PHARMA DEVILS

QUALITY CONTROL DEPARTMENT

STANDARD OPERATING PROCEDURE	
Department: Quality Control	**SOP No.:**
Title: Post Media Fill Cleaning and Startup of Production Line	**Effective Date:**
Supersedes: Nil	**Review Date:**
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1.0 OBJECTIVE:

To lay down a procedure for Post Media Fill Cleaning and Startup of Production Line.

2.0 SCOPE:

This SOP is applicable for Cleaning and Start-up of Production Line after Completion of Media Fill activity.

3.0 RESPONSIBILITY:

Officer / Executive – Production & QC (Microbiology)

4.0 ACCOUNTABILITY:

Head - Production

5.0 ABBREVIATIONS:

CIP	Clean in Place
IPA	Isopropyl Alcohol
LDPE	Low Density Polyethylene
Ltr.	Liter
No.	Number
QA	Quality Assurance
QC	Quality Control
SIP	Sterilization in Place
SOP	Standard Operating Procedure
SS	Stainless Steel
TOC	Total Organic Carbon
WFI	Water for Injection

6.0 PROCEDURE:

6.1 After Completion of Media Fill activity, Collect the used gown, hand gloves, mops, used Product filter and vent filters from Holding tank in a poly bag and send for destruction along with status label.

6.2 Used garments, Hand gloves & mop shall be cut into pieces vertically to make it unfit for reuse.

6.3 Product filter shall be sent to Microbiology Lab for sterilization and further destruction.

6.4 Remaining media solution shall be sent to Microbiology for decontamination in suitable SS Bin.

6.5 CLEANING & STERILIZATION OF COMPOUNDING VESSEL / HOLDING VESSEL:

6.5.1 Cleaning of vessel shall be carried out immediately after transfer of complete media for further process without any hold.

6.5.2 Compounding/Holding Vessel shall be filled with Water for Injection (Approx. 40% of Vessel Capacity or 100 Litre whichever is less).

6.5.3 Run the stirrer for 15 minutes (If vessel having stirrer) or and collect the drain in separate vessel.

Note: In case vessel doesn't have the stirrer facility, drain the WFI immediately and collect the rinse in separate vessel.

6.5.4 Add the NaOH into the collected rinse necessary get the pH between 8.0 - 10.0.

6.5.5 Check the pH of rinse and drain the solution in drain.

6.5.6 Sanitize the drain point as per respective SOP.

6.5.7 Perform the CIP & SIP of vessels as per SOP.

6.5.8 Printout of CIP & SIP cycle to be verified for proper cleaning and Sterilization parameters.

6.5.9 After successful completion of CIP of vessel, rinse shall be taken from vessel and shall be sent to Microbiology for bio burden analysis and Quality Control lab for pH, Conductivity and TOC Analysis.

6.5.10 For another 2 consecutive days CIP & SIP of vessels shall be performed and printouts shall be verified for accuracy of cleaning and sterilization process and rinse sample shall be sent to Microbiology for bio burden analysis and Quality Control lab for pH, Conductivity and TOC Analysis.

6.5.11 In case of Dry powder injection line, Media vessel shall be sent to Microbiology lab along with remaining media after decontamination of outer surface by 2.5% of NaOCl solution for further decontamination and discarding.

6.6 CLEANING & STERILIZATION OF FILLING / SEALING MACHINE PARTS, UNUSED PRIMARY PACKAGING MATERIAL:

6.6.1 Immediately after Completion of Filling operation, dismantle the silicone tubes and dip into 5% Acitar solution for 10 minutes and transfer to unit preparation area.

6.6.2 Allow the Silicone tubing in 5% Acitar solution for 10 minutes.

6.6.3 Remove the silicone tubing from disinfectant solution and dip in to another bucket having NaOH solution (pH 8.0 – 10.0) for 15 minutes and drain the disinfectant solution in drain.

6.6.4 After 15 minutes, drain the NaOH solution in drain trap followed by sanitization of drain as per respective SOP.

6.6.5 Cut the silicone tubes to make it unfit for further use and collect in poly bag and Send for further discarding with status label.

6.6.6 Machine Parts shall be dismantled and Media contact parts of machine shall be dipped immediately into 5% Acitar solution for 10 minutes and transfer to unit preparation area.

6.6.7 Non-contact parts of machine shall be transferred to Unit preparation area and shall be dipped in 5% Acitar solution for 10 minutes.

6.6.8 Keep the Machine Parts in 5% Acitar solution for 10 minutes.

6.6.9 Remove the Machine parts from disinfectant solution and sanitize with 70% IPA.

6.6.10 Drain the remaining disinfectant solution through drain point followed by sanitization of drain point as per respective SOP.

6.6.11 Clean the Machine parts as per respective SOP for Cleaning. Collect the rinse and send to QC for pH, Conductivity, TOC and Bioburden analysis.

6.6.12 Sterilization of machine parts shall be performed as per respective SOP.

6.6.13 Sterilization printout of autoclave shall be checked for accuracy of sterilization process.

6.6.14 Microbiologist shall be informed to collect the swab samples of sterilized machine parts.

6.6.15 For another 2 consecutive days cleaning and sterilization of machine parts shall be performed and autoclave printouts shall be verified for accuracy of sterilization process.

6.6.16 Remaining rubber bungs, Vials / Ampoules & flip off seals, LDPE bottles. three piece bottles, plastic nozzles, plastic caps & FFS vials shall be sent to Unit preparation area and dip in 5% Acitar solution for 10 minutes and drain the disinfectant solution in drain point.

6.6.17 All primary packaging material shall be collected in a poly bag and sent to scrap yard for destruction.

6.7 CLEANING & SANITIZATION OF AREA:

6.7.1 Cleaning and Sanitization of Aseptic area, manufacturing area and unit preparation area shall be performed as per respective SOP.

6.7.2 Mounted parts of Equipment i.e. Platform of Filling and Sealing machine / Dynamic Pass Box / Autoclave surface inside and outside of aseptic area, Laminar Air Flow etc shall be cleaned with 70% IPA solution as per SOP twice.

6.7.3 After complete cleaning of area, Fogging shall be performed as per respective SOP.

6.7.4 After fogging, Microbiologist shall performed Microbiological environmental monitoring of area as per respective SOP.

6.7.5 Cleaning, fogging and Microbiological Monitoring of area shall be continued for consecutive three days in static condition.

6.8 Microbiological monitoring of drain point shall be performed for 3 days.

6.9 Record the details of Post Media fill cleaning for Liquid Injection line as per format "**Post Media Fill Cleaning Record for Liquid Injection Line**" as shown in **Annexure-I**.

6.10 Record the details of Post Media fill cleaning for Dry Powder Injection line as per format "**Post Media Fill Cleaning Record for Dry Powder Injection Line**" as shown in **Annexure-II**.

6.11 On the basis of 3 consecutive days CIP / SIP cycle of vessels & machine parts, cleaning and sanitization of area etc. and based on the 72 Hrs. (Third Day) microbiological observations of first day Settle Plate Exposure, production line shall be allowed for routine production activity.

6.12 ACCEPTANCE CRITERIA:

6.12.1 Rinse sample should comply the specification of Water for Injection for Bioburden, pH, Conductivity and TOC.

6.12.2 Swab samples of sterilized machine parts should comply the sterility test.

6.12.3 Area Environmental monitoring should comply as per respective SOP.

6.13 In case any non-compliance of any test result, Product manufactured after media fill shall be put on hold and further decision shall be taken based on the investigation findings.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Post Media Fill Cleaning Record for Liquid Injection Line	
Annexure-II	Post Media Fill Cleaning Record for Dry Powder Injection Line	

8.0 DISTRIBUTION:

- Controlled Copy No. 01 Head Quality Assurance
- Controlled Copy No. 02 Head Production
- Controlled Copy No. 03 Head Warehouse
- Controlled Copy No. 04 Head Quality Control
- Controlled Copy No. 05 Head Engineering
- Master Copy Quality Assurance Department

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

POST MEDIA FILL CLEANING RECORD FOR LIQUID INJECTION LINE

Activity	Done By (Production / QC) Sign & date	Checked By (QA) Sign & Date
Collection of Garments/Component Exposed during Media Fill:		
Used garments, Hand gloves & mop shall be cut into pieces vertically to make it unfit for reuse		
Collect all gaskets, media filters and vent filters and sent to be Microbiology Lab for discarding.		
Remaining media solution of batch sent to be Microbiology for decontamination		
Cleaning & Sterilization of Compounding Vessel:		
Initial flush of compounding vessel with WFI approx 40% of vessel capacity or 100 Ltr. whichever is less.		
Collect initial flush of WFI of compounding vessel in separate vessel		
Add the NaOH to rinse (flush) of vessel		
Check the pH of rinse (pH 8.0 - 10)		
Drain the rinse (flush) solution in drain point		
Sanitize the drain point as per respective SOP		
CIP of Compounding vessel		
Verify the CIP printout		
SIP of Compounding vessel		
Verify the SIP printout		
Collect the rinse sample from compounding vessel and sent to Microbiology lab for Bioburden & Quality Control lab for pH, Conductivity and TOC Analysis.		
For another 2 consecutive days CIP & SIP of compounding vessels shall be performed.		
Verify the printouts of CIP & SIP.		
Cleaning & Sterilization of Holding Vessel:		
Initial flush of holding vessel with WFI approx 40% of vessel capacity or 100 Ltr. whichever is less.		
Collect initial flush of WFI of holding vessel in separate vessel		
Add the NaOH to rinse (flush) of vessel		
Check the pH of rinse (pH 8.0 - 10)		
Drain the rinse (flush) solution in drain point		
Sanitize the drain point as per respective SOP		
CIP of Holding vessel		
Verify the CIP printout		

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Activity	Done By (Production / QC) Sign & date	Checked By (QA) Sign & Date
SIP of Holding vessel		
Verify the SIP printout		
Collect the rinse sample from holding vessel and sent to Microbiology lab for Bioburden & Quality Control lab for pH, Conductivity and TOC Analysis.		
For another 2 consecutive days CIP & SIP of holding vessel shall be performed.		
Verify the printouts of CIP & SIP.		
Cleaning & Sterilization of Filling / Sealing Machine Parts, unused Primary Packaging Material:		
Dismantle the silicone tubes after completion of filling operation.		
After dismantle silicone tubes dip into 5% Acitar solution for 10 minutes and transfer to unit preparation area		
Remove the silicone tubing from disinfectant solution		
Dip the Silicone tubing in to another bucket having NaOH solution (pH 8.0 – 10.0) for 15 minutes		
After 15 minute, drain the NaOH solution in drain trap followed by sanitization of drain		
Cut the silicone tubes and collect in poly bag and Send for further discarding with status label		
Machine Parts shall be dismantled and Media contact parts of machine shall be immersed into 5% Acitar solution for 10 minutes and transfer to unit preparation area		
Non-contact parts of machine shall be transferred to Unit preparation area and shall be dipped in 5% Acitar solution for 10 minutes.		
Remove the Machine parts from disinfectant solution and sanitize with 70% IPA		
Drain the remaining disinfectant solution through drain point followed by sanitization of drain point.		
Clean the Machine parts as per respective SOP for Cleaning. Collect the rinse and send to QC for pH, Conductivity, TOC and Bioburden analysis.		
Sterilization of machine parts shall be performed as per respective SOP.		
Verify the Sterilization printout		
Collect the swab samples of sterilized machine parts by Microbiologist		
For another 2 consecutive days cleaning and sterilization of machine parts shall be performed		
Verify the autoclave printouts for accuracy of sterilization process		
Remaining rubber bungs, Vials / Ampoules & flip off seals, LDPE bottles. three piece bottles, plastic nozzles, plastic caps & FFS vials shall be sent to Unit preparation area and dip in 5% Acitar solution for 10 minutes.		

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Activity	Done By (Production / QC) Sign & date	Checked By (QA) Sign & Date
All primary packaging material collect in a poly bag and sent to scrap yard for destruction		
Cleaning & Sanitization of Area:		
Cleaning and Sanitization of Aseptic area, manufacturing area and unit preparation area shall be performed as per respective SOP		
Mounted parts of Equipment i.e. Platform of Filling and Sealing machine / Dynamic Pass Box / Autoclave surface inside and outside of aseptic area, Laminar Air Flow etc shall be cleaned with 70% IPA solution as per SOP twice		
After complete cleaning of area, Fogging shall be performed as per respective SOP		
After cleaning, fogging, Microbiologist shall performed Microbiological environmental monitoring of area as per respective SOP for consecutive three days in static condition.		

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ANNEXURE-II

POST MEDIA FILL CLEANING RECORD FOR DRY POWDER INJECTION LINE

Activity	Done By (Production / QC) Sign & date	Checked By (QA) Sign & Date
Collection of Garments/Component Exposed during Media Fill:		
Used garments, Hand gloves & mop shall be cut into pieces vertically to make it unfit for reuse		
Collect all gaskets & vent filters sent to be Microbiology Lab for discarding.		
Remaining media solution of batch sent to be Microbiology for decontamination		
Media Vessel Cleaning:		
Dismantle the silicone tubes after completion of filling operation.		
After dismantle silicone tubes dip into 5% Acitar solution for 10 minutes and transfer to unit preparation area		
Cleaning & Sterilization of Filling / Sealing Machine Parts, Unused Primary Packaging Material:		
Dismantle the silicone tubes after completion of filling operation.		
After dismantle silicone tubes dip into 5% Acitar solution for 10 minutes and transfer to unit preparation area		
Remove the silicone tubing from disinfectant solution		
Dip the Silicone tubing in to another bucket having NaOH solution (pH 8.0 – 10.0) for 15 minutes		
Drain the NaOH solution in drain trap followed by sanitization of drain		
Cut the silicone tubes and collect in poly bag and Send for further discarding with status label		
Machine Parts shall be dismantled and Media contact parts of machine shall be immersed into 5% Acitar solution for 10 minutes and transfer to unit preparation area		
Non-contact parts of machine shall be transferred to Unit preparation area and shall be dipped in 5% Acitar solution for 10 minutes.		
Remove the Machine parts from disinfectant solution and sanitize with 70% IPA		
Drain the remaining disinfectant solution through drain point followed by sanitization of drain point.		
Clean the Machine parts as per respective SOP for Cleaning. Collect the rinse and send to QC for pH, Conductivity, TOC and Bioburden analysis.		
Sterilization of machine parts shall be performed as per respective SOP.		
Verify the Sterilization printout		
Collect the swab samples of sterilized machine parts by Microbiologist		
For another 2 consecutive days cleaning and sterilization of machine parts shall be performed		
Verify the autoclave printouts for accuracy of sterilization process		

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Activity	Done By (Production / QC) Sign & date	Checked By (QA) Sign & Date
Remaining rubber bungs, Vials & flip off seals shall be sent to Unit preparation area and dip in 5% Acitar solution for 10 minutes.		
All primary packaging material collect in a poly bag and sent to scrap yard for destruction		
Cleaning & Sanitization of Area:		
Cleaning and Sanitization of Aseptic area and unit preparation area shall be performed as per respective SOP		
Mounted parts of Equipment i.e. Platform of Filling and Sealing machine / Dynamic Pass Box / Autoclave surface inside and outside of aseptic area, Laminar Air Flow etc shall be cleaned with 70% IPA solution as per SOP twice		
After complete cleaning of area, Fogging shall be performed as per respective SOP		
After cleaning, fogging, Microbiologist shall performed Microbiological environmental monitoring of area as per respective SOP for consecutive three days in static condition.		