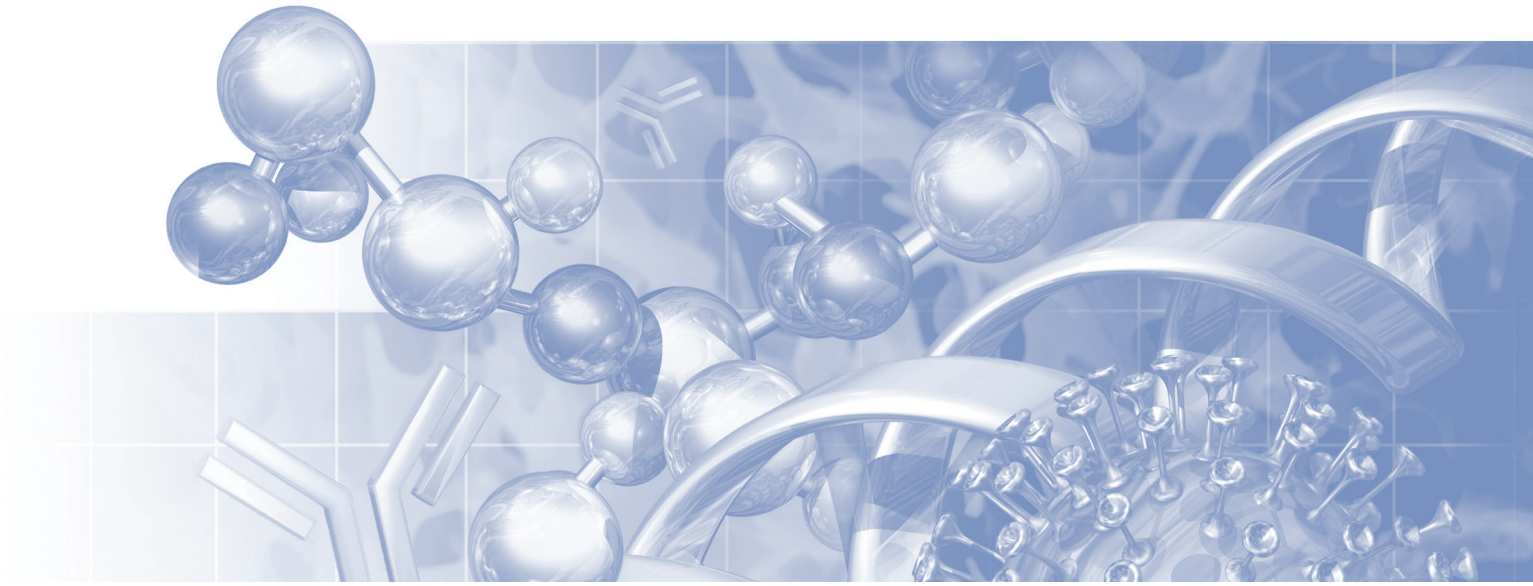
Biotech

User Guide

USD3297

Wetting and Flushing of Pall Microbially-Rated Filter Cartridges and Capsules



*Filtration. Separation. Solution.*SM

General Considerations on Filter Preparation for Use

Microbially-rated membrane filter cartridges and capsules are widely used throughout the biotechnology and pharmaceutical industries for bioburden reduction, fluid sterilization, as well as mycoplasma clearance. Integrity testing, either out-of-box, after sterilization/pre filtration (both can be referred to as “pre use”), and/or post filtration, is imperative in many applications.

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 (water, buffer, product, etc.). This thorough wetting allows the integrity test to be appropriately conducted and avoids false failures due to incomplete wetting, where air can freely flow through non-wetted or incompletely wetted pathways.

Flushing of filters pre-use is also recommended to reduce the presence of particles downstream of the filter assembly and to reduce leachables from the filter. An appropriately designed flushing regime can therefore address all three aspects in a filtration process. The parameters described further below in this document aim at achieving complete filter wetting for integrity testing. For leachables and particle reduction, other (typically less) flushing volumes may be required depending on the application and filter assembly. Flushing to reduce leachables should be carried out post-sterilization, as the sterilization process typically stimulates formation of leachables. The amount and composition of filter leachables after flushing will vary depending on 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.

Water in the filtration medium may restrict the flow of steam during SIP procedures and may lead to filter damage due to high differential pressure at elevated temperatures. Pall Application Note USTR805: Steam Sterilization of Pall® Filter Assemblies Utilizing Replaceable Filter Cartridges contains detailed instructions how to conduct *in-situ* steaming of a filter in either a dry or wetted state.

Some applications may require filter drying prior to filtration. *In-situ* drying is typically achieved by applying pressurized gas above the filter bubble point and exposing the filter to gas flow, and needs to be qualified assembly and application-specifically.

Flushing Information for Wetting

Pall’s general recommendations for filter wetting with aqueous fluids for the purpose of integrity testing are as follows:

For 0.2 µm microbially-rated liquid service filters:
4-8 L/min per 254 mm (10 in.) filter for 10 minutes

For 0.1 µm microbially-rated liquid service filters:
2-4 L/min per 254 mm (10 in.) filter for 10 minutes

Generally, enhanced flow rate and differential pressure, prolonged wetting fluid contact time, and back pressure are physical factors that will aid complete wetting for the purpose of integrity testing, and can therefore be applied in case of an integrity test failure. When using water as a wetting liquid, differential pressure of up to 500 mbar (7.2 psi), wetting time of up to 30 minutes, and back pressure up to 2 barg (30 psig) can be considered as “enhanced” conditions.

It should be noted that backpressure is not reverse pressure. Back pressure is achieved by placing a restriction on the outlet of the filter assembly during forward flushing, by using a valve, smaller piping size, tubing clamp, or similar constriction, maintaining a pressure differential from upstream to downstream. The use of backpressure during flushing helps to ensure uniform flow distribution through the filter, i.e. it helps overcome the fluid tendency to flow through the ‘path of least resistance’, i.e. larger flow pathways. Backpressure also facilitates the removal of air entrapped in the membrane pleats by further solubilizing the air by increased system pressure and by compressing air bubbles to a size where they may 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.

Table 1 shows the above recommended flow rates of 4-8 L/min and 2-4 L/min for 0.2 µm and 0.1 µm microbially-rated 254 mm (10 in.) filters converted for smaller filters sizes.

Table 1

Aqueous flow rates for various filter sizes to achieve complete wetting

Filter Style Description	Associated Part Number Prefix	Typical Filtration Area	Wetting Flow Rate for 0.2 µm filters	Wetting Flow Rate for 0.1 µm filters
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
125 mm (5 in.) Kleenpak Nova capsule or AB-style cartridge	NP5 / AB05	0.27 – 0.55 m^2	2 – 4 L/min	1 – 2 L/min
254 mm (10 in). Kleenpak Nova capsule or AB-style cartridge	NP6 / NT6 / AB1	0.55 – 1.1 m^2	4 – 8 L/min	2 – 4 L/min
508 mm (20 in.) Kleenpak Nova capsule or AB-style cartridge	NP7 / NT7 / AB2	1.1 – 2.2 m^2	8 – 16 L/min	4 – 8 L/min
762 mm (30 in.) Kleenpak Nova capsule or AB-style cartridge	NP8 / NT8 / AB3	1.6 – 3.3 m^2	12 – 24 L/min	6 – 12 L/min

For cases of filter wetting with alcohol/water mixtures, half of the above flow rates are typically sufficient. 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

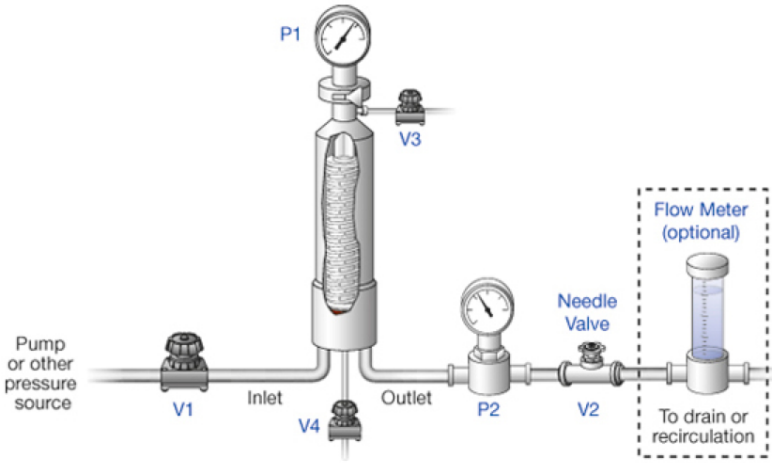
Flushing Installation and Procedure

Refer to Figure 1 (below) for recommended apparatus setup. 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 >8 L/min for a 254 mm (10 in.) 0.2 µm microbially-rated filter, and > 4 L/min for a 254 mm (10 in.) 0.1 µm rated filter with an inlet pressure of > 2 barg (30 psig). Please consult Table 1 for recommendations on other filter styles.

Figure 1

Flushing procedure – apparatus set up for flushing applying back pressure



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 barg, Y psig) at upstream pressure gauge P1, open outlet valve V2 until a backpressure of > 1 barg (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 the desired time.
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.
10. Perform integrity test.

In the case of integrity test failures, a defined Standard Operation Procedure (SOP) should be followed, involving:

1. Checking the system for leaks.
2. Rewetting with enhanced flush conditions (extending flush time, increasing backpressure, increasing flow rate, or all 3 parameters). Flush with increased liquid temperature will also aid wetting. The integrity test should then be carried out at the original temperature, i.e. requires active or passive cooling of the filter assembly prior to integrity testing.
3. Use of alcohol/water mixture as wetting liquid.

Note: Based on purely scientific considerations, an unlimited number of re-wetting and re-testing is possible: A true leak point in the filter will always manifest itself by a gas flow above limit value; thus, there is no risk that a damaged filter will display a gas flow below the gas flow limit (false pass) due to test repeats, as long as the test procedures specified by the filter manufacturer are followed. However, good practice in a GMP environment is to define a respective SOP, including a clear sequence of:

- System checks for leaks
- Enhanced wetting methods
- Limited number of test repeats

Closing Remark

The flushing procedure included in this document is one possible approach to appropriately flush a filter 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.

PALL Biotech

Corporate Headquarters
Port Washington, NY, USA
+1.800.717.7255 toll free (USA)
+1.516.484.5400 phone

European Headquarters
Fribourg, Switzerland
+41 (0)26 350 53 00 phone

Asia-Pacific Headquarters
Singapore
+65 6389 6500 phone

Filtration. Separation. Solution.SM

Visit us on the Web at www.pall.com/biotech
Contact us at www.pall.com/contact

International Offices
Pall Corporation has offices and plants throughout the world in locations such as: Argentina, Australia, Austria, Belgium, Brazil, Canada, China, France, Germany, India, Indonesia, Ireland, Italy, Japan, Korea, Malaysia, Mexico, the Netherlands, New Zealand, Norway, Poland, Puerto Rico, Russia, Singapore, South Africa, Spain, Sweden, Switzerland, Taiwan, Thailand, the United Kingdom, the United States, and Venezuela. Distributors in all major industrial areas of the world. To locate the Pall office or distributor nearest you, visit www.pall.com/contact.

The information provided in this literature was reviewed for accuracy at the time of publication. Product data may be subject to change without notice. For current information consult your local Pall distributor or contact Pall directly.

2/19, PDF, GN19.07281