Simplifying Progress

Case Study: Robustness Study for Virus Filtration of mAb Processes

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1. Introduction

All biopharmaceutical products derived from human or animal origins must have a proven virus safety concept to ensure the final patient's health before the product is released to commercial manufacturing or even clinical trials. The concept must cover known and unknown potential virus contaminations. Regulators require that manufacturers perform a risk analysis and have a strategy to remove contaminating viruses during downstream processing. The industry considers filtration to be a robust method. Virus filtration relies on the principle of size-exclusion and can remove all types of viruses.

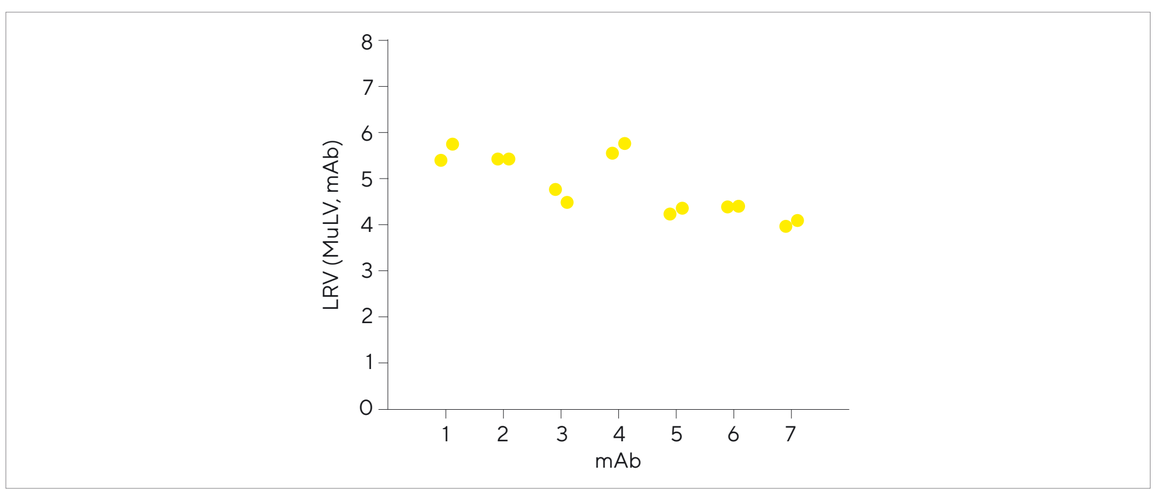
Retention during virus clearance unit operations is calculated as log10 reduction value (LRV). Typical model viruses used in the industry as well as by filter manufactures are summarized in the table below.

Virus	Description	Enveloped	Genome Type	Size [nm]
MVM	Model virus for small non-enveloped virus	No	ssDNA	18 – 26
MuLV	Model virus for large enveloped viruses	Yes	ssRNA	80 – 110
PP7	Proven bacteriophage model for parvoviruses	–	ssRNA	26

Data showing no virus breakthrough is indicated in the figures with filled points and data with virus breakthrough is unfilled respectively.

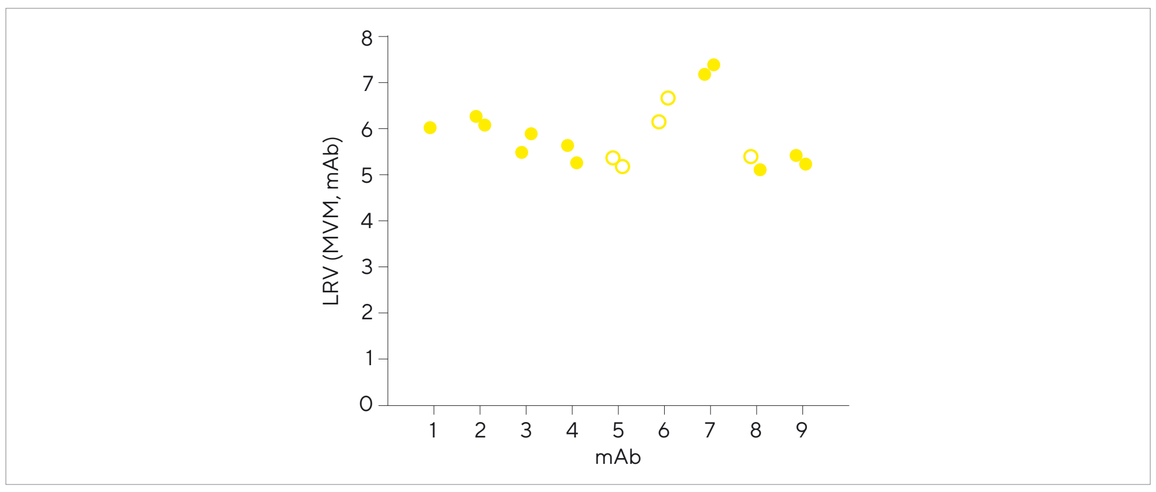
2. MuLV Retention

Murine Leukemia Virus (MuLV) is a standard model virus used to validate the clearance of large enveloped viruses in products derived from cell lines. MuLV retention results were summarized from different individual studies all performed at different contract testing organizations. The results indicate high LRVs with no virus breakthrough detected.



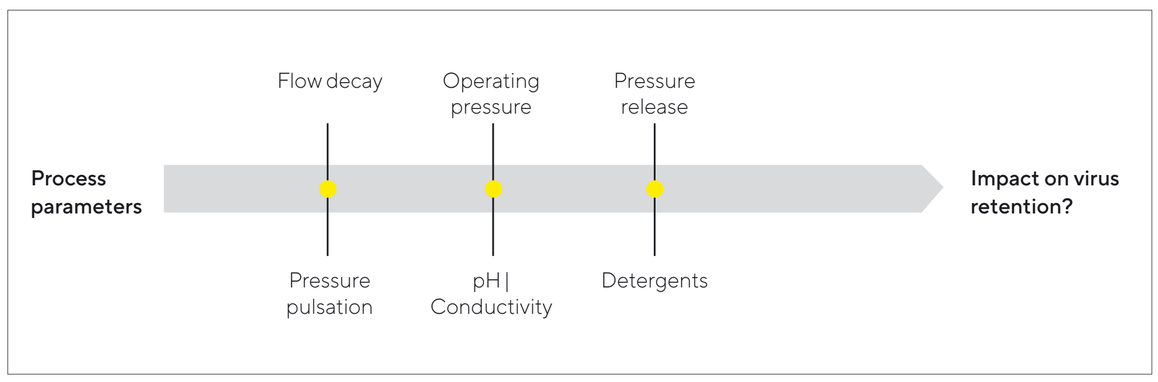
3. MVM Retention

Minute Virus of Mice (MVM) is a standard model virus used to evaluate the clearance of small-non enveloped viruses in products derived from cell lines. Different studies were performed with Virosart® HF lab modules showing MVM retention in duplicate runs. The studies were all performed by external contract laboratories. Virosart® HF meets the retention requirements of a high-performance parvovirus-retentive filter with minimal lot-to-lot variability.



4. Retention under Challenging Conditions

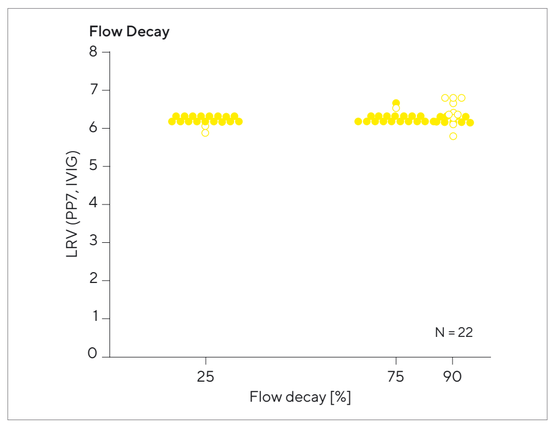
Investigators have recently discovered that under specific conditions with some virus removal membranes, virus breakthrough can occur as indicated in the drawing below.

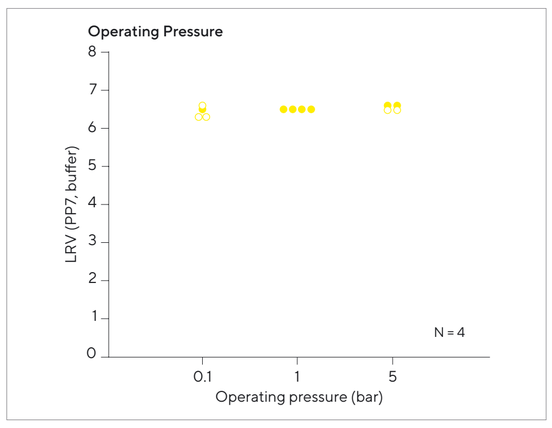


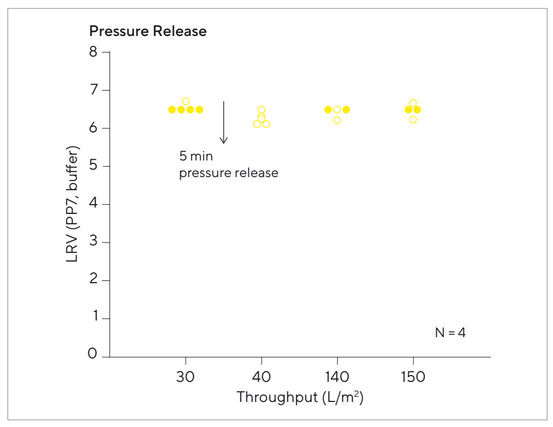
Experimental Details

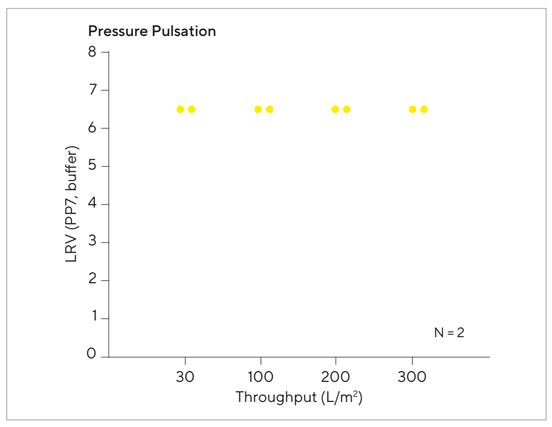
Virus	Filter	Pressure	Feed
▪ Pseudomonas aeruginosa bacteriophages PP7 ▪ Challenge level: >10^7 pfu/mL	▪ Commercial available virus filter (Virosart® HF) ▪ Down-scale device: 1.7 | 5 cm^2	▪ Standard: 2.0 bar ▪ Low: 0.1 bar ▪ High: 5.0 bar	▪ Buffer: 20 mM KPi Buffer, pH 7.2 ▪ IVIG: 1g/L in 20 mM Kpl buffer, pH 7.2 ▪ Tween | SDS: 0.1 % in 20 mM KPi Buffer, pH 7.2

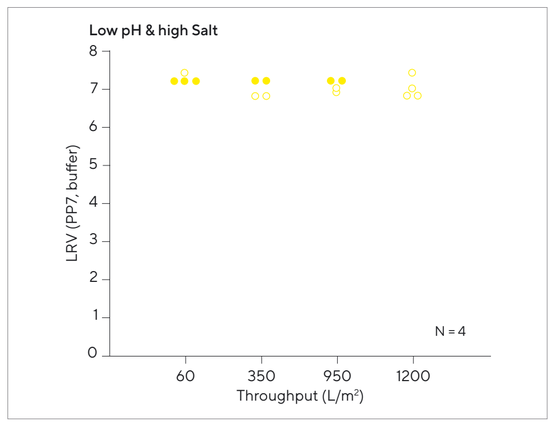
Results

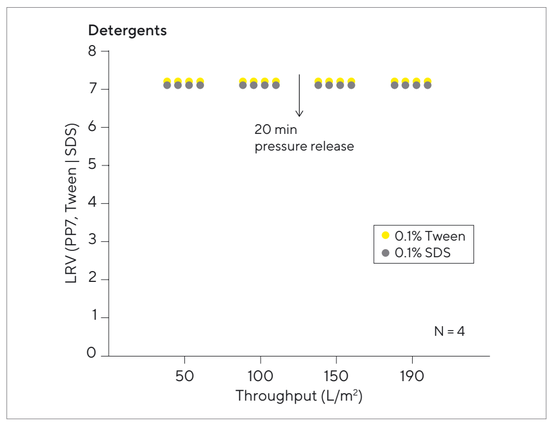












The results of a robustness study with Virosart® HF looking at various process parameters known to potentially impact virus retention show:

- Flow decay up to 90 % with no impact
- Consistent and high LRVs during pressure release, high and low operating pressure as well as pressure pulsation
- Robust retention at low pH and high salt as well as detergents being present in the feedstream