



Bubble Point Integrity Test Procedure

Prepared By: Martin Capati and Onyx S Ahmad

Approved By: Allen Y Zanki

Date: March 24, 2020



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Scope

This procedure defines protocols necessary to determine if, after use, a filter has maintained its integrity. To accomplish this goal, the bubble test method is employed. Because the surface tension of the end user's filtered solution is unknown, a solution of 60% isopropanol alcohol (IPA) and 40% deionized (di) water is used to flush the solution from the filter and wet the pores within the membrane of the filter. Pressurized air is then used in the filter's inlet to force the liquid from the pores. If a pressure of 18 psi can be achieved before bubbles are seen in the downstream side, the filter is considered capable of maintaining sterility of the product filtered. An article on bubble point theory is available on request.

100% Di Water can also be used for the test fluid, the acceptable bubble point value is 50 psi, see Table 3. The benefit of using the 60% IPA and 40% DI water is that the pressure required in the tubing is much lower making the operation safer for the operator and the test filter is easier to wet with the alcohol/water mixture.

Since pharmacist routinely keep 70% IPA and 30% water on hand it can also be used. The acceptable value is 17.5 inches of water, see table 3.

Filtering Medication Using the Filter

Using Table 1, select the correct size filter required to ensure that, under normal conditions, the complete batch of medication can be filtered through one filter. International Filter Products' has six different size filters for the Pharmacists' to select from, see Table 1 for reference. Larger capsules are available if required, they come in three sizes, the SKL-H (680 cm²), SKL-S (1,380 cm²), and SKL-L (2,550 cm²).



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Table 1: Filter Size and Volume Filtered Capability

Filter Part Number	Filter Area – cm ²	Volume Filtered - ml
D40CS020LFLM-PH-ETO	10.5	230 ml to 330 ml
D40CF020LFLM-PH-ETO	10.5	265 ml to 380 ml
D50CS020LFLM-PH-ETO	15.9	350 ml to 505 ml
D50CDS065S020LFLM-PH-ETO	15.9	525 ml to 760 ml
D50CF020LFLM-PH-ETO	15.9	400 ml to 580 ml
D50CF100020LFLM-PH-ETO	15.9	600 ml to 870 ml
D65RS020LFLM-PH-ETO	27	600 ml to 890 ml
D65RDS065S020LFLM-PH-ETO	27	900 ml to 1,335 ml
D65RF020LFLM-PH-ETO	27	720 ml to 1,070 ml
D65RF100020LFLM-PH-ETO	27	1,080 ml to 1,600 ml
D90RS020LFLM-2Z(6"LS)-PH-ETO	60	1,350 ml to 2,550 ml
D90RDS065S020LFLM-2Z(6"LS)-PH-ETO	60	2,025 ml to 3,825 ml
D90RF020LFLM-2Z(6"LS)-PH-ETO	60	1,620 ml to 3,060 ml
D90RF100020LFLM-2Z(6"LS)-PH-ETO	60	2,430 ml to 4,590 ml
D90RS020LFLM-PH-ETO	60	1,350 ml to 2,550 ml
D90RDS065S020LFLM-PH-ETO	60	2,025 ml to 3,825 ml
D90RF020LFLM-PH-ETO	60	1,620 ml to 3,060 ml
D90RF100020LFLM-PH-ETO	60	2,430 ml to 4,590 ml
JKPS020LFLM-PH-ETO	260	4.0 Liters to 8 Liters
JKPDS065S020LFLM-PH-ETO	230	6.0 Liters to 12.0 Liters
MKPS020DLFLM-PH-ETO	500	9 Liters to 15 Liters
MKPDS065S020DLFLM-PH-ETO	460	12.5 Liters to 22.5 Liters
MKPF020DLFLM-PH-ETO	500	10.8 Liters to 18 Liters
MKPF100020DLFLM-PH-ETO	460	15 Liters to 27 Liters
MKPS020DLF2Z(6"LS)-PH-ETO	500	9 Liters to 15 Liters
MKPDS065S020DLF2Z(6"LS)-PH-ETO	460	12.5 Liters to 22.5 Liters
MKPF020DLF2Z(6"LS)-PH-ETO	500	10.8 Liters to 18 Liters
MKPF100020DLF2Z(6"LS)-PH-ETO	460	15 Liters to 27 Liters

Option 1

Setup

1. Unpack the filter disc or capsule from its package.
2. Place the Luer Loc cap(s) found in the filter package onto the filter vent ports. This doesn't apply to the 40 mm and 50 mm filter discs as there is no Luer Loc vent port.
3. Connect the outlet tubing from the repeater pump (Luer Male) to the Luer Female on the Inlet side of the filter.
4. Open the bleed port on the filter. Slowly start the repeater pump and run until all air is bled from the filter and only medication is coming out. Close the bleed port and turn the repeater pump up to normal speed and continue until the batch is finished.



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Flushing the Filter

The medication must be flushed from the filter before conducting the Bubble Point Test. This is required because the surface tension of all end user medications is not known, and a known fluid surface tension is required to conduct an accurate bubble point test.

A 60% IPA and 40% Di water solution is going to be used as the test fluid to conduct the bubble test. Two (2) methods are available to flush the filter. A Table listing the flushing volume is provided as reference:

Table 2: Flushing Volume Based on Filter Series

Filter Series	Flushing Volume
D40 Discs	100-300 mL
D50 Discs	100-300 mL
D65 Discs	100-300 mL
D90 Discs	100-300 mL
JKP Capsules	300-600 mL
MKP Capsules	300-600 mL
SKL Capsules	600-2000 mL
SKP Capsules	600-2000 mL
SKV Capsules	600-2000 mL

Note: If using DI water, the flushing volume needs to be increased by roughly 20%

Bubble Point Testing

A 60 ml syringe can be used. Draw 60 ml from the 60% IPA and 40% Di water reservoir and connect to Luer Loc on the syringe to the filter's inlet as shown in Figure 1. Depress the plunger as rapidly as possible flushing the medication from the filter. Repeat until the appropriate amount of the IPA and water mixture has been flushed through the filter according to Table 2. (**Note:** It may be too difficult to force the 60% IPA and 40% Di water solution through the dirty filter, if so, use the second option.)



Figure 1: Depiction of a Syringe Connected to Inlet side of the Filter



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Option 2

Setup

1. Upon arrival, the bubble point test stand may have already been assembled. This means that the regulator, pressure gauges, and fittings are put together.
2. Some general assemblies require connecting the pressure pot's inlet and outlet to the bubble point test stand and connecting two more disc filters with Oil Removal Pre-Filter and Moisture Removal Pre-Filter. A picture of the set up can be seen below in Figure 2.

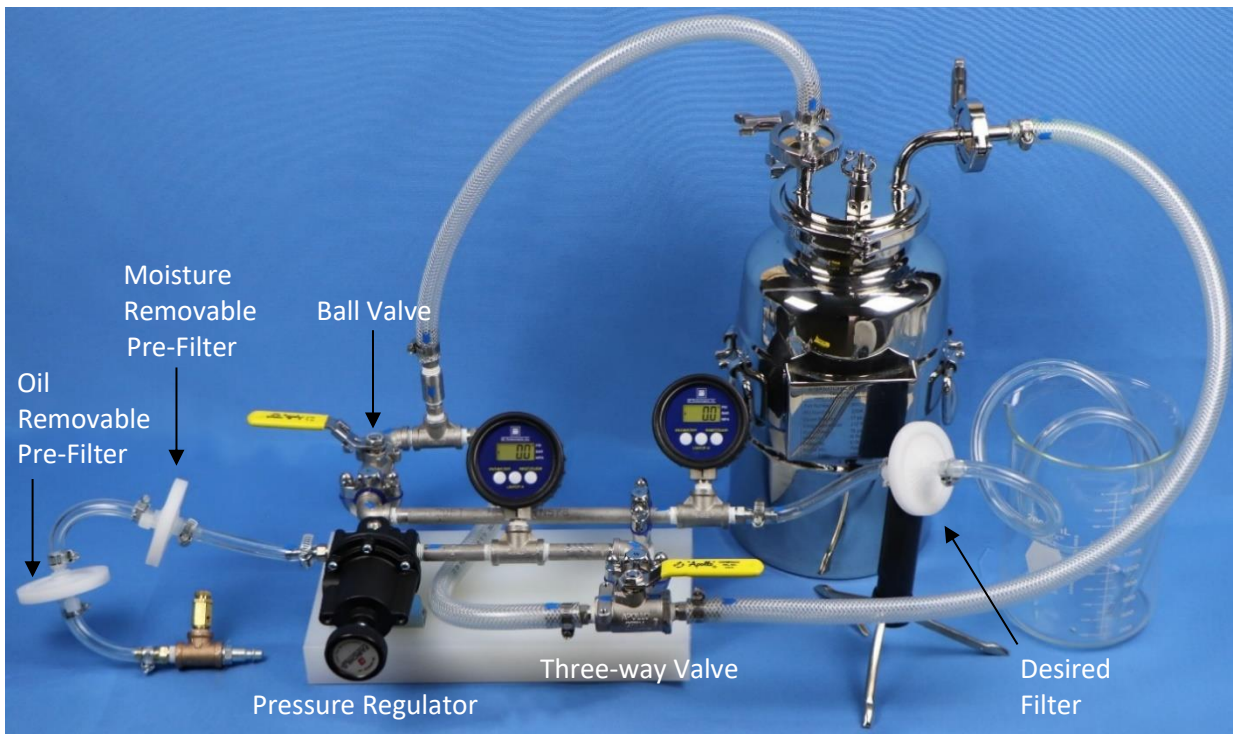


Figure 2: Bubble Point Test Apparatus

3. For less confusion, hoses have been labeled with letters A-G. Hose A will be connected to the air compressor and the inlet of the disc filter with Oil Removal Pre-Filter Membrane. The Oil Removal Pre-Filter Membrane will filter out the oil particles from the air compressor. As a precautionary measure, the recommended starting pressure for the air compressor is 20-40 psi. A pressure relief valve will be provided with the package to avoid excess starting pressure. The valve will be set at 30 – 35psi by default and can be adjusted when required. (**Note:** The testing requires different pressure input depending on the testing fluid, shown in Table 3. The pressure range can be altered on the relief valve by setting the adjustment screw accordingly.)
4. Hose B will be connected to the outlet of the disc filter with Oil Removal Pre-Filter Membrane to the inlet of the disc filter with Moisture Removal Pre-Filter Membrane. The Moisture Removal Pre-Filter will absorb the moisture from the air.



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5. Link the disc filter with Moisture Removal Pre-Filter Membrane to the pressure regulator with Hose C, followed by connecting Hose D to the tee connector and outlet of the pressure pot, while Hose E is connected to the threaded diverting valve and inlet of the pressure pot.
6. Hose F will be connecting the second pressure gauge and to the inlet of your desired testing filter. Before connecting the Hose F to the filter of your desired connection please see section “Flushing the Filter: Steps 1-4”.
7. Lastly Hose G will be connected to the outlet of your desired testing filter. Meanwhile, hang excess hose into a beaker (at your discretion) to drain the testing fluid.
8. Fill up the pressure pot with enough fluid to use for bleeding out air from the hoses, flushing the filter, and bubble point test (recommended volume is 2-5Liters). Seen below in Figure 4.
(**Note:** Table 2 shows the suggested amount of solution for flushing volume.)

Below shows a flow chart to reflect the steps of the apparatus setup labeled Figure 3.

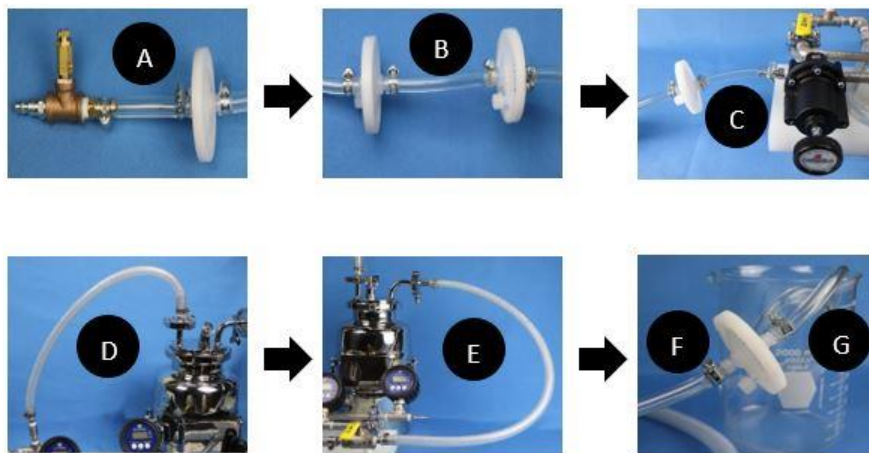


Figure 3: Flow Chart Setup



Figure 4: Filling the Pressure Pot

Note: Before testing, make sure all Hose connections in the system have clamps secured at the connection points to ensure that there are no leaks in the system. See Figure 5.



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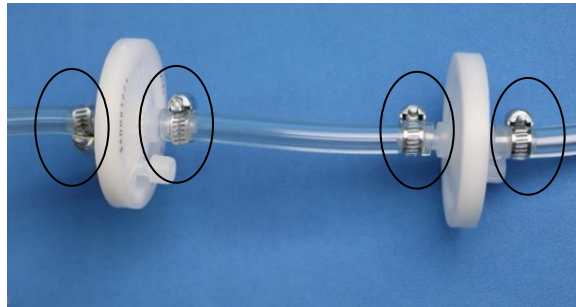


Figure 5: Disc Filters Connected

9. Connect the quick disconnect hose coupling with quick coupler from your air compressor. Pull the coupler body and insert the quick-disconnect hose. See Figure 6.

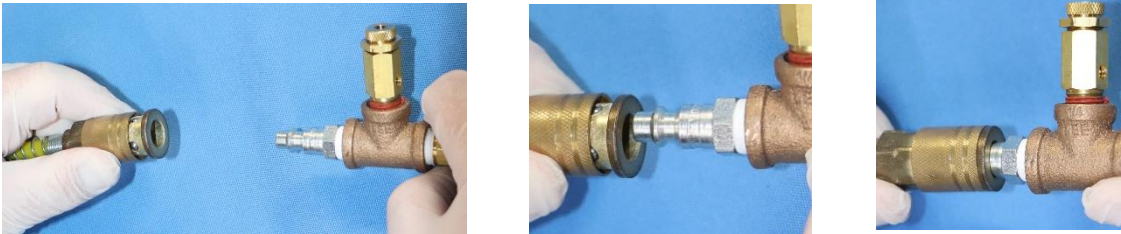


Figure 6: Connection the Air supply

Note: If there's hissing coming from the pressure relief valve, the incoming air pressure has mechanically activated the relief valve, this means the air compressor is set at higher value than accepted and the valve is releasing the excess pressure. Adjust the air compressor regulator to 40-45 PSI. Refer to your air compressor manual for operating instructions.

Flushing the Filter

1. Orient the handles on the three-way valve shown in Figure 7 (left) and ball valve shown in Figure 7 (right) as such. The compressed air will bypass the pressure pot and will allow air to flow out of the system.



Figure 7: Handle Position: Three-way valve to allow air to flow (left) and Ball valve in open position (right)



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2. Turn on all pressure gauges by pressing the on/off/unit button. The first pressure gauge connected to the pressure regulator should read 0-5 psi at the start. Slowly turn the pressure regulator in a clockwise direction to allow air to flow through. See Figure 8.



Figure 8: Pressure Gauge and Pressure Regulator

3. Turn the handle on the three-way valve to allow air to flow through the pressure pot in order to push the alcohol/water solution out through the system bleeding out the air from the testing line into the beaker. (Note, the test filter has not been installed.)

(Note: This will reduce the pressure, time, and alcohol/water solution needed to flush and properly wet the filter for testing.)

4. Turn the ball valve to the closed position and turn the pressure regulator in a counterclockwise direction until pressure reading is back to 0 psi. Return the three-way valve handle back to its original position to bypass the pressure pot. The handles should be oriented as such, once completed shown in Figure 9.

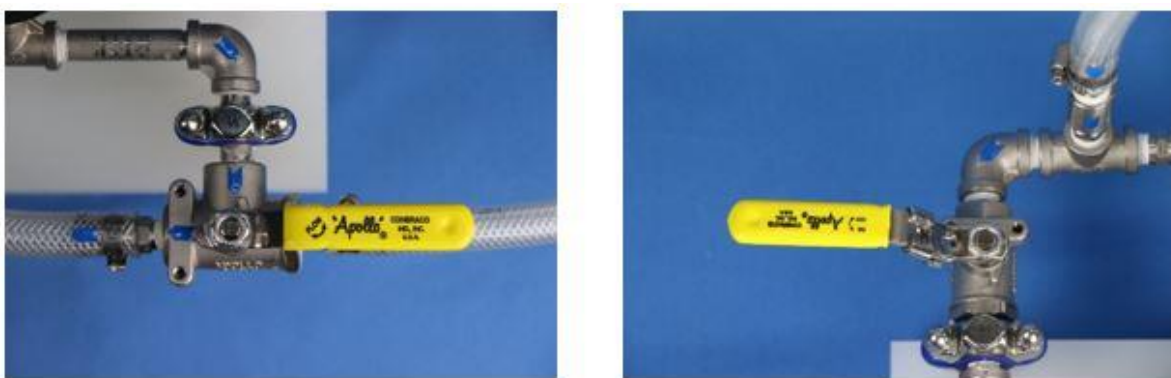


Figure 9: Handle Position: Three-way valve to bypass pressure pot (left) and Ball valve in closed position (right)



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- Now connect the filter you want to test, with the connection fitting that is most applicable to your filter shown in Figure 10.

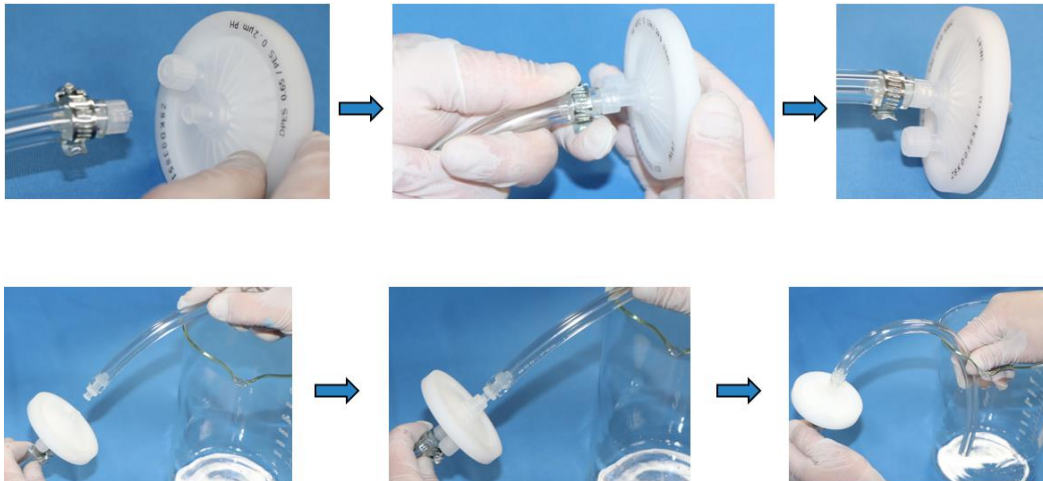


Figure 10: Filter connection setup. (Note your filter may be different than shown).

- Now that the test filter is connected, slowly turn the pressure regulator in a clockwise direction to allow air to flow through the pressure pot. This will push the solution through the system. The pressure gauge should read no more than the acceptable Bubble Point pressure mentioned in Table 3.

Table 3: Acceptable Bubble Point Values

Bubble Point Fluid	PES – BP value			PTFE – BP value			Nylon – BP value			PE – BP value		
	<i>psi</i>	<i>Bar</i>	<i>MPa</i>	<i>psi</i>	<i>Bar</i>	<i>MPa</i>	<i>psi</i>	<i>Bar</i>	<i>MPa</i>	<i>psi</i>	<i>Bar</i>	<i>MPa</i>
Water	50	3.445	0.345	50	3.45	0.345	50	3.45	0.345	50	3.45	0.345
60% IPA/ 40% H ₂ O	18	1.24	0.124	18	1.24	0.124	18	1.24	0.124	18	1.24	0.124
70% IPA/ 30% H ₂ O	17.5	1.21	0.121	17.5	1.21	0.121	17.5	1.21	0.121	17.5	1.21	0.121



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7. Switch the three-way valve (allow air to flow through the pressure pot to push the solution) and ball valve to the open position to allow the solution to flow through the system and down through the filter as shown in Figure 11. The second pressure gauge reading should start increasing in pressure.

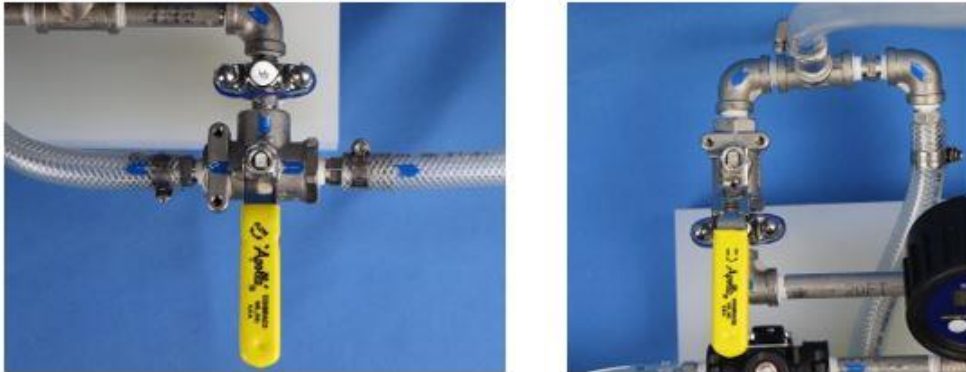


Figure 11: Handle Position: 3-way valve to flow through pressure pot (left) and Ball valve in open position (right)

8. Repeatedly turn the lever on and off on the 2-way ball valve displayed in Figure 12. This will create pulses or surges allowing the solution to force out the medication currently saturating the outer edges of the filter membrane filter. After few repetitions, leave the 2-way ball valve completely open. Allow solution to flow from the filter until no significantly large air bubbles are present in the downstream flow.

(Note: If medication fluid on the outer edges of the filter membrane are not forced out, this would lead to a faulty test.)

(Note: As seen in the picture below, it is a good idea to connect the hose to the outlet side of your desired testing filter and elevate the end of the hose in such a manner that the air bubbles can be seen easily. Make sure the connection on the outlet of the filter is tight and secure. The outlet tube might create a siphon affect and suck in air from any loose connection creating a faulty reading.)



Figure 12: Handle on 2-Way Valve Motion, Test filter orientation



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9. Once all the large air bubbles as well as any left-over medication have all been flushed from the testing filter, turn the ball valves to the off position shown in Figure 13. Now the bubble point testing can begin.



Figure 13: Handle Position to Discontinue the Flow of Air into the System

Bubble Point Testing

1. Now that bubble point testing is about to occur, set the air compressor to regulate an airflow of 10-15 psi to pass through the system. The 10-15 psi reading can be confirmed by taking a reading from the pressure gauge connected next to the regulator or adjusting the dial on the air compressor shown in Figure 14.

(Note: The range of pressure also changes with respect to the Bubble Point Fluid shown in Table 3.)



Figure 14: Adjusting regulator knob and setting pressure.



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2. Turn the 3-way valve to the other direction as seen in Figure 15 as to allow the flow of compressed air to go directly to the bubble point stand.



Figure 15: Handle Position to Allow for Flow of Air to Bypass Pressure Pot

3. Turn on the ball valve shown in the Figure 15 and let the pressure gauge attached on the other end of the ball valve to measure the pressure of the incoming air flow.
4. Once the air source is flowing in the direction to bypass the pressure pot, keep an eye on the outlet hose coming out of the filter for large air bubbles. Since it should be filled with solution, air bubbles should be easily seen.
5. Slowly increase the air pressure by turning the knob on the regulator until 17.5 psi, 18.0 psi or 50 psi is achieved on the second pressure gauge depending on the bubble point fluid. Continue to monitor the outlet hose of the filter for large bubbles.
6. **If there are no bubbles, the filter passed the bubble test and product filtered should be sterile.** If there are bubbles, they will flow in a continuous stream and will therefore consider this a failure of the bubble point test.

(Note: we suggest the technician continue to increase the pressure slowly past bubble point fluid value, after approximately every 0.5 psi increase to check the outlet of the filter. Sometime around 4-5 psi increase bubbles should appear. This will demonstrate what the technician is looking for during a failed test but at lower pressure levels.)



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Maintenance

This is intended to establish recommended practice as well as to give general advice and guidance in the maintenance of the equipment and operations.

Weekly Quick Check:

1. Inspect all fasteners for tightness, including clamps, nuts, and bolts.
2. Check for leaks throughout the system.
3. Check all tubing and high-pressure hoses for wear and abrasion.
4. Check all electrical components are operating correctly.

Apparatus: Make sure to turn off all air sources and relieve any air pressure that may be stored in the system.

Pressure Pot: Drain, clean, and dry the fluid from the pressure pot after daily use. Leaving fluid or residue for long periods promotes contamination, thus compromising the integrity of the test.

IMPORTANT: Pull up the key ring on the pressure pot until all air pressure is relieved, shown in **Figure 16**. If this is not done correctly and the lid is opened while the pot is pressurized, severe injury may occur.

Pre-Filters: To keep the system running at peak performance, replace oil removing filters and moisture removing filters after an average of **120-150 trials** or **every 4 months** due to the build-up of dirt and debris.



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Trouble Shooting Abnormalities

This section deals with abnormal occurrences of the Bubble Point Test stand. Some unusual occurrences might take place during different steps of the testing. Any unplanned incidents can be prevented by following the troubleshooting guideline. Some common issues and its troubleshooting are described below:

1. Leaks: The integrity test involves fluid flow due to pressure, and the technician might experience leaks in the system. Usually, leaks might occur on a hose or at the connection. It's highly recommended to check for leaks every time before testing to prevent any unwanted occurrence. If a leak is spotted on the body of a hose, replace it with a new hose. If leakage occurs at the connections, reconnect the joint and fasten tightly with the provided worm-drive clamps. It is also recommended to handle the filter connection carefully as most filters are constructed with thermoplastic or synthetic polymers, which tends to deform if not appropriately handled. Any damage to the connection will require replacement of the filter.
2. Unusual noise from the Pressure Relief Valve: If there is unusual noise or hissing from the pressure relief valve, that means the relief valve is releasing excess pressure from the air compressor. The noise can be reduced or stopped by adjusting the input air pressure from the compressor. However, the testing requires different pressure input depending on the testing fluid, and the pressure range can be altered on the relief valve by setting the adjustment screw accordingly. Check if the adjustment is accurate by reading the pressure gauge connected to it, otherwise repeat the calibration until the desired pressure is achieved.
3. Set the correct unit on the Pressure gauge: The provided pressure gauges can measure pressure in three different units, which are Psi, Bar, and MPa.
4. Unexpected Fluid Flow: If the fluid flow is not as planned, review the manual and orient the valve handle according to the referred figure.
5. Excess Fluid Drain: If the technician experiences a continuous surge of fluid and air while bleeding out the air or flushing the filter, that means there's an excess fluid drain from the system; thus, the pressure pot is running out of fluid. In such cases, discontinue the airflow immediately. The pressure pot will need to refill with fluid in order to bleed out all the air and to wet the filter. Ensure that the filter is thoroughly and uniformly wet such that all the pores are filled with fluid. Failure to wet the filter may result in premature airflow resulting in a false failure. It is important to release all the pressure from the pot by pulling pressure relief valve key ring all the way up before refilling the pot.
6. Over Venting the testing filter: It is suggested to vent air from the desired testing filter while flushing if there is any vent valve on it. The air particles vent immediately as soon as the vent valve is discharged, and the fluid starts leaking. Shut the vent valve on the filter instantly once the fluid starts leaking.
7. Inlet and outlet connection of filter: The pre-filters and desired testing filter can be damaged if not appropriately oriented to the system. All filters indicate the inlet or outlet on its body. The operation capacity of maximum reverse pressure is significantly less than the maximum forward pressure in a filter. Therefore, incorrect orientation will result in breakage on the membrane and deformation of the filter body. Replacement of the filter is necessary in such cases.



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WARNING: For safety reasons make sure to turn off all air sources and relieve any air pressure that may be stored in the system. This is especially important in the case of the pressure pot as it is dangerous to open before relieving pressure via the pressure relief valve. Pull up on the key ring as shown in Figure 16 until all air pressure is relieved. If this is not done properly and the lid is opened while the pot is pressurized, severe injury may occur.



Figure 16: Pressure Relief Valve Key Ring