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Application Note

April 10, 2018

Keywords or phrases:
Risk mitigation upstream, virus retention, chemically defined cell culture media, virus filtration, lot-to-lot performance consistency

Evaluating Lot-to-Lot Performance Consistency of Chemically Defined Cell Culture Media During Filtration With the Virosart® Media Filter

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Abstract

The contamination of bioreactors with adventitious agents such as bacteria, mycoplasma, and viruses is a potential risk to patient safety. Viruses have been the cause of multiple bioreactor contamination events in recent years. A number of biopharmaceutical companies have reported production-scale bioreactor contamination events by small non-enveloped viruses such as minute virus of mice (MVM) or vesivirus[1]. The consequences of such an event may be severe and result in GMP facility contaminations, along with drug shortages and financial losses. Therefore, several biopharmaceutical operations are evaluating risk mitigation strategies for the minimization of contamination by adventitious agents. Classical sterilizing-grade filters and even 0.1 µm-rated filter membranes cannot prevent contamination by small non-enveloped viruses[2].

Size exclusion-based filtration is the preferred technology for viral clearance, as it is robust and non-invasive. The Virosart® Media filter mitigates virus contamination risks which may arise from the addition of nutrients and other additives into the bioreactor system.

Find out more: www.sartorius.com/virosart-media

Introduction

The Virosart® Media filter has been developed specifically for chemically defined cell culture media. The filter is an asymmetric polyethersulfone hollow fiber membrane with 20 nm nominal pore size rating. It has a high capacity (~1000 L/m² at 2 bar in 4 hour filtration time) for chemically defined cell culture media while providing logarithmic reduction values (LRV) of ≥ 4 $\log_{10}$ for small non-enveloped viruses and ≥ 6 $\log_{10}$ for large enveloped viruses[3,4].

The purpose of this study was to evaluate the consistency of filtration capacities over a range of chemically defined cell culture media (table 1). Five different chemically defined cell culture media from one production lot were each tested with five different membrane lots of the Virosart® Media filter.

	Power CHO™ 3	Ex-Cell® CD CHO-325	CD CHO	Power CHO™ 2	ProCHO™ 5
Supplier	Sartorius	Sigma-Aldrich	Thermo Fisher	Sartorius	Sartorius
Cat. No	12-772Q	C1490-1L	10743-029	BE12-771Q	WPW-045D
Cell line	CHO (DG44, CHO-S, CHO K1, DHFR-...)	CHO	CHO	CHO (DG44, CHO-S, CHO K1, DHFR-...)	CHO (DG44, CHO-S, CHO K1, DHFR-...)
NAO*	Yes	N/A	Yes	Yes	Yes
Protein free	Yes	Yes	Yes	Yes	Yes
Peptide free	No	N/A	Yes	No	No
CD**	Yes	N/A	Yes	Yes	No
Gln containing	No	No	No	No	No
Polaxamer containing	Yes	N/A	Yes	Yes	0.1%

Table 1: *Chemically Defined Cell Culture Media Used to Evaluate the Lot-To-Lot Performance Consistency With Virosart® Media Filter*
*Yes = Contained in the Cell Culture Media, No = Not Contained in the Cell Culture Media, N/A = Information Not Available[5,6] * Non-animal Origin; ** Chemically Defined*

Materials and Methods

Filtration runs were performed with the Virosart® Media lab modules (1 cm², R & D samples) using five different membrane lots. The five dehydrated media described in table 1 were reconstituted in deionized water each according to the manufacturer's instructions. For all filtration runs the same lot of cell culture media was used. Before each run, the filters were flushed for 15 minutes with deionized water at 2.0 bar | 30 psi using compressed air and the water flux was recorded. The deionized water in the reservoir was replaced with the cell culture media to be tested. The filtration was performed at room temperature (20 – 22 °C | 68 – 71.5 °F) at a constant pressure of 2.0 bar | 30 psi. The weight of the collected filtrate was recorded at specific time points to calculate the flow rate, flux and flux decay.

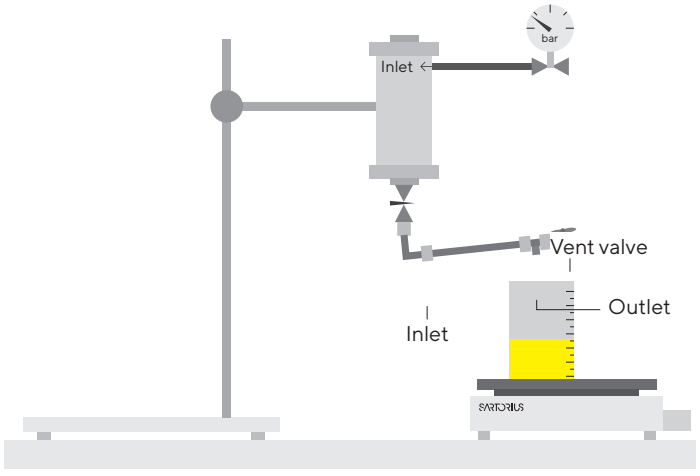

Figure 1: *Experimental Set-up of Small-Scale Filtration Using Virosart® Media Lab Modules*

Results and Discussion

During commercial processing but also during development, lot-to-lot membrane consistency of virus retentive filters such as Virosart® Media is of extreme importance. The permeability [LMH/bar] vs. capacity [L/m²] for each cell culture media was consistent when performed with Virosart® Media filter from different membrane lots.

The data presented in figure 2 shows that volumes of media that could be processed varied widely depending on the composition of the media. Some media tended to block the filter relatively quickly whereas other media did not appear to block the filter at all. Power CHO™ 2 (figure 2D) has been chosen as a worst case media known to show high blocking. Meanwhile Power CHO™ 2 has been updated by Power CHO™ Advanced, showing much higher permeability[4].

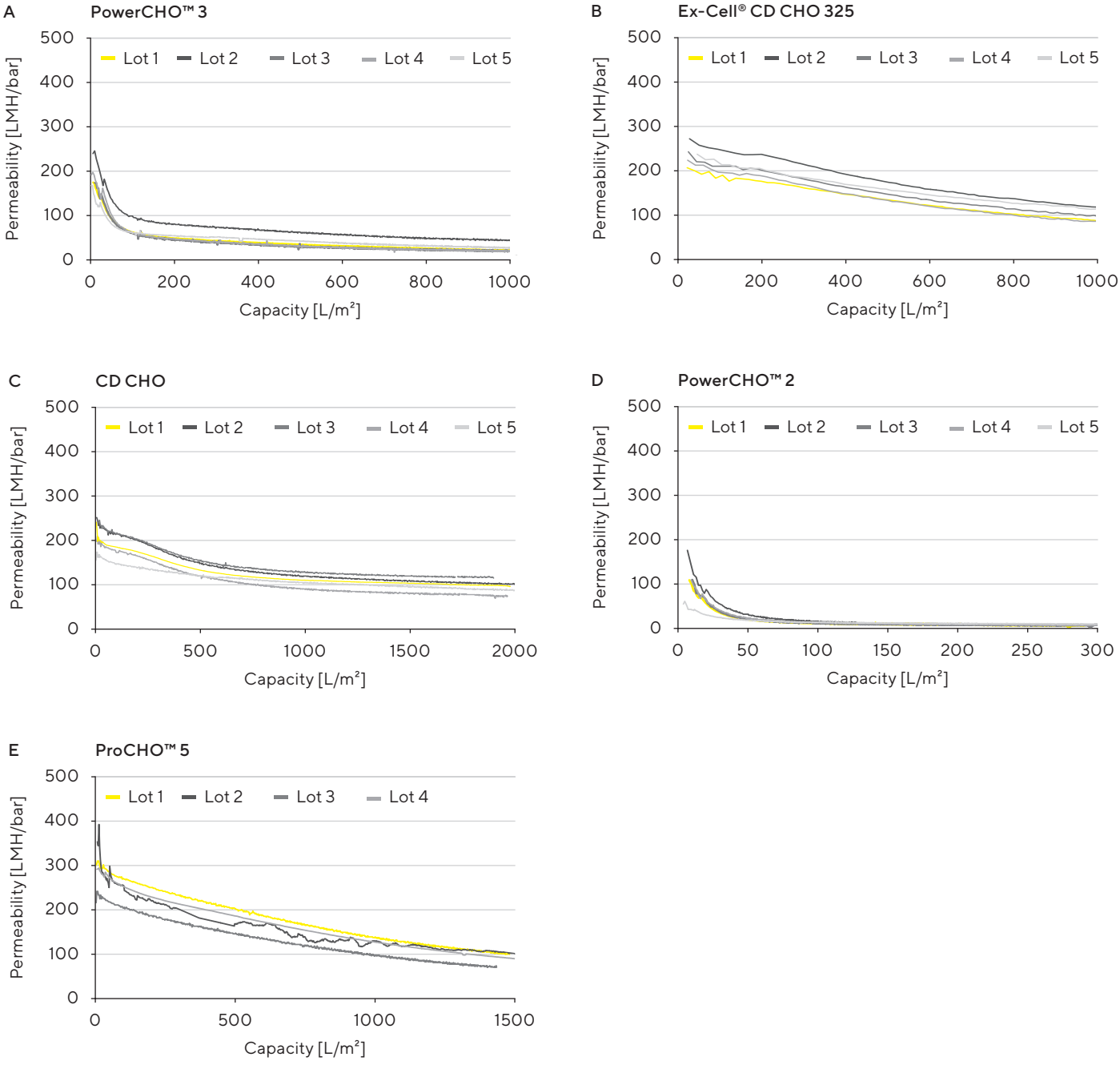

Figure 2: *Permeability Versus Capacity. Consistent Lot-To-Lot Filterability Performance for 5 Different Cell Culture Media Tested With 4 – 5 Different Membrane Lots of Virosart® Media Filter Each at 2.0 bar | 30 psi.*

Figure 3 shows the total capacity of the Virosart® Media filter for the different cell culture media after 4 hour filtration time at 2.0 bar | 30 psi. The Virosart® Media filter showed highest capacity with Ex-Cell® CD CHO-325 (figure 3A), CD CHO (figure 3C) and ProCHO™ 5 (figure 3E) of 1000 L/m² or more after 4 h filtration. Consistent capacity is shown for all five cell culture media with variation in capacity being in the range of ± 10% for the five different membrane lots tested.

This variation is low compared to the water flow rate specification of the membrane, which is ± 25%, that could possibly be attributed to variations in the cell culture media rather than the membrane. The maximum variation to be expected from the membrane is the specification of the water flow rate.

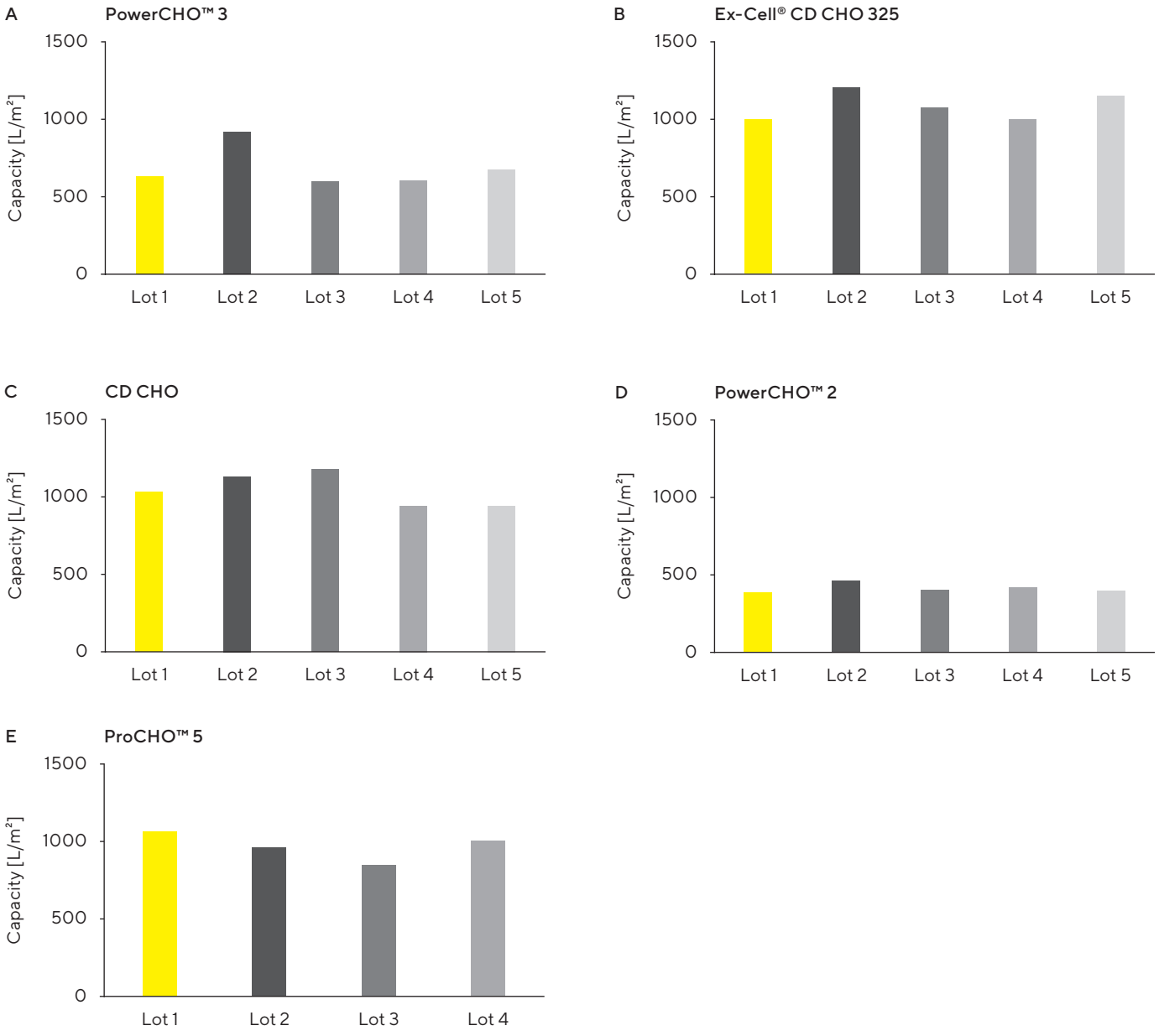

Figure 3: *Lot-To-Lot Filter Performance Consistency [L/m²] Tested With 4 to 5 Different Membrane Lots of Virosart® Media Filter for 5 Different Cell Culture Media After 4 Hours of Filtration at 2.0 bar | 30 psi.*

Summary and Conclusions

The data demonstrates that the Virosart® Media filter is the filter of choice for upstream applications where biomanufacturers require high capacities and low process costs. This makes Virosart® Media an economically feasible method for the consistent batch preparation of chemically defined cell culture media while reducing the risk of viral contamination. The 20 nm Virosart® Media filter has a high total capacity of approximately 1000 L/m² for several commercially available cell culture media tested during a 4-hour filtration at 2 bar | 30 psi. Repeated runs with multiple membrane from different lots showed variation in capacity in the range ± 10%.

References

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5) Link: https://www.thermofisher.com/
6) Link: http://www.sigmaaldrich.com/

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Order No.: 1000053370 | Status: 06 | 08 | 2022