STANDARD OPERATING PROCEDURE

Title: Operation and Cleaning of Integrity Tester Machine

SOP No.:		**Department:**	Production	
		Effective Date:		
Revision No.:	00	**Revision Date:**		
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1.0 OBJECTIVE:

To lay down a Procedure for Operation and Cleaning of Integrity Tester Palltronic Flowstar IV.

2.0 SCOPE:

This SOP is applicable for the Operation and Cleaning of Integrity Tester to be used for Filter integrity test (Hydrophobic and Hydrophilic Type filter) in production department.

3.0 RESPONSIBILITY:

Operating Person – Production
Data Backup - IT
Data Verification - IT/ Production/IPQA

4.0 ACCOUNTABILITY:

Head – Production

5.0 ABBREVIATIONS:

%	Percentage
IPA	Iso Propyl Alcohol
LTD	Limited
Mbar	Milli Bar
No.	Number
PVT	Private
QA	Quality Assurance
SOP	Standard Operating Procedure
WFI	Water for Injection
BPT	Bubble Point test
FFT	Forward Flow test
FRL	Filter Regulator & Lubricator
WIT	Water Intrusion Test
PDA	Parenteral Drug Association
QMS	Quality Management System.
NLT	Not Less Than
IT	Information Technology

6.0 PROCEDURE:

6.1 General Instructions for User Identities (for Equipment ID…….).

6.1.1 Four user levels are available in integrity tester machines (Equipment ID…….), refer point no.6.3.8 for user level rights.

6.1.2 Each user has to login with his own user ID and password.

6.1.3 Upto 250 active user identities can be set up on the Palltronic Flowstar IV instrument.

6.1.4 Provision for Electronic Signatures Management is available with the machine.

6.1.5 Never share password to anyone and follow below procedure for creating user identities, use of a new identity and deactivating/ deleting user identities :

6.1.5.1 Creating User Identities:

6.1.5.1.1 The system administrator has to select 'access management', followed by 'Edit user list'.

6.1.5.1.2 To enter new users into the system, select 'Create new user'.

6.1.5.1.3 The administrator has to enter a user name, a User ID and password as well as an access level into the blank boxes on the screen and then press the 'OK' button.

6.1.5.1.4 Each user must have a unique User ID and user name.

6.1.5.2 First Use of a new Identity:

6.1.5.2.1 New users should use the initial password given to them by the system administrator to access the Palltronic Flowstar IV instrument. They are forced by the instrument to change their password before getting full access.

6.1.5.2.2 Users who have forgotten their password must contact the administrator who can set a new initial password**.**

6.1.5.3 Deactivating/ Deleting User Identities:

6.1.5.3.1 The system administrator has to select 'Access management', followed by 'Edit user list' and choose the user to be deactivated/ deleted.

6.1.5.3.2 Deactivating a user means that the user remains stored on the instrument and can be reactivated later.

6.1.5.3.3 Deletion means that the record is no longer stored on the instrument and must be reentered to regain access.

6.1.5.3.4 The first user 'Administrator' cannot be deactivated or deleted. This is to prevent access to the system menu from being lost.

6.2 Precautions:

6.2.1 Filter shall be wetted for NLT 10 minutes with receptive wetting agent at ambient temperature.

6.2.2 In case Hydrophilic filters do wetting with Water for Injections and In case of hydrophobic filters, do wetting with 70/30 or 60/40 IPA v/v as filter certificate specification given by filter manufacturer before proceeding the Integrity test.

6.2.3 Record of filter wetting time shall be done as per annexure-I (for respective section)

6.2.4 Proceed the fitter sterilization after filter Integrity test compliance

6.2.5 Don't touch the Screen of integrity tester with any hard material.

6.2.6 Check supply air pressure (5000-6000 mbar) before start the test.

6.2.7 Check and ensure the all tube fittings connection are properly assembled and leak proof.

6.2.8 Never open the filter housing during the operation.

6.2.9 Check & insure FRL should be working condition which is installed in Air Line to remove any moisture.

6.2.10 Audit trail review shall be done by QA and Interpretation of filter integrity results shall be performed as per defined procedure.

6.2.11 Recording of each and every test i.e. Pass/ Fail / Abort / Error and self-test shall be done as per Annexure-I "**Operation and Cleaning Record of Integrity Tester".**

6.2.12 In case routine Filter integrity test is reported as "FAIL" then **Follow the Integrity Test Failure Report Decision Tree** Annexure-III ie (one routine test followed by 3 consecutive test as per **Decision Tree**)

6.2.13 Follow annexure-IV for action plan in case of any error observed.

6.2.14 Test result having test discrepancy has to attached with subsequent test result compliance.

6.3 Bubble Point Test of Cartridge or Capsule Filter:

6.3.1 Prior to conduct Bubble Point Test of the Filters, it should be assembled in respective housing or lines.

6.3.2 Attach the inlet of filter housing or capsule filter inlet with "Air Outlet" of Integrity Tester by cleaned tubes.

6.3.3 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.

6.3.4 Attach the compressed air line to the "Air Outlet" of Integrity Tester (Air Supply pressure 5000-6000 mBar).

6.3.5 Switch "ON" the Instrument starting screen shall display as below:

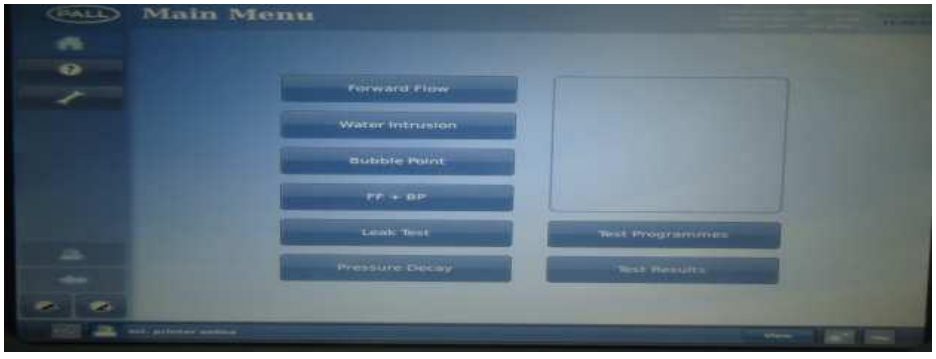
6.3.6 Press the button at back side of instrument to open the upper flap of the integrity tester.

6.3.7 For logging in integrity tester machines (Equipment ID……..): each user has to login with his user ID and password.

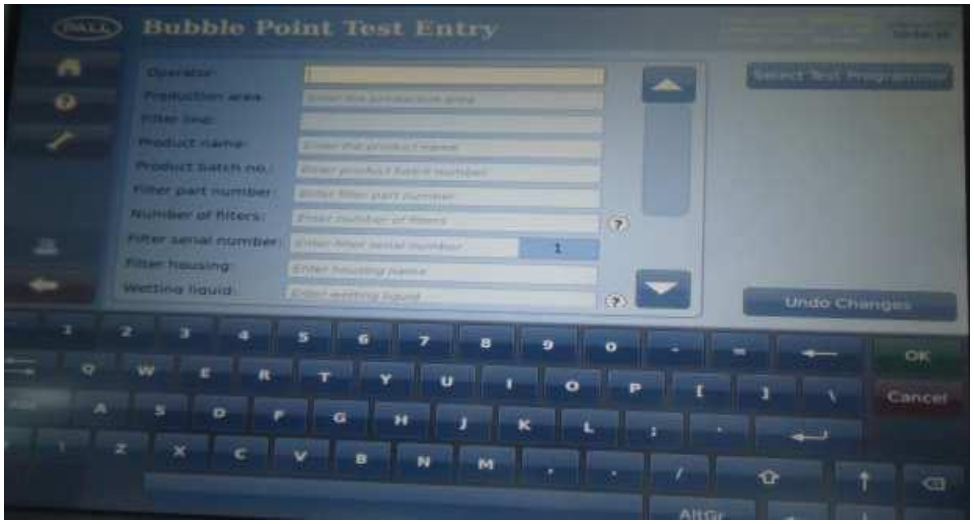
6.3.8 There are four user levels in integrity tester machines (Equipment ID…….

a) **Level 1:** Operator- Can perform filter tests
b) **Level 2:** Supervisor- Can create/ modify test programs and perform a backup
c) **Level 3:** Administrator- Can modify the configuration, the date/time and the access management
d) **Level 4:** Super administrator- Can modify the configuration, the date/time and the access management exempt from password aging.

6.3.9 Main Menu will display after some time as below.



6.3.10 Select or Click on type of test perform and press the icon (Bubble Point) to start the integrity test of filters, the screen of tester will show as below:



6.3.11 Select and fill the all detail about the respective filters (Manufacturer Certificate Detail). Ex.

Operator	XXX
Production Area	Unit Preparation Area
Filter line	Nitrogen/ Compressed Air
Product name	N/A
Product batch no.	N/A
Filter part no.	…….
Number of filters	01
Filter serial no.	…….
Filter housing	Capsule/ Cartridge
Wetting liquid	70 % IPA
Test gas	Compressed Air
Module factor	1
Minimum BP	1520 mbar
Maximum pressure	6000 mbar

6.3.12 Click/Press on the “OK” to continue the operational process.

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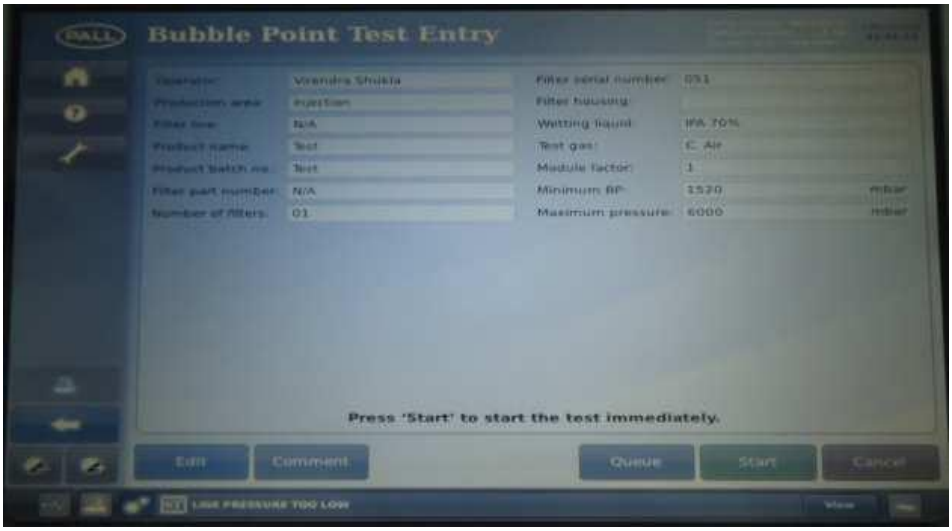
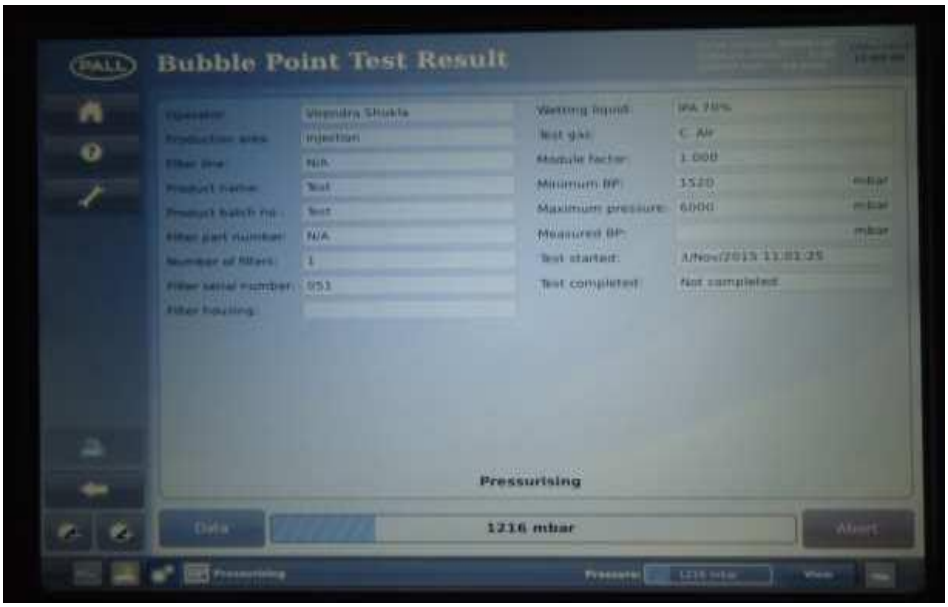


6.3.13 Check the filled detail/ parameters if it is ok then press the "START" icon to start the process.

6.3.14 After pressurize the filter, screen will show as:



6.3.15 After completion of the test Bubble point value shall display on the screen and report shall auto saved in the system.

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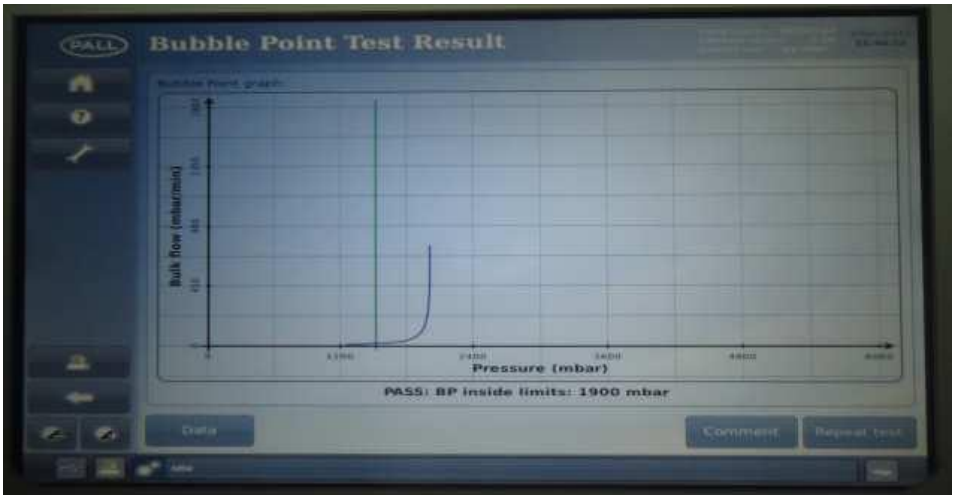
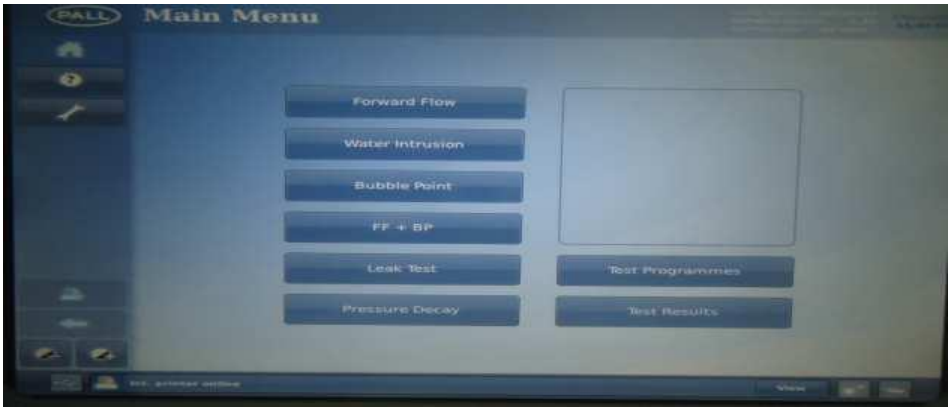
6.3.16 Click on the "Graph" to see the graph of the pressure raise during "Bubble Point Test"



6.3.17 Click on the Icon  to print the test report.

6.3.18 Click on "Home" Icon on the screen for "Main Menu" and the screen will show as:



6.3.19 To view the previously saved report click on the "Test Results".

6.3.20 All the saved report shall display on the screen.

6.3.21 Select the report to print the saved test report.

6.3.22 Click on the Icon  to view the report, test report shall display on the screen.

6.3.23 Click on the Icon  to print the test report.

6.4 Interpretation of Result:

6.4.1 If the test values measured by the equipment for the individual test is within limits as mentioned in its "Manufacturer Quality Certificate" or as per product BMR it indicates that the filter integrity is "PASS".

6.4.2 In case routine Filter integrity test is reported as "FAIL" then **Follow the Integrity Test Failure Report Decision Tree** Annexure-III ie; (One routine test followed by three consecutive test as per **Decision Tree**)

Test level	Line of Action plan after test failure	Interpretation
In case of Routine test failure	• Follow Decision Tree compliance after routine test failure as • Do the verification first as system set up followed by test parameters **SYSTEM SETUP CHECKS.** • Check that the test set up is assembled and functions properly. • Check that the test equipment has been properly calibrated. • Check that there are no Leaks in the system. • Check that the correct filter has been installed.	• As per point no. 6.3.2 and Record the observation in respective operation log book • Repeat for 1st test as define action plan in decision tree to conclude test • Record the 1st test observation in

	• Check that the temperature has remained, within the specified range during testing ***TEST PARAMETER CHECKS*** • Check that the appropriate Integrity test has been selected. • Check that the correct test parameters are being used. • Check that the correct wetting fluid and wetting procedure are being used. • Only Competent personnel shall perform the test	respective operation log book
Test level	**Line of Action plan after test failure**	**Interpretation**
• 1st fails after decision tree recommendation	• Increase flush volume / time. • Increase differential Pressure. • Apply back pressure	• Repeat for 2nd test as define action plan in decision tree to conclude test and Record the 2nd test observation in respective operation log book
• 2nd fails after decision tree recommendation	• Flush filter with a low surface tension reference wetting liquid to enhance the wetting per manufacturer's instruction. • Repeat integrity test using appropriate test parameters and limits for the low surface tension reference wetting liquid	• Repeat for 3rd • test as define action plan in decision tree to conclude test and Record 3rd test the observation in respective operation log book
• 3rd fail after decision tree recommendation	• Raise the incident and based on the outcome of investigation, the decision shall be taken for further activity.	• Record the observation in respective operation log book

6.4.3 All BPT details like (PASS/FAIL/ERROR/ABORT) shall be recorded in log book as per Annexure-I "**Operation and Cleaning Record of Integrity Tester"**

6.4.4 In-case system is showing test result as Error record the observation as per Annexure-I "**Operation and Cleaning Record of Integrity Tester"** and proceed as per line of action in Annexure IV "**Error Messages During Operation of Filter Integrity Machine**"

6.4.5 Record all the activities like cleaning and operation results of each and every test i.e. Pass/ Fail / Abort / Error as per Annexure-I "**Operation and Cleaning Record of Integrity Tester"**

6.4.6 Install a new filter after its integrity test compliance Refer **Annexure-I** of SOP on **"Issuance, Usage, Replacement and Integrity Testing of Filters"** and perform the integrity test as per **Annexure no. II** "**Integrity test values of filters"**

6.4.7 Audit trail shall be reviewed by QA person as per SOP "**Audit Trail Review of Filter Integrity Tester (Paltronic Flow Star IV)**".

6.5 Cleaning Procedure:

6.5.1 Switch "OFF" the main supply of Integrity Tester.

6.5.2 Dissemble all tube lines of the Integrity Tester.

6.5.3 Wipe the dry mop external surface of Integrity Tester machine followed by wet mob soaked with 70 % IPA.

6.5.4 Dip the tubes in 70 % IPA for 10 min, after that rinse with WFI and dry it by flushing of compressed air.

6.5.5 Record the activity in respective log book.

6.6 During the Breakdown of the Filter Integrity Machine:

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

6.6.2 Record the integrity test details in respective block log book.

6.6.3 After breakdown of the filter Integrity Machine perform the system leakage test and then released for routine integrity test.

6.6.4 Yearly servicing shall be done at the time of yearly calibration of the filter integrity machine.

6.7 Stored data from filter integrity tester machines shall be transferred to sever via pen drive with the help of IT department at a frequency of 2 months ±10 days and record the details in Annexure-V "Integrity Tester Machine Data Backup Record".

6.8 The saved data files (at least 01 file) shall be verified at every Year ± 01 Month to check whether file is getting open or not and record the details as per Annexure-VI "Restored Data Verification Results Record".

Frequency of Data Backup: Every 2 Months ±10 Days.

7.0 ANNEXURES:

ANNEXURE No.	TITLE OF ANNEXURE	FORMAT No.
Annexure-I	Operation and Cleaning Record of Integrity Tester	
Annexure-II	Integrity Tester Machine, Servicing and Calibration Record	
Annexure-III	Action Plan in case of Integrity failure of Hydrophobic and Hydrophilic Filters	
Annexure-IV	Error Messages during Operation of Filter Integrity Machine.	
Annexure-V	Integrity Tester Machine Data Backup Record	
Annexure-VI	Restored Data Verification Results Record	

ENCLOSERS: SOP Training Record.

8.0 DISTRIBUTION:

- Controlled Copy No. 01 — Quality Assurance
- Controlled Copy No. 02 — Production
- Master Copy — Quality Assurance

9.0 REFERENCES:

PDA Technical Report No.26.
SOP: Audit Trail Review of Filter Integrity Tester (Paltronic Flow Star IV).

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
OPERATION AND CLEANING RECORD OF INTEGRITY TESTER

Equipment ID No.: **Line/Location:**

Make : **Model No.:**

Date	Filter Wetting Time		Operation		Done By	Checked By	Verified By	Cleaning		Done By	Checked By	Remarks
	From	To	From	To				From	To			

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ANNEXURE-II
INTEGRITY TESTER MACHINE, SERVICING AND CALIBRATION RECORD

Equipment Name: Integrity Tester Machine Equipment ID:

S.No.	Equipment Servicing / Calibration date.	Equipment Next, Servicing / Calibration Due date.	Done by	Checked by	Verified by	Remarks

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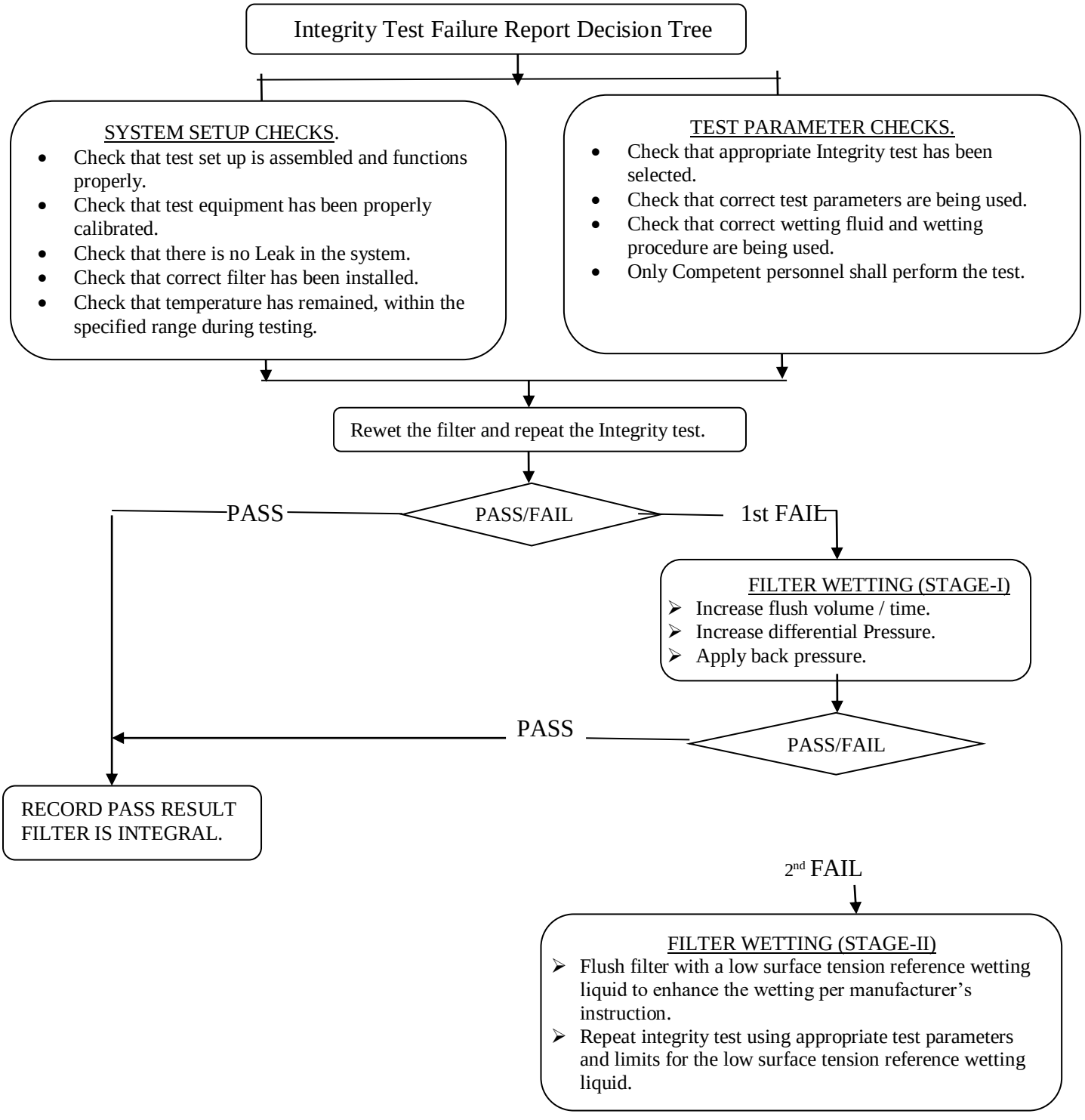
ANNEXURE-III
ACTION PLAN IN CASE OF INTEGRITY FAILURE OF HYDROPHOBIC AND HYDROPHILIC FILTERS



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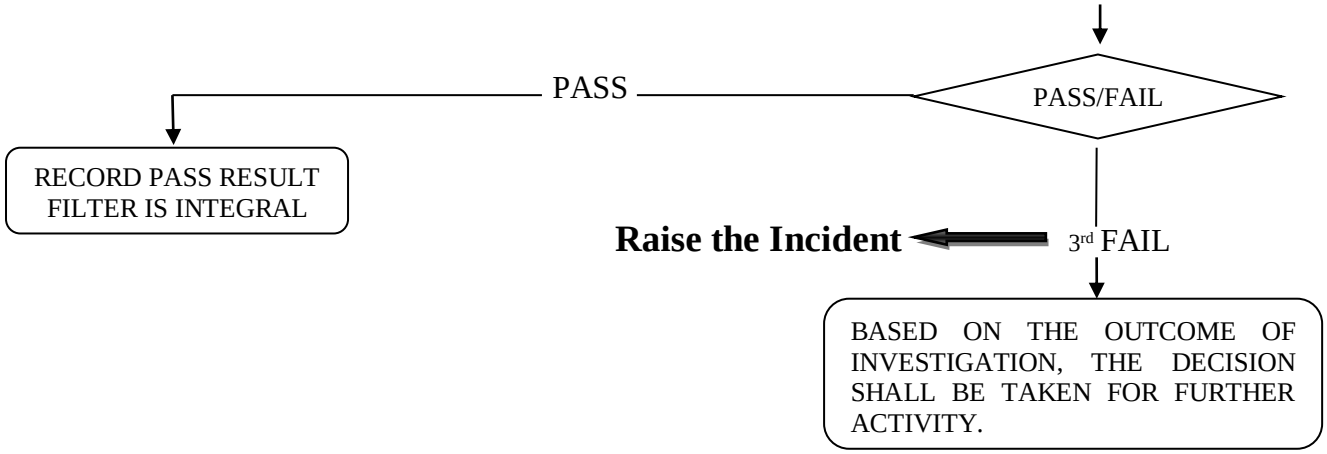

Note 1: All BPT details like (PASS/FAIL/ERROR/ABORT) shall be recorded in log book as per Annexure-I "Operation and Cleaning Record of Integrity Tester". Remark shall be written on the test print and test print shall be attached with BMR/documents.

Note 2: In case if filters observed fail after treatment of stage –II, then incident shall be initiated and based on the outcome of investigation the decision shall be taken for further activity.

ANNEXURE-IV
ERROR MESSAGES DURING OPERATION OF FILTER INTEGRITY MACHINE

❖ The Table below enumerates most common error messages and their possible causes. The error messages are displayed on the screen can be printed out. If errors are encountered that are not described here, please contact pall.

SELF TEST

S.No.	Error Messages	Possible causes	Action
1.	**Line pressure too low**	Line pressure below 3000 mbar (43.5psi), subsequent not completed.	Increase in the Line pressure.
2.	**Line pressure Unstable**	Line pressure not stable enough	Check pressure supply.
3.	**Self-test failed**	Self-test failure	Check self-test printout for additional information. Repeat self-test with pressure supply. If service message continues to be displayed, then further service is required.
4.	**Internal Error**	Internal communication of the instrument disturbed.	Restart the self-test. If not successful contact pall instrument services.

FILTER TEST (WIT)

S.No.	Error Messages	Possible causes	Action
1.	**Set up Error**	Pressurization could not start.	Check if filter is connected and remote vent valve is operating.
2.	**Line pressure is too low**	Line pressure is too low or there are fluctuations in the compressed air supply.	Check/increase the line pressure.
3.	**Line pressure unstable**	Line pressure not stable enough	Check pressure supply.
4.	**Pressure not obtainable**	• Major leak in the filter system under test. • Filter not wetted completely. • Filter has a major defect. • Line pressure too low or fluctuating.	• Check systems for leaks. • Rewet and retest filter. • Replace filter if needed. • Check line pressure.
5.	**Flow outside limits**	• Leak in the filter system. • Non-Integral filter. • Filter not completely wetted.	• Check system for leaks. • Replace filter if needed. • Rewet (FF-Test) and re-test the filter.

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S.No.	Error Messages	Possible causes	Action
6.	**Flow too high**	• Flow >1000ml/min (FF test) or >50 ml/min (WIT) • Leak in the filter system. • Non-Integral filter or filter not completely wetted.	• Check systems for leaks. • Replace filter if needed. • Rewet (FF Test) and retest filter.
7.	**Flow too Low**	• Flow < 0.05 ml/min (FF test) or <0.001ml/min (WIT). • Connection between filter and instrument interrupted/closed. • Flow value for the filter too low to be measured (Small filters only).	• Check the test system. • Re-wet (FF-Test) and re-test the filter. • Replace filter if needed.
8.	**Flow Unstable**	• Fast increase in flow during the measurement due to a leak filter de-wetting during the test. • Fluctuating pressure. • Fluctuating temperature.	• Check test systems. • Check for temperature conditions.
9.	**Downstream pressure too high.**	• Filter not installed or filter has a major defect.	• Check/Replace filter.
10.	**External Valve Error**	• External valve not connected. • External valve not opening.	• Check External valve.
11.	**External Pressure Transducer (PT) Error.**	• External pressure transducer not connected. • External pressure transducer defect.	• Check external pressure transducer. • Check configuration if external pressure transducer is not used.

FILTER TEST (BPT)

S.No.	Error Messages	Possible causes	Action
1.	**Set up Error**	Pressurization could not start.	Check if filter is connected and remote vent valve is operating.
2.	**Line pressure too low**	Line pressure too low or fluctuations in the compressed air supply. **Note :** Line pressure must be >500mbar (7.25 psi) above the minimum BP.	Check/increase line pressure.
3.	**Pressure not Obtainable**	• Major leak in the filter system under test. • Filter not wetted completely.	• Check systems for leaks. • Re-wet and re-test filter.

S.No.	Error Messages	Possible causes	Action
		• Filter has a major defect. • Line pressure too low or fluctuating.	• Replace filter if needed. • Check line pressure.
4.	**Leak test Failure**	• Major leak in the filter system under test. • Filter not wetted completely. • Filter has a major defect.	• Check system for leaks. • Re-wet and retest filter. • Replace filter if needed.
5.	**BP not obtainable**	• Final pressure is line pressure – 250 mbar (7.3 psi): Insufficient line pressure. • Unusual BP curve does not allow detection of the bubble point.	• Check line pressure. • Check connection between instrument and filter. • Re-wet and re-test the filter. • Replace filter if needed.
6.	**Maximum pressure Reached.**	• Maximum pressure defined in the test parameters reached but no BP is detected.	• Check connection between instrument and filter. • Retest the filter in a system with the higher tolerance. • Replace filter.
7.	**BP outside limits**	• Non-Integral Filter. • Filter not completely wetted.	• Rewet and retest the filter. • Replace filter if needed.
8.	**Downstream pressure too high.**	• Filter not installed or filter has a major defect.	• Check/Replace filter.
9.	**External Valve Error**	• External valve not connected. • External valve not opening.	• Check External valve.
10.	**External Pressure Transducer (PT) Error**	• External Pressure transducer not connected. • External pressure transducer defect.	• Check external pressure transducer.

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ANNEXURE-V
INTEGRITY TESTER MACHINE DATA BACKUP RECORD

Equipment Name: Integrity Tester Machine **Section:**
Data Backup Frequency: Every 2 Months ±10 Days.

S.No.	Date of Data Back-Up	Instrument ID No.	Done By (IT)	Verified By (IPQA)	Data Back-Up Due Date	Remarks

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ANNEXURE-VI
RESTORED DATA VERIFICATION RESULTS RECORD

Equipment Name: Integrity Tester Machine **Section:**
Data Verification Frequency: Yearly ±1 Month

S.No.	Date of Restored Data Verification	Instrument ID No.	Done By (IT)	Verified By (IPQA)	Restored Data Verification Due Date	Remarks