Wetting Out Pall Microbially-Rated Filter Cartridges and Capsules for Integrity Testing and/or Pre-Use Flushing

Wetting Out Pall Microbially-Rated Filter Cartridges and Capsules for Integrity Testing and/or Pre-Use Flushing

Introduction

The use of microbially-rated filters membrane filter cartridges and capsules is widely used throughout the biotechnology and pharmaceutical industries. These membrane filters are used in pre-filtration, particulate removal, bioburden reduction, fluid sterilization, as well as mycoplasma clearance. In certain applications, it is recommended that membrane filters be flushed and integrity tested before use (whenever possible after sterilization).

Integrity testing of membrane filter cartridges and capsules by Forward Flow (diffusion) or Bubble Point-type tests requires complete wetting of the membrane such that all flow pathways are filled with the wetting liquid. The flushing procedure for wetting of a membrane filter for integrity testing is similar to the procedure used for pre-use flushing to reduce filter leachables and any downstream particles. Moreover, wetting a membrane filter for the purpose of integrity testing, simultaneously serves as the pre-use flush.

Subsequent drying of the wetted filter serves to prepare it for use in situ steam sterilization (Steam-in-Place, SIP) and/or processing. Residual water in the filtration medium of either liquid service (hydrophilic) or gas/vent (hydrophobic) filters can restrict the flow of steam during SIP procedures. This makes the filters susceptible to damage due to high differential pressure at elevated temperatures. For filters where it is recommended that they are steam sterilized in a wet state, a separate procedure is followed. Refer to Pall Application Note USTR805: Steam Sterilization of Pall® Filter Assemblies Utilizing Replaceable Filter Cartridges.

When integrity testing is done after sterilization, post-test drying still serves a role of removing residual water to remove the potential of dilution from liquid service filters.

Flushing Information

As noted in the introduction, the objectives of a pre-use flush are three-fold: to reduce the presence of particles downstream of the filter and assembly, to reduce leachables from the filter, and to wet the filter membrane prior to pre-use integrity testing. The objective of a flush to wet the filter membrane for an integrity test is to fill all the fluid pathways with the specified wetting liquid (water, buffer, product, etc.). This thorough wetting allows the integrity test to be appropriately conducted and avoids false failures that may be due to incomplete wetting (where air can flow through non-wetted or incompletely wetted pathways).

Pall's general recommendations for filter wetting/flushing are as follows:

- For 0.2 µm air and microbial-rated liquid service filters: 4 - 8 L/min per 10" cartridge element for 10 minutes with up to 30 psig (~ 2 bar g) of backpressure
- For 0.1 µm liquid service filters: 2 – 4 L/min per 10" cartridge element for 10 minutes with up to 30 psig (~ 2 bar g) of backpressure

Note that backpressure is not reverse pressure. It is a restriction placed on the outlet of the filter assembly during forward flushing, by using a valve, smaller piping size, tubing clamp, or similar constriction. The use of backpressure during flushing helps to ensure a uniform flow distribution through the entire length of the filter, i.e. it helps overcome the fluid tendency to flow through the "path of least resistance" such as only the largest flow pathways. Backpressure also facilitates the removal of air entrapped in the membrane pleats, by further solubilizing the air (due to increase pressure in the system) and by compressing air bubbles to a size where they can freely pass through the membrane.

Flushing can be done either with a pump, whereby flow rate is measured, or with pressurized transfer, in which case pressure on the upstream and downstream side (backpressure) is monitored. Similar to the constant flow method, this will be more than sufficient to wet the filter for integrity testing or for a pre-use flush.

Refer to Table 1 for reference filter sizes and corresponding recommended flushing guidelines.

Table 1 – *Flush Parameters for Various Filters*

Filter Capsule / Cartridge Description	Associated Part Number Prefix	Typical Filtration Area	Wetting / Flush Flow Rate for 0.2 µm filters[1]	Wetting / Flush Flow Rate for 0.1 µm filters[1]
Mini Kleenpak™ Syringe Filter Capsules	KM2	2.8 cm^2	3 mL/min*	1 mL/min*
Mini Kleenpak 20 Capsules	KM5	20 cm^2	10 mL/min	5 mL/min
Mini Kleenpak Capsules	KA02	200 – 220 cm^2	125 mL/min	60 mL/min
Kleenpak Capsules Junior Cartridges or Novasip Capsules	KA1/ MCY1110/ CL1	375-500 cm^2	250 mL/min	125 mL/min
Kleenpak Capsules Junior Cartridges or Novasip Capsules	KA2/ MCY2220/ MCY 3330/ C(L)2	750-1200 cm^2	500 mL/min	250 mL/min
Kleenpak Capsules Junior Cartridges or Novasip Capsules	KA3/ MCY4440/ MCY4463/ C(L)3	1500-2000 cm^2	1 L/min	500 mL/min
Kleenpak Capsules	KA4	3300-5000 cm^2	2 L/min	1 L/min
5” Kleenpak Nova Capsule or AB-style Cartridge	NP5 / AB05	0.27 – 0.55 m^2	2 – 4 L/min	1 – 2 L/min
10” Kleenpak Nova Capsule or AB-style Cartridge	NP6 / NT6 / AB1	0.55 - 1.1 m^2	4 - 8 L/min	2 - 4 L/min
20” Kleenpak Nova Capsule or AB-style Cartridge	NP7 / NT7 / AB2	1.1 – 2.2 m^2	8 - 16 L/min	4 - 8 L/min
30” Kleenpak Nova Capsule or AB-style Cartridge	NP8 / NT8 / AB3	1.6 – 3.3 m^2	12 - 24 L/min	6 - 12 L/min

**These may also be wetted and flushed via a syringe.*

The amount of filter leachables after flushing will vary, depending upon the membrane type and the method of sterilization. Please refer to the appropriate Pall datasheets and/or validation guides for extractables data from specific filters for further information

The parameters described in Table 1 are robust wetting parameters for the purposes of effectively flushing and wetting a filter for an integrity test, without the need to repeat. For pre-use flushing for leachables removal, significantly less flushing could be needed to achieve the task of flushing the membrane.

For cases of filter wetting with alcohol:water mixtures, half of the above flow rates are typically all that is required. Note there are two primary cases for utilizing an alcohol:water mixture:

- For integrity test wetting of hydrophobic membrane filters
- For rinsing of hydrophilic filters, post-use, when trapped contaminants interfere with the effective wetting of the membrane with water alone.

Flushing Procedure

Refer to Figure 1 (below) for recommended apparatus set-up. The flow meter, located downstream of the test filter assembly, is optional. With smaller filters, a graduated beaker or cylinder can be sufficient to check the flow rate through the filter.

The pump or pressure source should be capable of delivering >4 L/min for a 10” 0.2 µ sterilizing grade filter, and > 2 L/min for a 10” 0.1 µ rated filter with an inlet pressure of >30psig. Filters different from these standard sizes should use flow rates correspondingly higher or lower, based on effective filtration area. Please consult Table 1 for specific recommendations.

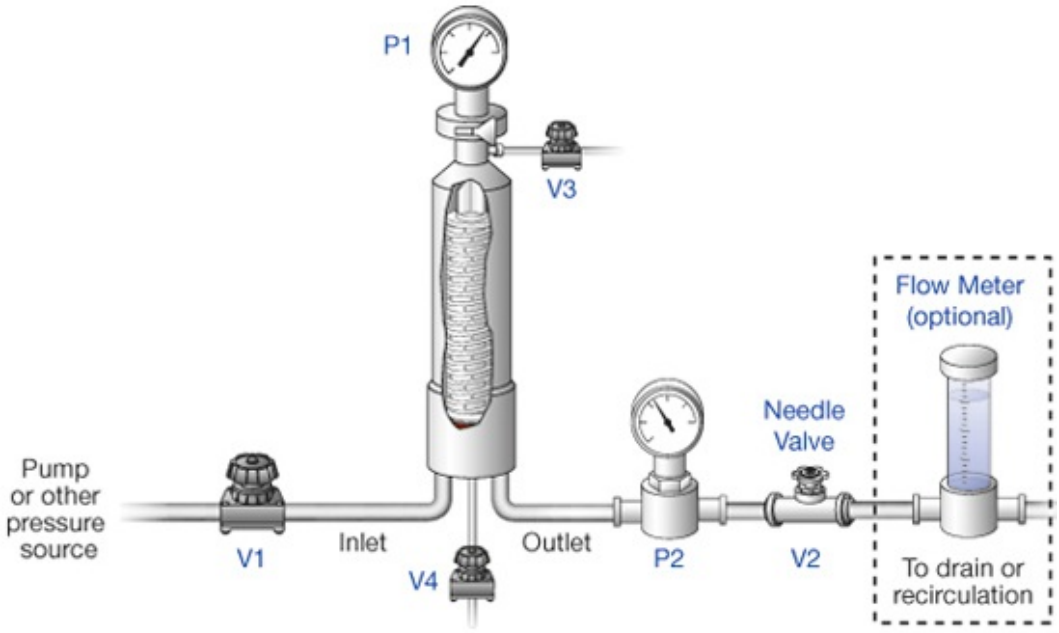

Figure 1: Flushing Procedure – Apparatus Set Up

1. Start with all valves closed. Open inlet V1, and vent V3 valves.
2. Start pump/open pressure source slowly and bleed all air from assembly through V3. When trapped air is no longer seen, close V3.
   Note: *If flushing a capsule filter or using in-line filter cartridge housing, ensure that the vent is located at the highest point during this venting phase.*
3. After bleeding and closing V3, while maintaining inlet pressure of (X psig, Y bar g) at upstream pressure gauge P1, open outlet valve V2 until a backpressure of >15 psig is indicated on downstream pressure gauge P2.
4. Check flow rate for the appropriate flow (see above). Adjust V1 or pressure source as necessary.
5. Adjust V2 as necessary to maintain the flow/pressure and backpressure conditions. A flow rate higher than is recommended is acceptable, as is a backpressure higher than recommended.
6. Flush for approximately 10 – 15 minutes.
7. Stop pump or release pressure source, and allow system to depressurize without any manipulation of any valves.
8. Drain system by opening V4, then V3.
9. Close V1, V4, V3. Fully open V2. Perform integrity test (if required).
   - For marginal integrity test failures, the procedure can be repeated by either extending the flush time, increasing the backpressure, increasing the flow rate, increasing the flush liquid temperature, or all 4 parameters, prior to a retest.
   - For gross integrity test failures, check the system for leaks, rewet and retest.

Recommendations

Flushing and wetting of membrane filter cartridges and capsules are recommended before use to rinse the membrane, reduce leachables and presence of any handling or installation residue in the downstream system, and to wet the filter prior to a pre-use integrity test. The reduction of leachables and downstream particles are intrinsic benefits of a membrane flush to wet for integrity testing and do not require separate actions.

The procedure included in this Application Note is not intended to include all ways a filter can be appropriately flushed prior to use. Pall is pleased to provide more customized approaches for specific applications based on individual process flushing requirements. Contact your Pall representative for further details.

[1]*Note: Suggested target flow rates for cartridges and capsules larger than 5" may incorporate high area filters and therefore have a broader suggested target wetting/flushing flow rate range. Time for wetting/flushing is up to 10 minutes with up to 30 psig (2 bar g) backpressure.*