

TECHNICAL BRIEF

Microfluor® II Filter Cartridge Integrity Testing

INTRODUCTION

The integrity test is the End User's method to confirm the structural integrity of a membrane filter before and after use. It is a non-destructive test that has been correlated to bacteria retention and validates the performance of the filter cartridge. An "in specification" result confirms the porosity of filter membrane and that the cartridge is structurally integral.

Compressed gas and tank vent filters are typically sterilized in-place as part of the production process system to ensure the equipment has maintained sterility after in-situ sterilization and that the equipment is ready to receive sterile product. Compressed gas and tank vent filters are non-product contact filters and are usually used over an extended period of time as compared to liquid filters that are typically discarded after a single product batch has been filtered. Hydrophobic compressed gas and tank vent filters are typically subjected to multiple sterilizations and; therefore, integrity tested multiple times as compared to filters used in liquid filtration applications.

Filter integrity can be determined by any of the following four test methods.

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

Unlike the typical hydrophilic filter medium filters used for liquid filtration applications, compressed gas and tank vent filters are fabricated with hydrophobic filter medium. Hydrophobic filter medium prevents the bulk flow of aqueous based product through the filter at differential pressures below the intrusion pressure of the medium, while permitting the free passage of gas through the filter. Integrity testing of hydrophobic filters by three of the four conventional integrity test methods listed previously (FFIT, BPT and PHT) require the use of wetting agents, such as alcohol or an alcohol and water mixture, to thoroughly wet the filter membrane prior to integrity testing. All three of these tests must be performed off-line to prevent the wetting fluid from contaminating the sterile downstream side of the filter membrane.

The fourth integrity test (WIT) can be performed in-situ using sterile water. This eliminates the use of wetting agents and does not require the penetration of the filter membrane by the wetting fluid.

All four tests can be conducted either manually or with an automated integrity test device, such as the CUNOCheck® 2 Automatic Integrity Tester.

The following procedures provide the instructions for integrity testing 10" cartridges. Contact CUNO Technical Service for details on how to integrity test other cartridge and capsule configurations.

FORWARD FLOW INTEGRITY TEST

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 wetting fluid 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, and the surface area of the membrane. The diffusion rate is measured at the minimum completely retentive membrane bubble point pressure. The Forward Flow Integrity Test (FFIT) may be employed with multi-cartridge housings.

The Forward Flow Integrity Test is the preferred test method to determine if the membrane and cartridge are structurally integral. The diffusion rate is typically measured at a test pressure at or near the minimum completely retentive bubble point pressure. The Forward Flow Integrity Test has been shown to be both a quantitative measurement and to correlate to bacteria retention. The bubble point of the membrane can be a subjective determination and does not always correlate to bacteria retention.



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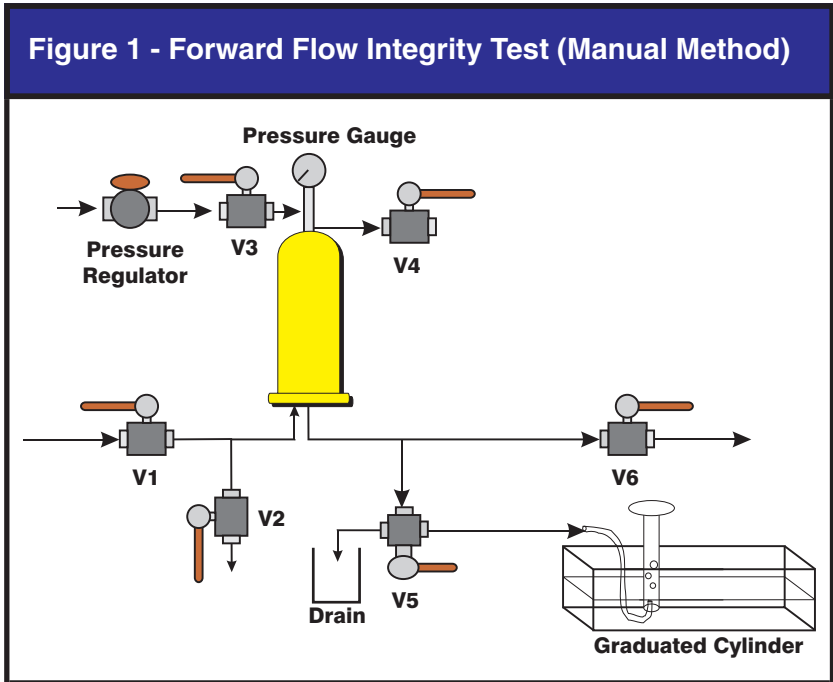
The bubble point of a membrane containing small defects will not correlate to bacteria retention due to the limited sensitivity of the bubble point test method to detect these small defects. Only the bubble point of a completely defect-free membrane will correlate to bacteria retention.

Selecting a test pressure for the Forward Flow Integrity Test at the Industry Standard Practice of 80% of the initial membrane bubble point does not ensure the integrity or the retention capability of the filter. This leaves a region between the test pressure and the membrane bubble point that is not tested and; therefore, the integrity of the membrane can not be ensured in this region. This is analogous to testing at 80% of the expected membrane bubble point.

Therefore, membrane filters should be tested at a more aggressive test pressure to ensure both the integrity and the correct pore size of the membrane. It is,

therefore, recommended that the Forward Flow Integrity Test be conducted at a test pressure at or near the minimum completely retentive membrane bubble point.

Integrity testing can be performed manually or using the CUNOCheck[®]2 Automated Integrity Tester. For more information about using the CUNOCheck 2 Tester to perform an integrity test, refer to CUNOCheck 2 Operator Manual (LITCCK2OPS).



2. Procedure (Manual Testing - Figure 1)

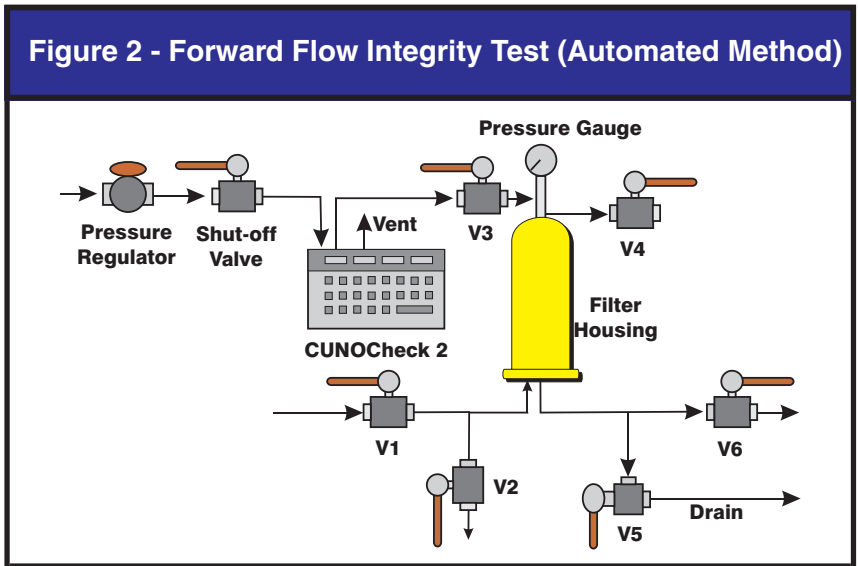
- A. Configure the system as shown in Figure 1.
- B. Install the filter in the housing and flow wetting fluid (55% / 45% **IPA** - Isopropyl alcohol / water (v/v) or 25% / 75% **TBA** - Tertiary butyl alcohol / water (v/v)) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.
- C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.
- D. Connect one end of a flexible tube to the outlet port V5 and submerge the other end in a container of water*. Position V5 to direct flow to the container of water.
- E. Open V3 and slowly adjust the pressure regulator to pressurize the system to the specified FFIT pressure value and allow the system to equilibrate for a maximum of 2 minutes, or until steady bubbling is seen from the submersed end of the tube.
- F. Place the opening of the tube under an inverted graduated cylinder or burette (calibrated in milliliters or cubic centimeters) of an appropriate size filled with and submersed under sterile water.
- G. Measure the air flow for 3 minutes. Calculate the diffusion rate in cc/min.
- H. When the test is complete, compare the result to the cartridge FFIT specification.
- I. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the water from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge in service.

* 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.

- 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 wetting 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?

3. Procedure (Automated Testing - Figure 2)

- A. Configure the system as shown in Figure 2.
- B. Install the filter in the housing and flow wetting fluid (see NOTE 1) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.
- C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.



- D. Close the housing inlet valve V1 and connect the CUNOCheck 2 Automated Integrity Tester at V3 and initiate the automated forward flow integrity test protocol. When prompted, program a stabilization time of 2 minutes and a test time of 3 minutes.
- E. When the test is complete, compare the measured Forward Flow Integrity value against the acceptable limit for the filter cartridge under test.
- F. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the wetting fluid from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge in service.
- G. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.

Microfluor II Grade	DFT Pressure - psi (bars)	DFT Specification (cc/min) per 10" equivalent
PFS020	16 (1.1)	< 14.7 (55%/45% IPA/Water)
		< 8.7 (25%/75% TBA/Water)

BUBBLE POINT TEST

1. Definition

The bubble point is the minimum gas pressure required to overcome the surface tension holding a wetting fluid in a membrane filter's largest pore.

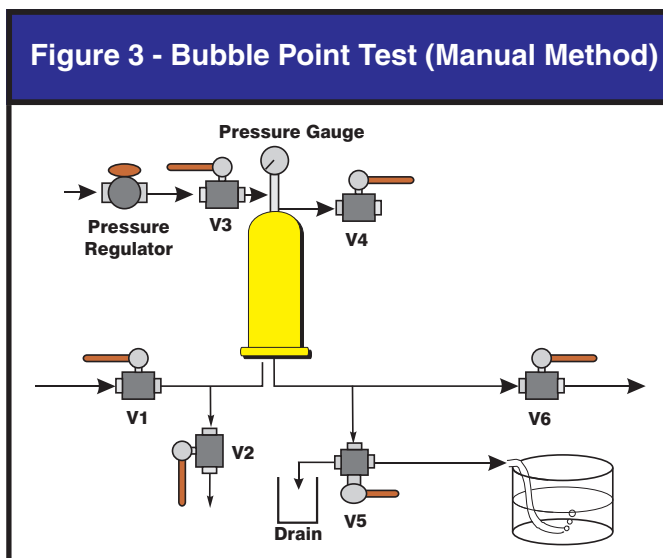
The bubble point pressure measurement is **only recommended** for single 10-inch cartridge filters or smaller. When more filter area is on line, it becomes difficult to distinguish diffusional flow from the true bulk flow which occurs at the bubble point pressure. For assemblies with 2 or more 10-inch equivalent cartridges, diffusion flow or pressure hold measurements are recommended.

The CUNOCheck 2 Automated Integrity Tester can be used to perform a bubble point test. When using the CUNOCheck 2 Tester, follow the installation instructions for connecting the unit to the upstream valve as shown in Figure 4. Consult the appropriate CUNO literature for the filter cartridge bubble point value for the filter to be used and program this value into the CUNOCheck 2 Tester when requested during the test set-up.

2. Procedure (Manual Testing - Figure 3)

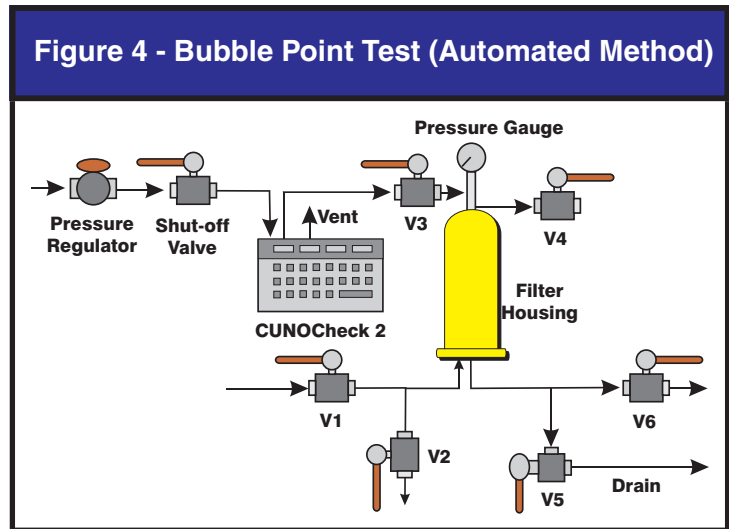
- A. Configure the system as shown in Figure 3.
- B. Install the filter in the housing and flow wetting fluid (55% / 45% IPA/water (v/v)) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.
- C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.
- D. Connect a tube from the outlet port V5 to a container of sterile water*.
- E. Open V3. Using the pressure regulator, slowly pressurize the system with air or nitrogen (DO NOT USE CO₂), raising the pressure 5 psi (0.34 bar) per minute. When within 5 psi (0.34 bar) of the expected bubble point pressure, make only very gradual 1 psi (0.07 bar) increases allowing 5 - 10 seconds between pressure increases to observe evidence of bubbling.
- F. Observe any air flow from the tube connected to the downstream port. A modest flow of small bubbles is diffusion flow only. When a continuous flow of large 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 Bubble Point value for the filter cartridge under test.
- H. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the water from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge 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 wetting fluid and filter ambient?
 - Was the filter seated correctly in the housing and were the o-rings undamaged?

* 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.



3. Procedure (Automated Testing - Figure 4)

- A. Configure the system as shown in Figure 4.
- B. Install the filter in the housing and flow wetting fluid (55% / 45% IPA/water (v/v)) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.
- C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.
- D. Disconnect the wetting fluid supply line and allow the wetting fluid to drain from the housing. Leave V5 or V6 open to atmosphere.
- E. Close V1 and connect the CUNOCheck 2 Automated Integrity Tester at V3 and initiate the automated bubble point test protocol.
- F. When the test is complete, compare the measured Bubble Point value against the acceptable limit for the filter cartridge under test.
- G. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the water from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge in service.
- H. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.



Microflur II Grade	Minimum Bubble Point Pressure - psi (bars)
PFS020	16 (1.1)

PRESSURE HOLD TEST

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 decay of pressure in a closed volume on the upstream side of the membrane as the gas diffuses through the membrane. PHT values are dependent on the volume of the specific filter housing employed, less the volume of the installed cartridges. Therefore, they must be determined on a case by case basis. Please contact CUNO Technical Service for assistance, if necessary.

The CUNOCheck 2 Automated Integrity Tester can be used to perform a pressure hold test. When using the CUNOCheck 2, follow the installation instructions for connecting the unit to the upstream valve as shown in Figure 6. Consult the appropriate CUNO literature for the test pressure and PHT value for the filter cartridge to be used or calculate the maximum allowable value using the following equation. Program these values into the CUNOCheck 2 Tester when requested during the test set-up.

The following equation can be used to calculate the PHT value:

$$\frac{\Delta P}{T} = \frac{D (P_a)}{V_{hsg}}$$

D= Manufacturer's maximum allowable diffusion rate for all the installed filters in cc/min (see FFIT specifications)

T= Time (typically 3 minutes)

P_a= Atmospheric pressure

V_{hsg}=Upstream housing volume (cc) less the volume occupied by the cartridge(s)

ΔP=Allowable pressure loss

2. Procedure (Manual Testing - Figure 5)

A. Configure the system as shown in Figure 5.

B. Install the filter in the housing and flow wetting fluid (55% / 45% IPA/water (v/v) or 25% / 75% TBA/water(v/v)) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.

C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.

D. Disconnect the wetting fluid supply line and allow the wetting fluid to drain from the housing. Leave V5 or V6 open to atmosphere.

E. Open V3 and slowly adjust the pressure regulator to pressurize the system to the specified PHT pressure value and allow the system to equilibrate for a maximum of two minutes.

F. Using a stopwatch, measure the pressure decay for 3 minutes. Calculate the pressure decay over the 3 minute period in psi/min.

G. When the test is complete, compare the measured Pressure Hold value against the acceptable pressure hold value for the filter cartridge under test

H. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the wetting fluid from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge in service.

I. If the pressure decay 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 wetting fluid and filter ambient?

Was the stabilization time adequate?

Was the test time adequate?

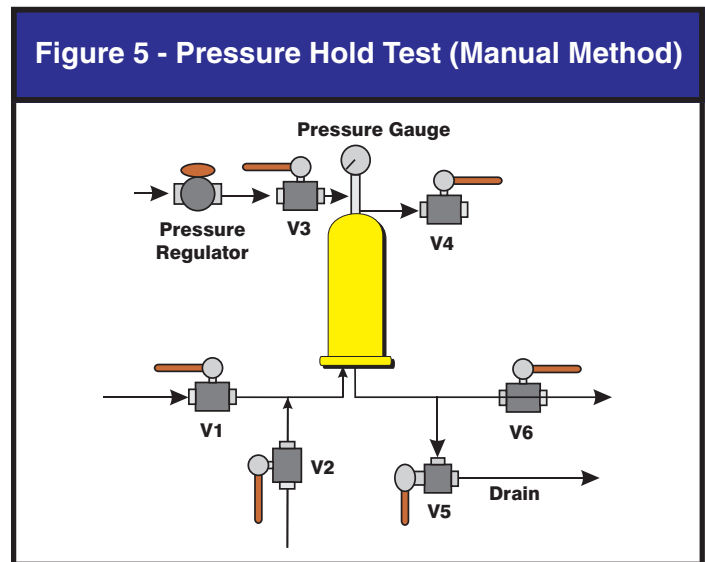
Was the filter seated correctly in the housing and were the o-rings undamaged?

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

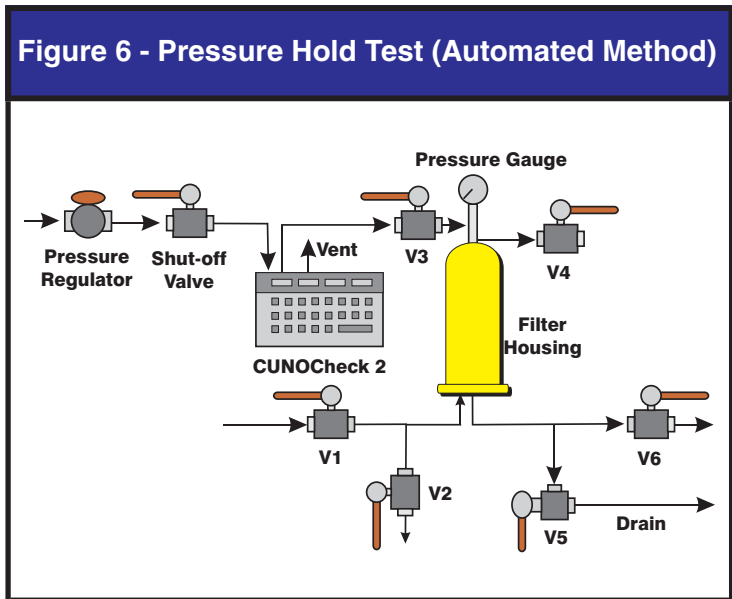
3. Procedure (Automated Test - Figure 6)

A. Configure the system as shown in Figure 6.

B. Install the filter in the housing and flow wetting fluid (55% / 45% IPA/water (v/v) or 25% / 75% TBA/water(v/v)) through the filter at a rate of approximately 1 gpm/10" cartridge for a minimum of 2 minutes.



- C. Close inlet V1 and outlet valve V6 to isolate the housing. Drain all the wetting fluid from the upstream side of the filter by positioning V5 to direct flow to drain. Adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen (DO NOT USE CO₂). Slowly open V3. Close V3 when wetting fluid discharge is no longer evident.
- D. Disconnect the wetting fluid supply line and allow the wetting fluid to drain from the housing. Leave V5 or V6 open to atmosphere.
- E. Close V1 and connect the CUNOCheck 2 Automated Integrity Tester at V3 and initiate the pressure hold test protocol. Close the housing inlet valve V1 and connect the CUNOCheck 2 Automated Integrity Tester at V3 and initiate the automated forward flow integrity test protocol. When prompted, program a stabilization time of 2 minutes and a test time of 3 minutes.
- F. When the test is complete, compare the measured Pressure Hold value against the acceptable limit for the filter cartridge under test.
- G. After the test is complete, flush the wetting fluid from the assembly with clean, filtered water and drain the water from the housing or adjust the pressure regulator to deliver 3 – 5 psig of air or nitrogen. Slowly open V3. Close V3 when wetting fluid discharge is no longer evident. Dry the cartridge before placing the cartridge in service.
- H. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.



WATER INTRUSION TEST

1. Definition

The WIT is only used with hydrophobic filters. The pores of a hydrophobic filter will resist the passage of water up to a certain pressure. The pressure at which water will pass through the pores of a hydrophobic filter is inversely proportional to the size of the pore.

The WIT offers several advantages over the previously described conventional integrity tests that are usually conducted with an alcohol or alcohol water mixture.

Safety – no flammability issues

Contamination – no wetting fluid or alcohol contamination of product

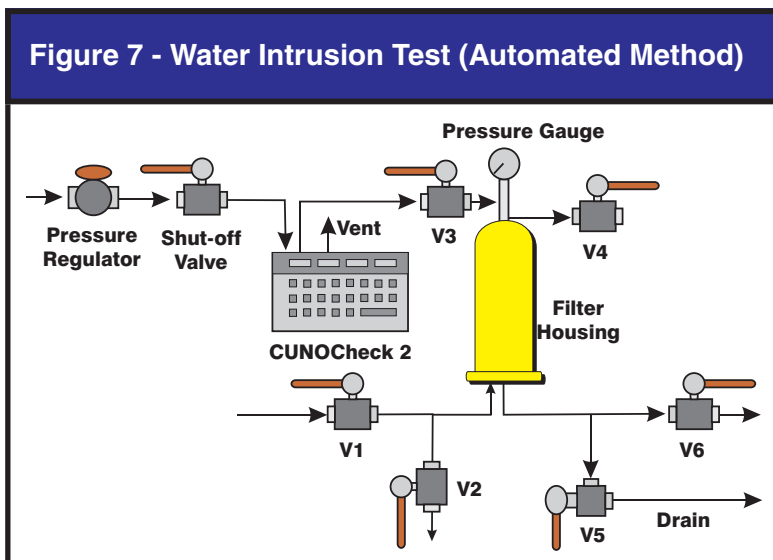
Time – no drying of the filter required before placing back into service

The CUNOCheck 2 Automated Integrity Tester can be used to perform a water intrusion test. When using the CUNOCheck 2 Tester, follow the installation instructions for connecting the unit to the upstream valve as shown in Figure 7. Consult the appropriate CUNO literature for the test pressure and WIT value for the filter cartridge to be used and program these values into the CUNOCheck 2 Tester when requested during the test set-up.

2. Procedure (Automated Testing - Figure 7)

- A. Configure the system as shown in Figure 7.
- B. Install the filter(s) in the housing and close all valves.
- C. Open V4. Fill the upstream side of the system with water through either V1 or V2. When water emerges from V4, stop the water flow and close whichever valve was used to introduce the water to the system.
- D. When water stops flowing from V4 close V4.

- E. Connect the CUNOCheck 2 Tester to the pressurized gas source, open the shut-off valve, and, using the regulator, adjust the pressure to the CUNOCheck 2 Tester to the necessary level for the test being conducted.
- F. Close the housing inlet valve V1 and connect the CUNOCheck 2 Automated Integrity Tester at V3 and initiate the automated water intrusion test protocol. When prompted, program a stabilization time of 5 minutes, a test time of 5 minutes and set the volume calculation to type "3".
- G. When the test is complete, compare the test result to the WIT specification for the filter being tested.



- H. After the test is complete, drain the water from the housing and place the cartridge in service.
- I. Disconnect the CUNOCheck 2 Automated Integrity Tester from the housing.
- J. If the WIT value is higher than the specification, consider the following questions and re-test if necessary:
 - Was the filter dry and free of solvents or surfactants prior to starting the test?
 - Was the correct pore size filter installed?
 - Was the temperature of the water and filter ambient?
 - Was the temperature stable during the test period?
 - Was the water free of solvents and/or surfactants?
 - Was the stabilization 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?

Microfluor II Grade	WIT Pressure - psi (bars)	WIT Specification (cc/min) per 10" equivalent
PFS020	40 (2.7)	0.59



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Cuno Incorporated

400 Research Parkway
 Meriden, CT 06450, U.S.A.
 Tel: (800) 243-6894
 (203) 237-5541
 Fax: (203) 630-4530
 www.cuno.com