TECHNICAL BRIEF

Integrity Testing BioASSURE™ PDA020 Filters

INTRODUCTION

The integrity test is a non-destructive method for the End User to confirm the structural integrity of a BioASSURE filter before and after use. An “in specification” result confirms the porosity of the filter membrane and that the cartridge is structurally integral. Three methods can be employed to integrity test hydrophilic (water wettable) BioASSURE filters. These methods are:

1. Forward Flow Integrity Test (FFIT)
2. Bubble Point Test (BPT)
3. Pressure Hold Test (PHT)

All three integrity tests can be performed manually or with the CUNOCheck®2 Automated Integrity Tester. For more information about using the CUNOCheck 2 tester to perform an integrity test, refer to the CUNOCheck 2 Operator Manual (LITCCK2OPS).

FILTER WET-OUT (Refer to Figure 1)

Prior to performing an integrity test, the filter membrane must be thoroughly wet with water. Typically, WFI or SWFI is used to wet the filter. (Note: if the process requires wetting the filter with a fluid other than water, testing will be required to correlate water integrity test values to test values obtained in the test fluid). Testing has shown that the BioASSURE PES membrane is easily wet with water. Any of the following three methods may be used to ensure the cartridge membrane is thoroughly wet prior to the integrity test:

1. Close valves V2, V3 and V5. With the housing vent valve V4 open and the downstream valve V6 slightly opened (or completely closed), open V1 and fill the housing with water. When water begins to exit through the housing vent valve V4, close the vent valve V4, close the downstream valve V6 and stop the flow of water into the housing by closing V1. Allow water to remain in the housing for approximately 10 minutes to statically wet the cartridge(s). Open the vent valve V4, the housing drain valve V2 and the downstream valves V5 and V6 to drain the housing. After the housing has completely drained close V1, V2, and V4. Leave V5 and/or V6 open. Perform the required integrity test. **(Note: the drain port for valve V5 should be of sufficient size to permit the cartridge core to completely drain under gravity when opened.)**
2. Close valves V2, V3, V5, and V6. Open valve V4. Fill the housing with water by opening valve V1. When water begins to exit through the housing vent valve V4, close the vent valve V4 and slowly open valve V6 (if the rinse water is to be directed through the downstream system) or slowly open V5 if rinse water is to be directed to the drain. Flow water through the housing for approximately 5 minutes at 11.4 liters per minute (3 gpm) per 10” cartridge with 0.35 bar (5 psig) back pressure. After flowing water through the cartridge(s) for 5 minutes, stop the flow by closing valve V1. Open the vent valve V4, housing drain valves V2 and V5 to completely drain housing. After the housing has completely drained close V1, V2 and V4. Leave V5 and/or V6 open. Perform the required integrity test.
3. Close valves V2, V3, V5, and V6. Open valve V4. Fill the housing with water by opening valve V1. When water begins to exit through the housing vent valve V4, close the vent valve V4 and slowly open valve V6 (if the rinse water is to be directed through the downstream system) or slowly open V5 if rinse water is to be directed to the drain. Flow water through the housing for approximately 5 minutes at 11.4 liters per minute (3 gpm) per 10” cartridge with 1.7 bar (25 psig) back pressure. After flowing water through the cartridge(s) for 5 minutes, stop the flow by closing valve V1. Open the vent valve V4, housing drain valves V2 and V5 to completely drain housing. After the housing has completely drained close V1, V2 and V4. Leave V5 and/or V6 open. Perform the required integrity test.

FORWARD FLOW INTEGRITY TEST (Refer to Figure 1)

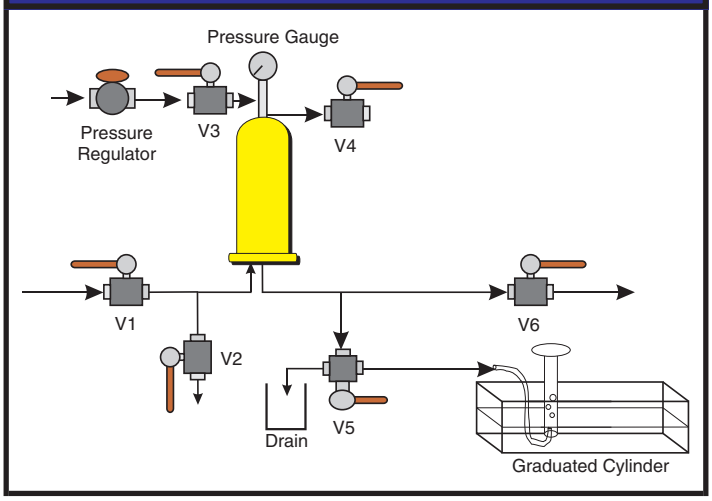
1. Definition

According to Fick's Law of Diffusion, when a differential gas pressure exists across a wetted membrane, the gas molecules will "diffuse" through the water filling the pores of the membrane. The rate of passage is proportional to the solubility of the gas in the wetting fluid, the surface tension of the wetting fluid, the differential pressure, the thickness of the membrane, the pore size, and the surface area of the membrane. The diffusion rate is measured at a pressure below the membrane bubble point pressure. If no bulk flow exists, then there are no pores large enough to compromise the filter's integrity. The Forward Flow Integrity Test (FFIT) may be employed with a multi-cartridge housing.

2. Procedure (Manual Testing – Figure 1)

(Note: Because this method requires opening the sterile side of the filter system, take appropriate steps to maintain sterility.)

Figure 1 - Forward Flow Integrity Test (Manual Method)



A. Configure the system as shown in Figure 1. Connect a pressure regulator to a sterile compressed air source **(Do Not Use CO_2)** capable of delivering a minimum of 0.7 bar (10 psig) more than the required test pressure. *FFIT test pressure for BioASSURE PDA020 is 2.8 bar (40 psig).* Connect a length of clear flexible tubing (3-6 mm I.D.) to the outlet port of drain valve V5. Fill the reservoir to a depth of approximately 5 cm (2 inches) with sterile water. Fill a graduate cylinder or burette of an appropriate size with sterile water, invert and submerse the open end 1.2 cm (0.5 inch) under the sterile water.

B. Install filter(s) into housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in "Filter Wet-Out".

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2, V4 and V6 are closed.

D. Position V5 to direct flow to the water reservoir. (Note: ensure that the open end of the tubing is NOT under the inverted graduate cylinder/burette at this time).

E. Open V3 and slowly adjust the pressure regulator to pressurize the system (approximately 2-3 psig/sec [150 - 200 mb/sec]) to the specified FFIT test pressure (2.8 bar, 40 psig). Allow the system to equilibrate for a minimum of one minute, or until steady bubbling is observed from the submersed end of the tubing.

F. Record the starting level of the water in the inverted graduate cylinder (or burette). Simultaneously, place tubing end under the submersed end of the inverted graduated cylinder or burette and start a timer.

G. After 5 minutes, remove tubing from under the inverted graduate cylinder and record the water level in the graduated cylinder. Determine the water volume displaced and calculate the air diffusion rate in cc/minute.

H. When the test is complete compare the results to the filter FFIT specification in Table 1.

I. After the test is completed, drain any residual water from the housing and place the filter into service.

J. If the diffusion rate is higher than the specification, consider the following questions and re-test if necessary:

- Was the filter completely wet out?
- Was the correct pore size filter installed?
- Was the temperature of the water and filter ambient?
- Was the stabilization time adequate?
- Was the test time adequate?
- Was the filter seated correctly in the housing and were the o-rings undamaged?
- Are there any leaks on the upstream side of the filter?

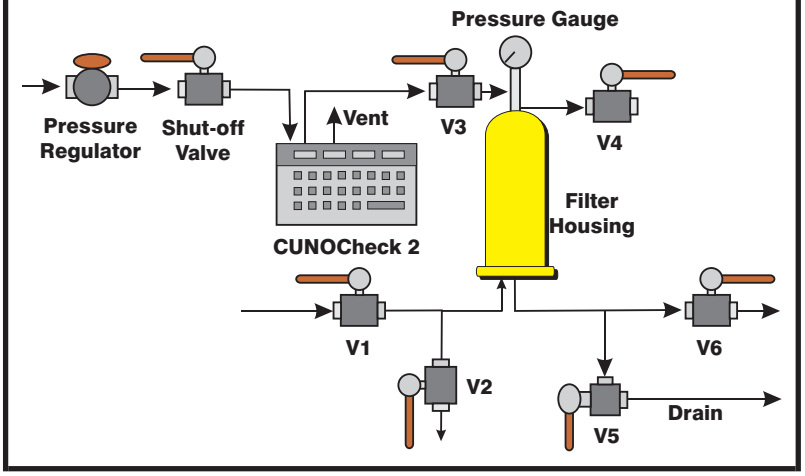
3.Procedure (Automated Method - Figure 2)

A. Configure the system as shown in Figure 2. Connect a pressure regulator to a sterile compressed air source **(Do Not Use CO_2)** capable of delivering a minimum of 0.7 bar (10 psig) more than the required test pressure. *FFIT test pressure for BioASSURE PDA020 is 2.8 bar (40 psig).*

B. Install filter(s) into housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in "Filter Wet-Out".

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2 and V4 are closed. Open valve V5 and or V6 if not already open.

Figure 2 - Forward Flow Integrity Test (Automated Method)



D. Connect the CUNOCheck 2 Automated Integrity Tester to valve V3. Adjust the pressure regulator to deliver a minimum of 3.5 bar (50 psig) to the CUNOCheck 2. Open valve V3.

E. Initiate the appropriate automated Forward Flow Integrity Test program stored in the CUNOCheck 2.

F. When the test is complete, close valve V3. The CUNOCheck 2 will indicate a pass or failed test on the printout.

G. After the test is complete and system pressure has been vented, drain any residual water from the housing by opening V2 and V4 before placing the cartridge in service.

H. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.

I. If the pressure decay is higher than the specification, consider the following questions and retest if necessary:

Is the CUNOCheck 2 programming correct for the filter being tested?

Was the filter completely wet out?

Was the correct pore size filter installed?

Was the temperature of the water and filter ambient?

Was the stabilization time adequate?

Was the test time adequate?

Was the filter seated correctly in the housing and were the o-rings undamaged?

Are there any leaks on the upstream side of the filter?

BUBBLE POINT TEST (Refer to Figure 3)
1. Definition

The bubble point is the minimum gas pressure required to overcome the surface tension holding water in a membrane filter's pores.

The bubble point pressure measurement is **only recommended** for single 10-inch or smaller cartridge and capsule filters. When more filter area is online, it can become difficult to distinguish diffusional flow from the true bulk flow which occurs at the bubble point pressure. For systems with two or more 10-inch equivalent cartridges, Forward Flow or Pressure Hold measurements are recommended. The CUNOCheck 2 Automated Integrity Tester can be used to perform a bubble point test. Prior to conducting a bubble point test the filter must be full wetted (see "Filter Wet Out" section). When using the CUNOCheck 2 tester, follow the installation instructions for connecting the unit to the upstream valve as shown in Figure 4.

Minimum Bubble Point value for BioASSURE PDA020 is 3.10 bar (45 psig)

2. Procedure (Manual Testing - Figure 3)

(Note: Because this method requires opening the sterile side of the filter system, take appropriate steps to maintain sterility.)

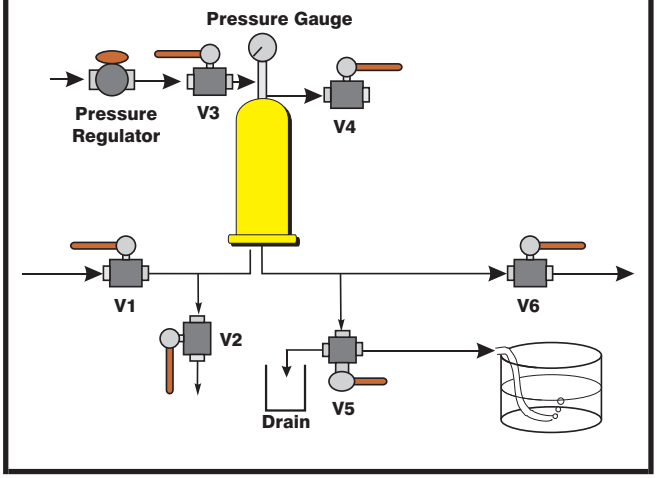
A. Configure the system as shown in Figure 3. Connect a pressure regulator to a sterile compressed air source **(Do Not Use CO_2)** capable of delivering a minimum of 1.4 bar (20 psig) more than the required test pressure. *Minimum Bubble Point test pressure for BioASSURE PDA020 is 3.1 bar (45 psig).* Fill a reservoir to a depth of approximately 5 cm (2 inches) with sterile water. Connect a length of clear flexible tubing (3-6 mm I.D.) to the outlet port of drain valve V5 and place other end into reservoir.

B. Install the filter(s) in the housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in “Filter Wet-Out”.

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2, V4 and V6 are closed.

D. Position valve V5 to direct flow to the water reservoir.

Figure 3 - Bubble Point Test (Manual Method)



E. Open V3. Using the pressure regulator, slowly pressurize the system with air (DO NOT USE CO_2), raising the pressure approximately 0.35 bar (5 psig) per minute. As the pressure is being increased observe the submersed end of the tube for a vigorous steady stream of bubbles which would be indicative of either a damaged filter device or inadequate filter wetting (Rewet the filter with method 3 described in the “Filter Wet-Out” section and retest). When within 0.35 bar (5 psig) of the specified bubble point pressure (3.1 bar, 45 psig), make only very gradual 0.07 bar (1 psig) increases allowing 10 - 15 seconds between pressure increases to observe evidence of bubbling.

F. Observe air flow from the tube connected to the downstream port. A modest flow of small bubbles is diffusional flow only. When a vigorous continuous stream of bubbles appears, the filter’s bubble point has been reached.

G. When the test is complete, compare the measured bubble point value against the acceptable limit (3.1 bar, 45 psig) for the filter cartridge under test.

H. After the test is complete, drain any residual water from the housing and place the cartridge back in service.

I. If the bubble point is less than the recommended value, consider the following questions and re-test if necessary:

- Was the filter completely wet out?
- Was the correct pore size filter installed?
- Was the temperature of the water and filter ambient?
- Was the stabilization time adequate?
- Was the test time adequate?
- Was the filter seated correctly in the housing and were the o-rings undamaged?
- Are there any leaks on the upstream side of the filter?

3. Procedure (Automated Testing - Figure 4)

A. Configure the system as shown in Figure 4. Connect a pressure regulator to a sterile compressed air source **(DO NOT USE CO_2)** capable of delivering a minimum of 1.4 bar (20 psig) more than the required test pressure. *Minimum Bubble Point test pressure for BioASSURE PDA020 is 3.1 bar (45 psig).*

B. Install filter(s) into housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in “Filter Wet-Out”.

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2, and V4 are closed. Open valve V5 and or V6 if not already open.

D. Connect the CUNOCheck 2 Automated Integrity Tester to V3.

E. If this the first time the CUNOCheck 2 Bubble Point test program is being used, follow the instructions in the CUNOCheck 2 Operator Manual to edit the “Max. Pressure Drop” field in the program. Set the Max. Pressure Drop to 28 mbar (0.4 psig) and when prompted, save the file.

F. Call up the edited program and initiate the automatic Bubble Point Test.

G. When the test is complete the CUNOCheck 2 will indicate a pass or fail on the printout based on the parameters programmed.

H. After the test is complete, disconnect the CUNOCheck 2 Automatic Integrity Tester from the housing.

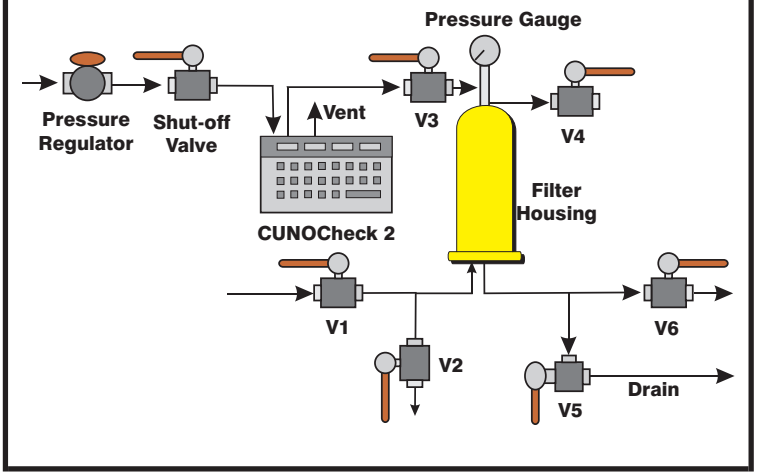
I. Drain any residual water from the housing and place the cartridge in service.

J. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.

I. If the bubble point is less than the recommended value, consider the following consider following questions and re-test if necessary:

Was the filter completely wet out?
Was the correct pore size filter installed?
Was the temperature of the water and filter ambient?
Was the stabilization time adequate?
Was the test time adequate?
Was the filter seated correctly in the housing and were the o-rings undamaged?
Are there any leaks on the upstream side of the filter?

Figure 4 - Bubble Point Test (Automated Method)



PRESSURE HOLD TEST (see Figure 5)

1. Definition

A variation of the FFIT is the Pressure Hold Test (PHT). Instead of measuring the diffusion rate of gas across the membrane, the PHT uses a sensitive pressure gauge to measure the pressure decay of a precisely know closed volume on the upstream side of the membrane as the gas diffuses through the wetted membrane. The pressure measuring device used must be capable of accurately measuring a pressure change of 10 mbar (0.15 psig). PHT value is dependent on the **total** upstream volume of the filter system being tested. Table 1 provides PHT values based on valve V1 being connected directly the housing inlet port. In systems where V1 is not directly connected to the housing inlet port, calculate the additional volume between the inlet port and V1. Add that volume to the upstream volume shown in Table 1 and recalculate the maximum allowable pressure loss using Equation 1. Contact CUNO technical services for assistance if necessary.

The CUNO Check 2 Automatic Integrity Tester can be used to perform a PHT. When using the CUNOCheck 2 tester, follow the installation instructions for connecting the unit to the upstream valve as shown in Figure 6. Consult CUNO for the appropriate PHT value for your filter housing. Program these values into the CUNOCheck 2 tester when prompted during test set-up.

Equation 1:

$$\frac{\Delta P}{T} = \frac{K(Pa)}{Vhsg}$$

Pa = Manufacturer's maximum allowable diffusion rate for all the installed filters in cc/min (see Forward Flow Integrity specifications)

T = Time (typically 5 minutes)

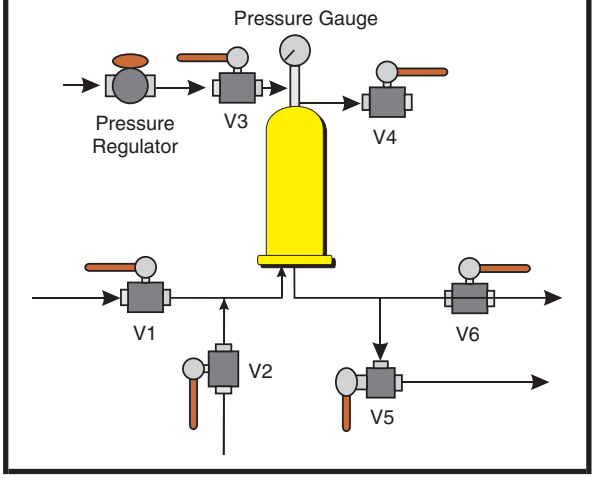
K = Atmospheric pressure, 1.01 bar (14.7 psig)

Vhsg = Upstream housing volume (cc) less the volume occupied by the cartridge(s). See note in Table 1.

ΔP = Allowable pressure loss

2. Procedure (Manual Testing – Figure 5)

Figure 5 - Pressure Hold Test (Manual Method)



A. Configure the system as shown in Figure 5. Connect a pressure regulator to a sterile compressed air source **(Do Not Use CO_2)** capable of delivering a minimum of 0.7 bar (10 psig) more than the required test pressure. *PHT test pressure for BioASSURE PDA020 is 2.8 bar (40 psig).*

B. Install filter(s) into housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in "Filter Wet-Out".

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2 and V4 are closed. Open valve V5 or V6 if not already open.

D. With V5 or V6 open to atmosphere, open V3 and slowly adjust the pressure regulator to pressurize the system, raising the pressure approximately 1.4 bar (20 psig) per minute. Allow the system to equilibrate for a minimum of two minutes.

E. At the end of the two minute equilibration record the pressure as the initial pressure (Pi). Close V3 and immediately start a stopwatch. After 5 minutes, record the pressure as the final pressure (Pf). (Note: if the pressure decay is less than the capability of the pressure measuring device, then increase the test time to 10 or 15 minutes). Determine the pressure decay by subtracting Pf from Pi, divide this value by the number of minutes in the test to obtain the pressure decay per minute.

F. When the test is complete, compare the result to the specified PHT value in Table 1.

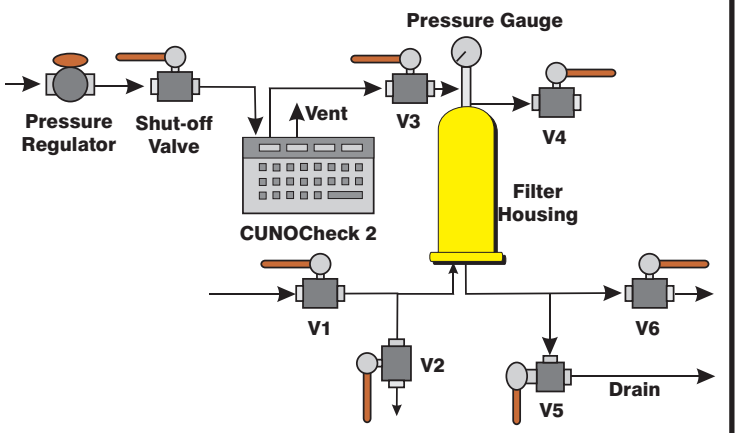
G. After the test is complete, drain any residual water from the housing and place the cartridge back in service.

H. If the pressure decay is higher than the specification, consider following questions and re-test if necessary:

Was the filter completely wet out?
Was the correct pore size filter installed?
Was the stabilization time adequate?
Was the test time adequate?
Was the filter seated correctly in the housing and were the o-rings undamaged?
Are there any leaks on the upstream side of the filter?

3. Procedure (Automated Testing - Figure 6)

Figure 6 - Pressure Hold Test (Automated Method)



A. Configure the system as shown in Figure 6. Connect a pressure regulator to a sterile compressed air source **(Do Not Use CO_2)** capable of delivering a minimum of 0.7 bar (10 psig) more than the required test pressure. *PHT test pressure for BioASSURE PDA020 is 2.8 bar (40 psig).*

B. Install filter(s) into housing and thoroughly wet with clean, ambient temperature, WFI or SWFI using one of the three wetting procedures previously described in "Filter Wet-Out".

C. Ensure all water has been drained from both upstream and downstream sides of the filter and valves V1, V2, and V4 are closed. Open valve V5 or V6 if not already open.

D. Connect the CUNOCheck 2 Automated Integrity Tester to valve V3. Adjust the pressure regulator to deliver a minimum of 3.5 bar (50 psig) to the CUNOCheck 2. Open valve V3.
E. Select the CUNOCheck 2 program that uses the appropriate upstream housing volume from Table 1 (or calculated from Equation 1) and the specified PHT test pressure.
F. Initiate the automated Pressure Hold Integrity Test program.
G. When the test is complete, the CUNOCheck 2 will indicate a pass or fail on the printout.
H. After the test is complete, drain residual water from the housing and place the cartridge back in service.
I. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.

NOTE: It is important to make an aseptic connection and to close the outlet port immediately after the system has been integrity tested to prevent contamination.

Table 1. Integrity Test Values

CUNO Filter Housing	# EQSL†	Forward Flow Integrity Test Maximum Acceptance Value (cc/min)	Upstream Housing Volume†† (cc)	Pressure Hold Test bar/min (psig/min)
1ZVS1	1	38	1,987	0.019 (0.28)
1ZVS2	2	71	3,188	0.023 (0.33)
1ZVS3	3	104	4,373	0.024 (0.35)
1ZVS4	4	137	5,557	0.025 (0.36)
1ZMS1	1	38	2,119	0.018 (0.26)
1ZMS2	2	71	3,319	0.022 (0.32)
1ZMS3	3	104	4,504	0.023 (0.33)
1ZMS4	4	137	5,705	0.024 (0.35)
4ZWC1	4	137	11,200	0.012 (0.18)
4ZWC2	8	264	14,400	0.019 (0.27)
4ZWC3	12	390	19,600	0.020 (0.29)
4ZWC4	16	516	24,800	0.021 (0.31)
8ZWC1	8	264	20,400	0.013 (0.19)
8ZWC2	16	516	28,800	0.018 (0.26)
8ZWC3	24	765	37,200	0.021 (0.30)
8ZWC4	32	1013	45,600	0.023 (0.33)
11ZWC1	11	359	27,300	0.013 (0.19)
11ZWC2	22	703	42,600	0.017 (0.24)
11ZWC3	33	1044	54,900	0.019 (0.28)
11ZWC4	44	1384	67,200	0.021 (0.30)
21ZWC1	21	672	65,300	0.010 (0.15)
21ZWC2	42	1323	80,600	0.017 (0.24)
21ZWC3	63	1970	100,900	0.020 (0.29)
21ZWC4	84	2616	136,200	0.019 (0.28)

†EQSL = (Equivalent Single Length) The number of standard 10 inch cartridge lengths.

††Upstream housing volumes assume that the inlet valve is directly connected to the housing inlet. If the inlet valve is not connected directly to the housing inlet then the upstream housing volume column must be adjusted to include the volume between the valve and housing inlet.