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Application Note

Improved Vent Filtration for Large Scale Single-Use Assemblies

Streamline filling without compromising sterility

Introduction

Single-use technologies are increasingly being implemented throughout the biomanufacturing workflow to improve efficiency and provide manufacturing flexibility. These single-use technologies are used for both small- and large-scale manufacturing processes and for many different modalities. Presterilized mixing assemblies are frequently used to prepare buffers and other sterile solutions for processing, and depending on the process, a sterilized vent filter may be needed to inflate a mixing bag during assembly installation. Media or buffer ingredients are then added to the mixing bag, and the air in the assembly is displaced through the vent filter.

Proper selection and sizing of a sterilizing-grade vent filter for inflation and filling of single-use bags is important not only to maintain sterility, but also to avoid stretching, bursting or compromising the single-use components as a result of pressure increases inside the bag. For closed processes this is especially important. To minimize the effects of pressure increases, end users venting large-scale containers may use more than one vent filter.

Ideally, a vent filter for single-use applications should be gamma-compatible and have sufficient membrane area and high permeability to provide minimal pressure drop across the filter during routine operations. Millipore Express® SPG filters are gamma-compatible vent filters containing sterilizing-grade polyethersulfone (PES) membrane, with capsule formats designed to provide a venting solution for single-use applications at both small- and large-scales, Table 1.

Table 1.

Millipore Express® SPG filter formats and membrane area.

Capsule Format	Opticap® XL50	Opticap® XL300	Opticap® XL5	Opticap® XL10
Filtration Area	19.6 cm^2	480 cm^2	0.39 m^2	0.87 m^2

The purpose of this study was to compare the performance of Millipore Express® SPG membrane in Opticap® XL5 and XL10 capsules and other commercially available filters for venting large-scale single-use mixing assemblies. By understanding the flow rate and pressure drop across these filters, we provide a foundation for implementing these filters in the bioprocessing workflow.

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Test Methods

The mixing assembly filling study was conducted with Mobius® 1000 L Power MIX bags (catalog number MIX1000LSPB03) in a Mobius® 1000 L stainless steel Mobius® Power MIX system with an integrated load cell (catalog number MXRJ1000TLA). A diagram of the test setup is shown in Figure 1 and illustrates the relative location of measuring equipment and the method of liquid transfer from a storage vessel to the mixing vessel. A pressure transducer was connected to the bag side of each vent filter to record and monitor bag pressure during inflation and ensure that pressures did not exceed 0.25 psi, to keep the pressure below the pressure rating for the Mobius® bag (0.25 psi). To directly compare the vent filters, the same bag, pump, connections, and tubing were used for each test system: tubing for filling and venting was 1.0" ID and utilized 1.5" sanitary flange (TC).

The test filters are listed in Table 2. Prior to each test, bags were inflated and held at 0.1 psi. Next, bags were filled with reverse osmosis (RO) water via the bottom port and vented through the top port to atmosphere. A target water filling rate of 100 L/min was used for most filters; for Filter B which had a smaller filtration area than the other test filters, a lower flow rate of 85 L/min was used to maintain pressure below 0.25 psi. Filling continued until each mixing bag was filled with 1000 L of water. After each test, the bags were drained and re-inflated to 0.1 psi in preparation for the next test.

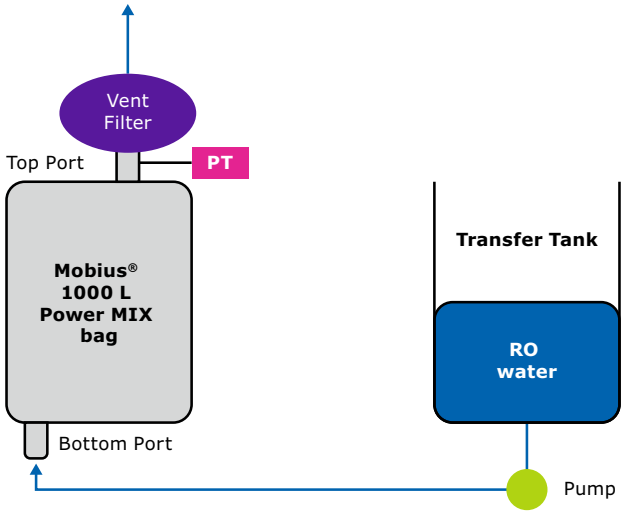

Figure 1.

Schematic of bag filling with RO water. PT is a pressure transducer.

Separately, the pressure across each filter was measured under a range of ambient air flow rates from 0.45 to 50 standard cubic feet per minute (SCFM). Air flow entering the filter was set using a mass flow controller and the pressure was measured at one end of the filter with the other side of the filter venting to atmosphere. Once pressure and flow reached an equilibrium, data were recorded.

Table 2.

Vent filters tested with 1.0" ID tubing and 1.5" sanitary flange (TC) connection.

Filter	Manufacturer	Effective Filtration Area [m²]	Gamma Sterilized	Membrane	Water Flow Rate Tested [L/min]
Millipore Express® SPG, Opticap® XL5 Capsule	Merck	0.39	Yes	PES[1]	100
Aervent® 0.2 µm, Opticap® XL5 Capsule	Merck	0.32	No[2]	PTFE[3]	100
Filter A1	A	0.34	Yes	PES[1]	100
Filter B	B	0.17	Yes	PVDF[4]	85
Millipore Express® SPG, Opticap® XL10 Capsule	Merck	0.87	Yes	PES[1]	100
Aervent® 0.2 µm, Opticap® XL10 Capsule	Merck	0.65	No[2]	PTFE[3]	100
Filter A2	A	0.53	Yes	PES[1]	100

[1] Polyethersulfone (PES).
[2] Aervent® filters are not compatible with gamma irradiation but can be sterilized with ethylene oxide.
[3] Polytetrafluoroethylene (PTFE).
[4] Polyvinylidene fluoride (PVDF).

Results and Discussion

When selecting a vent filter for an application, it is important to correctly size the filter to ensure a low operating pressure and avoid stretching, bursting or compromising presterilized single-use components. The performance of Millipore Express® SPG membrane in Opticap® capsules, was benchmarked against other commercially available sterilizable encapsulated membranes filters to assess bag pressure during filling; results are shown in Figure 2.

All filters, except for Filter B, maintained pressures below 0.25 psi, the upper pressure limit, when filled with water at 100 L/minute. Of the gamma-compatible filters, the Millipore Express® SPG capsule showed the lowest pressure increase in the single-use bag. The bag pressure when using the Millipore Express® SPG membrane in Opticap® XL5 capsule was 10% and 40% lower than for Filters A1 and B, respectively. Note, the filtration area for Filter B is approximately 2× lower than the 5-inch filters tested so this filter was limited to a flow rate of 85 L/min to ensure a bag pressure lower than 0.25 psi. Although the Aervent® 0.2 µm Opticap® XL5 capsule had approximately 30% lower pressure than the Millipore Express® SPG membrane in Opticap® XL5 capsule, this filter is not compatible with gamma sterilization and requires additional considerations for implementation.

If lower pressures are desired, or if larger volume assemblies are being used, the 10" Millipore Express® SPG membrane in Opticap® XL10 capsule is a good option for venting. These filters have 60% lower pressure compared to the smaller Opticap® XL5 capsules.

Comparing filters from different manufacturers, 5" and 10" capsules exhibited similar performance trends. However, the combination of higher filtration area and similar membrane permeability of the Millipore Express® SPG membrane in the Opticap® XL10 capsule (0.87 m^2) format as compared to the 10" Filter A2 capsule (0.53 m^2) results in ~50% lower pressure. This lower pressure may reduce the number of vent filters needed for any one assembly and offers the opportunity for faster filling without risking the integrity of the bag or single-use assembly components.

Figure 3 provides guidance for filter selection for a range of flow rates or pressure limitations with two filter connections. For both Opticap® XL5 and XL10 capsules containing Millipore Express® SPG membrane, a 1.5" sanitary flange (TC) connection will have lower pressure than a $^9/_{16}$" hose barb (HB) connection.

Millipore Express® SPG membrane in Opticap® XL5 and XL10 capsules are an attractive option for vent filtration in single-use applications. These gamma-compatible filters have higher filtration areas and air permeability within 10% of other commercially available gamma-compatible filters. These characteristics enable these Millipore Express® SPG capsule filters to support high flow venting applications without the pressure increases that could compromise the sterility or integrity of a single-use system.

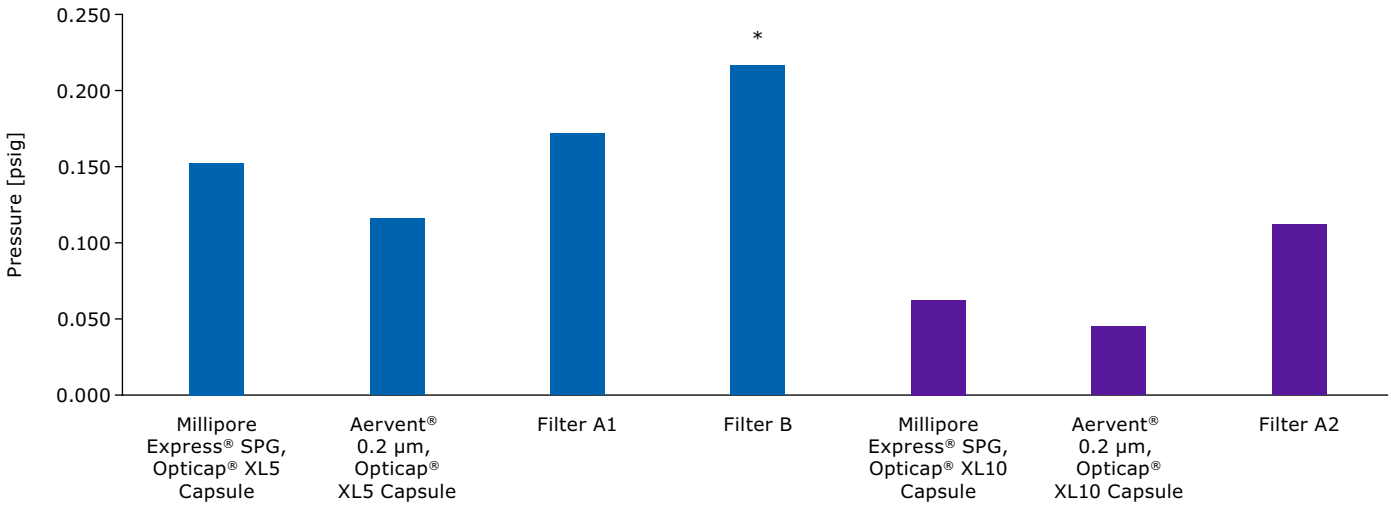

Figure 2.

1000 L Mobius® MIX bag pressure while flowing at 100 L/min into the bag. The * indicates the flow rate was at 85 L/min.

Conclusion

The goal of this study was to quantify the performance of different gamma-sterilized vent filters for use on a single-use mixing assembly. The pressure for each filter was monitored while filling with water at a constant flow rate.

- Millipore Express® SPG membrane in Opticap® XL5 and Opticap® XL10 formats maintained low pressure (<0.25 psi) when filling 1000 L single-use bags at a flow rate of 100 L/min.
- When compared to other gamma sterilized commercially available vent filters, these filters offered superior venting performance and avoided the pressure increases inside the bag that could compromise single-use integrity.

The higher filtration area of Millipore Express® SPG membrane in Opticap® XL5 and XL10 capsules enables operating at higher flow rates, without the risk of pressure increase, and reduces the number of vent filters needed to maintain low pressures with single-use mixing assemblies.

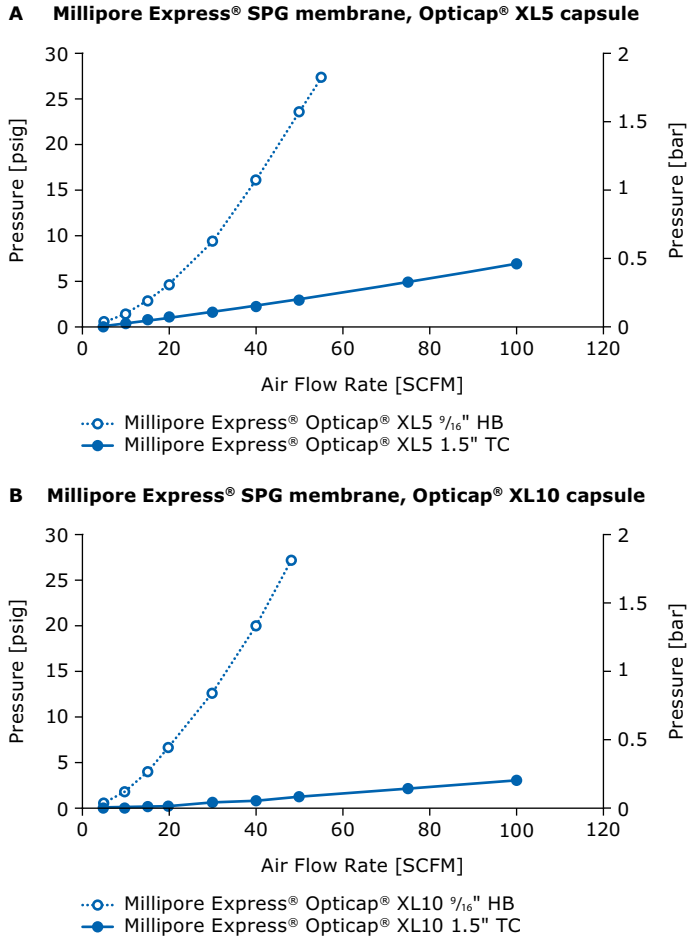

Figure 3.

Flow dP Curves for Millipore Express® SPG, Opticap® capsules with 1.5" TC and 9/16" hose barb connections on the inlet/outlet for (**A**) 5" and (**B**) 10" capsules.

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