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Consideration of Filter Design Space for Validation of Virus Filtration in Continuous Processing Applications

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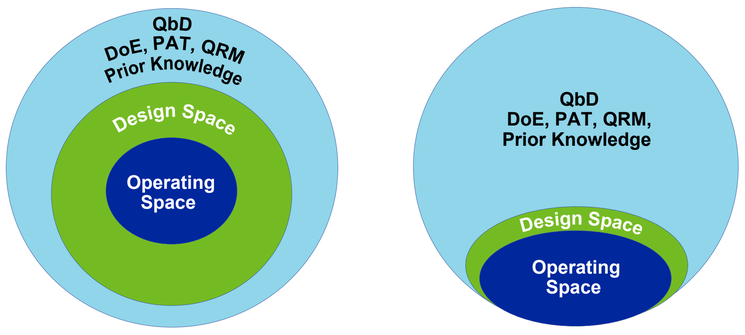
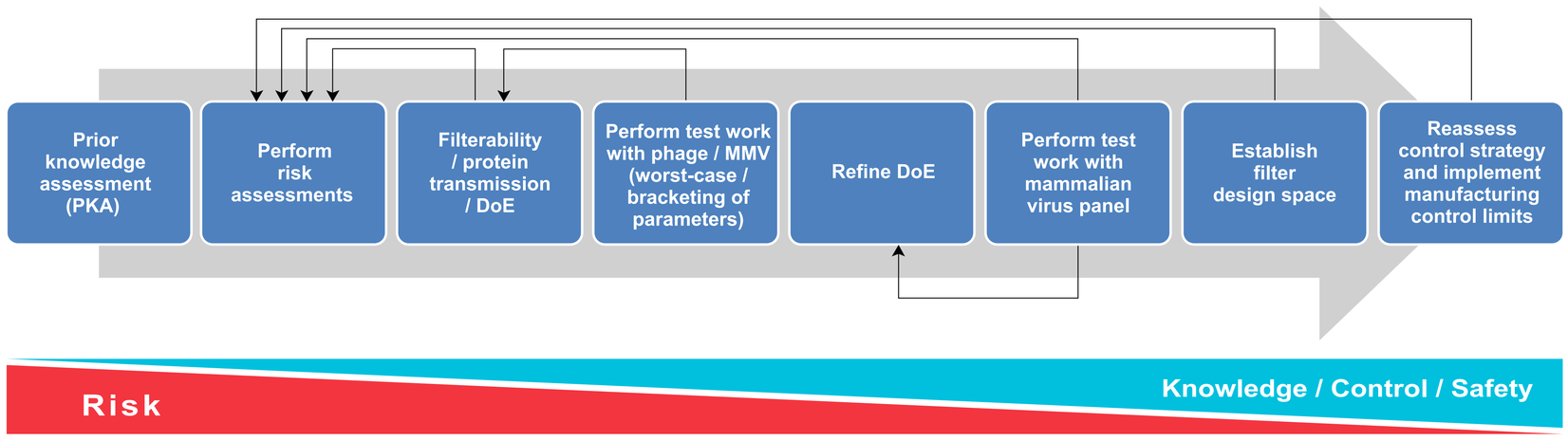
UNDERSTANDING FILTER DESIGN SPACE



Low Risk Operating Space **High Risk Operating Space**

- Partnership between filter manufacturer and end user required for effective quality by design (QbD):
  - Shared knowledge of existing data and understanding utilizing design of experiments (DoE), process analytical technology (PAT) and quality risk management (QRM)
- Establishing the filter design space ensures a safe, high quality product
- Creating a balanced operating space within the filter design space will minimize risk of requiring post approval changes

BUILDING A VIRUS FILTER DESIGN SPACE



- Building a design space is an iterative process and continuously re-visiting the risk assessment is important
- Determine critical quality attributes (CQA), e.g., >4 log reduction value (LRV) for viruses
- Determine critical process parameters (CPP) and material attributes (MA)
- Establish a CPP / MA filter design space bracketing the operating design space
- Implement manufacturing control limits

POTENTIAL CRITICAL PROCESS PARAMETERS AND MATERIAL ATTRIBUTES

Volumetric Throughput | **Protein Purity** | **Protein Aggregation** | **pH / Ionic Strength** | **Operating Pressure / Flux** | **Processing Time** | **Process Interruptions**

Figure 1
Strong parvovirus (MMV) retention of Pegasus™ Prime virus membrane, bracketing mAb throughput and purity

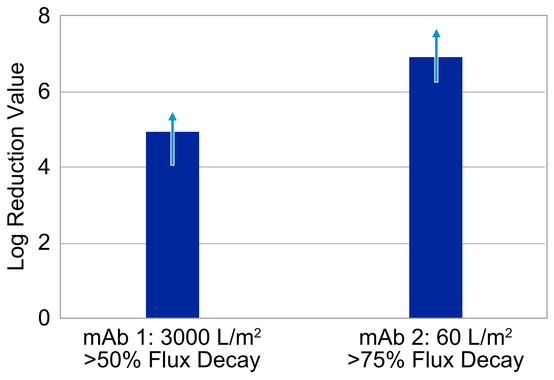


Figure 2
Consistently high Pegasus Prime virus membrane bacteriophage retention at the extremes of buffer design space in IgG

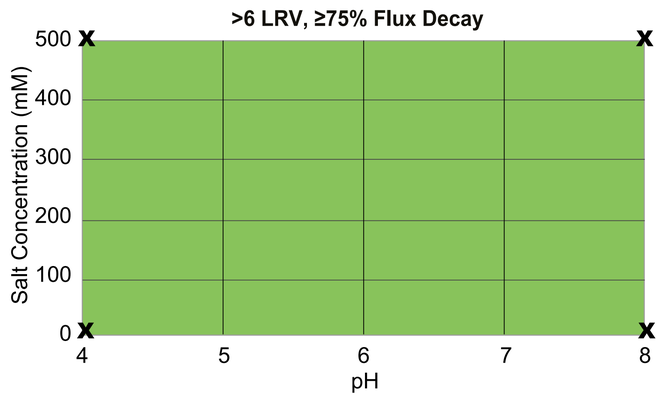
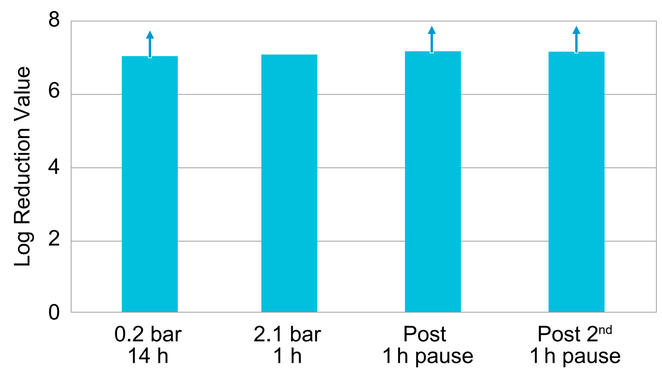


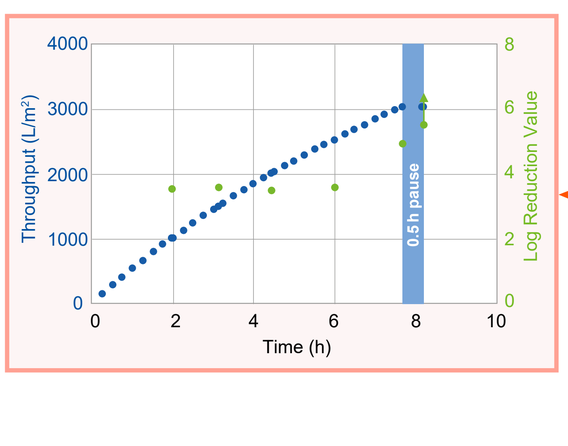
Figure 3
Reproducible Pegasus Prime virus membrane retention of bacteriophage (PP7) in IgG. Worst case of long processing time and low pressure and after process interruptions



NEW CONTINUOUS DESIGN SPACE

- Lower flow rates throughout the continuous process require virus filtration at lower operating pressures
- Significant operational and risk advantages to reduced filter replacement and long processing times
- Prior knowledge: low pressure or flow is now considered worst-case and must be validated
- Pegasus Prime virus membrane robustness in the new continuous design space is detailed in Figures 4 and 5

Figure 4
Pegasus Prime virus membrane retention robustness of parvovirus (MMV) in a batch mAb process



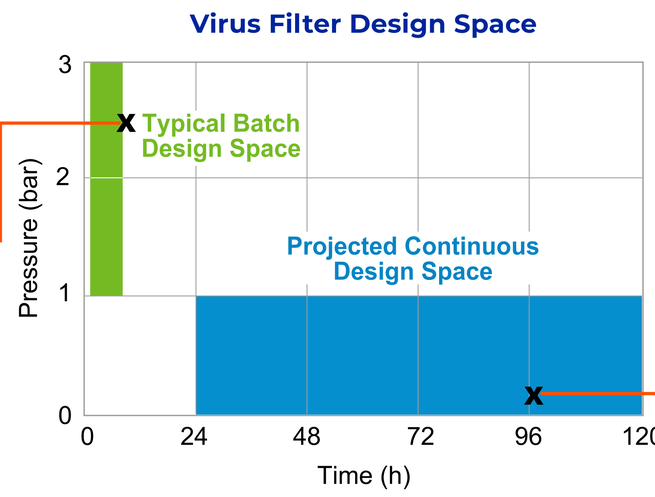
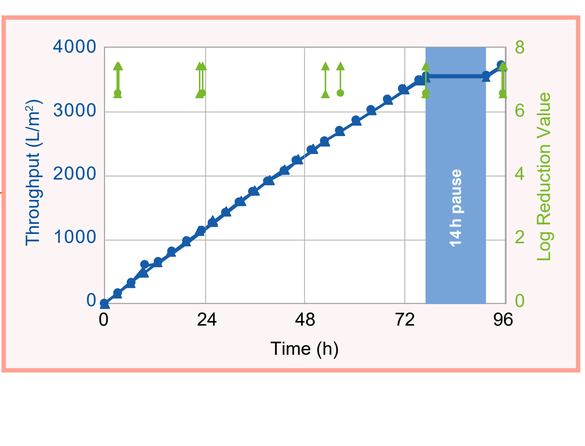


Figure 5
Pegasus Prime virus membrane retention robustness of bacteriophage (PP7) in PBS under extended continuous processing conditions



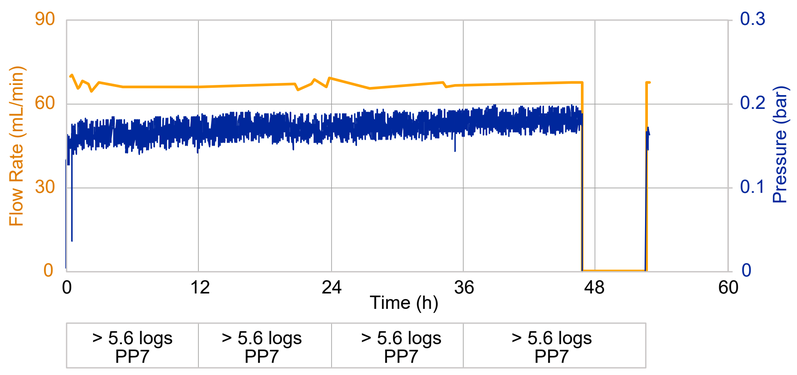
PROCESS SIMULATION

- Process simulation under continuous design space conditions
- Phosphate buffered saline (PBS) spiked with PP7 bacteriophage:
  - Eliminates chance of protein-virus interaction
  - Focuses on risk of virus diffusion in the design space
- Single-use sterilized system including:
  - Allegro® 3D biocontainer (200 L) for feed
  - Pegasus Prime 1 in. virus filter capsule
  - Allegro™ bioprocessing workstation for aliquot collection

Figure 6
Single-use virus filtration system operation

- 1,800 L/m² throughput achieved over approximately two days
- Consistently high LRV observed in all aliquots:
  - Process pause incorporated in the final aliquot

Figure 7
Extended processing of a Pegasus Prime 1 in. virus filter capsule under continuous processing conditions up to a volumetric throughput of 1800 L/m²



CONCLUSIONS

- **QbD principles are important to minimize the risk of a changing design space**
- **New continuous virus filter design space generates increased processing time and low pressure risk factors**
- **Pall supports the industry in exploring progressive process boundaries with innovative new product designs**
- **All Pegasus Prime filters show robust retention in the new continuous design space without compromise**

FIND OUT MORE ABOUT PALL'S VIRUS FILTRATION AND CONTINUOUS PROCESSING SOLUTIONS

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