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Application Note

Efficient Vent Filtration for Single-Use Bioreactors

Introduction

Vent filters play a critical role in assuring sterility and preventing microbial ingress during biomanufacturing. In upstream applications such as media preparation or operating a bioreactor (e.g. filling, draining, sparging), vent filters provide a sterile gas transfer barrier which maintains the sterility of the system.

Ideally, a vent filter for a single-use application should have sufficient membrane area and permeability to have minimal pressure drop during operation. Millipore Express® SPG filters are gamma-compatible capsules containing sterilizing-grade hydrophobic polyethersulfone (PES) membrane. These capsule filters are offered in various sizes to meet the needs of small- and large-scale single-use applications. **Table 1** summarizes the filter formats and filtration areas.

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

For flow rates less than 141 L/min (5 cubic feet per minute – SCFM), Millipore Express® SPG capsules in Opticap® XL5 and XL10 formats have initial pressure drops well below 0.25 psi, which is a common pressure limit for single-use bioreactor bags (**Figure 1**). This low initial pressure drop enables these filters to be used for a range of flow rates on small- and large-scale bioreactors, without the risk of exceeding the pressure specifications for a bioreactor bag.

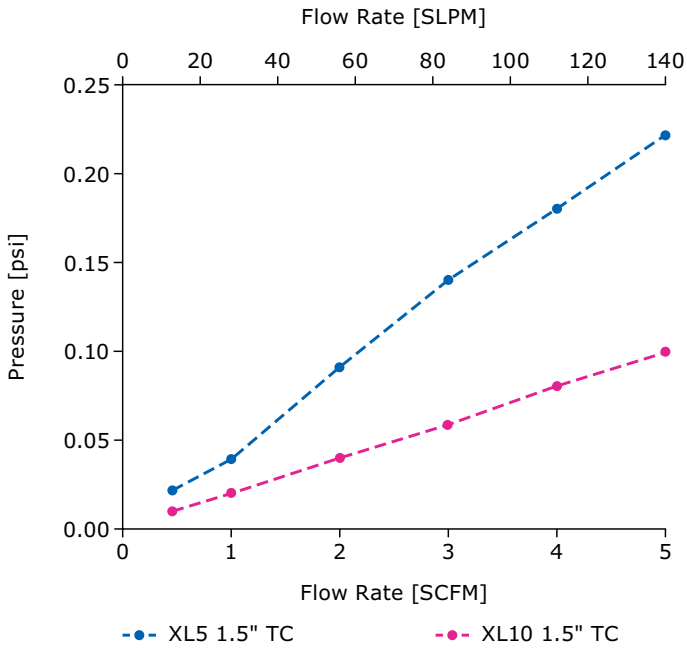

Figure 1.

Flow dP curves for Millipore Express® SPG capsules in Opticap® XL5 (blue) and XL10 (pink) formats with 1.5" TC connections for the inlet/outlet.

The purpose of this study was to benchmark the performance of Millipore® Express SPG capsules in the Opticap® XL5 format with other commercially available vent filters in a 14-day mock bioreactor run. The filters were sized to have an initial pressure <0.02 psi when sparging air at 12.5 L/min (0.44 SFCM) through a mock cell culture media. At this constant sparging rate, the differential pressure across the filter as a function of time was monitored. These studies provide a foundation for sizing and implementing Millipore® Express SPG filters in a bioreactor venting application.

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Test Methods

A bioreactor simulation was created using a 200 L mock cell culture media (MCCM) formulated with 10× PBS, 50 ppm antifoam, 4 g/L poloxamer, and reverse osmosis water. A Mobius® 200 L bioreactor and control unit was utilized in tandem with a circulation chiller to maintain the MCCM at 37 °C. A 200 L PureFlex™ baffled bioreactor bag was used inside the bioreactor. The open-pipe sparger was set to a flow rate of 12.5 ± 0.5 LPM and the agitation rate was set to 40 W/m^3. The vent filter being tested was attached to the bioreactor bag with 1" ID tubing and the air flowed in the direction of the arrow on the capsule.

A thermocouple was used directly upstream and downstream of the vent filter. A pressure transducer monitored bag pressure and a second pressure transducer was on the bioreactor bag to determine an emergency system shutoff pressure at 0.20 psi ensuring pressure operations below the bag limit of 0.25 psi. The air flow rate was recorded using the built-in software for the Mobius® bioreactor. A diagram of the test setup is shown in **Figure 2**.

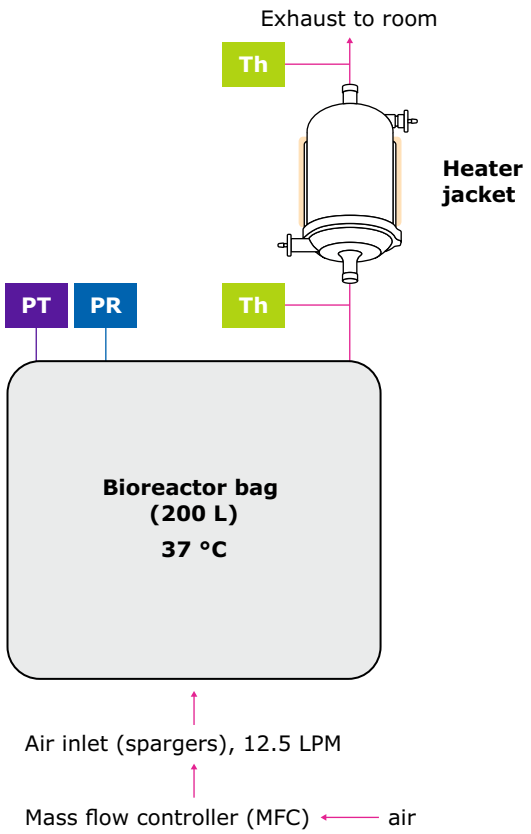

Figure 2.

Diagram of bioreactor setup where PT is a pressure transducer, Th is a thermocouple, and PR is pressure relief valve.

A polytetrafluoroethylene (PTFE) layered heating jacket was placed around each filter while it was tested on the bioreactor. The heater jackets were snug to the filter capsule and covered the whole filter area between the top and bottom vent ports. The heater jacket temperature was set such that the surface of the filter was 60 °C. Each filter was tested on the bioreactor for 14 days or until the shutoff pressure of 0.20 psi was reached, whichever came first. The filters tested are outlined in **Table 2**.

Millipore Express® SPG capsules in Opticap® XL5 format, were compared to commercially available gamma sterilized encapsulated membrane filters. Although not compatible with gamma sterilization, Aervent® 0.2 µm capsules in Opticap® format were included in this study for comparative purposes. Aervent® filters contain PTFE membrane and can be sterilized by ethylene oxide treatment for use in single-use assemblies.

Table 2.

Vent filters tested on 200 L Mobius® bioreactor, all with 1.0" ID tubing and 1.5" sanitary TC connections.

Filter	Manufacturer	Membrane	Area [m^2]	Gamma Sterile?
Aervent® 0.2 µm, Opticap® XL5 Capsule	MilliporeSigma	PTFE[2]	0.32	N[1]
Millipore Express® SPG, Opticap® XL5 Capsule	MilliporeSigma	PES[3]	0.39	Y
A	Competitor A	PES[3]	0.34	Y
B	Competitor B	PVDF[4]	0.17	Y

[1] Aervent® filters are not compatible with gamma irradiation but can be sterilized with ethylene oxide

[2] Polytetrafluoroethylene (PTFE)

[3] Polyethersulfone (PES)

[4] Polyvinylidene fluoride (PVDF)

Results and Discussion

Each vent filter remained below the bag pressure limit when tested during the 14-day operation (**Figure 3**). During this time, Millipore Express® SPG filters had similar pressure to Filter A and 5× lower than Filter B. The Aervent® 0.2 µm capsule had slightly lower pressure than the Millipore Express® SPG capsule; however, this filter is not compatible with gamma sterilization and requires additional considerations for implementation. The pressure curves for each vent filter were similar except for some deviation with Filter B which experienced gradual pressure increases over the 14 days. The bioreactor temperature was set to 37 °C with a measured vent filter exhaust between 40–43 °C for each filter except for Filter B which was only at 38 °C. This suggests Filter B was less efficiently heated and was more prone to condensation build up within the vent filter during the experiment compared to the other filters tested. For all the other filters, the bioreactor pressure remained constant and the filter exhaust temperatures for each filter were above 40 °C, which helped mitigate moisture build up in the filters.

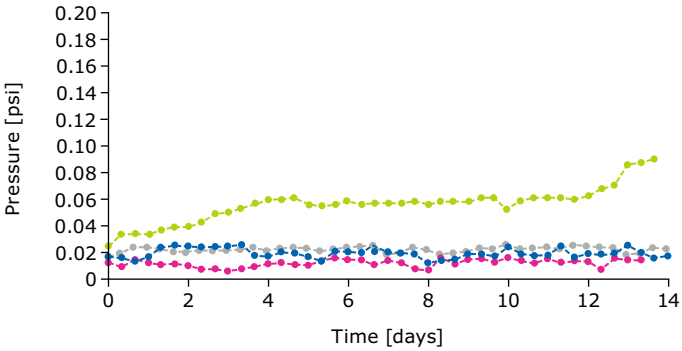

Figure 3.

Bioreactor pressure vs. time. Filter A (grey), Millipore Express® SPG capsule (blue), Aervent® 0.2 µm capsule (pink), and Filter B (green).

To avoid rapid pressure rise and to maintain filter productivity throughout the duration of upstream cell culture processes, vent filters should be sufficiently heated to avoid water condensation within the device.

Conclusions

The goal of this study was to quantify the performance of different gamma-sterilized vent filters, including Millipore® Express SPG capsules, for use with single-use bioreactors. Pressure across the vent filters was measured over a 14-day mock bioreactor run. Compared to competitor vent filters, Millipore Express® SPG filters have similar or lower pressure at a given gas flow rate. When adequately sized and heated, Millipore Express® SPG vent filters in Opticap® formats are ideally suited for maintaining the sterility and pressure of single-use bioreactors during extended operations.

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