SeproPor® Filters

MEISSNER

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SepraPor® Filters

SepraPor® are tangential flow filtration (TFF) devices containing hollow fiber membranes (HFM). SepraPor® filters are ideal for use in a variety of biopharmaceutical applications, including cell concentration, continuous cell culture perfusion, and protein concentration and diafiltration. SepraPor® filters are available in a range of sizes in both capsule and cartridge configurations. Cartridges are designed to fit inside stainless steel housings for steam-in-place (SIP) sterilization and operation. SepraPor® capsules are available as standalone filters or as part of single-use assemblies.

Materials of Construction

SepraPor® filters are manufactured using high quality components, which are all animal component free (ACF), nontoxic, and biologically inert. The materials are listed for food contact use in the Code of Federal Regulations (CFR), Title 21, or meet Commission Regulation (EU) No 10/2011, as below:

Components

All devices:		
Hollow fibers:	Polysulfone	CFR Title 21, 177.1655
Fiber bundle netting:	Polypropylene	CFR Title 21, 177.1520
Capsule housing/Cartridge sleeve	Polysulfone	CFR Title 21, 177.1655
Fiber encapsulation:	Epoxy	CFR Title 21, 175.300
Cartridges:		
End O-rings:	Silicone	CFR Title 21, 177.2600
Capsules:		
Permeate Ports:	Polysulfone	CFR Title 21, 177.1655
Retentate Ports:	Polysulfone	CFR Title 21, 177.1655

The SepraPor® filters meet the requirements as specified in the USP 43 Biological Reactivity Tests, *in vitro* <87> (cytotoxicity) and *in vivo* <88> (Class VI Plastics).

Configurations

SepraPor® filters can be manufactured in a variety of configurations and lengths for XFM cartridges and XFC capsules. See the "Ordering Matrix Descriptions" section at the end of this document for configuration part numbers and Figure 1 and Figure 2 for drawings of capsules and cartridges, respectively.

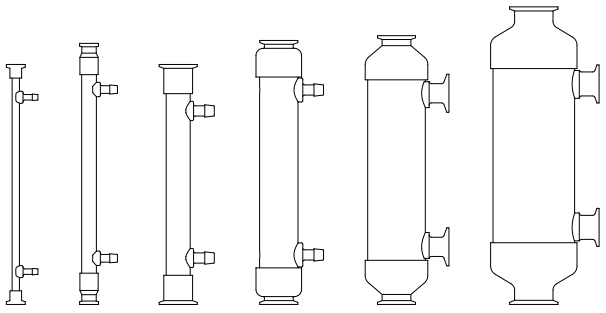

Figure 1: Standard configurations for SepraPor® hollow fiber capsule filters with 30 cm path length capsules shown.

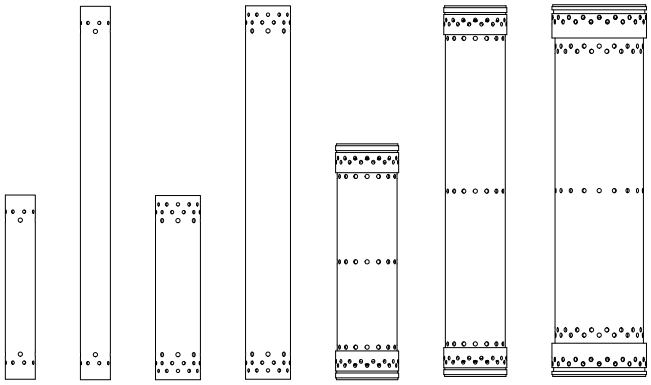

Figure 2: Standard configurations for SepraPor® hollow fiber cartridge filters for Steam-In-Place (SIP) use.

Dimensions

All hollow fibers for capsules and cartridges have an inner diameter (I.D.) of 1.0 mm and an outer diameter (O.D.) of 1.5 mm.

Capsules

Table 1: Dimensions of SepraPor® capsule filters.

Filter Diameter	Porosities	Fluid Path Length (Nominal)	Filter Length	Effective Filtration Area
3/8" (0.95 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	12.5" (31.8 cm)	0.12 ft² (0.011 m²)
3/8" (0.95 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	25.0" (63.5 cm)	0.25 ft² (0.023 m²)
¾" (1.9 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	13.6" (34.5 cm)	0.45 ft² (0.042 m²)
¾" (1.9 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	26.0" (66.0 cm)	0.91 ft² (0.085 m²)
1" (2.5 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	12.5" (31.8 cm)	0.81 ft² (0.075 m²)
1" (2.5 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	25.0" (63.5 cm)	1.6 ft² (0.15 m²)
1¼" (3.2 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	12.5" (31.8 cm)	1.3 ft² (0.12 m²)
1¼" (3.2 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	25.0" (63.5 cm)	2.5 ft² (0.23 m²)
2" (5.1 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	13.8" (35.1 cm)	3.9 ft² (0.36 m²)
2" (5.1 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	25.0" (63.5 cm)	9.0 ft² (0.84 m²)
3" (7.6 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	14.0" (35.6 cm)	9.9 ft² (0.92 m²)
3" (7.6 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	26.5" (67.3 cm)	23 ft² (2.1 m²)
4¼" (10.8 cm)	0.1, 0.2, 0.4 µm	12" (30 cm)	19.8" (50.3 cm)	27 ft² (2.5 m²)
4¼" (10.8 cm)	0.1, 0.2, 0.4 µm	24" (60 cm)	28.8" (73.2 cm)	47 ft² (4.4 m²)

Cartridges

Table 2: Dimensions of SepraPor® cartridge filters.

Filter Diameter	Porosities	Fluid Path Length (Nominal)	Filter Length	Effective Filtration Area
2" (5.1 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	12.3" (31.2 cm)	4.3 ft² (0.40 m²)
2" (5.1 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	24.9" (63.2 cm)	8.6 ft² (0.80 m²)
3" (7.6 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	12" (30 cm)	12.3" (31.2 cm)	9.7 ft² (0.90 m²)
3" (7.6 cm)	0.1, 0.2, 0.4 µm 10, 30, 50, 100, 300, 500, 750 kDa	24" (60 cm)	24.9" (63.2 cm)	22.6 ft² (2.10 m²)
4" (10.2 cm)	0.1, 0.2, 0.4 µm	12" (30 cm)	15.5" (39.4 cm)	24.8 ft² (2.30 m²)
4" (10.2 cm)	0.1, 0.2, 0.4 µm	24" (60 cm)	24.5" (62.2 cm)	45.2 ft² (4.20 m²)
5.9" (15 cm)	0.1, 0.2, 0.4 µm	24" (60 cm)	24.6" (62.5 cm)	89.3 ft² (8.30 m²)

Operating Characteristics

Cartridges and Capsules

Operating Temperature Range: 32 °F to 100 °F (0 °C to 38 °C)
Maximum Operating Temperature: 122 °F (50 °C) for short-term operation such as cleaning

Table 3: Operating pressures for SepraPor® microfiltration porosities.

Porosity (µm)	Maximum Transmembrane Pressure (TMP)	Maximum Feed Pressure
0.4	10 psig @ 77 °F (0.7 bar @ 25 °C)	15 psig @ 77 °F (1.0 bar @ 25 °C)
0.2	15 psig @ 77 °F (1.0 bar @ 25 °C)	25 psig @ 77 °F (1.7 bar @ 25 °C)
0.1	20 psig @ 77 °F (1.4 bar @ 25 °C)	30 psig @ 77 °F (2.1 bar @ 25 °C)

Table 4: Operating pressures for SepraPor® ultrafiltration porosities.

Porosity (kDa)	Maximum Transmembrane Pressure (TMP)	Maximum Feed Pressure
750	45 psig @ 77 °F (3.1 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
500	45 psig @ 77 °F (3.1 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
300	45 psig @ 77 °F (3.1 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
100	45 psig @ 77 °F (3.1 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
50	45 psig @ 77 °F (3.1 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
30	50 psig @ 77 °F (3.5 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)
10	50 psig @ 77 °F (3.5 bar @ 25 °C)	65 psig @ 77 °F (4.5 bar @ 25 °C)

Cartridge Installation

Meissner SepraPor® cartridge filters are available in a number of different adapter and O-ring configurations designed to fit inside stainless steel cartridge housings. The filter cartridge should fit snugly in the housing. Improper installation can impair filtration efficiency and compromise system sterility.

1. Verify that the correct filter part number for the application has been selected.
2. Assemble the stainless steel filter housing.
3. Remove the SepraPor® filter from its packaging and install into the stainless steel housing. SepraPor® filters are symmetrical so there is no top or bottom orientation.
4. Ensure that the filter is securely and evenly seated in the base of the housing.
5. To assist with proper installation, see Meissner's Cartridge Insertion Tool instructions.
6. Install the filter upper support of the housing, ensuring that it sits snugly and evenly around the top of the filter.
7. Ensure that all O-rings are seated evenly.
8. Proceed with housing assembly and rinsing of the SepraPor® filter per the instructions below.

Water Conservation Rinsing Procedure

Rinsing Procedure for New Filters

Standalone non-sterile hollow fiber filters contain glycerol as part of the manufacturing process. Although highly permeable, rinsing of new filters is essential prior to integrity testing, sterilization, sanitization, or direct use. Ultrafiltration membranes can be soaked in 60% isopropanol (IPA) or ethanol for 30 to 60 minutes to help wet the membrane and enhance glycerol removal during new filter rinsing. Additionally, warm water is recommended to facilitate wetting if alcohol is not used. This step is highly recommended for membranes with a molecular weight cut-off (MWCO) lower than 100 kDa due to the smaller pore sizes. For more information on ultrafiltration rinsing procedures, please contact Meissner.

NOTE: If you have water supply constraints, a recirculation scheme such as the “Water Conservation Rinsing Procedure” below may be used. This rinse scheme reduces water usage and is presented as an example. However, the standard rinsing procedure is recommended for more thorough reduction of total organic carbon (TOC).

This rinsing procedure is provided only as an example of a reduced water usage rinsing scheme. Final rinsing parameters must be validated by each user. The water conservation rinsing procedure is recommended only if the standard rinsing procedure presented above is not possible due to water supply constraints.

Microfiltration TOC Flush Volumes

1. Following installation of the filter cartridge into a stainless steel housing, or if using a capsule filter, connect the retentate and permeate lines to waste containers.
2. Fill a feed reservoir with room temperature or warm (up to 50 °C [122 °F]) deionized water (DIW) for rinsing. Rinsing with a feed pressure of 5 psig (0.34 bar) for at least 5 minutes is recommended.
3. Start the feed pump at a slow flow rate and adjust feed pressure to 5 psig (0.34 bar) for all microfiltration pore sizes, adding more water as required. Slowly close the retentate outlet valve to increase the permeate flow to improve the clean water flux through the fibers while maintaining the cross-flow to a trickle from the retentate outlet

Below are the TOC results for autoclaved and gamma irradiated microfiltration SeparPor® Filters.

Autoclave Flush Results

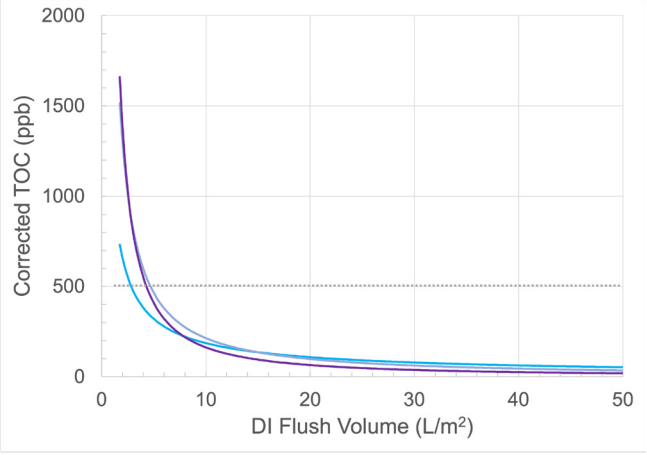

Figure 3. Typical TOC flush results for an autoclaved SepraPor® hollow fiber microfiltration capsule filter (Part No. XFCM20C024-7711; EFA 0.023 m²) showing the power function curve fit for the three lots tested.

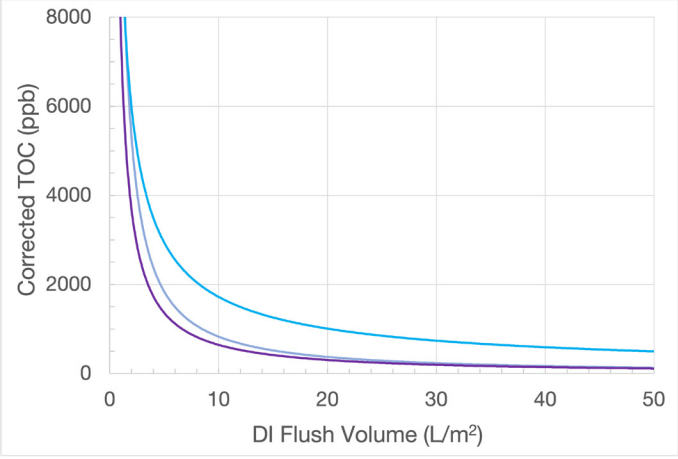

Figure 4. Typical TOC flush results for an autoclaved SepraPor® hollow fiber microfiltration capsule filter (Part No. XFCM20C124-7722; EFA 0.085 m²) showing the power function curve fit for the three lots tested.

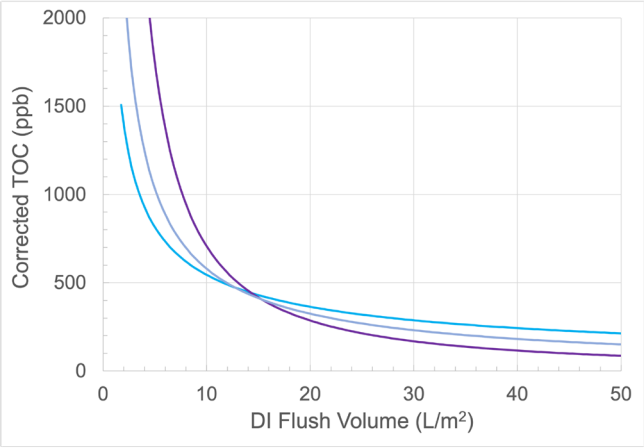

Figure 5. Typical TOC flush results for a gamma irradiated SepraPor® hollow fiber microfiltration capsule filter (Part No. XFCM20C024-7711; EFA 0.023 m²) showing the power function curve fit for the three lots tested.

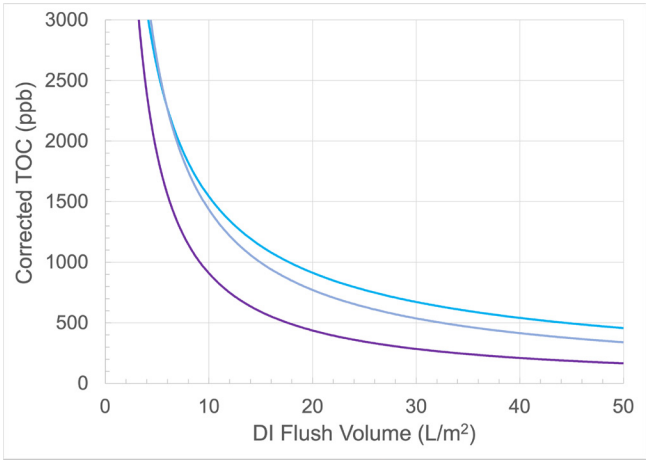

Figure 6. Typical TOC flush results for a gamma irradiated SepraPor® hollow fiber microfiltration capsule filter (Part No. XFCM20C124-7722; EFA 0.085 m²) showing the power function curve fit for the three lots tested.

Measuring Clean Water Flux

After establishing integrity of the filter and system, the next step with a new SepraPor® filter is to obtain baseline clean water flux data. Water flux is important to correlate with bubble point data to confirm the desired porosity of the HFM. Baseline water flux also allows post-use, post-cleaning flux to be compared for cleanability and reusability of the HFM. Baseline data should be generated under easily repeatable conditions so comparisons with water flux data after cleaning cycles can be made directly. Parameters to control for reproducibility are:

- Water temperature
- Cartridge inlet pressure
- Cartridge outlet pressure
- Permeate flow rate
- System piping

"Clean" water, defined as ≤10 kDa ultrafiltration permeate, or water for injection (WFI), is required to ensure contaminants are not present which could negatively impact membrane performance.

Water flux is measured most reliably at low pressure. Minimal crossflow is required, and the retentate valve only needs to be slightly cracked open to ensure elimination of air trapped on the lumen side of the HFM. Care should be taken not to restrict permeate flow, such as with small diameter tubing or long fluid path lengths.

Procedure:

1. Fully open the permeate valve.
2. Crack open the retentate valve.
3. Start the feed pump, increasing flow to a feed pressure of 1 – 5 psig (0.07 – 0.3 bar) for microfiltration devices. The objective is to attain a consistent, measurable permeate flow at low inlet pressure. Use 2 or 3 psig (0.1 or 0.2 bar) inlet pressure. Inlet pressures up to 10 psig (0.7 bar) may be required to attain a measurable permeate flow for MWCO lower than 100 kDa due to the smaller pore sizes. Record the outlet pressure as well.
4. Start the measurement with the outlet valve cracked open to vent the air. Then close the outlet valve until only a trickle of water is observed.
5. Measure the permeate flow in mL/min and calculate the flux in L/m²/hr/bar (LMH/bar) per the following equation: flux needs to be in LMH/bar.

$$Normalized\ Flux\ (LMH/bar) = \frac{Permeate\ flow\ (mL/min)}{Filtration\ area\ (m^2)}\ x\ 0.06\ /\ TMP\ (bar)$$

$$TMP = \left(\frac{P_{inlet} + P_{outlet}}{2}\right) - P_{permeate}$$

NOTE: $P_{permeate}$ *is assumed to be 0 psi at low* P_{inlet}

6. Measure the temperature of the water.
7. Record inlet and outlet pressures, permeate flow rate, and temperature into a data log form or spreadsheet.
8. Normalize the flux temperature to 25°C per the following equation:

$$Temperature\ Corrected\ Flux = Flux\left(\frac{T_1}{T_2}\right)$$

Where T_1 *= Reference temperature (e.g., 25 °C) and* T_2 *= Actual temperature (°C)*

Typical Clean Water Flux Ranges

Nominal Pore sizes (µm)	Normalized Clean Water Flux (LMH/bar @ 25 °C)
0.4	≥ 7,500
0.2	≥ 3,300
0.1	≥ 1,800

Table 5: Minimum flux for SepraPor® microfiltration porosities.

Molecular weight Cut-off sizes (kDa)	Normalized Clean Water Flux (LMH/bar @ 25 °C)
750	840 - 1,300
500	465 - 1,200
300	325 - 600
100	215 - 550
50	100 - 480
30	70 - 265
10	50 - 165

Table 6: Typical flux ranges for SepraPor® ultrafiltration porosities.

Integrity Testing

The bubble point and diffusive flow tests are industry accepted nondestructive methods for verifying the integrity of a membrane filter. These tests may be performed manually as described in this section or with the use of an automated integrity tester such as Meissner's AccuFlux® Integrity Tester. In each method, the test pressure varies directly with the surface tension of the wetting fluid. For test values using wetting fluids other than those used in the procedures below, please contact Meissner.

Diffusive Flow Test Procedure

The Diffusive Flow Test may be performed on SepraPor® hollow fiber filter cartridges or capsules. The filter is wetted, drained, and a constant air pressure is applied. Diffusive air flow through the membrane is measured.

Procedure:

1. A system setup for performing the Diffusive Flow Test is shown in Figure 6.
2. Close all valves.
3. Open V_1 and V_2. Thoroughly wet the filter with water, opening vent V_4 to allow trapped air to escape. The complete wetting of the filter is crucial to the accuracy of the test. An incompletely wetted filter will fail. Slower flow rates can be used for longer periods. Back pressure should be applied by partially closing V_2 while flowing wetting solution through the filter. Do not exceed the recommended maximum transmembrane pressure rating of the porosity of the filter being tested.
4. Drain excess water from the housing shell using V_5 and V_2. If using an air flow meter, ensure the shell is sufficiently drained of water such that displaced water does not enter the flow meter.
5. Close V_1, V_5, and V_2.
6. Open V_3 and apply air pressure of 15 psi (1.0 bar) for microfiltration filters or 30 psi (2.1 bar) for ultrafiltration filters to the inlet side of the system. This will push the upstream volume of water through the filter.
7. If necessary, open V_5 to drain the downstream volume of water. Water remaining downstream of the filter may cause an inaccurate diffusion reading by interfering with the air flow in the outlet tube. Close V_5.
8. Open V_4.
9. Verify the test pressure and adjust as necessary. Allow the air flow to stabilize.
10. Fill a graduated cylinder with water and invert into a container of water. Place the outlet tubing from V_4 underneath the opening of the cylinder and measure the volume of air diffused per minute. The recorded flow rate must not exceed the normalized flow rate related to filter surface area.

SepraPor ® Hollow Fiber	Maximum DF (mL/min/f2)	Maximum DF (mL/min/m2)
Microfiltration: 0.1, 0.2, 0.4 µm	≤ 2.79 @ 15 psi	≤ 30 @ 15 psi
Ultrafiltration: 10 - 750 kDa	≤ 2.79 @ 30 psi	≤ 32 @ 30 psi

Table 7: Diffusive flow values for integral SepraPor® hollow fiber filters, wetted with 100% water.

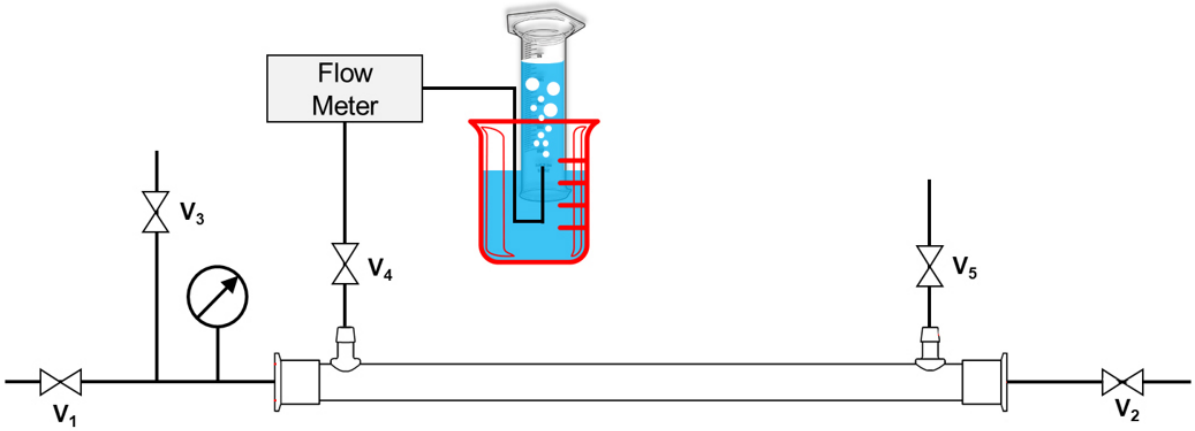

Figure 6: Diffusive Flow Test Schematic.

Bubble Point Test Procedure

This procedure outlines the steps required to perform a bubble point test on SepraPor® filter cartridges or capsules. The manual bubble point test requires a wetted filter, a calibrated pressure gauge, a regulated gas pressure source (usually compressed air or nitrogen), narrow diameter downstream tubing, and a beaker of water in which the tubing outlet is submerged. Air pressure is applied to the wetted filter and gradually increased until a steady stream of bubbles is observed to come from the submerged tubing.

Procedure:

1. A system setup for performing the bubble point test is shown below in Figure 7.
2. Ensure hollow fiber membrane is fully wetted out with 60%/40% IPA/Water (v/v).
3. Close all valves.
4. Open V_1 and V_2. Thoroughly wet the filter with the wetting solution by opening V_4 and slowly closing off V_2, letting the wetting solution permeate through the fibers and fill the housing.
5. Open V_5 to allow trapped air to escape, then close V_5. The complete wetting of the filter is crucial to the accuracy of the test. An incompletely wetted filter will fail. Once the housing is filled with the solution, the fibers should be sufficiently wetted.
6. Close V_1.
7. Drain excess solution from the housing shell using V_5 and V_2. If using an air flow meter, ensure the shell is sufficiently drained of solution such that displaced solution does not enter into the flow meter.
8. Close V_5 and V_2.
9. Open V_3 and apply air pressure of 5 psi to the inlet side of the system. This will push the upstream volume of wetting solution through the filter.
10. Increase the air pressure slowly at about 1 psig/second until a constant stream of bubbles is observed in the beaker or water bath. Alternatively, a more accurate method of carrying out the measurement is to use a digital flow meter with a low volume range.
11. The initial stream of air is usually entrapped air and may produce a large amount of bubbling that will decrease rapidly and be replaced by regularly spaced bubbles produced by air diffusing through the filter membrane. Slowly increase the pressure while observing for *continuous bubbling* from the bubble point tube. Do not confuse the additional bubbles produced by a rapid increase in air pressure with the bubble point. Observe the bubbles when the air pressure has stabilized. The bubble point is the pressure at which a marked change in the rate of bubbling occurs.
12. When a *steady* stream of bubbles is detected, the bubble point pressure has been reached.

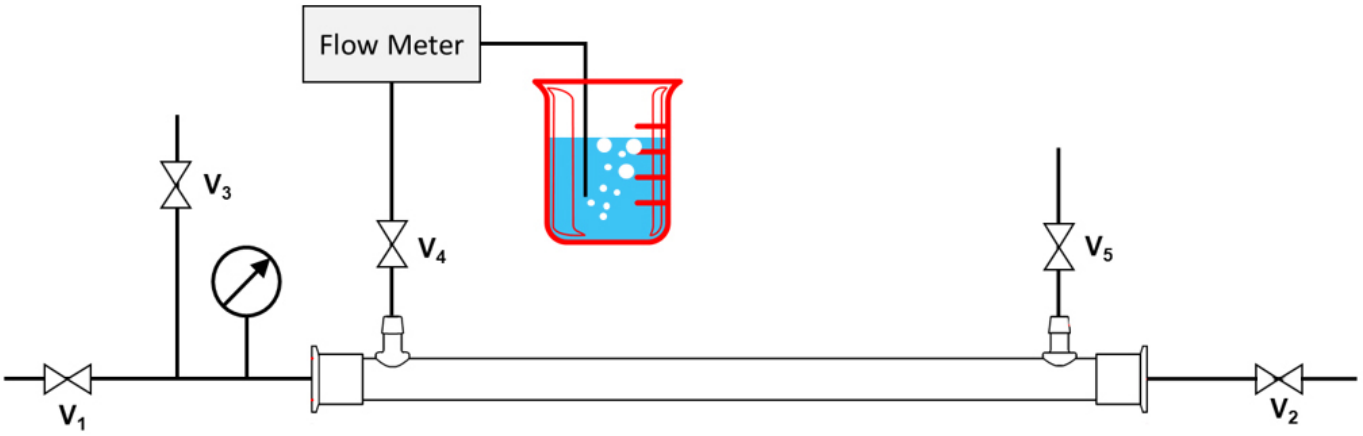

Figure 7: Bubble Point Test Schematic.

Correlating Clean Water Flux to Bubble Point

Once Bubble Point and Clean Water Flux have been measured, ensure that the values lie within the ranges provided in the table below to confirm porosity of the HFM.

Normal Pore Size (µm)	Bubble Point In 60%/40% IPA Water (v/v)	Normalized Clean Water Flux (LMH/bar @25 °C)
0.4	9 - 17 psi (0.6 - 1.2 bar)	≥ 7,500
0.2	18 - 25 psi (1.2 - 1.7 bar)	≥ 3,300
0.1	26 - 38 psi (1.8 - 2.6 bar)	≥ 1,800

Table 8: Bubble point and normalized clean water flux for SepraPor® microfiltration porosities.

Ultrafiltration Characterization: Passage

Molecular weight cut-off values are assigned using a rigorous characterization method with a minimum of three molecular weight (Mw) markers. Each MWCO has a designated passage band based on three Mw markers, which a lot of membrane must perform within to be assigned that MWCO. These passage bands are distinct to minimize overlap between membranes of different MWCO and improve membrane lot-to-lot consistency.

Passage is calculated using the following formula:

$$Passage\ \% = \frac{Permeate\ concentration}{Retentate\ concentration}\ x\ 100$$

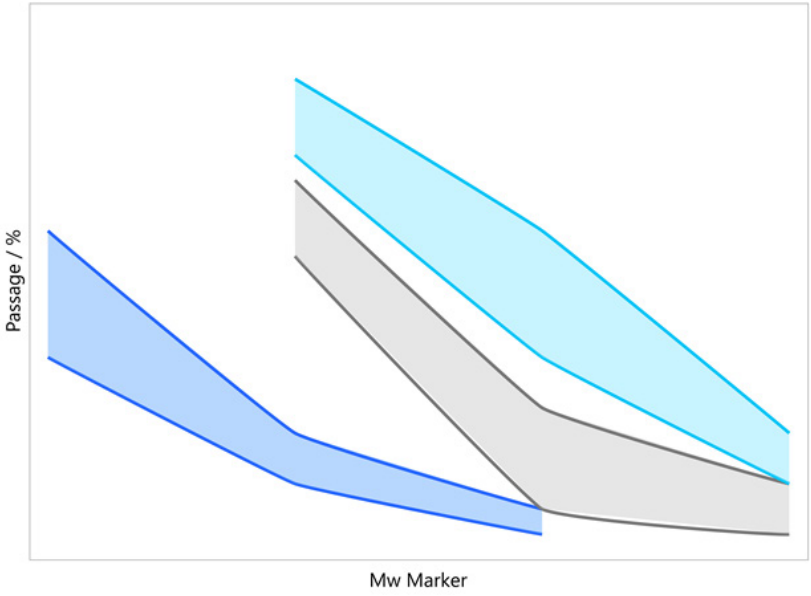

Figure 8: Example passage bands used for ultrafiltration MWCO characterization.

Sterilization Instructions

For critical pharmaceutical and biotechnology applications, the sterility of the SepraPor® filter must be ensured prior to process use. Steam-in-place (SIP) and autoclaving are commonly used methods of sterilization for SepraPor® filters.

When using steam to sterilize SepraPor® filters, it is important to use gentle and gradual temperature and pressure gradients to heat and cool the filter and to not exceed 121 °C (250 °F). The recommended rate of heating and cooling is 1 °C/minute.

The longevity of a hollow fiber filter is correlated to steam sterilization cycle, cycle time, temperature, and number of sterilization cycles.

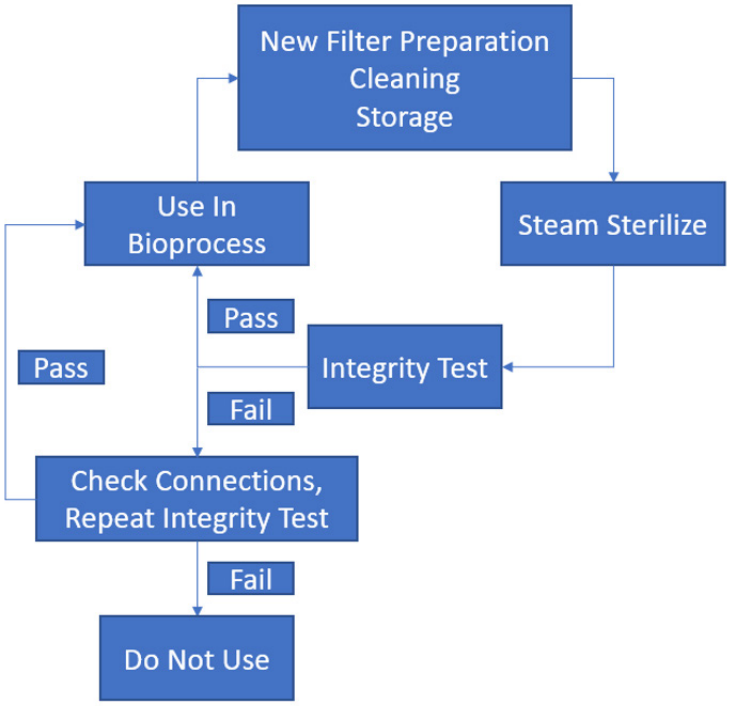

Figure 9: Flow chart for sterilization, integrity testing, and use of SepraPor® filters.

Steam-In-Place (SIP) Sterilization

SIP sterilization should be performed at 121 °C (250 °F) for a minimum of 30 minutes. A validated procedure that ramps temperature and pressure slowly to and from final sterilization temperature and pressure is required.

The procedure outlined below is intended as an initial starting point for developing an SIP process, and is specific to the 6-inch diameter SepraPor® cartridge in a stainless steel housing. Users may carry out their own proprietary SIP procedures, but in all cases, users should validate their SIP cycle parameters and equipment used to perform SIP sterilization.

1. Prepare filter for steaming by rinsing according to the new filter rinsing and preparation instructions.
2. Close the feed inlet valve (V1), retentate outlet valve (V2), permeate outlet valve (V3), low-point permeate drain (V4), and air inlet/vent valve (V5).
3. Open the retentate steam inlet valve (V6) and permeate steam inlet valve (V7).
4. Open the feed steam trap bypass valve (V8).
5. Close steam trap isolation valves (V9 and V10).
6. Introduce steam by cracking open the steam inlet valve (V11) or adjusting steam regulator to 1 psig (0.07 bar). Steam and water should trickle from the feed steam trap bypass valve (V8). Adjust the steam inlet valve so that the system outlet temperature heats up to 100 °C (212 °F) at a rate of 1 °C/minute.
7. Once outlet temperature reaches 100 °C (212 °F), wait 5 minutes and open the permeate steam trap bypass valve (V4). Wait 5 more minutes, then close both steam trap bypass valves (V4 and V8).
8. Open the steam trap isolation valves (V9 and V10), maintaining steam flow into both the retentate and permeate sides of the filter. Condensate will drain from the steam traps.
9. Open the retentate valve (V2) slightly and slowly open the steam inlet valve (V11). Adjust the steam inlet valve so that the system outlet temperature heats up to 121 °C (250 °F) at a rate of 1 °C/minute.

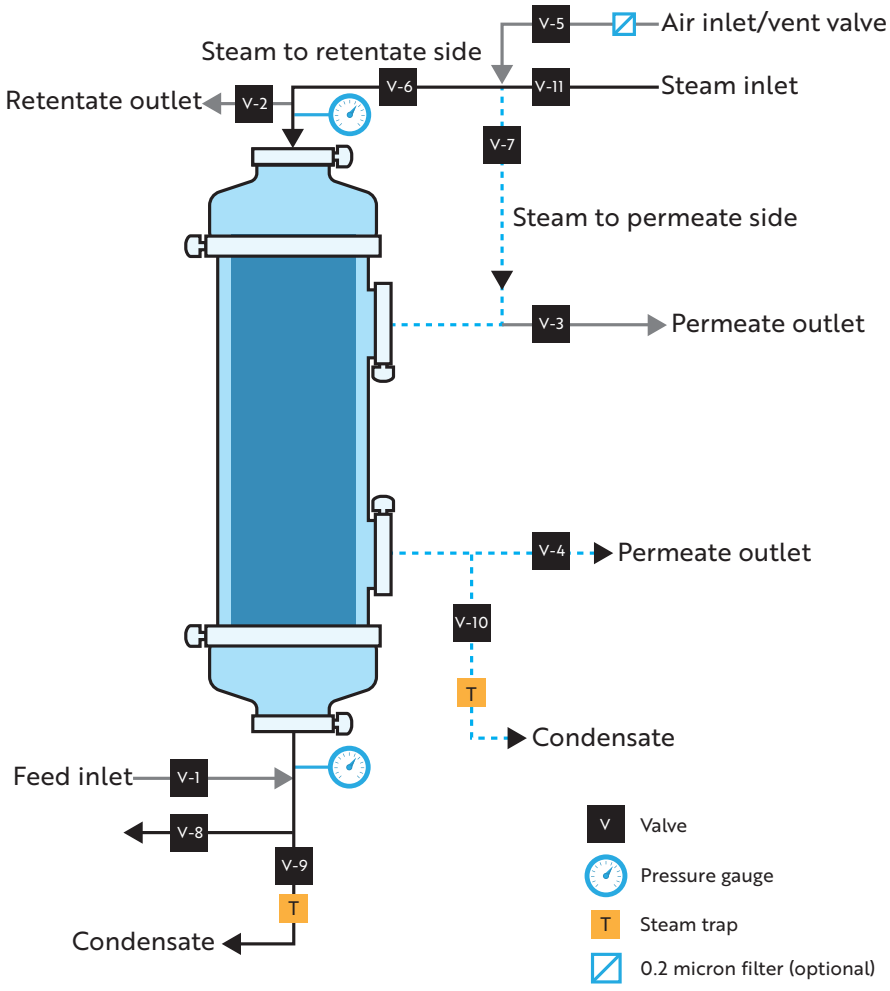

Figure 10: Typical configuration for SepraPor® SIP.

10. Open the feed inlet valve (V1), retentate outlet valve (V2), and permeate outlet valve (V3) slightly.
11. If introducing steam to the remainder of the process system, slowly open the feed inlet valve (V1) and retentate outlet valve (V2), ensuring steam pressure does not drop. When the remainder of the process system comes up to pressure, fully open valves V1 and V2.
12. Steam for a minimum of 30 minutes at the specified pressure.
13. To cool the cartridge and housing, close all valves starting with those furthest from the steam source and working toward the source. Finish by closing the steam inlet valve (V11).
14. Pressurize the system to 15 psi (1.0 bar) by opening the air inlet/vent valve (V5). Crack open one of the steam trap bypass valves (V4 or V8) to release pressure and maintain air flow through the filter assembly.
15. Allow the cartridge and system to cool gradually to ambient temperature. To help preserve filter integrity, maintain a cool down rate of -1 °C/minute.

16. Integrity test the filter post-sterilization is optional but recommended and sometimes required in critical applications. If performing an integrity test, close all valves except the air inlet/vent valve (V5), retentate steam inlet valve (V6), and permeate steam trap bypass valve (V4). See Figure 11.
17. Attach flexible tubing to the permeate steam trap bypass valve (V4) and immerse in a beaker of water.
18. Perform pressure hold integrity test by introducing air at approximately 5 psig (0.3 bar) through the air vent. Watch for bubbles coming from the permeate outlet. If only small bubbles form, the cartridge is integral.
19. To configure the filter system for processing, close the air inlet/vent valve (V5), retentate steam inlet valve (V6), permeate steam inlet valve (V7), steam trap bypass valves (V4 and V8), and steam trap isolation valves (V9 and V10).
20. Open feed inlet valve (V1), permeate outlet valve (V3), and retentate outlet valve (V2).
21. The filter system is now ready for processing.

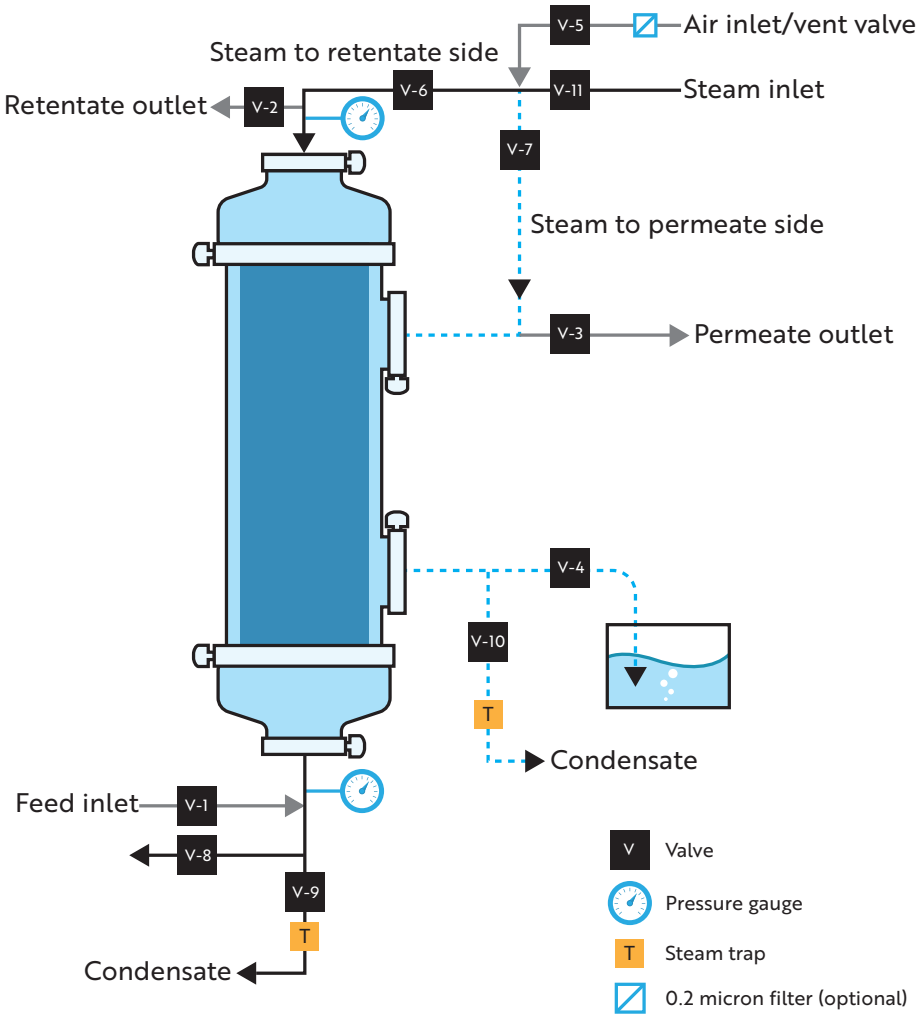

Figure 11: Typical configuration for integrity testing SepraPor® post-SIP.

General SIP Recommendations:

Meissner offers the following recommendations and techniques to help ensure efficient and effective operation of the filter system.

- Do not shock or expose the filter cartridge to pressure surges, as this can compromise filter integrity.
- Ensure that temperature increases and decreases are gradual, approximately 1 °C/minute during the heating and cooling cycles.
- Fully wet the filter membrane before performing autoclave or steam sterilizations.
- Ensure differential pressure across the membrane does not exceed 5 psid (0.3 bar).
- Introduce steam simultaneously through both the retentate and permeate sides of the filter to prevent filter damage.

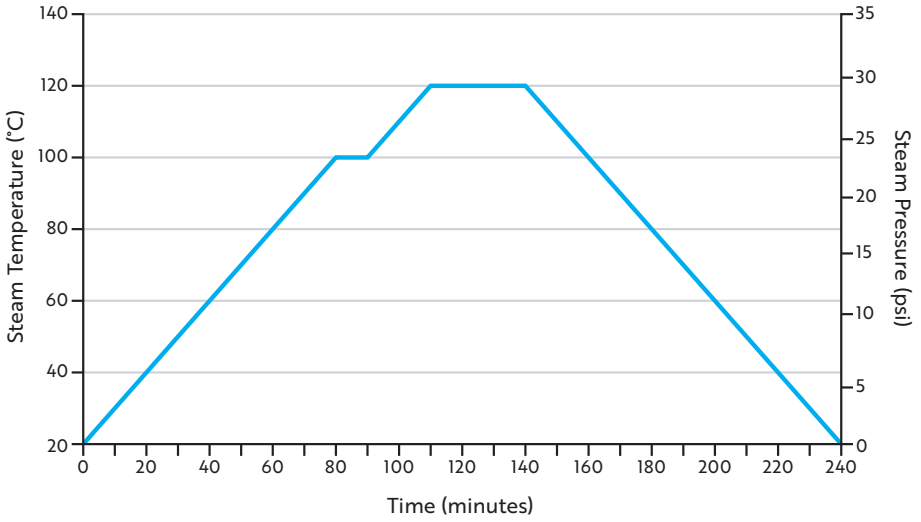

Figure 12: Recommended SIP sterilization cycle for the 6" SepraPor® cartridge at a temperature change rate of 1 °C/minute.

- Monitor steam temperature and pressure to ensure effective sterilization without compromising filter integrity.
- Steam must be free of rust and other particulates.
- Filter housing should be clean before the cartridge is installed.
- To ensure thorough sterilization, steam pressure in the system must be maintained at ≥ 15 psi.
- Establish a sterilization procedure that provides consistent sterilization results, and validate the procedure.
- Superheated steam can overheat the filter, causing damage to the cartridge and affecting membrane performance. Maintain sterilization temperature at 121 °C (250 °F), or as close to this temperature as possible.
- Always check valve positions before operating or steaming the filter.
- Do not apply back pressure on the membrane.

Autoclave Sterilization

Sterilize the SepraPor® filter at 121 °C (250 °F) and 15 psi (1.0 bar) for a minimum of 30 minutes, using a temperature ramp of no more than 1 °C/minute above 121 °C (250 °F). A validated procedure that ramps temperature and pressure slowly to final sterilization temperature and pressure is required.

For users who do not have access to a programmable autoclave, instructions are provided below solely as a guide, and the user is ultimately responsible for properly validating their sterilization process.

1. Wet the filter following the new filter rinsing and preparation instructions on Pages 7-8.
2. Warm the module in an oven at 100 °C (212 °F) for at least 90 minutes.
3. Transfer the warmed SepraPor® filter into the autoclave and sterilize at 121 °C (250 °F) for at least 30 minutes.
4. Allow the unit to cool to room temperature slowly for a minimum of 3 hours before use.

Gamma Sterilization

SepraPor® XFC filters are designed for gamma sterilization and can be included as part of a OneTouch® single-use assembly. Sterility validation is currently available for the M10, M20, and M40 filters. SepraPor® microfiltration hollow fiber filter capsules may be gamma irradiated with 25 - 40 kGy once. It is not recommended to autoclave or SIP an irradiated filter

System Start-Up

Start-up occurs after the rinsing of the filter and ensuring complete wetting of the hollow fiber membrane to avoid "entrapped" air within the pores. Improper start-up of high-flux microfiltration membranes can result in rapid gel layer formation leading to a decline in flux. During start-up, close both permeate valves to establish the cross flow velocity as needed. If possible, circulate water or buffer solution initially to obtain the proper cross flow velocity before introducing your product solution.

During processing, aim to maintain an inlet pressure of less than 10 psig (0.7 bar) for microfiltration membranes and less than 50 psi (3.5 bar) for ultrafiltration membranes. Please refer to the maximum operating condition for additional details on Page 5. Low inlet pressures will help prevent pore plugging by small particulates or cell fragments in microfiltration applications. Ultrafiltration processes can be operated at higher pressures from the beginning given the typically lower bioburden load of these solutions. Retentate pressure should be approximately 0 psi (0 bar) at start-up before applying any type of back pressure.

After establishing the desired cross flow rate, begin permeate withdrawal by fully opening the permeate tubing valve. If you observe rapid flux decline, throttle the permeate tubing valve on subsequent trials to create back pressure in the permeate line. Controlling permeate flow rate can stabilize flux and improve long-term system productivity. This technique, called permeate flow control, is recommended for all microfiltration separations, particularly when using membrane rated at 0.4 µm.

Post-Use Cleaning

Following is a general guideline for cleaning SepraPor® hollow fiber filters.

Reasons for Cleaning:

- Remove residual product to prevent possible cross-contamination
- Remove fouling materials to maintain and/or recover filtration efficiency
- Prevent microorganism growth and remove metabolites to maintain a sanitary system

An insufficiently cleaned filter will have reduced flux and shortened usable life. Using such filters may lead to extended manufacturing times and reduced processing capacity, resulting in process interruption and filter replacement.

Cleaning effectiveness may be influenced by process solutions, process conditions, cleaning chemicals, and cleaning methods. Different membranes may require different cleaning strategies, such as stronger or more concentrated cleaning chemicals, higher temperatures, longer cleaning durations, and higher cross flow rates. Due to different process requirements and fouling conditions, users should study and develop the most effective cleaning methods for their particular processes. For particularly difficult to clean processes, it may be most efficient to forego cleaning and begin each process with a new filter.

Key Factors for Cleaning

- Time: Typical cleaning durations are from 30 – 120 minutes; longer cleaning times generally lead to better cleaning results.
- Cleaning agent type and concentration: HFMs are typically cleaned with NaOH from 0.1 – 1.0 N. However, users should determine the most effective cleaning agent and the minimum effective concentration per cleaning time for their application due to differences in process conditions, contaminants, and cleanability.
- Temperature: Typical cleaning temperatures are between 25 °C – 50 °C; higher temperatures are usually more effective, especially for lipids and other oily contaminants, though care should be taken not to exceed the maximum operating temperature of the HFM.
- Cross flow rate: Higher cross flow rates produce better cleaning results. Carefully monitor inlet-, outlet-, and transmembrane pressures when cleaning at elevated cross flow rates.
- Water: It is recommended to use deionized water (DIW) or water for injection (WFI); poor quality water should not be used.

Common Cleaning Agents

Type	Agents	Foulant	Conditions
Alkalies	NaOH	Proteins, vaccines, bacterial cells, pyrogens, etc.	0.1 – 0.5 N 20 °C – 50 °C 30 – 60 min.
Alkalies	NaOH - NaOCl	Nucleic Acids	0.1 – 0.5 N NaOH 100 – 300 ppm NaOCl 30 – 60 min.
Acids	HNO_3 H_3PO_4 H_2SO_4	Nucleic Acids, inorganic, etc.	0.1 N 20 °C – 50 °C 30 min.
Surfactants*	SDS Triton X-100 Tween 80	Precipitated proteins, lipids, oils, antifoams, lipopolysaccharides	0.1%, pH 4 – 9 30 – 60 min.

Table 9: Recommended cleaning agents for various foulants of SepraPor® filters.

**Cleaning with surfactants is commonly performed in industry. However, the end user is ultimately responsible to validate their cleaning procedure.*

Evaluation of Cleaning Effectiveness

Determining the effectiveness of a cleaning protocol is usually done by water flux recovery (%), comparing the water flux rate of a filter after cleaning against its initial water flux rate:

$$WF\ recovery\ \% = \frac{WF_{after\ cleaning}}{WF_{initial}}\ x\ 100$$

Water flux recovery may vary widely (65% - 95%) after the first use, but subsequent recovery values should be near 90%. Lower recovery may indicate the need for cleaning method optimization. If cleaning has been optimized, membranes with low recovery should be replaced.

Although the most common assessment of cleaning efficiency, water flux is not the only criterion available. Certain applications may see low water flux recovery, but consistent sample flux.

Water flux is temperature sensitive and should be normalized to 25 °C. See the “Measuring Clean Water Flux” in this document for more information.

Used Membrane Storage

Filters must be stored appropriately to prevent membranes from drying out or developing microbial growth. Typical storage solutions and conditions are listed below, and filters should be sanitized before next use to ensure cleanness. Note: Storage conditions are based on industry standards.

Storage Solutions	Maximum Recommended Storage Time
NaOH (0.05 – 0.1 N)	< 6 months
NaOH (0.05 – 0.1 N) at 4 °C	< 1 year
Deionized H_2O + bactericide	< 1 month

Table 10: Recommended SepraPor® storage conditions.

Storage and Shelf Life

Meissner manufactures a complete line of filter products and One-Touch® single-use assemblies that can be integrated with SepraPor® capsule filters. Assemblies are suitably bagged and boxed for shipping and may be stored in the original packaging in a clean dry area at room termperature. The following gives the minimum shelf life expectancies for SepraPor® products. Filters may be used beyond their minimum expected shelf life if stored in original packaging and integrity tested prior to use and found to be within specification.

Filter product age can be determined from the date of manufacture on the product label, or the original Certificate of Conformance. For gamma irradiated filters, shelf-life starts from the date of irradiation and are distinguished with part numbers XFG.

Microfiltration

Autoclaved and gamma irradiated SepraPor® microfiltration filters are validated for a 2-year shelf life in cartridge and capsule configurations.

Ultrafiltration

Autoclaved SepraPor® ultrafiltration filter shelf-life studies are ongoing.

Quality Assurance

Each SepraPor® hollow fiber capsule filter is supplied with a Certificate of Conformance. SepraPor® Products are manufactured and packaged in a cleanroom facility that meets or exceeds FDA Good Manufacturing Practice Standards. To ensure product reliability, Meissner's Quality Assurance staff continually audits the manufacturing process for conformance to its Quality Management System. Each SepraPor® hollow fiber capsule filter is integrity tested during manufacture and is clearly marked with filter type, lot number, and serial number.

Cartridge Ordering Matrix Description

Retention Rating
M10 = 0.1 µm
M20 = 0.2 µm
M40 = 0.4 µm
010 = 10 kDa
030 = 30 kDa
050 = 50 kDa
100 = 100 kDa
300 = 300 kDa
500 = 500 kDa
750 = 750 kDa

To specify the correct part number, please choose a Retention Rating from the chart at left and insert the code in the spaces indicated with underscore marks in the Part Number field in the chart below.

Part Number	Fiber Lumen	Filter Diameter	Fluid Path Length (Nominal)	Effective Filtration Area	Housing Seal Configuration[1]	O-ring Seal Material
XFM [_ _ _] C412-AAS	1 mm	2" (5.1 cm)	12" (30 cm)	4.3 ft² (0.4 m²)	AA	Silicone
XFM _ _ _ C424-AAS			24" (60 cm)	8.6 ft² (0.8 m²)		
XFM _ _ _ C512-AAS		3" (7.6 cm)	12" (30 cm)	9.7 ft² (0.9 m²)		
XFM _ _ _ C524-AAS			24" (60 cm)	22.6 ft² (2.1 m²)		
XFM _ _ _ C612-CCS[2]		4" (10.2 cm)	12" (30 cm)	24.8 ft² (2.3 m²)	CC	
XFM _ _ _ C624-CCS[2]			24" (60 cm)	45.2 ft² (4.2 m²)		
XFM _ _ _ C824-AAS[2]		5.9" (15 cm)	24" (60 cm)	89.3 ft² (8.3 m²)	AA	

[1] *AA and CC configured cartridges are fitted with an O-ring at each open-face end that engage and seal the cartridge in the filter housing.*

[2] *Cartridges with these diameter sizes are only available for microfiltration (0.1, 0.2, and 0.4 µm retentions) and are not offered for ultrafiltration retentions.*

Capsule Ordering Matrix Description

Retention Rating
M10 = 0.1 µm
M20 = 0.2 µm
M40 = 0.4 µm
010 = 10 kDa
030 = 30 kDa
050 = 50 kDa
100 = 100 kDa
300 = 300 kDa
500 = 500 kDa
750 = 750 kDa

To specify the correct part number, please choose a Retention Rating from the chart at left and insert the code in the spaces indicated with underscore marks in the Part Number field in the chart below.

Part Number[1]	Fiber Lumen	Filter Diameter	Fluid Path Length (Nominal)	Effective Filtration Area	Retentate Ports	Permeate Ports
XFC _ _ _ C012-7711	1 mm	3/8" (0.95 cm)	12" (30 cm)	0.12 ft² (0.011 m²)	¾" sanitary flange	¼" hose barb
XFC _ _ _ C024-7711			24" (60 cm)	0.25 ft² (0.023 m²)		
XFC _ _ _ C112-7722		¾" (1.9 cm)	12" (30 cm)	0.45 ft² (0.042 m²)		3/8" hose barb
XFC _ _ _ C124-7722			24" (60 cm)	0.91 ft² (0.085 m²)		
XFC _ _ _ C212-00CC		1" (2.5 cm)	12" (30 cm)	0.81 ft² (0.075 m²)	1" sanitary flange	½" hose barb
XFC _ _ _ C224-00CC			24" (60 cm)	1.6 ft² (0.15 m²)		
XFC _ _ _ C312-FFCC		1¼" (3.2 cm)	12" (30 cm)	1.3 ft² (0.12 m²)	1½" sanitary flange	
XFC _ _ _ C324-FFCC			24" (60 cm)	2.5 ft² (0.23 m²)		
XFC _ _ _ C412-FFCC		2" (5.1 cm)	12" (30 cm)	3.9 ft² (0.36 m²)		
XFC _ _ _ C424-FFCC			24" (60 cm)	9.0 ft² (0.84 m²)		
XFC _ _ _ C512-FF00		3" (7.6 cm)	12" (30 cm)	9.9 ft² (0.92 m²)		1" sanitary flange
XFC _ _ _ C524-FF00			24" (60 cm)	23 ft² (2.1 m²)		
XFC _ _ _ C712-HH00[2]		4¼" (10.8 cm)	12" (30 cm)	27 ft² (2.5 m²)	2" sanitary flange	
XFC _ _ _ C724-HH00[2]			24" (60 cm)	47 ft² (4.4 m²)		

[1] *Irradiated capsule order numbers begin with XFG.*

[2] *Capsules with this diameter size are only available for microfiltration (0.1, 0.2, and 0.4 µm retentions) and are not offered for ultrafiltration retentions.*

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