SARTORIUS

Application Note

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Effect of Flux Decay on Virus Retention

Virus Clearance

Contact
E-Mail: Virussafety@Sartorius.com

Introduction

This application note describes virus retention properties of Virosart® CPV, the Sartorius 20 nm Polyethersulfone membrane virus filter. This application note outlines virus retention data for Virosart® CPV with increasing flux decay profiles for several different proteins.

Background

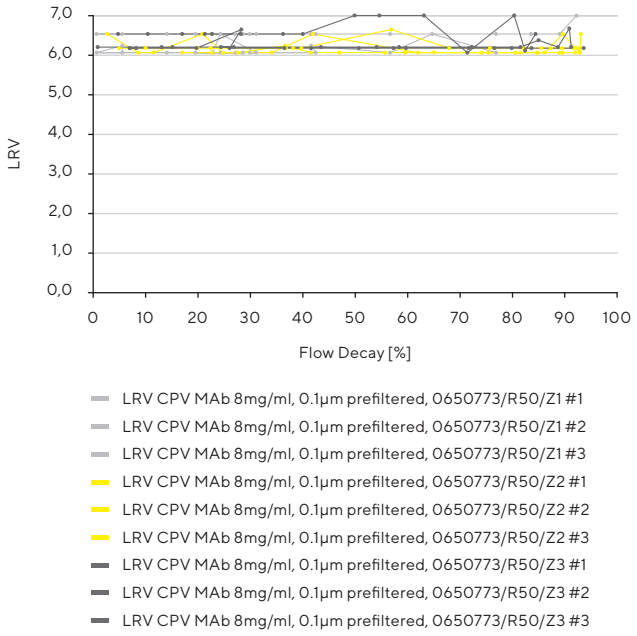
20 nm retentive virus removal filters are a well established, robust method for clearing both large and small viruses within a purification process. In order to validate the efficiency of these filters, a virus spiking trial must be performed. It has been shown that the virus reduction capability of some virus removal filters decreases with increasing flux decay (1). This decrease in log reduction value (LRV) is dependent on several factors including protein concentration, product purity and plugging mechanism (adsorptive vs. pore plugging). The influence of these parameters on the overall flow decay profile of each virus filter has to be examined case by case.

Material & Methods

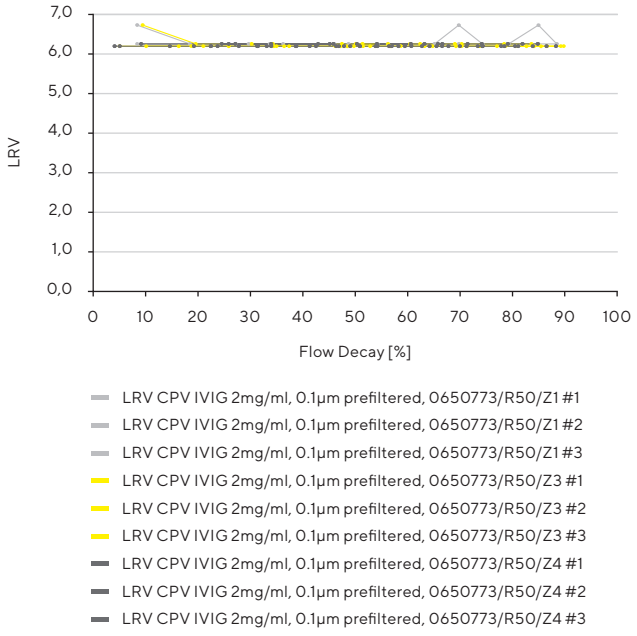
- Different protein types and concentrations have been used to determine LRV versus flux decay profiles for Virosart® CPV
- Spiking studies were performed with Virosart® CPV Minisart® using bacteriophage PP7, a small 25 nm non enveloped ss-RNA Pseudomonas phage (Leviviridae family) at different spiking concentrations.
- PP7 is the model virus widely used by filter manufacturers for the evaluation of retention characteristics of 20 nm virus filters
- Sartorius has shown the feasibility of PP7 as a model virus for mammalian viruses (2)
- Instantaneous samples were taken at various levels of flow decay and virus retention was determined.
- For each test, protein type, protein concentration, pH, buffer type and composition as well as the spiking concentration are outlined
- Graphs show LRV over Flow decay profile

Results

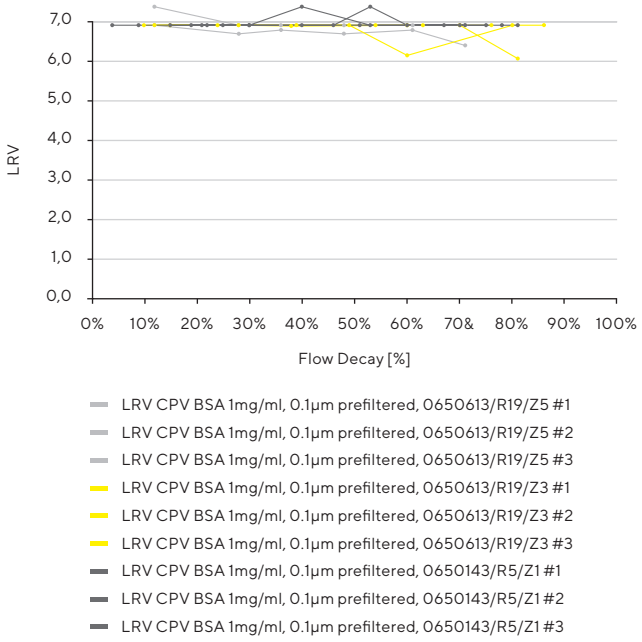
Graph 1: LRV versus Flow decay – Monoclonal Antibody
9 mg/ml MAb in 20 mM Tris, 25 mM NaCl, pH 7.2, Virosart® CPV Minisart® Lot number 0650773 | R50 | Z1; Upstream titer 3.0 × 107/ml



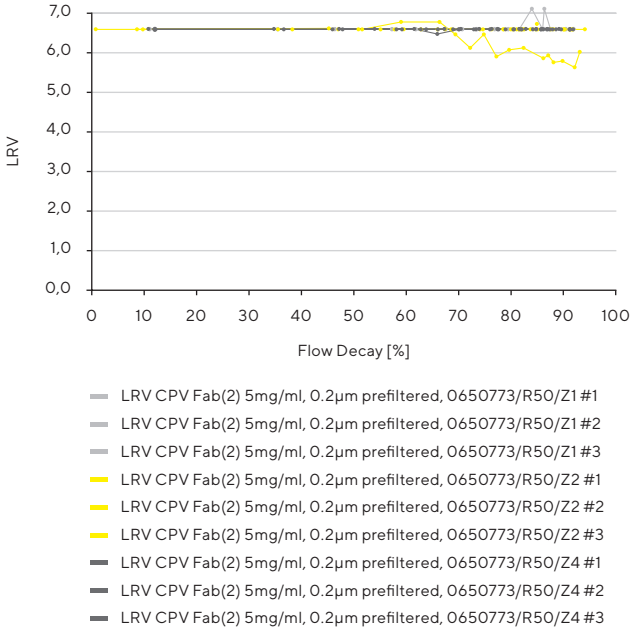
Graph 2: LRV versus Flow decay – Human Derived IVIG
IVIG 1.2% in 0.2 M glycine buffer, pH 7.1, Virosart® CPV Minisart® Lot number 0650773 | R50 | Z1-4, 2 bar, Upstream titer 2.2 × 107/ml



Graph 3: LRV versus Flow decay – BSA
BSA 0.1%, 20 mM potassium phosphate buffer, Virosart® CPV Minisart® Lot number 0650613 | R19 | Z5, 0650613 | R19 | Z3, 2 bar, Upstream titer 6.4 × 107/ml



Graph 4: LRV versus Flow decay – Fab_2
5 mg/ml in 25 mM Tris, pH 6.5, 2 bar, Virosart® CPV Minisart® Lot number 0650773 | R50 | Z1,2,4 Upstream titer 3.0 × 107/ml



Summary

The 20 nm Virosart® CPV membrane filter provides reliable virus retention of small viruses.

The capability of Virosart® CPV to retain more than 4 log of small non enveloped viruses is not necessarily correlated to the flux decay. Reliable retention of more than 4 log has been shown for flux decay profiles of up to 90%.

The data shown are typical examples for different protein types, buffers and concentrations. They can not, however, be used to predict the performance in general.

It is up to the end user to determine what level of flow decay and virus retention is acceptable for his process in order to achieve the desired virus retention.

References

[1] "Normal Flow Virus Filtration – Detection and Assessment of Endpoint in Bioprocessing", Mark Bailey, E. Lilly, May 2005 PDA Viral Safety Conference

[2] "The Sartorius virus and contaminant removal platform", K. Tarrach, Sartorius Downstream Technology Forum Barcelona, November 23rd 2004

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA
Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia, NY 11716
Toll-Free +1 800 368 7178

For further contacts, visit
www.sartorius.com

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