

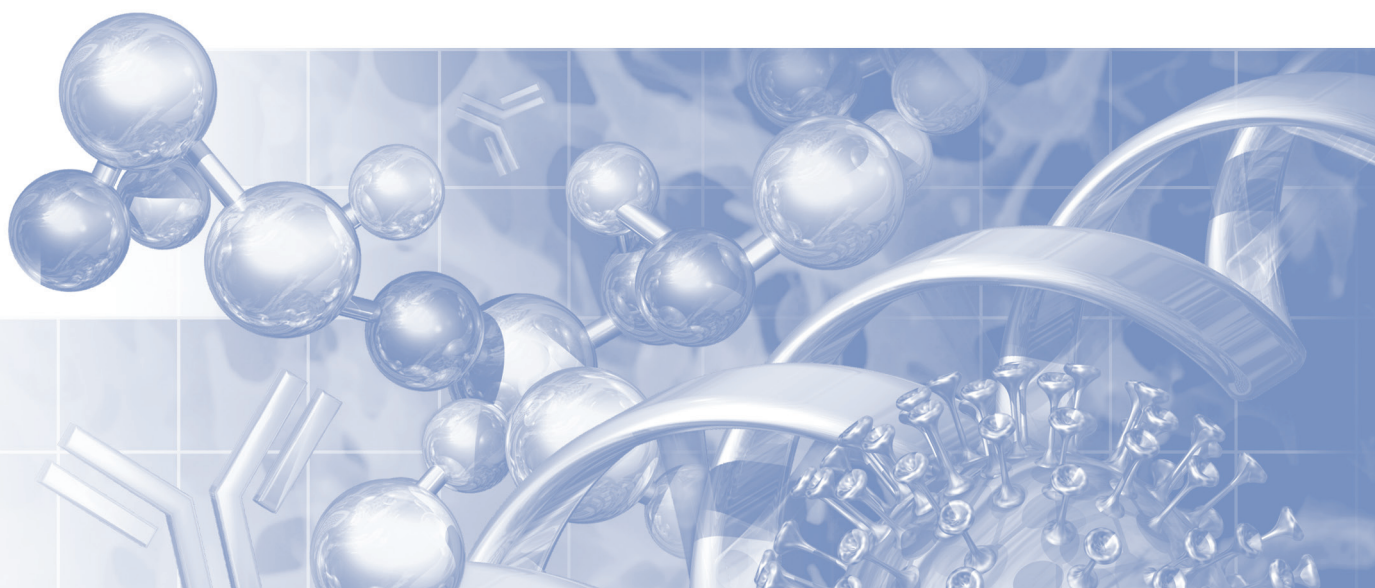


Life Sciences

Application Note

USD3159⁽¹⁾

Pegasus™ Prime Virus Filtration: Robust Retention after Pressure Interruptions (Stop and Start)



Introduction

Virus filtration is a robust technique which is a vital part of the overall viral clearance strategy (inactivation and removal). Filtration's size exclusion mechanism complements other inactivation or removal techniques by targeting the physical dimensions of the virus to enable a high degree of virus safety through a method orthogonal to inactivation or adsorption.

Flow pausing and/or filtration pressure interruption during virus filtration has been demonstrated to increase the risk of virus passage. Process interruption can sometimes occur in clinical or commercial scale manufacturing due to risk factors including:

Common Risk Factors

- Feed vessel switching
 - Product recovery flush
 - Multiple storage bags or tanks

Unlikely Risk Factors

- Power outages
- Mechanical failures
- Scheduling of personnel / shift breaks

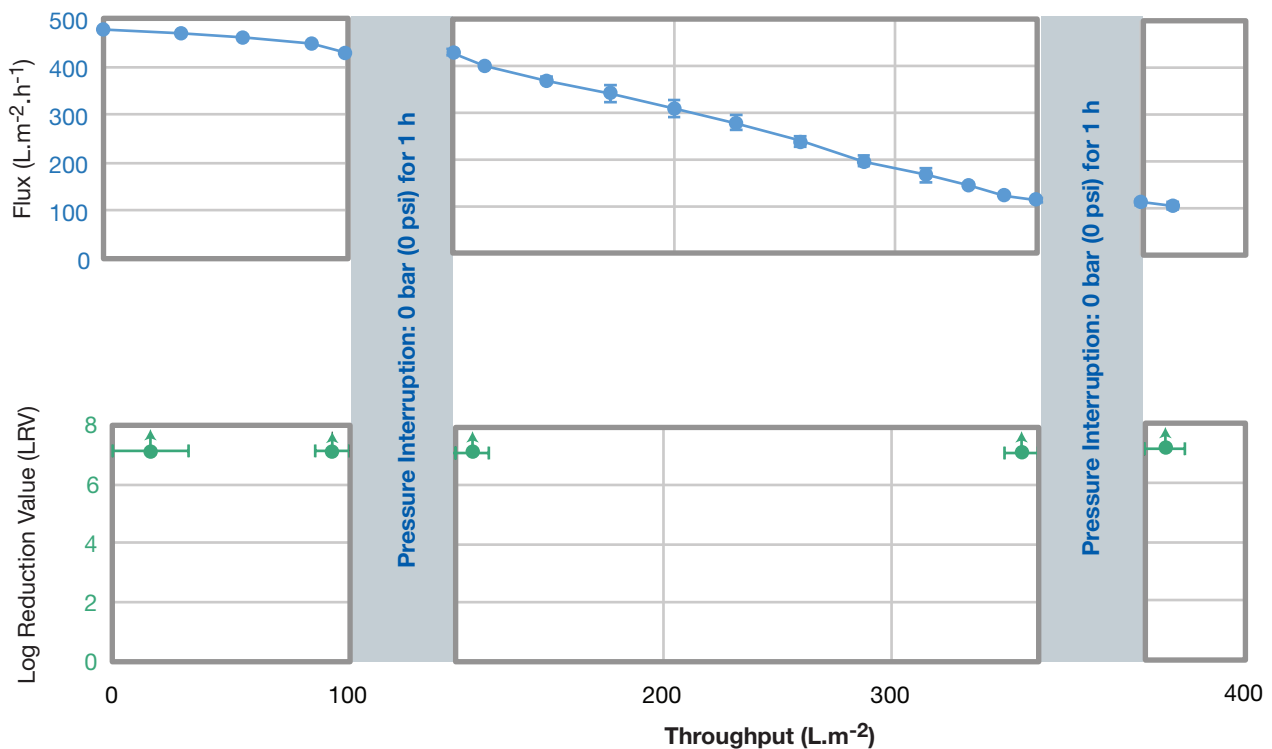
Cause/Mechanism

The loss of virus removal performance in some small virus retentive filters when the process is interrupted is primarily caused by diffusion. While size-exclusion is the primary retention mechanism for virus retentive filters, since the viruses are not permanently adsorbed, there is always a small chance that viruses can diffuse from fully-retentive areas of the membrane matrix to areas along a lower-retention flowpath. During normal processing the convective flow rate is much greater than the diffusion rate of viral particles and therefore minimizes this effect. However, where the convective flow is reduced or eliminated by pressure interruption, a small number of viruses may diffuse to a position where they could pass through the membrane.

Although multiple factors which relate to diffusion can be considered (temperature, viscosity, virus load), the key risk factors that exacerbate this phenomenon are:

- Duration of pressure interruption
- Magnitude of pressure interruption

Figure 1



Pegasus Prime Virus Removal Filters: Pall pressure interruption study (2 x 1 h pauses). IgG in PBS spiked with bacteriophage PP7 at 2.1 bar (30 psi). Data are the mean values from triplicate tests. LRV x-axis error bars represent the size of the aliquots taken for the data point shown. Flux y-axis error bars represent the standard deviation of the triplicate samples. All aliquot virus concentrations were below the limit of quantification therefore there is no observed difference in LRV before and after each 1 h stop.

Recommended Risk Mitigation Strategy

Everything should be done to minimize or avoid pressure interruption during process development and process scale. Best practice is to use state-of-the-art automated virus filter systems which can significantly reduce the impact or prevent the occurrence of pressure interruption where possible.

- Pressure interruption steps included in validation of virus filtration
- **Filter selection:** no virus filter can claim to be completely immune to this effect, but Pegasus Prime virus removal membrane is highly robust to process interruptions (Figure 1)
- Process control of pressure interruptions and pressure differentials
- Pressure differentials recorded in batch records
- Automated feed vessel switching using automated process-scale virus filtration systems (Figure 2)
- Prevent or mitigate the possibility of power outages
- Mitigate the probability of equipment failure (e.g pumps or valves) through appropriate maintenance schedules
- Schedule personnel to allow appropriate monitoring and control of the process

Figure 2

Process-scale virus filtration: Allegro™ MVP system with Pegasus SV4 virus removal filter capsules



Pressure Interruption Studies with Pegasus Prime Virus Removal Filters

Step 1 Evaluate the possible risks in your process-scale virus filtration for pressure interruption.

Step 2 Mitigate or eliminate the pressure interruption risks.

Step 3 Based on the process control limits implemented in step 2, a risk-based approach should be taken to define pressure interruptions during virus validation.

The data in this application note support the successful operation of Pegasus Prime virus removal filters with two separate pressure interruptions of 1 h. It is recommended to put process controls in place wherever practical, however validation can be carried out under these conditions and significantly beyond. The unique pore structure and pore size distribution of Pegasus Prime virus removal membrane from the macro to the nano-scale allows superior throughput performance but still restricts diffusion of captured viruses.



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