Pegasus™ SV4

VIRUS REMOVAL FILTER MEMBRANE
IN KLEENPAK™ NOVA FILTER CAPSULES

Single-use filter capsules with constant, stable flow rates providing efficient, high viral clearance and significantly reduced processing costs

With the ever-present risk of virus contamination in biologic products, potential sources of virus contamination of biotechnology products include viruses associated with the cell lines (endogenous viruses), or viruses introduced into the bioreactor from culture medium or during the production processes (adventitious viruses). Viruses could also potentially be present in donations for plasma derivatives.

Kleenpak™ Nova filter capsules with Pegasus™ SV4 virus removal filter membrane are encapsulated, direct-flow filters that combine robust, high viral clearance of parvovirus and larger viruses with high throughput capacity and stable flow rates, in both dilute and complex concentrated biological fluids. Consistent flow rates and high throughputs help control process performance and costs. The encapsulated format removes some operating costs associated with traditional formats, such as cleaning and maintenance of filter housings, and cleaning validation. Capsules can be autoclaved and supplied as part of a single-use processing system such as a filter/tubing/biocontainer set.

Fig 1. In-line and t-style Kleenpak Nova filter capsules.

Features and benefits

Features	Benefits
Incorporates Pegasus SV4 virus filter membrane	Offers robust, high parvovirus clearance (> 4 log reduction value)
Constant, stable flow-rate performance	Improves process and cost control, enables high 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 the cost of goods sold (COGS)
Suitable for automated *in situ* integrity test both pre-use and post-use	Provides reliable integrity testing, reducing labor costs and the risk of handling errors

Features	Benefits
Entirely encapsulated format	Reduces operating costs, no cleaning validation required
In-line sanitization or autoclaving capability	Helps to maintain low process bioburden
Suitable for inclusion in Allegro™ MVP systems for single-use, automated virus filtration	Enhanced process control

High parvovirus clearance

Pegasus SV4 virus removal filter membrane demonstrates efficient clearance of both small 'non-enveloped' viruses and 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.

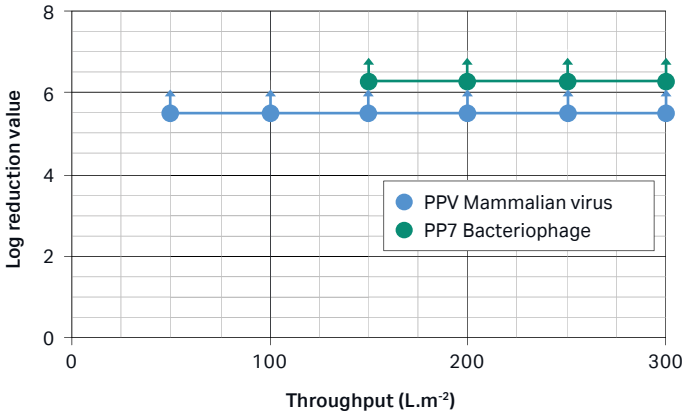

Fig 2. Retention of porcine parvovirus (PPV, n=4) and small spherical bacteriophage virus (PP7, n=9) by Pegasus Grade SV4 virus membrane in 1 g.L^{-1} BSA at 3.1 bar (45 psi).

Due to the high resistance to plugging and excellent throughput properties of Pegasus SV4 membrane, typical viral spikes will not have significant impact on flux decay during viral retention studies.

Constant, stable flow-rate performance, with outstanding throughput capacity

With the need to control the cost of goods sold one of the main points of consideration in downstream processing, Pegasus SV4 virus removal filter membrane has been designed to offer constant, stable flow rates and outstanding throughput capacity, thereby improving process and cost control and enabling excellent filtration economy and efficiency.

Efficient and economical

Pegasus SV4 virus removal filter membrane also demonstrates efficient clearance of both small 'non-enveloped' viruses and large viruses, providing constant flow rates with most biological fluids. It also offers stable pressure/flux capability with 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 membrane.

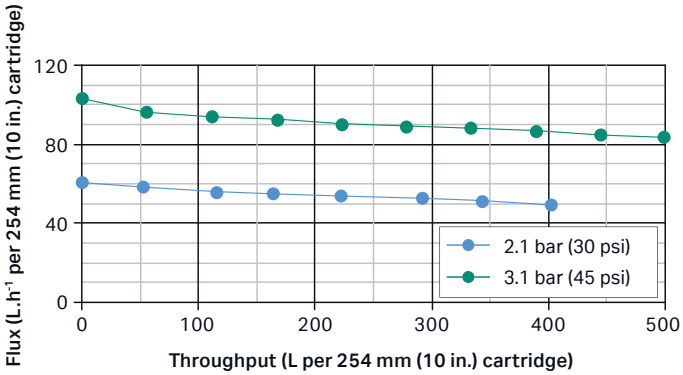

Fig 3. Calculated flux decay at 2.1 bar (30 psi) and 3.1 bar (45 psi) with 25 g.L^{-1} (2.5 %) MAb.

Reduces processing costs

Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane offer a high filter area (2.25 m² per 10 in. filter) due to their high-area filter laid-over pleating construction, which enables more filter membrane to be packed into each capsule. This helps to improve process productivity while reducing process costs, by the amount of filter capsules required per installation, and helps decrease the hold-up volume of the virus filter system.

Fig 4. Laid-over pleat construction utilized by Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane.

Exceptional process control

Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane offer exceptional process control in process scale virus filtration.

Process requirement: aseptic safety

Kleenpak Nova filter capsules with Pegasus SV4 virus removal membrane can be autoclaved and are suitable for inclusion into Allegro MVP virus filter systems.

Process requirement: easy, reliable integrity testing

Kleenpak Nova filter capsules with Pegasus SV4 virus removal membrane can be *in situ* integrity tested both pre-use and post-use.

Table 1. Sterilization and integrity testing of Kleenpak Nova filter capsules with Pegasus SV4 virus removal filters.

Product	Inlet
Steam in place (SIP)	No
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*)

Suitable for use with automated single-use systems

We offer automated Allegro systems for virus filtration with a single-use fluid path, enabling precise and consistent operation and improved process efficiency. The systems can be designed with automated integrity-test-in-place (ITIP) for the installed filter capsules, and enable exceptional manufacturing process performance.

Benefits include

- Reductions in cost of goods
- Reduced labor, materials and facility operating costs
- No cleaning or cleaning validation required
- Ease of use and flexibility for different processes increased productivity in manufacturing
- Better resource allocation
- Effective capacity utilization
- Robust operation and less risk of operator error
- Enables precise and consistent operation
- Built-in, non-destructive automated ITIP

Fig 5. The Allegro MVP single-use system for virus filtration.

Fig 6. Kleenpak Nova filter capsules undergoing integrity testing.

Rigorous quality testing at multiple stages of production

Throughout the process of manufacture of Kleenpak Nova filter capsules with Pegasus SV4 virus removal membrane, our rigorous quality control systems enable products to perform to their specification.

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

Full traceability, fast and efficient data entry

Capsules are manufactured under a quality management system certified to ISO 9001:2008, and is identified by a part number with specific lot and serial numbers, to allow traceability of the product manufacturing history, and to assist the user's own traceability systems.

High quality standards

The filter components have met 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

Product	Material of construction
Membrane	Hydrophilic modified polyvinylidenedifluoride (PVDF)
Support and drainage layers	Polyester
Core, cage and endcaps	Polypropylene
Internal o-rings	Silicone
Housing bowl and head	Polypropylene

Operating parameters

Recommended operating differential pressure	2.1 to 3.1 bard (30 to 45 psid)
Maximum operating pressure	5 barg (73 psig) [1]
Maximum differential pressure	3.1 bard (45 psid) for continuous service, 6.2 bard (90 psid) during integrity testing only for up to a maximum of 10 hours
Autoclave	Maximum 125°C, 2 × 1 hour cycles
Maximum operating temperature	40°C (104°F)

In compatible fluids that do not soften or swell, or adversely affect the filter or its materials of construction.
[1] For up to a maximum of 25 hours continuous service. Contact us for recommended procedures to qualify filters under actual conditions of use.

Pore size	20 nm (nominal)
Retention ratings (virus)	> 4 log reduction value for bacteriophage PP7 [2, 3]

[2] Claims based on challenge with parvovirus model bacteriophage (bacterial virus) PP7
[3] > 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
Filter area (nominal)	2.25 m^2 (24 ft^2) per 254 mm (10 in.) filter
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	9.6 cm^2	10MCFSV4
Filter disc (47 mm)	11 cm^2 (in FTK200 holder)	FTKSV4047
Mini Kleenpak™ capsule	0.058 m^2	KA02SV42FT [4]
25.4 mm (1 in.) Kleenpak Nova capsule	0.25 m^2	NP1LUSV4P1
254 mm (10 in.) filter cartridge	2.25 m^2	AB1USV47PH4
254 mm (10 in.) Kleenpak Nova capsule (in-line style)	2.25 m^2	NP6LUSV4P1
254 mm (10 in.) Kleenpak Nova capsule (t-style)	2.25 m^2	NT6USV4P1

Not all filter types can be steam sterilized. Consult individual product datasheets for technical specifications.
[4] Filterability tool version (FT). Not qualified for virus removal. For filterability tests only.

Ordering information

Product	Length (nominal)	Filter area (nominal)	Product code [5]
Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane (in-line style)	129 mm (5.1 in.)	0.25 m^2	NP5LUSV4P1
Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane (in-line style)	335 mm (13.2 in.)	2.25 m^2	NP6LUSV4Px
Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane (in-line style)	584 mm (23.5 in.)	4.5 m^2	NP7LUSV4Px
Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane (in-line style)	834 mm (32.8 in.)	6.75 m^2	NP8LUSV4Px
Kleenpak Nova filter capsules with Pegasus SV4 virus removal filter membrane (t-style)	349 mm (13.7 in.)	2.25 m^2	NT6USV4Px
Kleenpak Nova filter capsules with Pegasus virus removal filter membrane (t-style)	598 mm (23.5 in.)	4.5 m^2	NT7USV4Px
Kleenpak Nova filter capsules with Pegasus virus removal filter membrane (t-style)	848 mm (33.4 in.)	6.75 m^2	NT8USV4Px

[5] x = Add additional code for desired connection option, see 'connection options' table below.

Connection options

Connection type	Applicable product(s)	Code
1 to 1½ in. sanitary flange inlet and outlet	In-line style and t-style	1
1 to 1½ in. sanitary flange inlet and 13 mm (½ in.) single barb hose barb outlet	In-line style only	16
1 to 1½ in. sanitary flange inlet and 25 mm (1 in.) single barb hose barb outlet	In-line style and t-style	19

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