No.	Port wheel size	Piston size	Fill weight range
1.	1/4	85 mm	60 mg to 250 mg
2.	3/4	80 mm	250 mg to 750 mg
3.	3/4	65 mm	750 mg to 1250 mg
4.	3/4	55 mm	1250 mg to 1750 mg

- 6.2.1.11** Adjust the known depth of all dosing pistons.
- 6.2.1.12** Set the piston and wheel on the machine.
- 6.2.1.13** Adjust the doctor blade of hopper and place it above the wheel.
- 6.2.1.14** Load the powder in the hopper with the help of sterilized spatula.
- 6.2.1.15** Adjust the fill weight by adjusting the depth of port to increase or decrease the fill weight with the help of wheel type D-spanner. For decreasing fill weight, rotate the spanner in clockwise direction and for increasing the fill weight, rotate the spanner in anticlockwise direction.
- 6.2.1.16** Adjust the depth of all the remaining of filling ports.
- 6.2.2 Machine parts assembling for media fill.**
- 6.2.2.1** Before assembling, ensure that machine parts should be dry.
- 6.2.2.2** Compressed air purging (pre and post) is to be done instead of nitrogen.
- 6.2.2.3** Ensure the availability of Compressed air (0.5-1.5 kg /cm²) and Vacuum (400-760 mm of Hg).
- 6.2.2.4** Set the railing guard and assemble the piston, piston tips, “O” ring, doctor blade, star wheel, vial separator and fix the port wheel with screw on filling head.
- 6.2.2.5** Set the powder collector on both side of port wheel and assemble the powder hopper on filling head with universal joint.
- 6.2.2.6** Assemble the pneumatic piston, silicon tube with needle for liquid media fill.
- 6.2.2.7** Set the media fill volume of vial according to media fill BMR.



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6.3 Stoppering unit setting:

- 6.3.1 Set the rubber stopper hopper on the machine.
- 6.3.2 Adjust the height of chute according to the vial size.
- 6.3.3 Place rubber stoppers inside the stopper hopper.
- 6.3.4 Switch ON the vibrator and adjust the vibrator with the help of knob to ensure the proper feeding of rubber stopper in rubber stopper chute.
- 6.3.5 Record the operation details in “**Filling of Machine Utilization Record**” in SOP of Titled “**Filling of Machine Utilization Record**”.

6.4 Filling Operation:

- 6.4.1 Operator shall check and ensure that powder hopper, powder wheel, pistons, piston tips, “O” ring, bung hopper, bung chute, railing guard, doctor blade, star wheel, vial separator pre & post nitrogen needle and silicon tube are as per vial size.
- 6.4.2 Set the empty vial for adjustment of powder dosing and bunging.
- 6.4.3 Operator shall check and ensure the availability nitrogen supply and adjust the Nitrogen pressure (limit 0.5 – 1.5 kg/cm²), purging gauge (pre nitrogen limit 0.5 Psi & post nitrogen limit 0.2 Psi).
- 6.4.4 Pass vial through conveyor rails to ensure line smoothness.
- 6.4.5 Press the inching button and adjust the speed of filling machine to match it with the same of the empty vial supplied under filling wheel.
- 6.4.6 Turn off all the switches before checking all parameter of the machine operation.
- 6.4.7 Vials handling section of the machine will be completely adjusted.
- 6.4.8 Set the infeed and outfeed Turn table speed for easy movement of feeding vials and receiving vials from the conveyor belt and transfer the vial on the sealing machine.
- 6.4.9 Initially, production & IPQA person shall check weight of 08 vials respectively. Ensure that weight of individual vial is within permissible weight limit, discard the in-process vials and record the same in respective BMR.
- 6.4.10 After getting line clearance from IPQA, filling operation shall be started.
- 6.4.11 In process check shall be done by production and IPQA person as per frequency mentioned in respective BMR.
- 6.4.12 During filling operation, check relative humidity, room temperature and fill weight at every hour.
- 6.4.13 If any excursion observed in environmental conditions, then handle the same as per SOP.



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6.5 Cleaning of Filling and Rubber Stoppering Machine:

- 6.5.1 Switch “OFF” the Mains and Machine.
- 6.5.2 Turn off the supply of Nitrogen Gas and Vacuum.
- 6.5.3 Dismantle filling parts: - Powder hopper, Powder Wheel, Pistons, piston tips, “O” Ring, bung hopper, bung chute, railing guard, doctor blade, star wheel, vial separator pre & post nitrogen needle and silicon tube etc. from filling and stoppering.
- 6.5.4 Cover the dismantled machine parts with Dacron bags and transfer it to equipment washing area through the dynamic pass box for cleaning.
- 6.5.5 Remove all the powder from the machine and outer surface of the machine using lint free cloth.
- 6.5.6 Clean all the guards, Machine body and conveyor belt, tunnel dead plate and turn table using WFI.
- 6.5.7 Clean all the guards, Machine body and conveyor belt, tunnel dead plate and turn table using 70% IPA.
- 6.5.8 Clean the surrounding area of the machine using scheduled disinfectant solution and 70% IPA.

6.6 Filling and Stoppering Machine Parts Cleaning:

- 6.6.1 Dismantle the powder hopper with docking system in below sequence:
 - 6.6.1.1 Open the clamp and disassemble the powder container.
 - 6.6.1.2 Detach the butterfly valve using LN key.
- 6.6.2 Dip the dismantled parts (e.g. Powder hopper, Powder hopper container, Butterfly valve powder wheel, pistons, piston tips, “O” Ring, bung hopper, bung chute, railing guard, doctor blade, star wheel, vial separator pre & post nitrogen needle and silicon tube) in PW for NLT 10 min.
- 6.6.3 Apply 0.1% non-ionic SLS soap solution on all parts and it by using nylon scrubber.
- 6.6.4 Wash all the dismantled parts thoroughly with Purified Water NLT 5min.
- 6.6.5 Wash all the dismantled parts with WFI NLT 5min.
- 6.6.6 Finally rinse the parts with WFI and intimate QA to collect the sample of final rinse water from Powder Filling and Sealing Machine change parts for Rinse water analysis.
- 6.6.7 After QA clearance dry all parts using 0.2 µ filtered compressed air.
- 6.6.8 Record the cleaning steps of filling and stoppering machine parts cleaning as per annexure-I.
- 6.6.9 Affix the ‘Status Label’ for cleaned status of the machine parts.



PHARMA DEVILS

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6.7 Record the cleaning details of vial filling and stoppering machine “**Filling of Machine Utilization Record**” in SOP Titled “**Filling of Machine Utilization Record**”.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure- I	Cleaning Checklist For Filling machine parts	
Annexure- II	Nitrogen Challenge Test	

ENCLOSURES: SOP Training Record

8.0 DISTRIBUTION:

- Controlled Copy No. 01 Quality Assurance
- Controlled Copy No. 02 Production
- Master Copy Quality Assurance

9.0 REFERENCES:

Not Applicable.

10.0 REVISION HISTORY:

CHANGE HISTORY LOG

Revision No.	Change Control No.	Details of Changes	Reason for Change	Effective Date	Updated By



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ANNEXURE – I CLEANING CHECKLIST FOR FILLING MACHINE PARTS

S.No.	CLEANING	STATUS
1.	Dip the dismantled parts in PW for NLT 10 min.	
2.	Apply 0.1% non-ionic SLS soap solution on all parts and it by using nylon scrubber.	
3.	Wash all the dismantled parts thoroughly with Purified Water.	
4.	Wash all the dismantled parts with WFI.	
5.	Finally rinse the parts with WFI and intimate QA to collect the sample of final rinse water from Powder Filling and Sealing Machine's change parts for Rinse water analysis.	
6.	After QA clearance dry all parts using 0.2 μ filtered compressed air.	
7.	Affix the 'Status Label' for cleaned status of the machine parts.	

* Put '√' mark if activity performed satisfactorily OR Put 'X' if the activity not performed.

Done By:
(Production Operator)
Sign and Date:

Checked By:
(Operating Person – Production)
Sign and Date:

Verified By:
(Operating Person - QA)
Sign and Date:



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ANNEXURE – II NITROGEN CHALLENGE TEST

Date	
Product Name	
Batch No.	

S.No.	Test Description	Observation (OK/ Not OK)	Done by (Sign. and Date)
1.	Decrease the pressure of nitrogen below 0.5 Kg/ cm ² ; the Vial filling machine should stop immediately.		

Checked By Production
(Sign and Date)

Verified By QA
(Sign and Date)