Pegasus™ SV4

VIRUS REMOVAL FILTER CARTRIDGES

With the ever-present risk of virus contamination in biologic products, potential sources of virus contamination of biotechnology products include viruses associated with cell lines (endogenous viruses), or viruses introduced into the cell line or product from culture medium or during the production process (adventitious viruses). Viruses could also potentially be present in donations for plasma derivatives. Pegasus™ SV4 virus removal filter cartridges are direct flow filters combining robust, high viral clearance of parvovirus and larger viruses with high throughput capacity and demonstrating constant, stable flow rates in both dilute and complex/concentrated biological fluids. Such consistent, constant flow rates and excellent throughput performance allows a high degree of process control.

Fig 1. Pegasus SV4 virus removal filter cartridge.

Features and benefits

Features	Benefits
Incorporates Pegasus SV4 virus filter membrane	Offers robust, high parvovirus clearance (> 4 log reduction value)
Demonstrates constant, stable flow-rate performance	Improves process and cost control, enables significant virus filtration economy and efficiency
Resistant to filter 'plugging'	Shows excellent throughput capacity in both dilute and complex/ concentrated biological fluids
High filter area per cartridge	Reduces hold-up volume and system space requirements, reducing cost of goods sold (COGS)
Automated *in situ* integrity test both pre-use and post-use	Provides easy, reliable integrity testing, reducing labor costs and decreasing the risk of handling errors
Can be cleaned in place (CIP) and steamed in place (SIP)	High aseptic safety
Rigorous quality testing at multiple stages of production	Consistent performance as per the specification
Suitable for inclusion in Cytiva's fully-automated virus filtration systems	Enables a high level of process control and safety

High parvovirus clearance

Pegasus SV4 virus removal filter cartridges demonstrate efficient clearance of both small 'non-enveloped' viruses as well as large viruses. Figure 2 provides an example of its high parvovirus clearance by showing the typical performance of a Pegasus SV4 filter in a 1 g.L^{-1} BSA solution, as per the PDA's guidelines:

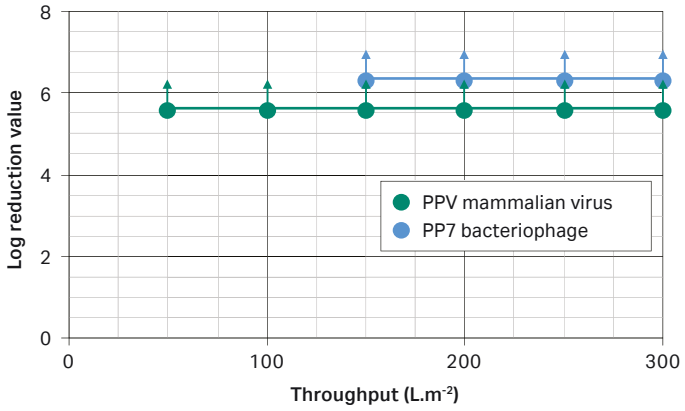

Fig 2. Retention of porcine parvovirus (PPV, n=4) and small spherical bacteriophage virus (PP7, n=9) by Pegasus grade SV4 virus membrane in 1 g.L^{-1} BSA at 3.1 bar (45 psi) [1].

[1] PPV retention testing carried out at an independent virus validation test laboratory using 47 mm filter discs

Due to its resistance to flux decay and excellent throughput properties, typical spikes will not have significant impact on the flux decay of Pegasus SV4 virus removal filter cartridges.

Constant, stable flow-rate performance with excellent throughput capacity

With the need to control the cost of goods sold (COGS) being one of the main points of consideration in downstream processing, Pegasus SV4 virus removal filter membrane has been designed to address this need by offering constant, stable flow rate performance and excellent throughput capacity, thereby improving process and cost control and enabling significant virus filtration economy and efficiency.

Efficient and economical

Pegasus SV4 virus filter membrane also demonstrates efficient clearance of both small 'non-enveloped' viruses and large viruses, even showing constant, stable flow rate performance when used with dilute or complex/concentrated biological fluids. It also offers stable pressure/flux capability in more complex or concentrated feeds, helping to improve virus filtration economy in highly concentrated protein solutions. Figure 3 shows a typical flux profile for Pegasus SV4 virus removal filter cartridges when challenged with a monoclonal antibody solution.

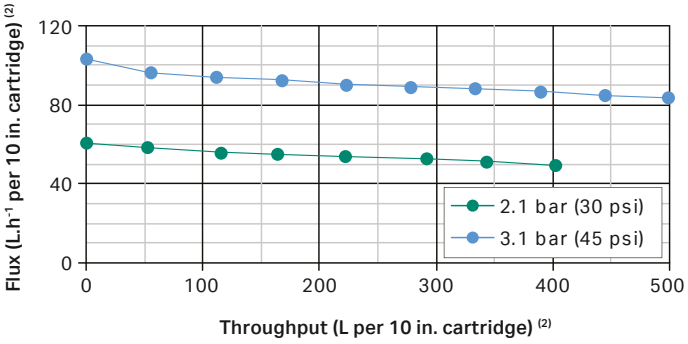

Fig 3. Results of filterability tests at 2.1 bar (30 psi, 0.21 MPa) or 3.1 bar (45 psi, 0.31 MPa) with up to 25 g.L^{-1} (2.5%) monoclonal antibodies (mAbs).

[2] Performance predicted from tests performed on Pegasus SV4 virus removal filter discs (47 mm)

Reduces processing costs

Pegasus SV4 virus removal filter cartridges offer a high filter area per cartridge (2.25 m^2) due to their patented laid-over pleat construction, which enables significantly more filter membrane to be packed into each cartridge (Fig 4). This helps to optimize process productivity while decreasing process costs, by reducing the number of filter cartridges required per installation, and helps reduce the hold-up volume of the virus filter system.

Fig 4. Laid-over pleat construction utilized by Pegasus SV4 virus removal filter cartridges.

Process control and safety

Pegasus SV4 virus removal filter cartridges offer a high level of process control in process-scale virus filtration.

Process requirement: aseptic safety

Best practice – Pegasus SV4 virus removal filter cartridges can be cleaned in place (CIP) and steamed in place (SIP), and are suitable for inclusion into available fully automated systems.

Process requirement: easy, reliable integrity testing

Best practice – Pegasus SV4 virus removal filter cartridges can be *in situ* integrity tested both pre-use and post-use.

Table 1. Integrity testing of Pegasus SV4 virus removal filter cartridges

Pegasus SV4 virus removal filter cartridges	
Steam in place (SIP)	Yes
Autoclavable by user	Yes
Integrity test pre-use	Yes (non-destructive, water-wet *in situ*)
Integrity test post-use	Yes (non-destructive, water-wet *in situ*)

Fig 5. Integrity testing Pegasus SV4 virus removal filter cartridges with a Palltronic® Flowstar filter integrity test instrument.

Suitable for inclusion in Cytiva's fully automated virus filtration systems

Cytiva also offers fully automated virus filtration systems that enable precise and consistent operation, together with process efficiency. The systems can be designed with steam in place (SIP), clean in place (CIP) and integrity test in place (ITIP) capabilities. The cluster filtration technology assures optimized filter integrity sensitivity. Cytiva's range of fully automated virus filtration systems provides a high level of manufacturing safety and process performance.

Rigorous quality testing at multiple stages of production

Throughout the process of manufacture of Pegasus SV4 virus removal filter cartridges, Cytiva's rigorous quality control systems support consistent performance, as per the product specification.

- Quality control at multiple production stages
- 100% fabrication integrity tested - correlated to PP7 bacteriophage removal
- Viral reduction tested with PP7 bacteriophage lot release test
- 100% fabrication water flow tested
- Protein transmission tested
- Visual inspection control

Full traceability, fast and efficient data entry

Each Pegasus SV4 virus removal filter cartridge is manufactured under a quality management system certified to ISO 9001:2008, and is easily identified by product code, lot number and a serial number, which is laser marked on the filter cartridge as a two-dimensional (2D) barcode (Fig 6). These codes can be read by a barcode reader, enabling traceability of the manufacturing history (Fig 7).

Fig 6. Pegasus SV4 virus removal filter cartridge showing 2D barcode.

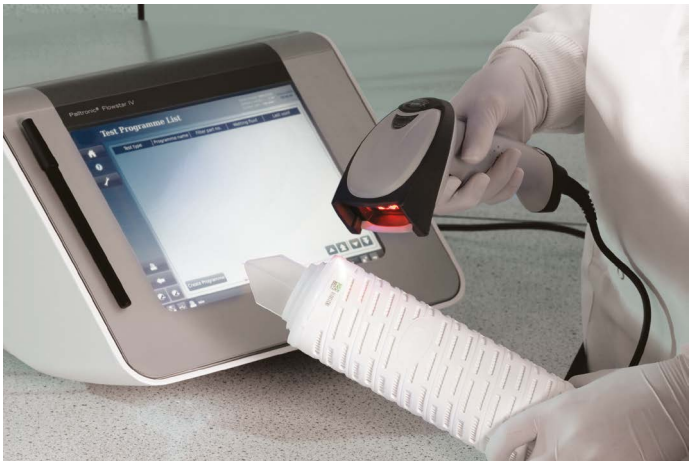

Fig 7. Scanning a barcode on a Pegasus SV4 virus removal filter cartridge using a Palltronic barcode reader and Palltronic Flowstar IV filter integrity test instrument.

High quality standards

The filter components have met the requirements for biological reactivity, *in vivo*, under USP <88> (for Class VI – 121°C plastics) and *in vitro*, under USP <87> (elution test).

- Meets cleanliness per USP <788> particulate matter in injections
- Non-fiber releasing per title 21 of the U.S. Code of Federal Regulations (CFR) parts 211.72 and 210.3 (b) (6)
- Non-pyrogenic per USP <85> bacterial endotoxins test

The filter cartridge does not contain materials of construction that are considered specified TSE or BSE-risk materials according to current legislation and guidelines (reference European CPMP EMA/410/01 and U.S. Code of Federal Regulations, title 21 part 189.5).

Technical specifications

Item	Materials of construction
Membrane	Hydrophilic modified polyvinylidene fluoride (PVDF)
Support and drainage layers	Polyester
Core, cage and endcaps	Polypropylene
Code 7 adapter	Polypropylene with encapsulated stainless steel reinforcing ring
O-rings	Silicone

Operating parameters [3]

Recommended operating differential pressure	2.1 to 3.1 bard
Maximum differential pressure	3.1 bard for continuous service 0.3 bard during steam sterilization 6.2 bard during integrity testing only
Autoclave/steaming	Autoclavable or steamable *in situ*
Maximum operating temperature	40°C

[3] In compatible fluids that do not soften or swell, or adversely affect the filter or its materials of construction. Contact Cytiva for recommended procedures to qualify filters under actual conditions of use.

Pore size (nominal)

20 nm

Retention ratings (virus)

> 4 log reduction value for bacteriophage PP7 [4, 5]

[4] Claims based on challenge with parvovirus model bacteriophage (bacterial virus) PP7
[5] > 4 log reduction value for bacteriophage PP7 per Parenteral Drug Association (PDA) technical report 41 rating method for small virus-retentive filters. > 4 log reduction value typically expected with mammalian parvoviruses.

Aqueous extractables (NVR)

Refer to validation guide for Pegasus SV4 virus removal filter cartridges

Filter area (nominal)

2.25 m^2 (24 ft^2) per 254 mm (10 in.) cartridge

Forward flow integrity test

Diffusional flow integrity test, carried out by standard upstream or downstream methods

Table 2. Process scale-up with Pegasus grade SV4 virus filters

Filter type	Filter area	Product code
Minidisc capsule	0.00096 m^2	10MCFSV4
Filter disc (47 mm)	0.0011 m^2 (in FTK200 Holder)	FTKSV4047
Mini Kleenpak™ capsule	0.058 m^2	KA02SV42FT [6]
1 in. Kleenpak Nova capsule	0.25 m^2	NP1LUSV4P1
10 in. filter cartridge	2.25 m^2	AB1USV47PH4
10 in. Kleenpak Nova capsule (in-line style)	2.25 m^2	NP6LUSV4P1
10 in. Kleenpak Nova capsule (T-Style)	2.25 m^2	NT6USV4P1

Not all filter types can be steam-sterilized. Consult individual product data files for technical specifications.
[6] Filterability Tool version (FT). Not qualified for virus removal. For filterability tests only

Ordering information

Item	Length (nominal)	Product code
Pegasus SV4 virus removal filter cartridge, code 7 double o-ring, bayonet lock and fin	254 mm (10 in.)	AB1USV47PH4
Pegasus SV4 virus removal filter cartridge, code 7 double o-ring, bayonet lock and fin	508 mm (20 in.)	AB2USV47PH4
Pegasus SV4 virus removal filter cartridge, code 7 double o-ring, bayonet lock and fin	762 mm (30 in.)	AB3USV47PH4

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