Simplifying Progress

Case Study: Virus Filters Enabling Reliable Process Development in Antibody Processes

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1. Introduction

The commercial manufacturing of therapeutic antibodies or recombinant proteins requires robust and reliable processes that are economical and deliver high yields, while generating a product that is adequate for human use. One factor posing a threat to the patients' health is the presence of viruses in the final product. A contamination of products derived from human or animal cells with viruses can have disastrous clinical consequences. Therefore, regulatory authorities stress the need to implement robust and orthogonal strategies for virus clearance in order to meet the requirements of a risk-based approach to virus clearance assessment. Virus filtration has traditionally been accepted as a robust method for virus clearance. This poster summarizes the performance of the Virosart® HF in its typical field of application. Virus filter throughput, constant performance, scalability is demonstrated using monoclonal antibodies (mAbs) as well as IVIG model feedstreams.

2. Virus Filtration of mAbs

Characteristics of Virosart® HF

Target Molecule
The main application for Virosart® HF, for virus retentive filtration, are monoclonal antibodies (mAbs), antibody fragments (Fab) or small recombinant proteins (< 150 kD).

Positioning
Virosart® HF is used towards the end of the purification process for viral filtration of the biopharmaceutical product.

Working principle
Virus filtration works based on sizes exclusion. Small non-enveloped and large enveloped viruses are retained by the 20 nm asymmetric membrane structure.

The Virosart® HF filter is specially developed for the filtration of mAbs and recombinant proteins. The filter was challenged with 10 different mAb solutions ranging in concentration from 3 to 30 g/L. High mass throughput of up to 12 kg/m² in 3 hours of filtration is demonstrated for Virosart® HF.

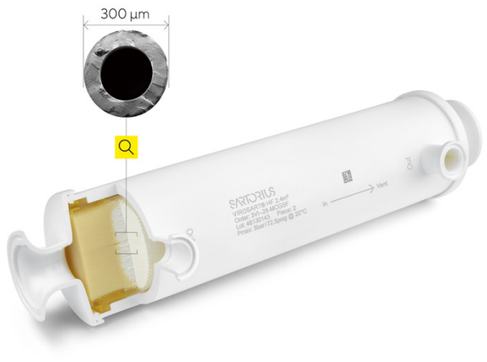
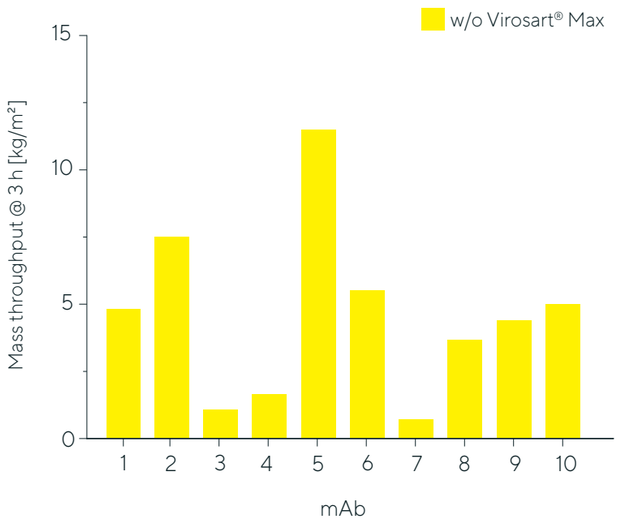
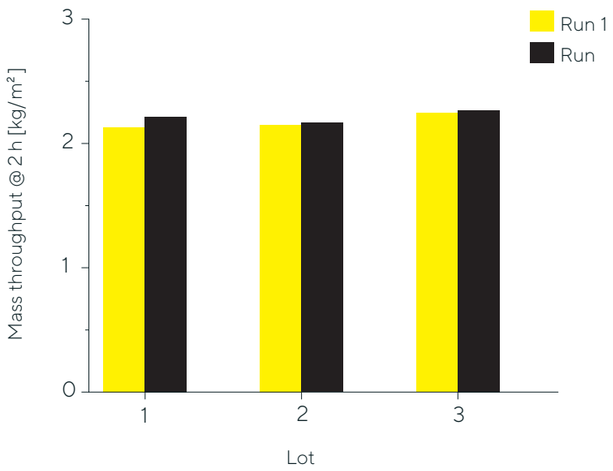


Figure 1: Virosart® HF



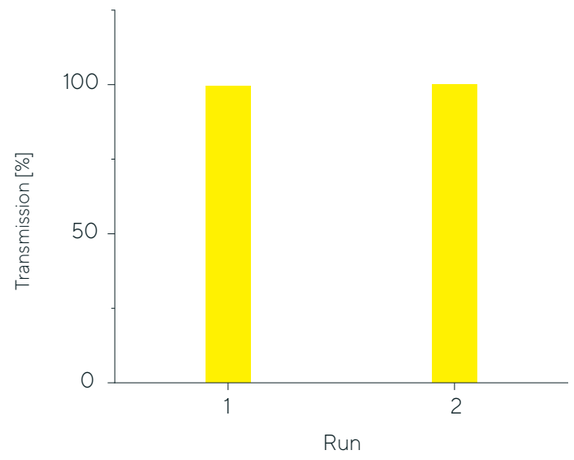
3. Consistent Filter Throughput

Biopharmaceutical manufacturers expect consistent and reproducible throughputs from virus filters. Three different filter lots were challenged with a mAb solution of 5 g/L. All runs were performed in duplicate at 2.0 bar | 30 psi operating pressure. Inter- and intra-lot consistency of Virosart® performance is confirmed with minimal variation of 5%.



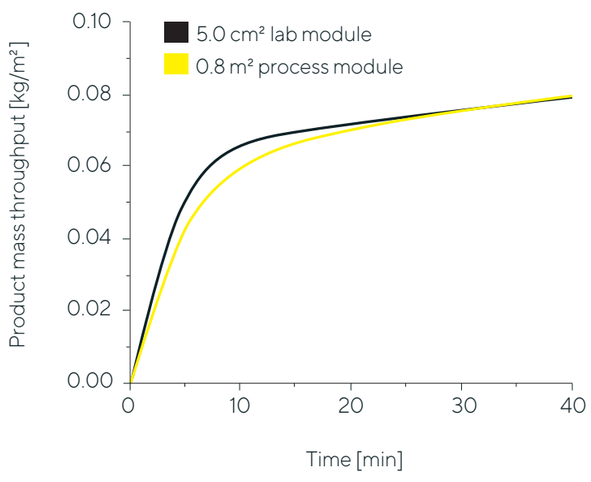
4. Protein Transmission

High yields also result from the high selectivity of the virus filter to retain viruses and to allow product to pass through the filter. A model feedstream of buffered IVIG was filtered through Virosart® HF in duplicate runs. The protein concentration was determined using a photometer at a wavelengths of 280 nm. Protein transmission in both runs exceeded 99%.



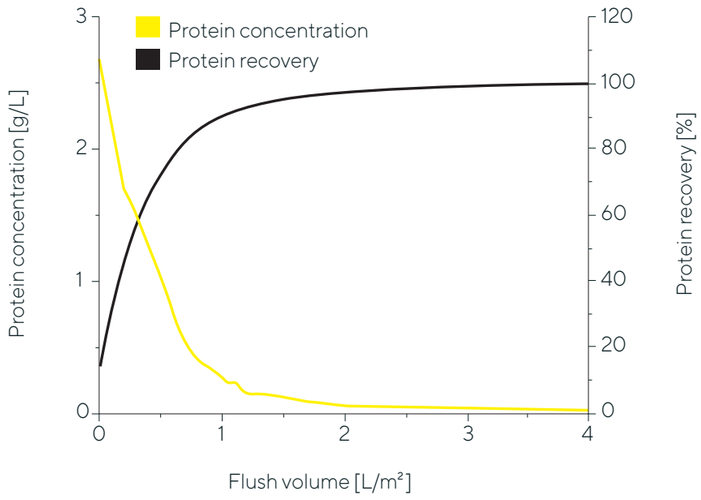
5. Scalability

From a process development perspective, scalability is a key factor to successfully transfer processes to large scale. Three different 5.0 cm² Virosart® HF lab modules and one 0.8 m² process module were challenged with 2 g/L buffered IVIG model solution until 95% flow decay was achieved. The results show that from down-scale modules can be scaled-up based on 2 to 3 down-scale experiments.



6. Post-Flushing Volume

A Post-use flush is often performed during the virus filtration step in commercial production in order to recover protein and increase yield. A Virosart® HF process module with 0.8 m² surface area was used to determine the flushing volume required to reach 88% product recovery after filtration of 2 g/L buffered IVIG solution. Minimal post flushing volumes are required with 3 L/m² to reach 99% product recovery.



7. Summary

The Virosart® HF could demonstrate:
- High protein throughput
- Consistent filter throughput
- Scalable filtration performance
- Minimal flushing volume