STANDARD OPERATING PROCEDURE

Title: Cleaning, Sterilization, Usage, Replacement and Integrity Testing of Filters

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

To lay down a procedure for Cleaning, Sterilization, Usage, Replacement and Integrity Testing of Filters.

2.0 SCOPE:

This SOP is applicable for Cleaning, Sterilization, Usage, Replacement and Integrity Testing of Filters of Hydrophilic and Hydrophobic in production Department.

3.0 RESPONSIBILITY:

Operating Person: Production

4.0 ACCOUNTABILITY:

Head Production

5.0 ABBREVIATIONS:

BPT	Bubble Point Test
IPA	Isopropyl Alcohol
Ltd.	Limited
Pvt.	Private
QA	Quality Assurance
QMS	Quality Management System
SOP	Standard Operating Procedure
WFI	Water for Injection
%	Percent
No.	Number
BFS	Blow-Fill & Seal
FFT	Forward Flow Test
M/C	Machine
NA	Not Applicable
SHWSS	Super-Heated Water Spray Sterilizer
WIT	Water Intrusion Test

6.0 PROCEDURE:

6.1 Precautions for Cleaning:

6.1.1 Handle the Filter carefully to avoid any possible damage / extraneous contamination.

6.1.2 Never remove the filters from line when it is in under operation.

6.1.3 Filter should be clean with their respective cleaning agent.

6.1.4 When observed any physical damage, filter should be replaced by new one and discard the damaged filter.

6.2 Cleaning and Sterilization of Filters:

6.2.1 Clean the filter housing with WFI.

6.2.2 Take out the Filter & Dip into 70%/60% IPA solution (Hydrophobic).

6.2.3 Clean the filter with WFI by flushing of WFI in case of hydrophilic Cartridge only.

6.2.4 Dry the filter by flushing of Compressed Air.

6.2.5 Perform the Sterilization process of the Cartridge filters as per respective SOP.

6.2.6 Record the filter cleaning, and sterilization cycle details mentioned in **Annexure-I**.

6.3 Filter Usage Policy:

6.3.1 Filter shall be used after satisfactory result of BPT/WIT.

6.3.2 Filter shall be used after insuring the pore size of filter as per requirement.

6.4 Procedure of Changing of Hydrophobic / Hydrophilic Cartridge Filters:

6.4.1 Ensure the availability of the following:

- Palltronic m/c
- Hydrophobic Cartridge Filter
- Filter Housing
- Water for injection
- 0.22µ filtered Compressed Air (6 Kg/cm^2)
- Power Supply (220V)

6.4.2 Hydrophobic Filters for BFS m/c (Blowing air, Ballooning air, Buffer air filters), Autoclaves (Garment/SHWSS), For mixing, Holding tank air vent, Air- line, Nitrogen line, Disinfectant air line:

6.4.3 Hydrophilic Filters for Mixing to Holding tank, (1.2µ, 0.65 µ, and 0.22µ) and on BFS machine (Two 0.22µ filters).

6.4.3.1 Check the cartridge filter integrity test (WIT, BPT & FFT) as per SOP of hydrophobic and Hydrophilic cartridge filters.

6.4.3.2 Maximum 80 SIP cycles permissible or as per its literature in Hydrophobic filters.

6.4.3.3 Maximum 25 SIP cycles permissible for Capsule Hydrophobic filters.

6.4.3.4 Maximum 25 SIP cycles permissible or as per its literature in Hydrophilic filters.

6.4.3.5 The smooth working of the m/c requires appropriate flow rate of filtered air, filter can be replace if physical condition is not proper (color change) while integrity of filter found ok.

6.4.3.6 Record the Filter Integrity Testing/Sterilization/Destruction Record, in **Annexure-I.**

6.5 Frequency of Filter Changing:

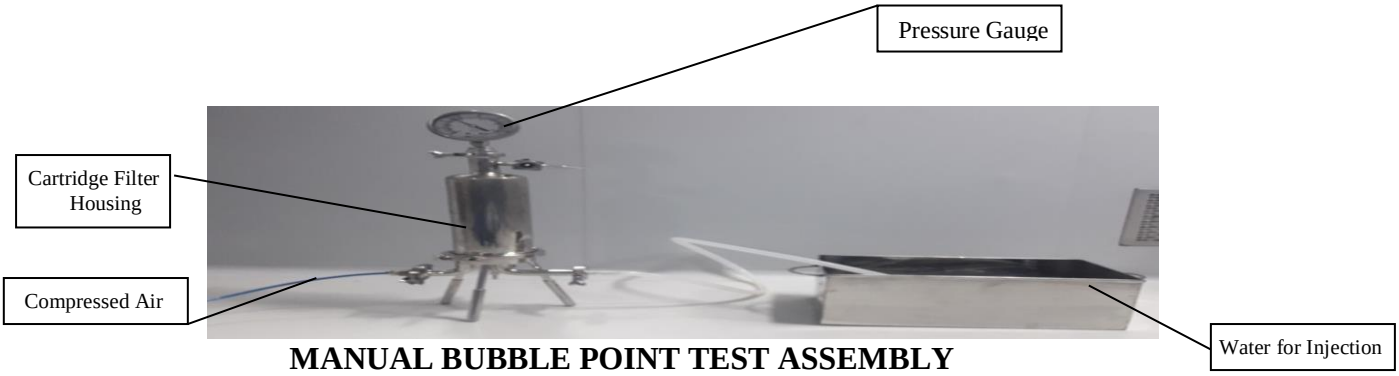
6.5.1 Whenever the WIT / BPT/ FFT, recommended three consecutive test fails.

6.5.2 Whenever there is slow filtration rate during the operation.

6.5.3 Whenever SIP cycles are over.

6.5.4 Whenever depend upon filter physical appearance.

6.6 Manual Integrity Testing of Cartridge, Capsule and Air Vent Filter:



MANUAL BUBBLE POINT TEST ASSEMBLY

6.6.1 Connect a piece of flexible tubing from the downstream port of the filter and another end of the flexible tube open in a container filled with water.

6.6.2 Connect the air pressure to the inlet of housing OR filter inlet in case of capsule/vent filter.

6.6.3 Slowly open the air supply, as per their minimum bubble pressure mentioned in **Annexure –II** and stabilizes for two minutes.

6.6.4 If no continuous stream of bubbles comes out from the cartridge outlet in Water for Injection (up to pressure mentioned in Annexure -II) the filter passes the test.

6.6.5 Disconnect the air supply and release the pressure by opening of release knob.

6.6.6 Record the testing details at specified place in relevant BMR respectively.

6.6.7 List of integrity test value of filters as shown in **Annexure-II**.

6.7 Frequency of Integrity Testing.

6.7.1 For Hydrophilic Filter (BPT/WIT) Pre and Post of Filtration or after completion of batch/ batch campaign.

6.7.2 For Hydrophobic Filters (WIT/BPT/FFT), (Air Vent Filter on Manufacturing Holding Tank, Filling machine, SHWSS, HPHV, N_2 line) – 15 day ±02 day.

6.7.3 Record the Filter Integrity Test/Sterilization cycle in **Annexure-I.**

6.8 Precautions:

6.8.1 During handling of cartridge filter, take precaution to avoid any damage / contamination of the cartridge filter / air- line.

6.8.2 After post integrity of particular cartridge filter, flush the filter with Water for Injection at Room Temperature for 10-15 minutes. After this dry the cartridge filter with filtered compressed air for 15-20 minutes at pressure of 1.0 to 1.5 kg/cm^2.

6.8.3 Ensure the proper drying of the filter and wrap the filter with bio-barrier paper.

6.8.4 Mention the product generic name, lot number and serial number of the filter on bio-barrier paper.

6.8.5 Store this filter in the designated storage cabinet.

6.9 Filter Storage Policy (Dedicated filter):

6.9.1 After Post-CIP / Flushing, dismantle filter for post integrity.

6.9.2 After completion of Integrity, dry the filter under Bench LAF in Cool Zone area.

6.9.3 Then Kept and store under LAF Cabinet for storage at tool room area as per molecule wise.

6.9.4 Before use of Filter it shall be clean with WFI & Check the pre integrity.

6.9.5 If any filter not used till 3 months then again filter shall be clean with WFI and sterilize it in the respective line, after drying, can be store for next 3 month.

6.9.6 If any filter stored and not use within 6 months or before its expiry, shall be discarded.

6.9.7 This dedicated filter storage policy shall be applicable for the each active molecule.

6.9.8 Hydrophilic / Hydrophobic filter's expiry consider for 5 Years. (As per vendor recommendations or its Literature).

6.10 During the breakdown of the Filter Integrity Machine in L-Block.

6.10.1 If the Integrity of the testing machine is malfunctioning, integrity of cartridge filter can be performed on integrity testing machine installed in other Section/Block using recipe for the respective filter. Data will be recorded in respective log book.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Filter Integrity Testing/Sterilization/Destruction Record	
Annexure-II	BPT/WIT Value For Hydrophobic And Hydrophilic Filters.	
Annexure-III	Location of Hydrophobic and Hydrophilic Filters .	

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
FILTER INTEGRITY TESTING/STERILIZATION/DESTRUCTION RECORD

Location of filter ……
Filter Make ……
Type of Filter ……
Filter Lot No. /Filter part no. ……
Filter Sr. No. ……
Date of Installation ……

Product Name: ……
Filter size/pore size: ……
Expiry Date: ……

Date	Type of Filter	Cleaning Time		Done By	Integrity		Done By	Sterilization Time		Cumulative Sterilization Cycle No.	Destruction By	Checked By Production	Verified By QA
		From	To		From	To		From	To				

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ANNEXURE-II
BPT/WIT VALUE FOR HYDROPHOBIC AND HYDROPHILIC FILTERS

S.No	Type of Filter	Make	Pore Size	Cat. No. / Lot No.	MOC	Size	WIT/BPT	WIT/BPT	Max. Sterilization Cycle.
01	Hydrophilic	Pall	0.2µ		PVDF	10”	BPT	2760 mbar	25
02	Hydrophilic	Millipore	0.2µ		PVDF	30”	BPT	3100 mbar	25
03	Hydrophilic	Sartorius	0.45µ+0.2µ		PES	10”	BPT	3200 mbar	25
04	Hydrophilic	Sartorius	0.45µ+0.2µ		PES	30”	BPT	3200 mbar	25
05	Hydrophobic	MDI	0.2µ		PTFE	5”	WIT/BPT	≤6.0 ml/10 min at 2.0 kg/cm^2, 1520 mbar	80
06	Hydrophobic	Pall	0.2µ		PTFE	5”	WIT/BPT	0.16 ml/min, 2500 mbar	80
07	Hydrophobic	Pall	0.2µ		PTFE	10”	WIT/BPT	5.5 ml/min, 1100 mbar	80
08	Hydrophobic	MDI	0.2µ		PTFE	20”	WIT/BPT	≤ 2.6 ml/min, 2000 mbar	80
09	Hydrophobic	Pall	0.2µ		PTFE	20”	WIT/BPT	≤ 0.16 ml/min, 1380 mbar	80
10	Hydrophobic	MDI	0.2µ		PTFE	10”	WIT/BPT	≤ 0.16 ml/min, 1520 mbar	80
11	Hydrophobic	Pall	0.2µ		PTFE	10”	WIT/BPT	≤ 5.5ml/min, 1100 mbar	80
12	Hydrophilic	Millipore	0.2µ		PVDF	10”	BPT	3100 mbar	25

13	Hydrophobic	Millipore	0.2µ		PTFE	5”	BPT	1100 mbar	80
14	Hydrophilic	MDI	0.2µ		PES	10”	BPT	3400 mbar	15
15	Hydrophobic	Millipore	0.2µ		PTFE	10”	BPT	1100 mbar	80
16	Hydrophobic	Sartorius (Capsule).	0.2µ		PTFE	5”	WIT	≤ 3.0 ml/min	25
17	Hydrophilic	Millipore	0.2µ		PVDF	20”	BPT	3100 mbar	25

Note: If any other filter use which is not mention in this Annexure, we can use the related literature of the filter for reference.

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ANNEXURE-III
LOCATION OF HYDROPHOBIC AND HYDROPHILIC FILTERS

Filter Type: Hydrophilic **Block:** LVP

S.No.	Location of filter	Pore size, Nos., Filter Size (inch)	Filter shape
1	On BFS machine (Filling Room)	0.2 (µ) , 2Nos , 10"	Cartridge
2	Mfg. to Holding (Filtration Room)	0.2 (µ) , 1Nos (10"/20"/30")	Cartridge
3	Disinfectant Filter	0.2 (µ) , 1Nos , 10"	Cartridge

Filter Type: Hydrophobic

4	Compress Airline filter mfg.01	0.2 (µ),1Nos,5"	Cartridge
5	HPHV autoclave vent filter	0.2 (µ),1Nos,5"	Cartridge
6	Manufacturing line N_2 Filter	0.2 (µ),1Nos,5"	Cartridge
7	Holding N_2 Filter	0.2 (µ),1Nos,5"	Cartridge
8	Holding airline Filter	0.2 (µ),1Nos,5"	Cartridge
9	Machine Balloon Filter	0.2 (µ),1Nos,5"	Cartridge
10	Machine blow Filter	0.2 (µ),1Nos,5"	Cartridge
11	Machine buffer Filter	0.2 (µ),1Nos,5"	Cartridge
12	Disinfectant Air line Filter	0.2 (µ),1Nos,5"	Cartridge
13	BFS Machine Airline Filter	0.2 (µ),1Nos,5"	Cartridge
14	BFS Machine N_2 Filter	0.2 (µ),1Nos,5"	Cartridge
15	Super-Heated Air filter (Loading side)	0.2 (µ),1Nos,20"	Cartridge
16	HPHV autoclave (Vent Filter)	0.2 (µ),1Nos,5"	Capsule

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17	Mixing tank 4 KL (Vent Filter)	0.2 (µ),1Nos,10"	Cartridge
18	Holding tank 4KL (Vent Filter)	0.2 (µ),1Nos,10"	Cartridge