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Bubble Point Integrity Test Procedure

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A	05/14/2021	Added Post Bubble Point Test Procedure Section	11
B	07/27/2021	Added Diffusive Flow Instruction	10

Scope

This procedure defines protocols necessary to determine if, after use, a filter has maintained its integrity. The bubble point test is the most reliable and commonly adopted method to test filter integrity. The surface tension of the end user's filtered solution is unknown; a solution of 70% isopropanol alcohol (IPA) and 30% Deionized (DI) water (*) or 60% isopropanol alcohol (IPA) and 40% Deionized (di) water (*) is used for flushing the solution from the filter and wetting 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 the pressure of 18 psi can be achieved before bubbles are seen on the downstream side, the filter can maintain the 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 70%/60% IPA and 30%/40% DI water (*) is that the tubing pressure is much lower, making the operation safer for the operator. The test filter is easier to wet with the alcohol/water mixture.

It is recommended to use 70% IPA since pharmacists routinely keep 70% IPA and 30% DI water(*) on hand. The acceptable value is 17.5 psi; see table 3.

(*) DI water can be substituted by RO water, Purified Water or Sterilized water.

International Filter Products offers affordable and compact Bubble Point Test Stand – Basic Model (shown in figure 1) for convenient filter integrity tests in the industry.

Figure 1: Fully assembled Bubble Point Test Stand Basic Model

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 cm^2), SKL-S (1,380 cm^2), and SKL-L (2,550 cm^2).

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

Flushing the Filter

Any filter prior to bubble point test using Bubble Point Test Stand Basic Model needs to be flushed. The filtered medication with an unknown surface tension must be flushed and replaced by known fluid surface tension to acquire an accurate bubble point value.
Capsule filters have pleated membrane or media, which makes it more challenging to flush the filter thoroughly. The pleated structure provides more folds and air pockets. It is highly recommended to repeat the flushing method twice or thrice if the capsules fail to obtain the bubble point value at the first few trials.

It is recommended to use 70% or 60% IPA solution as the flushing fluid. DI water is also considered as one of the flushing fluids. However, PTFE membrane are hydrophobic, and it can only be flushed using 70% or 60% IPA.

Benefits of using 70% IPA 0r 60% IPA:

- Flushes medication from the filter membrane quicker and better than DI water.
- The acceptable bubble point value is more than 50% less than DI water which means the maximum pressure within the device will be 50% less if flushed with IPA. The reduction of pressure increases safety significantly.
- PTFE membrane are hydrophobic, and it can only be flushed using 70% or 60% IPA. PES membrane or PP media can be flushed with both DI water and IPA solution. Therefore, IPA solution can flush all types of membrane/media and the laboratory does not need to keep multiple flushing fluid available.

Table 2 listing the estimated 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 20%-25%

Bubble Point Test Procedure

Acceptable Bubble Point Value:

Table 3: Acceptable Bubble Point Values

Bubble Point Fluid	PES – BP value			PTFE – BP value			Nylon – BP value			PE – BP value		
	psi	***Bar***	***MPa***	***psi***	***Bar***	***MPa***	***psi***	***Bar***	***MPa***	***psi***	***Bar***	***MPa***
Water (*)	50	3.445	0.345	NA	NA	NA	50	3.45	0.345	50	3.45	0.345
60% IPA/ 40% H_2O	18	1.24	0.124	18	1.24	0.124	18	1.24	0.124	18	1.24	0.124
70% IPA/ 30% H_2O	17.5	1.21	0.121	17.5	1.21	0.121	17.5	1.21	0.121	17.5	1.21	0.121

(*) Water can be substituted by DI water, RO water, Purified Water or Sterilized water.

Note: PTFE Membrane is hydrophobic, and the bubble point test can only be performed with an alcohol solution

Setup

1. Place the Bubble Point Test on a table top where the air-compressor nozzle is accessible. IFP-161-0002 Bubble Point Test Stand Basic Model is stable on the stand. However, there is the option to physically mount the device with a screw on the work table. Figure 2 shows the construction of the Bubble Point Test Stand while shipped to the customer.

Figure 2: Bubble Point Test Stand

2. Adjust the viewing angle where the pressure gauge is clearly visible. The stand allows to adjust the viewing angle between ± 30° . The feature makes it convenient for technicians with different heights. Figure 3 represents the adjustment on the stand.

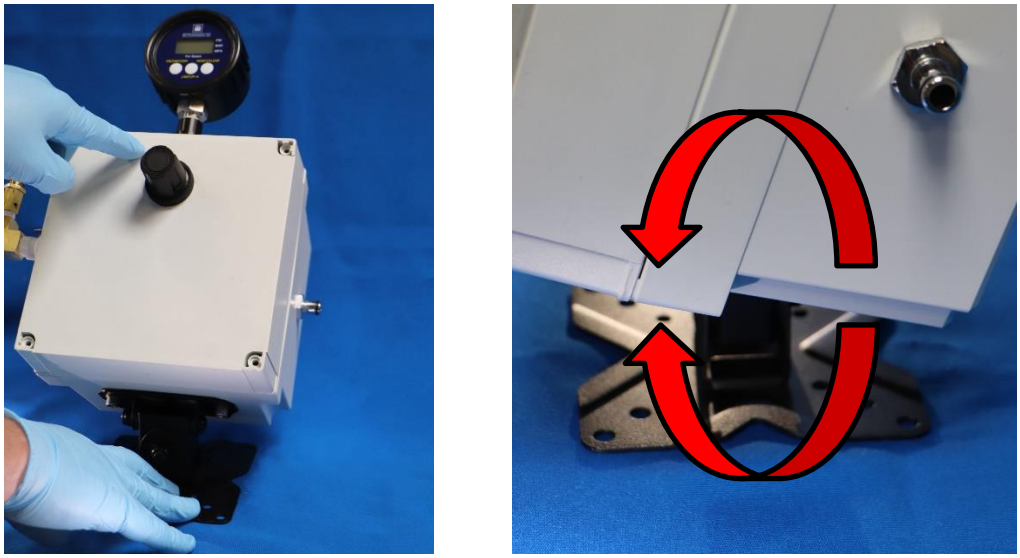

Figure 3: Adjustable mount

3. Hose A is provided with quick disconnect fitting on one side and filter (disk or capsule) inlet adapter on the other side. Connect Hose A with the Bubble Point Test Stand from the quick disconnect connection. Connect the filter (disk or capsule) inlet connection with the other end of Hose A. The steps are shows in the figure 4.

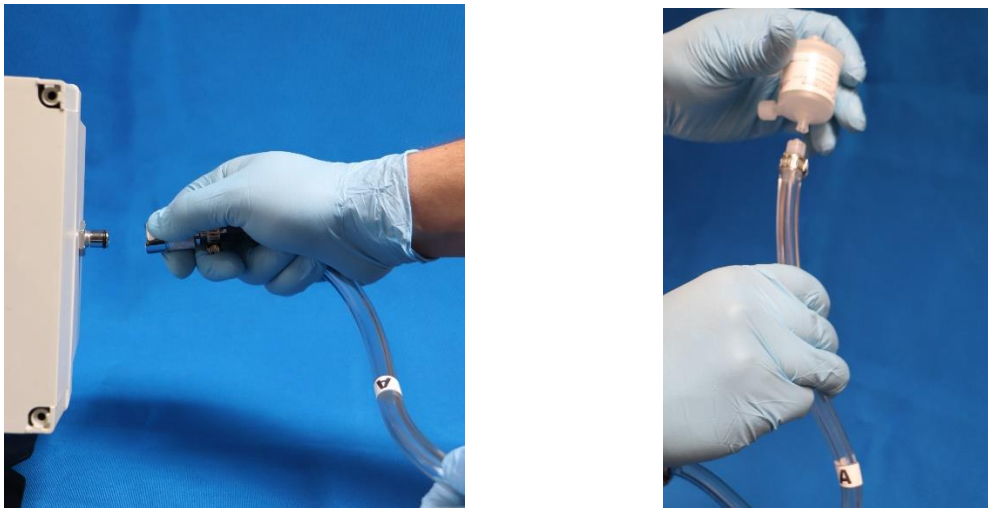

Figure 4: Hose A Connection with Test Stand and Test Filter

Note: The filter inlet adapter is subjected to change with the connection type of the test filter. The Bubble Point Test Stand will have Luer Loc Male and Luer Loc Female adapter by default. In case of hose barb connection, connect the test filter directly with Hose A without any adapter. For other connections, select an appropriate adapter or contact International Filter Products for assistance.

4. Hose B has test filter (disk or capsule) outlet adapter on one end and funnel on the other end. Connect the test filter (disk or capsule) outlet with the Hose B from the adapter side (shown in figure 5)

Figure 5: Hose B connection with Test Filter

As shown in figure 6, hang the Hose B vertically using a stand. The funnel will store water to trace the bubbles from the integrity test.

Figure 6: Funnel position

5. Turn on the pressure gauge and set the unit to PSI. The pressure gauge screen will be lit up if it is turned on correctly.

Figure 7: Switched on pressure gauge with lit screen

Note: The pressure gauge turns off automatically after few minutes of idle time. Make sure the pressure is always turned on while the bubble point test stand is connected to the air compressor.

6. Make sure the pressure regulator knob is turned all the way back. Turn the knob counterclockwise as (shown in figure 8) to double check.

Figure 8: Turning Pressure regulator to stop airflow in the system

7. The last step to set up the Bubble Point Tester is to connect with an air compressor. Connect the air-compressor nozzle with the Bubble Point Test Stand from the quick-disconnect hose coupling (shown in figure 9). The air coupling connection is also connected with a pressure relief valve to ensure safety in case the air-compressor is set at very high pressure. Initially, the pressure relief valve is set to release air at 55-60 psi. If there is a hissing noise or the relief valve activates after connecting to the air compressor, decrease the air pressure from the air compressor.

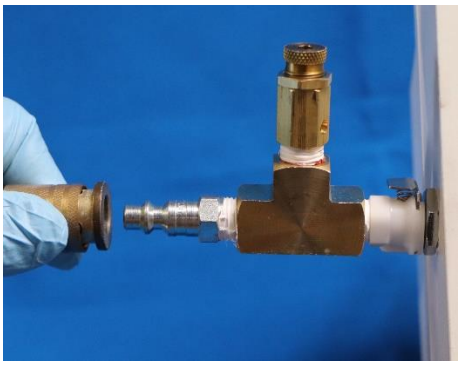

Figure 9: Connecting the Bubble Point Test Stand with air-compressor

Safety

1. Check the pressure indicator on the air compressor before connecting with the Bubble Point Test Stand. The air pressure should not exceed 60 psi. IFP-161-0002 is compatible with test filters (disk or capsule) that are flushed with both IPA and DI water (Table 3 represents the acceptable bubble point value). The highest pressure needed for test filters that are flushed with DI water (50 psi). Thus, limiting the air-pressure from the regulator at 60 psi restricts the device from getting over pressurized.
2. Check if the air relief valve is hissing after the air-compressor is connected. The air relief valve will be set at 55-60 psi by default. If hissing, adjust the air-compressor and lower the pressure from the supplied air. **Note**: The air relief valve can be adjusted if necessary. If the test filter (disk or capsule) is flushed with IPA, it is recommended to set the air-relief valve at 35 psi.
3. Check the pressure gauge and air regulator before performing the Bubble point test. Make sure the pressure regulator is reading 0 psi initially. If the pressure regulator is showing pressure more than 0 psi, turn the air -regulator knob counter-clockwise until the pressure gauge reading comes back to 0 psi.

Bubble Point Testing

1. Once the device is set up, fill the funnel on Hose B with water to trace the bubble from the integrity test. Add water with a syringe to the funnel. Make sure to be careful about spilling water while adding.

Figure 10: Adding water to the funnel

2. Slowly turn the knob of air regulator clockwise to let the air through the device. The representation is shown in figure 11.

Figure 11: Turning Pressure regulator to allow airflow in the system

3. The pressure gauge reading should increase at a slow increment (preferably 1-5 psi) to identify the pressure when the bubble starts coming out from the test filter.
   Diffusive Flow: Diffusive flow of bubbles will appear from downstream of the filter once the pressure increases. Keep increasing the pressure using the air regulator up to 50% of minimum Bubble Point Value at a slow increment and let the diffusive flow of bubbles settle down for 10 seconds.
4. 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 pressure gauge depending on the flushing fluid (see Table 3). Continue to monitor the outlet hose of the filter (Hose B) for bubbles. If there are no bubbles until the minimum accepted bubble point value, the filter passed the bubble test and product filtered should be sterile. If there are bubbles before that point, they will flow in a continuous stream and will therefore consider this a failure of the bubble point test.
   Note: In case of failure, it is recommended to flush and re-test the filter one more time. Follow table 2 for the estimated flushing volume for your filter (disk or capsule). If the filter (disk or capsule) is flushed long time after usage, some medication settles on the membrane/media and it is harder to flush. Capsule filters have pleated membrane or media, which makes it more challenging to flush the filter thoroughly. The pleated structure provides more folds and air pockets. It is highly recommended to repeat the flushing method twice or thrice if the capsules fail to obtain the bubble point value at the first trial. Experiments show that it is more convenient to use an alcohol solution as bubble point fluid for capsules or pre-wet the media/membrane with an alcohol solution before using DI water (*). Flushing filters (disk or capsule) from the downstream is also recommended before bubble point test.

Post Bubble Point Test Procedure

Once the bubble point test is completed it is import to safely turn-off the device and detach the test filter. Follow the following post bubble point test procedure,

1. Turn off the air flow within the device by turning the knob counterclockwise as (shown in figure 12) and disconnect the air compressor.

Figure 12: Turning Pressure regulator to stop airflow in the system

2. Have a container or beaker underneath the test filter before detaching (shown in figure 13).

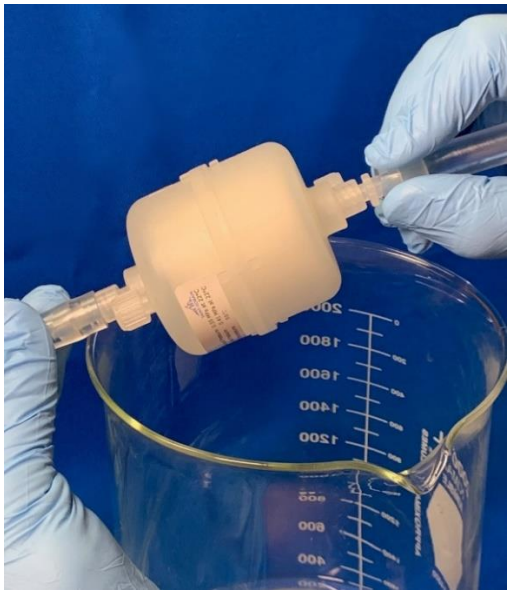

Figure 13: Detaching Test Filter after Bubble Point Test

As soon as the test filter is disassembled from Hose A and Hose B, the water from the funnel and the test filter will start draining. It is important to securely store the water and avoid spilling in the laboratory.

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 gauge and regulator are operating correctly.

Pre-Filters Replacement

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. The pre-filters are installed within the device. Unscrew the Bubble Point Test Stand from the back side to disassemble. Contact International Filter Products for replacement pre-filters. Use a screw driver to take off the clamps from the pre-filters before replacement (see figure 12).

Figure 14: Pre-filter installment

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 air 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 is 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, 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. 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.
5. 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.