



# PHARMA DEVILS

PRODUCTION DEPARTMENT

## STANDARD OPERATING PROCEDURE

**Title:** Clean and Sterilization in Place of Blow-Fill and Seal Machine

<b>SOP No.:</b>		<b>Department:</b>	Production
		<b>Effective Date:</b>	
<b>Revision No.:</b>	00	<b>Revision Date:</b>	
<b>Supersede Revision No.:</b>	Nil	<b>Page No.:</b>	1 of 4

### 1.0 OBJECTIVE:

To lay down a procedure for clean and sterilization in place of blow-fill and seal machine.

### 2.0 SCOPE:

This SOP is applicable for Clean and sterilization in place of blow-fill and seal machine (Make: **Weiler engineering**) make **603** in production Area.

### 3.0 RESPONSIBILITY:

Officer / Executive - Production

### 4.0 ACCOUNTABILITY:

Head – Production

### 5.0 ABBREVIATIONS:

°C	Degree Celsius
CIP	Clean in place
BFS	Blow-Fill & Seal
GMP	Good Manufacturing Practice
LHS	Left Hand Side
PLC	Programmable Logic Controller
QA	Quality Assurance
QC	Quality Control
RHS	Right Hand Side
SS	Steam Sterilization
SOP	Standard Operating Procedure
SIP	Sterilization in place
WFI	Water For Injection
WHO	World Health Organization

### 6.0 PROCEDURE:

#### 6.1 PRECAUTIONS:

**6.1.1 For CIP-**Check and ensure that the WFI Line is connected/supply properly to the BFS Machine from holding tank.

**6.1.2 For SIP-** Ensure that the BFS Machine CIP done prior to SIP.

**6.1.3** Check & ensure that the Pure Steam Line is connected properly.

#### 6.2 PHILOSOPHY:

**6.2.1 For CIP-** Clean in Place is carried out to perform Product Line cleaning. Remove all the traces of previous product from the machine pipe lines and all contact parts.



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**6.2.2** The CIP of the BFS Machine shall be performed for minimum 1800 sec or required more on basis of cleaning validation or until conductivity of final rinse not achieved, which is installed in drain line of BFS M/c.

**6.2.3** The CIP shall be performed during Batch Changeover/Before SIP or whenever its required.

**6.2.4 For SIP-** The Sterilization in Place is carried out at a temperature above than 121°C for 1800 sec to remove microbiological contamination and reduce the bio load using by Moist Steam.

**6.2.5** The Blow Down program (Filter Drying) requires 1800 sec for successful completion of the Filter Drying program.

**6.2.6** The SIP shall be performed during Batch Changeover/machine break down more than 6 Hrs/or whenever its required.

### 6.3 PROCEDURE:

**6.3.1 CIP and SIP** - of blow Fill and Seal Machine shall involves: Product Line Cleaning [Includes Cleaning of SS 316L Pipeline of product contact parts, Cleaning along with SS Housings, Air Filters installed over the BFS M/C, Filling Mandrels etc.

**6.3.2 VLC-** Vacuum Line Cleaning & Mould Cleaning.

### 6.4 PRODUCT LINE CLEANING IN PLACE(CIP):

**6.4.1** Ensure that the WFI Line attached to the BFS Machine (Product Line).

**6.4.2** Move the Mould carriage to Parison (back position) position.

**6.4.3** Operate the filling head and to down position.

**6.4.4** Attach the steam cups from its resting position and fix it on to the filling head.

**6.4.5** Select the Cleaning Program.

**6.4.6** Start the product pump of holding vessel to supply the WFI from holding vessel to BFS machine.

**6.4.7** Remove air pocket from the filter housing through vent valve for effective cleaning process.

**6.4.8** Let WFI flows and clean all those parts which come in to its contact from Holding area line to M/C, entire product line and drain it out till conductivity not achieved or found < 1.3 µs.

**6.4.9** Intimate the QA Officer / Executive to collect the Sample of Rinse Water at drain point after Product Line cleaning and send to QC for Analysis.

**6.4.10** Take line clearance for SIP and Start the SIP of BFS machine after completion of CIP.

**6.4.11** Record the CIP Operation Details in respective log book, and respective Batch Production and Control Record. Attach the CIP result in BMR as it complies from QC.



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### 6.5 PRODUCT LINE STERILIZATION IN PLACE(SIP):

- 6.5.1 Insure the availability of the Pure Steam supply to BFS m/c and product line both.
- 6.5.2 Attach the Filling Mandrel steam cups before starting the SIP procedure.
- 6.5.3 Open the Pure Steam Valve gradually, now pure steam is available to the Machine, set the Steam Pressure not exceeding 2.5 bars by manual valve.
- 6.5.4 Switch "ON" the Machine for the Sterilization cycle.
- 6.5.5 As soon as Steam is opened and flows through all Product Lines and also from Filling Nozzle, Blow Filter (Air Vent Filter) etc.
- 6.5.6 When the pre-set time reaches Sterilization elapsed message is displayed.
- 6.5.7 When the Steam temperature reaches at the set point of 121°C (sensed by all temperature Probes installed at 16 different locations in BFS m/c) the Sterilization Time starts for 1800 SEC.

PROBE Nos.	PROBE LOCATIONS
1	Steam inlet temp
2	Product filter 1 drain temp
3	Product filter 1 vent temp
4	Product filter 2 drain temp
5	Product filter 2 vent temp
6	Buffer tank filter drain temp
7	Buffer tank filter vent temp
8	Vent line temp
9	Steam cup drain temp
10	Blow filter drain temp
11	Fill nozzle blowing line temp-1
12	Fill nozzle blowing line temp-2
13	Blow filter outlet temp
14	Balloon filter drain temp
15	Balloon filter out let temp
16	Blow fill vent temp

- 6.5.8 Close the Steam Inlet Valve and intimate for stop the pure steam supply.
- 6.5.9 After completion of Sterilization, select the FILTER DRYING program from the Machine PLC for FILTER DRYING.
- 6.5.10 After completion of 'FILTER DRYING' select the program if heating.



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**6.5.11** LAF blower will automatically start after completion of 'FILTER DRYING' Cycle to maintain Class-100.

**6.5.12** Remove the Filling Mandrel steam cups and keep at designated place.

**6.5.13** Record the SIP Operation Details in respective log book and attaché the print out in respective Batch Production and Control Record.

### 6.6 VACUUM LINE CLEANING & MOLD CLEANING:

**6.6.1** This is carried out in case of Vacuum System with Product OR whenever required.

**6.6.2** The Vacuum Line Cleaning & Mold Cleaning shall be performed using Manual Operation Mode only.

**6.6.3** Remove the Vacuum Line and Connect the WFI Line. Ensure that the TC Clamp is connected properly and tight.

**6.6.4** Open the WFI Valve.

**6.6.5** Clean the Mold (Head Mold / Seal Mold, Main Mold and Holding Jaw) using WFI.

**6.6.6** Stop the Supply of Water For Injection.

**6.6.7** Empty the Vacuum Lines for 05 minutes by switching on the Vacuum Pump.

**6.6.8** Record the Vacuum Line Cleaning & Mold Cleaning operation details in respective m/c break down record.

### 7.0 ANNEXURES:

Not Applicable

**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:

- WHO & GMP

### 10.0 REVISION HISTORY:

#### CHANGE HISTORY LOG

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