STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	1 of 18

1.0 OBJECTIVE:

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

2.0 SCOPE:

This SOP is applicable for Issuance, Usage, Replacement and Integrity Testing of Filters of Hydrophilic and Hydrophobic Filters in production department.

3.0 RESPONSIBILITY:

Officer / Executive – Production

4.0 ACCOUNTABILITY:

Head – Production

5.0 ABBREVIATIONS:

BPT	Bubble Point Test
IPA	Isopropyl Alcohol
WFI	Water for Injection
QA	Quality Assurance
Pvt.	Private
Ltd.	Limited
SOP	Standard Operating Procedure
SWS	Single Window System
CIP	Clean In Place
SIP	Sterilization In Place
BMR	Batch Manufacturing Record

6.0 PROCEDURE:

6.1 FILTER USAGE POLICY:

6.1.1 Dedicated filters shall be used for filtration of each generic product.

6.1.2 Before issue and use of particular cartridge filter ensure the required specification like filter type (Hydrophobic/ Hydrophilic), MOC, make, Catalogue No, Filter size, Pore size,

6.1.3 Filter shall be used after satisfactory result of BPT.

6.2 FILTER ISSUANCE AND PHYSICAL VERIFICATION PROCEDURE:

6.2.1 Filter shall be issued from general store after getting the mail/ SWS system of filter receiving in store.

6.2.2 Verify the filters for its physical parameter like filter quantity; filter catalogue no., filter certificate, filter MOC, filter supplier, filter type (Hydrophobic/ Hydrophilic), Filter size, filter pore size and filter physical condition(if any damage of its gasket, lock, body, filter element) during receiving from general store.

6.2.3 Filter will be stored at their respective storage area in Almirah with Lock & Key in production area.

6.2.4 New shall be issued only after taking the authorization from Production Head/ Department Head.

6.3 FILTER REPLACEMENT POLICY:

6.3.1 Filter shall be replaced immediately:

6.3.1.1 If any physical damage observed in filter.

6.3.1.2 If recommended sterilization cycle of filter completed. Recommended sterilization cycle of filters is mentioned in the **Annexure-II.**

6.3.1.3 During use of filter ensure its self-life and shall be used within the expiry date of particular filter. The expiry date of particular filter shall be recorded in the **Annexure No-III** for product filters and in the **Annexure No-IX** for vent filters.

6.3.1.4 If filter observed chock during filtration process but pass in BPT then this filter shall be cleaned and destroyed in presence of IPQA. Rest qty. of solution shall be filter with new sterilized filter.

6.3.2 Action plan in case of integrity failure:

6.3.2.1 In case the failure of Preintegrity, follow the below action plan:

6.3.1.1.1 Issue the new cartridge filter as specified in the respective BMR.

6.3.1.1.2 Perform the pre integrity and sterilization as per procedure.

6.3.1.1.3 Filter the bulk solution as per procedure.

6.3.1.1.4 Perform the post integrity and start the filling operation.

6.3.1.1.5 Initiate the incident to find out the root cause.

6.3.2.2 In case the failure of Post integrity, follow the below action plan:

6.3.2.2.1 Transfer the bulk solution from holding vessel to another sterilized holding vessel.

6.3.2.2.2 Perform the CIP & SIP of holding vessel as procedure.

6.3.2.2.3 Issue the new cartridge filter as per specified in the respective BMR.

6.3.2.2.4 Perform the pre integrity and sterilization as per procedure.

6.3.2.2.5 Filter the bulk solution as per procedure.

6.3.2.2.6 Perform the post integrity and start the filling operation.

6.3.2.2.7 Initiate the incident to find out the root cause.

6.4 PRECAUTIONS DURING HANDLING AND INTEGRITY TESTING OF FILTERS:

6.4.1 Handle the filter carefully to avoid any possible damage / extraneous contamination.

6.4.2 Before start the integrity, ensure and check the physical condition of filter housing and its components like O ring, gasket, teflon tip, vent valve. If required replace with new one.

6.4.3 Never open the Filter Housing during the operation.

6.4.4 In case of failure of test, recheck for the possibility of any leakage (i.e. from the 'O' ring of cartridge if any) proper locking of Filter/Filter Housing/Membrane Holder etc. In case of capsule filter check the tube attached or joint clamps.

6.4.5 Prior to conduct Bubble Point Test of the Filter it is to be assembled in Test housing and the Filter must be completely wetted by flushing with Water for Injection at Room Temperature for 10-15 minutes in case of Hydrophilic Filter and with IPA 70% solution (Ratio-IPA:WFI 70:30) for 10-15 minutes in case of Hydrophobic Filter.

6.4.6 Take necessary precautions during handling of cartridge filter like integrity, transfer from one location to other location, flushing, drying, loading & unloading in autoclave and assembling to avoid any physical damage to the filter.

6.4.7 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.

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

6.4.9 Mention the product Generic Name, Lot Number and Serial Number of the filter on bio-barrier paper.

6.4.10 Store this filter in the designated storage cabinet.

6.5 INTEGRITY TESTING OF FILTERS BY USING THE PALLTRONIC FLOWSTAR:

6.5.1 Perform the Integrity of Filter as per respective SOP.

6.5.2 Prior to start Bubble Point Test, Check the physical condition of the filter and assemble into filter test housing.

6.5.3 Open the filter line or housing and check physical condition of the filter and the O-ring gaskets visually. If found "OK", re-assemble the filter in their respective housing.

6.5.4 Close the inlet valve of Filter housing.

6.5.5 Attach the air line in the inlet of Instrument and outlet of instrument to the air inlet of Filter housing.

6.5.6 Run the Palltronic Flowstar with pre defined specific parameters for particular filters.

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

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

6.5.9 In case any breakdown of Integrity Tester performs the Integrity test (Bubble Point) by manual method as follows.

6.6 MANUAL INTEGRITY TESTING OF MEMBRANE FILTER:

6.6.1 Assemble the membrane filter in their respective membrane holder, and wet the filter with cooled WFI.

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

6.6.3 Connect the air pressure to the inlet of membrane filter holder.

6.6.4 Slowly open the compressed air/Nitrogen supply, as per their minimum bubble pressure mentioned on filter "Quality Certificate" and stabilizes for two minutes.

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

6.6.6 Disconnect the compressed air/nitrogen supply and release the pressure by opening of release knob.

6.7 INTEGRITY TEST OF PRODUCT WETTED FILTERS FOR SPECIFIC PRODUCTS:

6.7.1 If new cartridge filter will be issued then during first pre integrity consider the pre integrity value as recommended in the manufacturer certificate.

6.7.2 After filtration of bulk solution consider the post integrity value as mentioned in **Annexure-V.**

6.7.3 From second time onwards during pre-integrity consider the pre integrity value as mentioned in **Annexure-V** for specific product.

6.8 INTERPRETATION OF RESULT:

6.8.1 If the values measured by the equipment for the individual test is within limits as mention in its "**Annexure -II**", it indicates that the filter is "OK", if not within limits, repeats the test, if still "NOT OK", Inform to department Head and take permission for discarding. Discard the filter and install a new filter after checking its integrity.

6.9 FREQUENCY:

6.9.1 For Hydrophilic Filter (Product) – Pre and Post of Product Filtration.

6.9.2 For Hydrophilic Filter (Water Filter) – 15 ±2 Days.

6.9.3 For Hydrophobic Filter (Air Vent Filter on Holding Tank) – 15 ±2 Days.

6.9.4 For Hydrophobic Filter (Capsule/ Other Air Line Vent Filter) - 15 ±2 Days.

6.10 CLEANING AND STERILIZATION OF CARTRIDGE & CAPSULE FILTER

6.10.1 **For hydrophilic filters**: Clean the cartridge & capsule filters by flushing with WFI for 10-15 minutes.

6.10.2 **For Hydrophobic Filters:** Clean the cartridge & capsule filters by dipping in IPA 70 % solution for 10-15 minutes.

6.10.3 After cleaning and wetting perform the integrity by using Paltronic filter integrity machine as per SOP.

6.10.4 For integrity value limit refer the integrity value limit mentioned in the **Annexure- II**, titled as **"Integrity Test Value of Filters"**

6.10.5 Record the result of integrity in **Annexure –I** titled as **"Filter Integrity Testing Record"** and proceed for sterilization.

6.10.6 Perform the sterilization of particular filters as per respective SOP.

6.10.7 Record the sterilization cycle detail in the **Annexure-III** titled as **"Issuance, Sterilization Cycle and Destruction Record of Product Filters"** and **Annexure No-IX** titled as **"Issuance, Sterilization Cycle and Destruction Record of Vent Filters".**

6.11 Perform the integrity of vent line filters as per **Annexure- VIII**, titled as **"Planner for Vent Filter Integrity".**

6.12 After integrity and sterilization of vent line filter affix the filter status label on the filter housing as per **Annexure-VII,** titled as **"Filter Status Label"**

Note:-

- Cartridge filter and Capsule Filter should be replaced by newer one when it is observed physically damaged.
- Cartridge filter and Capsule Filter {Hydrophilic and Hydrophobic (Vent Filter)} should be replaced by newer one when it is failure in BPT or after completion of recommended Sterilization Cycle in Annexure-II.
- Membrane filter should be replaced by newer one when it is failure in BPT or single time use only.
- 01 sterilization cycle of filter shall be used for the viscous product of ampoule section.
- In case, if integrity testing machine of respective section is malfunctioning / under breakdown, Integrity test can be done on defined recipe using integrity testing machine from other working production section of I/Q and update the test record in respective operation log book OR respective filter integrity testing machine can be transferred to working production section of I/Q considering the production planning along with respective logbook in case the machine kept at idle condition in any section.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Filter Integrity Testing Record	
Annexure-II	Integrity Test Value of Filters	
Annexure-III	Issuance ,Sterilization Cycle and Destruction Record of Product Filters	
Annexure-IV	Product Wetted Filter Integrity Test Value of Filter For Specific Products	
Annexure-V	Filter Status Label	
Annexure-VI	Planner for Vent Filter Integrity	
Annexure-VII	Issuance ,Sterilization Cycle and Destruction Record of Vent Filters	
Annexure-VIII	Action Plan In Case Of Integrity Failure Of Hydrophobic And Hydrophilic Filters	

ENCLOSURES: SOP Training Record.

8.0 DISTRIBUTION:

- Controlled Copy No.01 — Quality Assurance
- Controlled Copy No.02 — Production (I-Block)
- Controlled Copy No.03 — Production (Q-Block, Three Piece Line)
- 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

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters			
SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	7 of 18

ANNEXURE – I
FILTER INTEGRITY TESTING RECORD

Date	Type of Filter	Filter Catalogue No	Filter Lot No	Filter Serial No	Pore Size	Wetting Agent	Integrity		Integrity result (Pass/fail)	*Product Name/B.No	Done By	Checked By	Verified By	Remark
							From	To						

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	8 of 18

ANNEXURE – II
INTEGRITY TEST VALUE OF FILTERS

Category	Filter Size	Pore Size	Manufacturer	Catalogue Number	Test To Be Performed For Integrity		MOC	Maximum Sterilization Cycle
					BPT			
					Test Pressure	Test Value		
Hydrophilic	10 Inch	0.45µ+ 0.2 µ	Sartorius		3200 mbar	Bubble should not found below test value	PES	25
		0.45µ+ 0.2 µ	Sartorius		3200 mbar		PES	25
		0.2 µ	Millipore		3100 mbar		PVDF	25
			Pall		3180 mbar		PVDF	25
			MDI		3440 mbar		PES	15
			Pall		3180 mbar		N66 ULTIPORE	25
			Pall		3180 mbar		N66 POSIDYNE	25
			Pall		3655 mbar		PES	10
Hydrophobic	5 Inch	0.2 µ	Millipore		1100 mbar		PTFE	80
			Pall		1320 mbar		PTFE	80
			MDI		1520 mbar		PTFE	80
			MDI		1520 mbar		PTFE	80
			Millipore		1100 mbar		PTFE	80
			Pall		1380 mbar		PTFE	80
			Pall		1380 mbar		PTFE	80
Hydrophobic	10 Inch	0.2 µ	Pall		1380 mbar	Bubble should not found below test value	PTFE	80
Hydrophobic Capsule Filter	2 Inch	0.2 µ	Sartorius		1000 mbar		PTFE	80
	3.5 Inch		Sartorius		1000 mbar		PTFE	80
	5 Inch	0.2 µ	Pall		1380 mbar		PTFE	80

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters				
SOP No.:		**Department:**	Production	
		Effective Date:		
Revision No.:	00	**Revision Date:**		
Supersede Revision No.:	Nil	**Page No.:**	9 of 18	

			MDI		1520 mbar		PTFE	50
Hydrophobic Disk Filter	50 mm	0.2 µ	MDI		700 mbar		PTFE	30

Note: Other filter, which is not listed in above table, can be used after integrity testing as defined value of BPT and maximum number of sterilization cycle in "Manufacturer quality certificate".

Category	Filter Size	Pore Size	Maximum Sterilization Cycle
Hydrophilic cartridge Filter(Pre-filter)	10 Inch	1.0 µ (Micron) /2.0 µ (Micron)	25

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	10 of 18

ANNEXURE – III

ISSUANCE, STERILIZATION CYCLE AND DESTRUCTION RECORD OF PRODUCT FILTERS

Block: **Line:** **Section**:

1.Filter Detail & Issuance Record			
Generic name of Product			
Filter Make		**Filter Catalogue No**	
Filter Lot No		**Filter S.No.**	
Filter Size/Pore Size		**Expiry Date(MM/YY)**	
Date of issue			
Checked By (Sign & Date)			
Maximum Recommended Sterilization Cycle			

2. Sterilization Cycle Record					
Cycle No	**1**	**2**	**3**	**4**	**5**
Load No					
Sign/Date					
Cycle No	**6**	**7**	**8**	**9**	**10**
Load No					
Sign/Date					
Cycle No	**11**	**12**	**13**	**14**	**15**
Load No					
Sign/Date					
Cycle No	**16**	**17**	**18**	**19**	**20**
Load No					
Sign/Date					
Cycle No	**21**	**22**	**23**	**24**	**25**
Load No					
Sign/Date					

3.Destruction Record	
Reason of Destruction	

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	11 of 18

Destruction done By(Production)	
Checked By(Production)-Sign/Date	
Verified By(IPQA)-Sign/Date	

ANNEXURE – V
PRODUCT WETTED FILTER INTEGRITY TEST VALUE OF FILTER FOR SPECIFIC PRODUCTS

S.No.	Product Name	BPT value (mbar)
1.	Tobramycin Ophthalmic Solution	NLT 2520 mbar
2.	Hypromellose Ophthalmic solution	NLT 2240 mbar
3.	Olopatadine Hydrochloride Ophthalmic Solution IP 0.1%	NLT 2360 mbar
4.	Olopatadine Hydrochloride Ophthalmic Solution IP 0.2%	NLT 2580 mbar
5.	Gatifloxacin and Dexamethasone ophthalmic solution	NLT 2100 mbar
6.	Megabrom/ Bromfenac Eye Drop	NLT 2080 mbar
7.	Brimonidine Tartrate and Timolol Maleate Ophthalmic Solution	NLT 2280 mbar
8.	Cyclomune Eye Drop	NLT 2000 mbar
9.	Cyclosporine Eye Drop	NLT 2800 mbar
10.	Nepafenac Eye Drop	NLT 2100 mbar

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters			
SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	13 of 18

ANNEXURE-VII

FILTER STATUS LABEL	
Date	
Type of Filter	**Pore Size**
Location	**Catalog/Serial no**
Filter Installation Date-	**Total sterilization cycle-**
Integrity done on	**Integrity Due on**
Done By:	**Checked By:**

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters			
SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	14 of 18

ANNEXURE-VIII
PLANNER FOR VENT FILTER INTEGRITY

Department: **Year:**

Section Name: **Effective Date:**

S.No.	Location of filter	Filter Housing ID No./ Catalogue No.		Month											
				Jan.	Feb.	Mar.	Apr.	May	Jun.	July	Aug.	Sep.	Oct.	Nov.	Dec.
			P												
			A												
			P												
			A												
	Checked By QA														

P=Planned, A=Actual
Note: "□" tick mark on planned month for applicable filter integrity and mention actual date in DD/MM/YY
Remarks (If any):

	Prepared By Production	Reviewed By Department Head	Approved By Head QA
Name			
Sign			
Date			

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	15 of 18

ANNEXURE – IX
Issuance, Sterilization Cycle and Destruction Record of Vent Filters

Block: **Line:** **Section**:

1.Filter Detail & Issuance Record			
Location		**Equipment Name/ID No**	
Filter Make		**Filter Catalogue No**	
Filter Lot No		**Filter Sr. No**	
Filter Size/Pore Size		**Expiry Date(MM/YY)**	
Date of issue/Installation			
Checked By(Sign/Date)			
Maximum Recommended Sterilization Cycle			

2.Sterilization Cycle Record										
Cycle No	1	2	3	4	5	6	7	8	9	10
Load No										
Sign/Date										
Cycle No	11	12	13	14	15	16	17	18	19	20
Load No										
Sign/Date										
Cycle No	21	22	23	24	25	26	27	28	29	30
Load No										
Sign/Date										
Cycle No	31	32	33	34	35	36	37	38	39	40
Load No										
Sign/Date										
Cycle No	41	42	43	44	45	46	47	48	49	50
Load No										
Sign/Date										
Cycle No	51	52	53	54	55	56	57	58	59	60
Load No										
Sign/Date										
Cycle No	61	62	63	64	65	66	67	68	69	70
Load No										
Sign/Date										
Cycle No	71	72	73	74	75	76	77	78	79	80
Load No										

STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

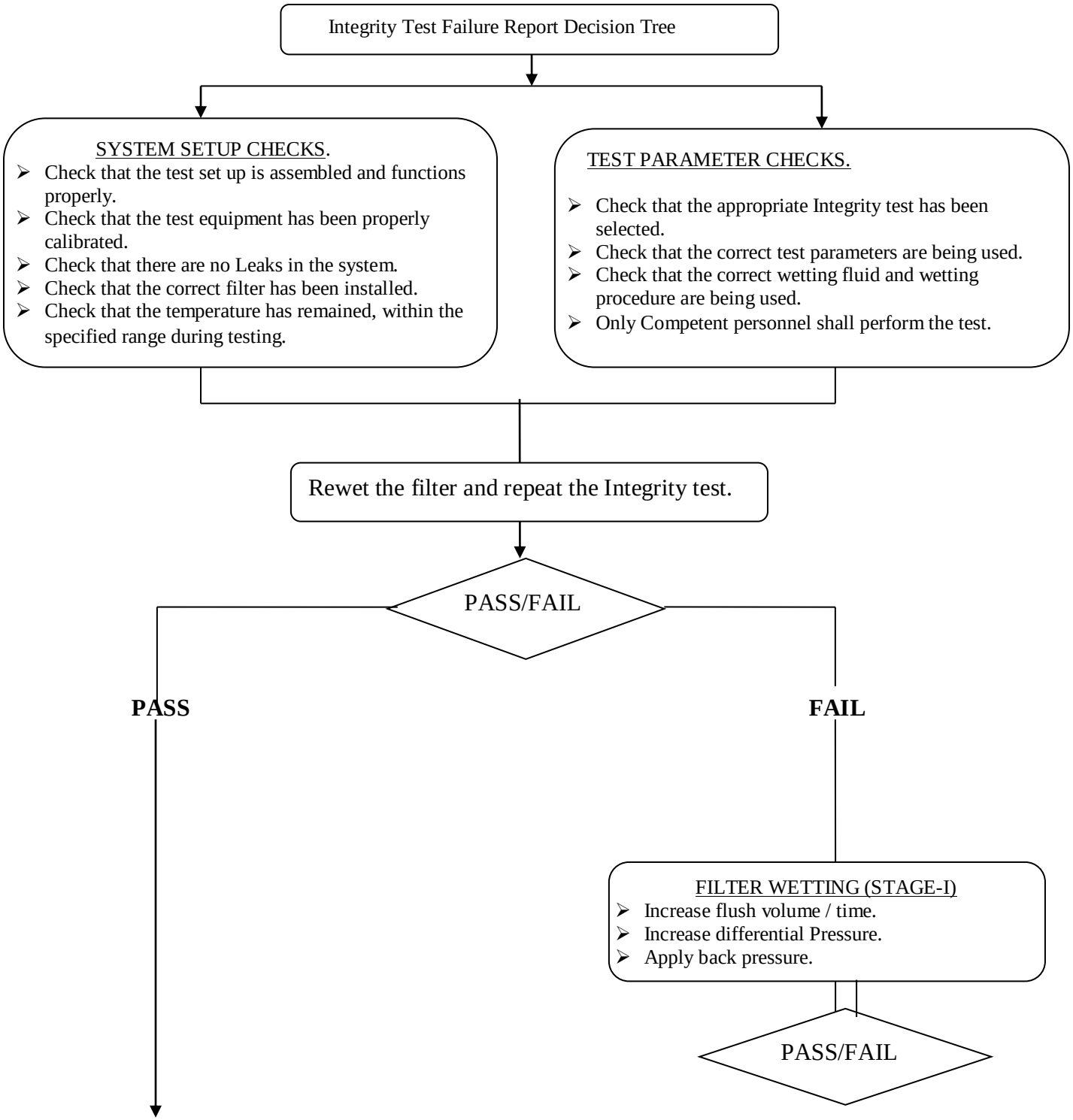
SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	16 of 18

Sign/Date										

3.Destruction Record	
Reason of Destruction	
Destruction done By(Production)	
Checked By(Production)-Sign/Date	
Verified By(IPQA)-Sign/Date	

STANDARD OPERATING PROCEDURE				
Title: Issuance, Usage, Replacement and Integrity Testing of Filters				
SOP No.:		**Department:**	Production	
		Effective Date:		
Revision No.:	00	**Revision Date:**		
Supersede Revision No.:	Nil	**Page No.:**	17 of 18	

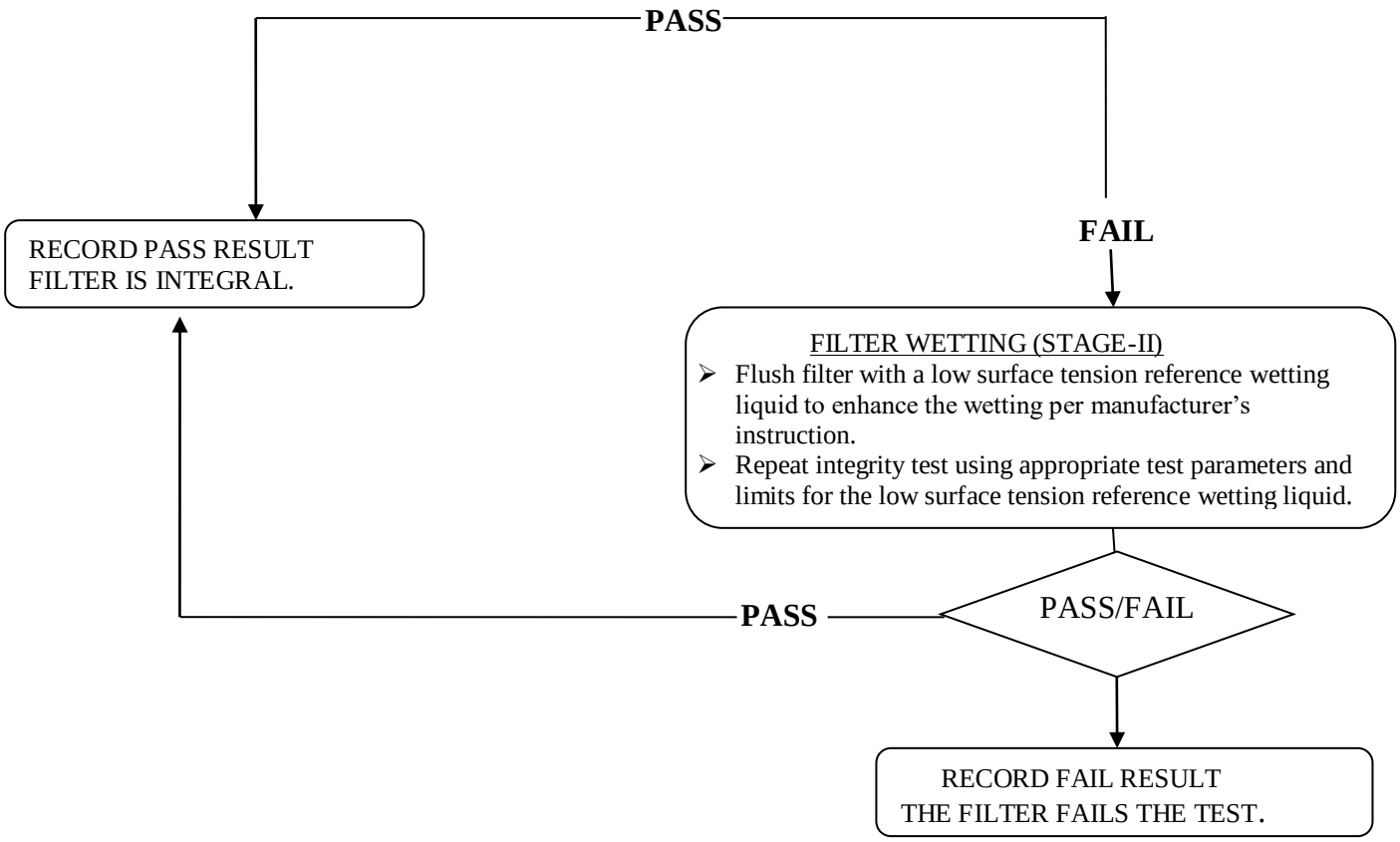
ANNEXURE-X
ACTION PLAN IN CASE OF INTEGRITY FAILURE OF HYDROPHOBIC AND HYDROPHILIC FILTERS



STANDARD OPERATING PROCEDURE

Title: Issuance, Usage, Replacement and Integrity Testing of Filters

SOP No.:		**Department:**	Production
		Effective Date:	
Revision No.:	00	**Revision Date:**	
Supersede Revision No.:	Nil	**Page No.:**	18 of 18



Note: 1. Failure interpretation shall be recorded in respective log book and related printout shall be Attached in respective documents.

2. Deviation/Incident shall be taken on the basis of outcome of investigation and Risk Assessment.

3. All the electronic data shall be verify by QA at the time of log sheet submission and Retrieval, also remarks and counter sign shall be done by QA.