



PHARMA DEVILS

PRODUCTION DEPARTMENT

STANDARD OPERATING PROCEDURE

Department: Production	SOP No.:
Title: Operation and Cleaning of Ampoule Filling and Sealing Machine	Effective Date:
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1.0 OBJECTIVE:

To lay down a Procedure for Operation and Cleaning of Ampoule Filling and Sealing Machine.

2.0 SCOPE:

This SOP is applicable for Operation and Cleaning of Ampoule Filling and Sealing Machine, Twelve Heads, (**Make:** TruKing) in Production area at

3.0 RESPONSIBILITY:

Officer/Executive – Production

4.0 ACCOUNTABILITY:

Head – Production

5.0 DEFINITIONS:

Not Applicable

6.0 PROCEDURE:

6.1 CHECKS AND PRECAUTIONS:

6.1.1 Ensure that proper electric supply & earthing are provided to the Machine.

6.1.2 Ensure Oxygen, LPG & Nitrogen Supply is ON.

6.1.3 Ensure that each & every ampoule rotating Bearing is working properly.

6.1.4 Ensure that LAF is 'ON' and Pressure differential in Magnehelic Gauge is within Range.

6.1.5 Ensure that Temperature of filling area is NMT 25°C.

6.1.6 Before starting the filling operation, ensure the machine setting by using empty ampoules for following:

6.1.6.1 Filling nozzle shouldn't touch the tip of ampoules to avoid any friction which may lead to generation of glass particles.



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6.1.6.2 Filling nozzle should be in the center of tip to avoid any spiking / deposition of solution over the neck of ampoules (Which may lead to charring of solution and results in generation of black particles).

6.1.7 Ensure cleaning & sanitization of aseptic area done before activity.

6.2 MACHINE SET UP:

6.2.1 Transfer the sterilized machine parts from cooling zone to filling room through Mobile LAF.

6.2.2 Take the machine parts from mobile LAF & assembled machine parts step by step as per requirement aseptically under LAF.

6.2.3 Machine parts shall be assembled step by step in the below mentioned sequence.

6.2.3.1 Transfer the piston from mobile LAF trolley to filling machine under LAF.

6.2.3.2 Open the filling machine safety guard, and assemble the Pistons manifolds as below.



6.2.3.3 Connect the inlet of piston with manifolds outlet by sterilized silicon tubing as below.



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6.2.3.4 Connect the outlet of piston with filter needles shown as below.



6.2.3.5 Assemble Pre & Post Nitrogen needles manifold & connect the Nitrogen manifold outlet with needles by sterilized silicon tubing as below.



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- 6.2.3.6** Connect the nitrogen supply to Manifold inlet by using sterilized hydrophobic vent filter as shown below.
- 6.2.4** After that Manifold inlet connected with outlet of buffer tank using product dedicated silicon tube.
- 6.2.5** Set the ampoule height & proper sealing by adjusting the flame with empty ampoule and measuring the ampoule height by using vernier caliper / calibrated SS Scale.
- 6.2.6** Cutting of ampoules to be done as per following parameters.
- For ampoules of volume 1ml, height of ampoule will be 48.0mm +/- 2mm.
 - For ampoules of volume 2ml, height of ampoule will be 58.0mm +/- 2mm.
 - For ampoules of volume 3ml, height of ampoule will be 65.0mm +/- 2mm.
 - For ampoules of volume 5ml, height of ampoule will be 69.0mm +/- 2mm.
- 6.2.7** Check nitrogen supply from pre & post nitrogen needle and adjust Nitrogen flow rate as per BMR by using Rota meter.
- 6.2.8** Start the filling machine, and initially flush out the solution from filling needles and then adjust fill volume as per BMR.
- 6.2.9** Initially check the fill volume by using Calibrated Measuring Cylinder or pre sterilized disposal syringe.
- 6.3 FILLING OPERATION:**
- 6.3.1** Perform Challenge test of sensors before start of operation and after any break-down of machine.



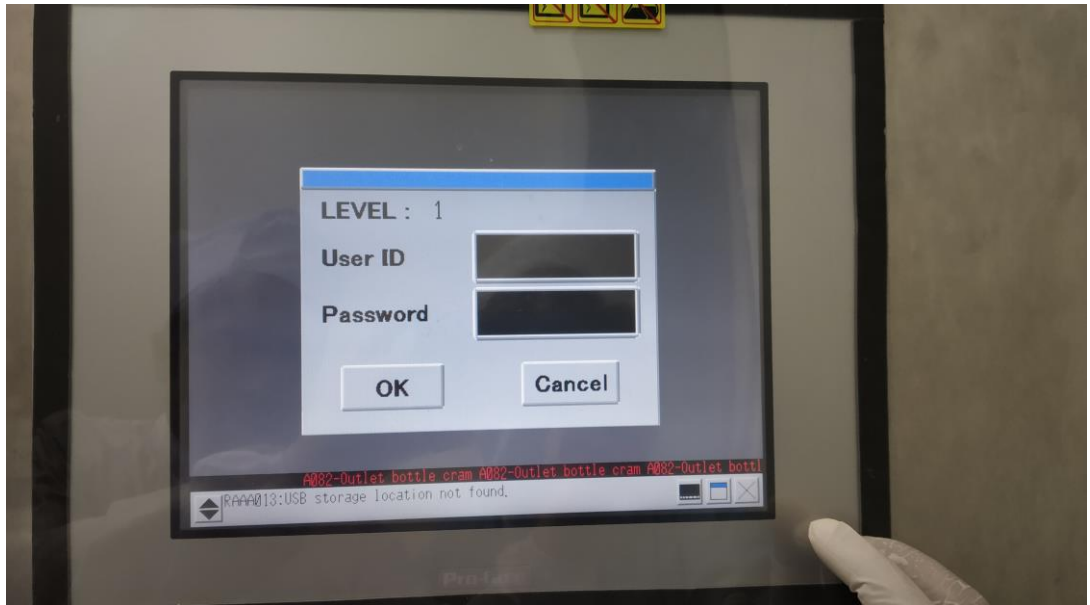
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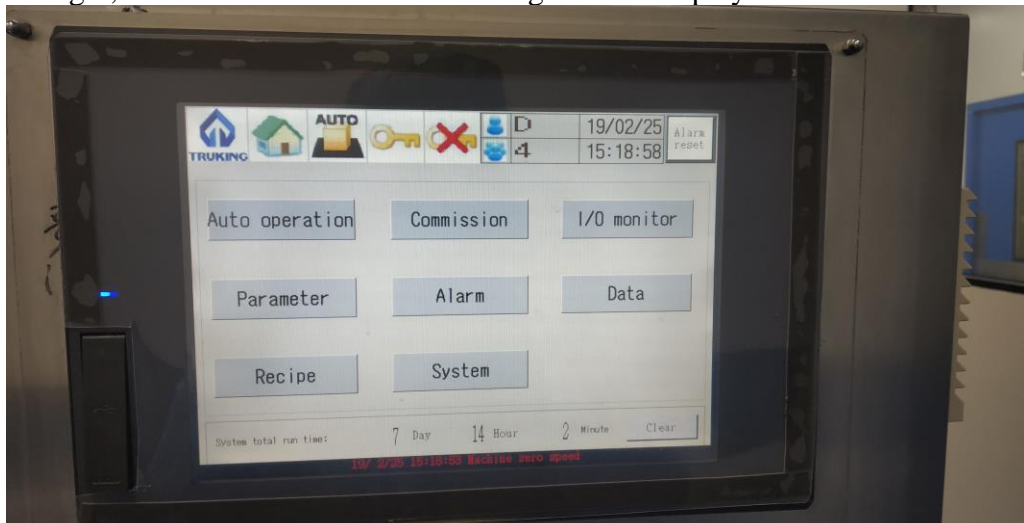
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- 6.3.2 Record the details of sensors challenge test in **Annexure-I**
- 6.3.3 Ensure that depyrogenated empty ampoules are ready for filling operation.
- 6.3.4 Ensure that Post BPT of first filtration complies. For filter used between compounding to holding vessel (Cartridge)
- 6.3.5 Switch On Machine. Following screen will get display, login the machine by user ID and password.



- 6.3.6 After Login, HMI screen will show following MENU display.



- 6.3.7 After selecting Auto –operation following display appear

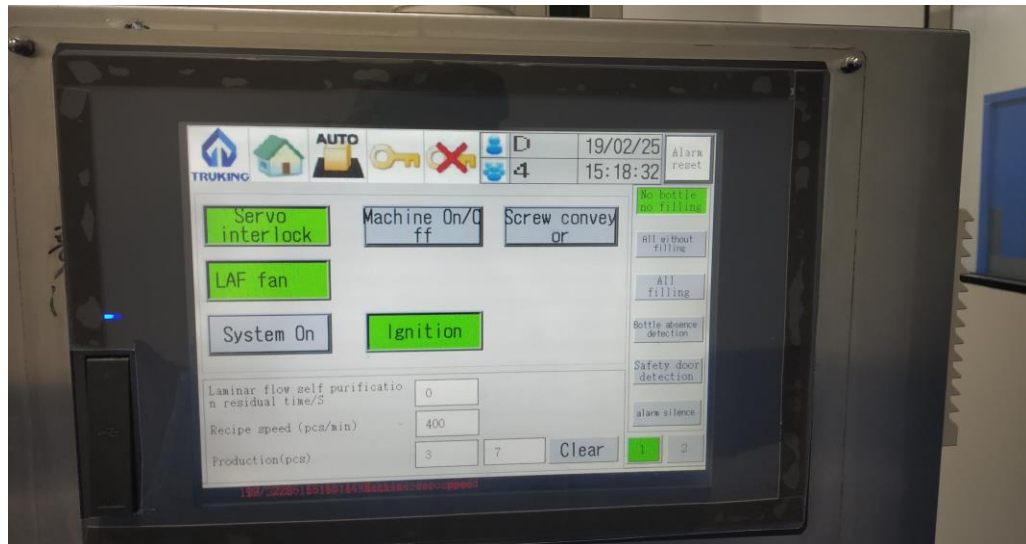


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- 6.3.8 Parameters settings and maintenance mode are allowed to run by authorized persons only.
- 6.3.9 Get detail of inputs and outputs.
- 6.3.10 Press Maintenance to check & run the machine equipments manually.
- 6.3.11 Press Parameters setting to set machine parameters.
- 6.3.12 After getting the required volume, check & adjust the pre and post Nitrogen flushing of the Ampoule.
- 6.3.13 Check the volume of ampoules from each needle respectively. Ensure volume of individual Ampoule is within permissible volume limit during initial setting as per BMR.
- 6.3.14 Adjust the oxygen and LPG using gas ON/OFF buttons for ampoule sealing.
- 6.3.15 Check the Sealed Ampoules for proper sealing.
- 6.3.16 Filled and Sealed Ampoules are collected in pre sterilized perforated SS trays.
- 6.3.17 Check the volume of each needle as per Batch Manufacturing Record.
- 6.3.18 Check the height of the Ampoule as per specification (Refer point no.6.2.6).
- 6.3.19 Record the operation details in Format Titled “**Equipment Log**” of SOP

6.4 CLEANING:

- 6.4.1 Switch off the electric supply of the machine



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- 6.4.2 Turn off the supply of nitrogen gas, oxygen gas and LPG.
- 6.4.3 Take filtered WFI in holding vessel and connected to final filter housing, and operate the filling machine and Flush out the WFI through filling needle
- 6.4.4 Dismantle the filling parts: - Syringes, Needles, Silicone Tubes etc. & transfer it to pre wash area through the Dynamic pass box for its cleaning and sterilization.
- 6.4.5 Remove the left over empty ampoules and transfer to pre wash area for destruction.
- 6.4.6 Remove all the spread solution from the outer and inner side of the machine
- 6.4.7 Take all unused filling machine parts and other accessories and transfer in to pre wash area.
- 6.4.8 Wipe all the guards, machine body & conveyor belt with WFI using lint free Moping pad
- 6.4.9 Clean all the guards, machinery & conveyor belt using 70% IPA solution spraying all over the Machine and by lint free Moping pad
- 6.4.10 Clean the surrounding area of the machine using disinfectant solution or and then sanitized the area as per SOP.
- 6.4.11 **CLEANING OF FILLING & SEALING MACHINE CHANGE PARTS (SYRINGES, NEEDLES, SILICONE TUBES ETC.):**
 - 6.4.11.1 Disconnect all machine parts, silicon tubes & needles.
 - 6.4.11.2 Connect each set of silicon tubing to manifold system installed in pre wash area and flush out purified water for 2 min. with pressure of WFI for 2 min with pressure.
 - 6.4.11.3 Clean the Manifolds & Needles individually with Purified water followed by WFI for 1 min each.
 - 6.4.11.4 Connect the inner side of manifold' to silicon tube and flush out with purified water for 2 min. & followed by WFI for 2 min.
 - 6.4.11.5 Dismantle all pistons and collect in a tray and dip in purified water and thoroughly cleaned by using lint free MOP.
 - 6.4.11.6 After cleaning with purified water, clean the pistons with WFI.
 - 6.4.11.7 Cleaning of Final filter and Filter housing shall be performed as per respective SOP.
 - 6.4.11.8 Cleaning process shall be verified by production & IPQA personnel and after proper cleaning, inspect the Machine Parts visually.



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6.4.11.9 IPQA person shall collect rinse water sample (if product change) for analysis.

6.4.11.10 After QA clearance, all machine parts and tubing to be sterilized in Autoclave as per validated load pattern.

6.4.11.11 If cleaned machine parts not used within 12 Hrs., then cleaning of machine parts shall be performed again before using as per above procedure.

6.4.11.12 Perform the cleaning of machine parts as per SOP and checklist details in Format Titled “Cleaning Checklist for Machine Parts”.

6.5 FREQUENCY:

Before use or every batch/product change over.

7.0 ABBREVIATIONS:

°C	Degree Centigrade
BPT	Bubble Point Test
ID No.	Identification Number
IPA	Isopropyl Alcohol
LAF	Laminar Air Flow
LPG	Liquid Petroleum Gas
Ltd.	Limited
Mm	millimeter
MMI	Man Machine Interface
No.	Number
QA	Quality Assurance
SOP	Standard Operating Procedure
SS	Stainless Steel
WFI	Water for Injection



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ANNEXURE-I

SENSOR CHALLENGE TEST RECORD

Frequency: Before Start of Operation and After Machine Break-Down

Date	Product Name	Batch No.	Sensor Details	Status (Ok / Not Ok)	Done By Sign & Date	Checked By Sign & Date	Verified By Sign & Date	Remarks
			No Ampoule No Filling Sensor					
			Counter Sensor					
			Nitrogen Pressure Low Sensor					
			Air Velocity Sensor					
			ORABS Sensor					