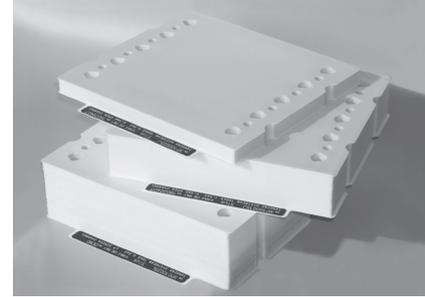


Sius™ Cassettes

Single-Use TFF Cassette

For Early Pilot Scale and Process Scale



Sius™ cassette family

Benefits of Selecting Disposable Sius™ Cassettes:

- **Disposable process scale tangential flow filtration cassettes**
 - 0.5 m², 1.5 m² and 2.5 m² membrane configurations
 - Three channel configurations
 - Reproducible and reliable scale-up performance from lab through to process
 - Two mPES membrane chemistries with ten MWCO's each
- **Purpose built for single-use disposability**
 - Ease and simplicity in processing
 - Pre-sanitized and ready-to-use
 - Cost-effective

Product Description

Sius™ is the first truly single-use tangential flow filtration cassette for the biopharmaceutical industry. These single-use cassettes have been designed to offer **comparable performance to reusable products at a fraction of the cost**. Each cassette arrives pre-sanitized, ready to be used for processing after equilibration with buffer. Sius™ cassettes are available in a range of **surface areas from 0.5 m² to 2.5 m²**. Cassettes can also be stacked together to provide greater surface areas. These cassettes have been developed using an innovative manufacturing approach that provides an efficient cassette production process that costs significantly less than comparably sized reusable products. Moreover, the cassettes are completely interchangeable with existing cassette hardware making them an ideal choice for many Tangential Flow Filtration (TFF) processes.

TFF cassettes are well established for the concentration and diafiltration of biomolecules. TFF cassettes are typically used in a process and then cleaned between uses with a Clean-In-Place (CIP) operation. This method of reuse requires a significant investment of raw materials, utilities, energy, and time. The cassette is used repeatedly until its process performance has deteriorated below acceptable limits and its productivity is reduced. Novasep now offers the **first purpose-built single-use tangential flow filtration cassette for the biopharmaceutical industry**. Additionally, each cassette arrives pre-sanitized, packaged in 0.2 M sodium hydroxide and **ready for processing** after equilibration with buffer. The cassette is simply installed, conditioned with buffer to neutralize the pH and ready for processing. Finally, validation of membrane cleaning studies and performance studies after reuse is eliminated.

Sius™ cassettes offer exceptional value when considering the basic steps of a TFF unit operation; those steps include pre-use activities, process and post-use activities. With reusable cassettes, typically only 50% of the total process time is devoted to processing the product; the remaining 50% is spent in preparing and cleaning the TFF system. With Sius™ single-use cassettes, the time needed in preparing and cleaning the cassette is drastically reduced allowing more time to be devoted to processing the product while increasing process efficiency and saving a significant portion of the overall process time.

Using Sius™ single-use cassettes also improves process safety by reducing the risk of cross-contamination. In addition, Novasep experts can provide you with any data and documentation needed to meet cGMP guidelines and pass regulatory inspections.



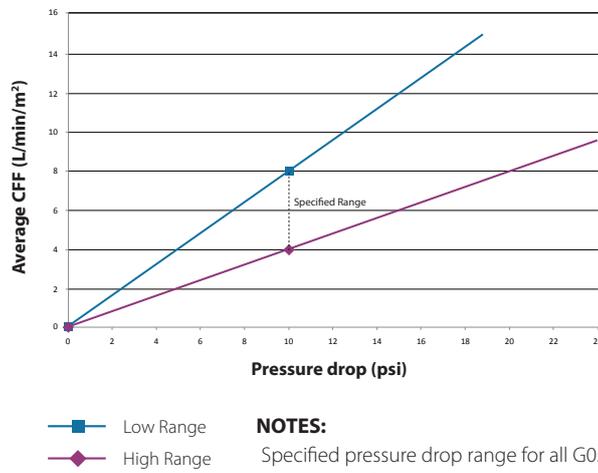
Pure Performance for the Lifes Sciences

Application Performance:

Sius™ conforms to industry standard size formats... use your existing filter holders or systems!

At pilot and process scale, the primary membrane has been chosen and process parameters have been established. Typically at the pilot stage, the production method is being verified and production materials produced for toxicology or pre-clinical trials and predictable scalability is imperative. In order to facilitate the manufacturing life cycle of a successful therapeutic candidate, cGMP manufacturing needs to begin at relatively small scale to facilitate human clinical trials. Manufacturing material for this early pilot scale manufacturing can easily and effectively be accomplished using the Sius™ single-use cassettes. Like the corresponding Sius™-LS process development cassettes, Sius™ pilot and process scale cassettes are available in a comprehensive range of options that are directly scalable from earlier development. Optimized channel geometry and enhanced device rigidity ensures hydraulic performance is maintained when scaling up through to process scale with the Sius™ cassette family resulting in optimal and reproducible scaling performance.

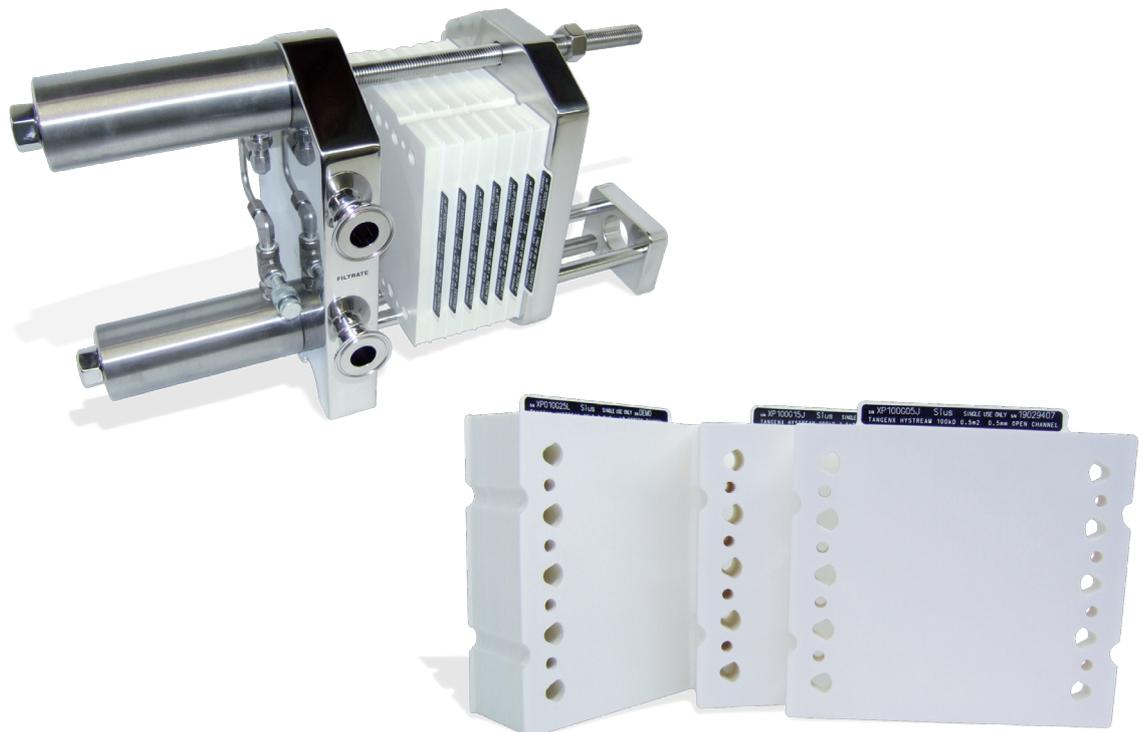
Graph 1 shows the pressure drop versus cross-flow specification for the Sius™ cassettes. A membrane's Normalized Water Permeability (NWP) is dependent on its Molecular Weight Cut-Off (MWCO). Therefore, there is a range of permeability rates for each cassette of a given MWCO. Therefore, there is a range of permeability rates for each cassette of a given MWCO. Table 1 shows typical water permeability rates for the Sius™ cassette with "LP" screen channel configuration.



Graph 1: Pressure drop vs. cross-flow flux - Sius™ "LP" screen

MWCO	Typical NWP Range (L/m²/h/psi)
1 kD	0.8 to 1.5
3 kD	1.5 to 3.8
5 kD	2.6 to 5.7
10 kD	8.6 to 24
30 kD	24 to 41
50 kD	34 to 56
100 kD	38 to 91
300 kD	82 to 129
0.1 µm	112 to 225
0.2 µm	138 to 284

Table 1: Typical NWP Range for Sius™ Cassettes

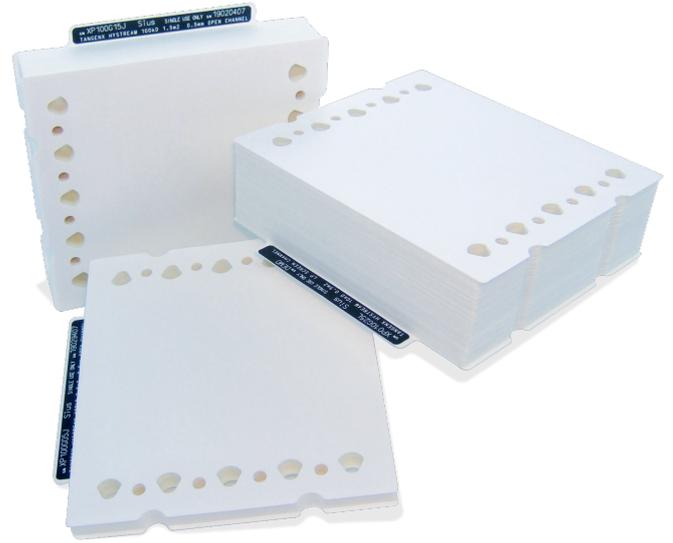


Cassette Selection and Optimization:

Ask us about our Sius™ FPI disposable flow path components!

Sius™ 0.5m², 1.5 m² and 2.5 m² devices are designed for processing volumes from tens of liters to thousands of liters when scaled to full capacity. This variety of device size allows for efficient processing over a wide range of operating volumes.

- ◆ Sius™ processing volume capability:
For example, depending on the characteristics of the feed stream, a 10 kD membrane run at 2 bar TMP typically handles 50 L/h for the 0.5 m², 150 L/h for the 1.5 m² and 250 L/h for the 2.5 m².
- ◆ Concentration factors obtained with Sius™:
Typically 3-100X when used in conjunction with a Novasep engineered system. Sius™ cassettes represent the latest development in tangential flow-filtration cassette design and performance. The Novasep line of cassettes has been designed to deliver optimal performance as well as demonstrate exceptional batch-to-batch reproducibility.



Many factors affect the type of cassette and membrane surface area that is best suited for a specific application. Significant differences from molecule to molecule and process to process demand that a range of cassettes be available to ensure the most advantageous balance of performance and capacity.

The Sius™ cassettes are available in a wide range of membrane pore sizes from 1 kD to 0.2 μm, in both ProStream™ (neutrally charged membrane designed for extremely low protein binding) and HyStream™ (extremely hydrophilic membrane designed for streams with a higher level of foulants) mPES membrane chemistries.

Sius™ cassettes are available with three different retentate channel configurations, each ideally suited for a specific type of feed stream:

- ◆ Medium “LP” Screen is ideal for low to medium viscosity streams where high flux and lower recirculation rates are desired.
- ◆ 0.5 mm “J” and 1.0 mm “K” open channels are ideal for streams of high viscosity or those containing particulates. This geometry is ideal for cell clarification.

Applications

Biopharma, Biotech, Life Sciences:

- ◆ Concentrate and desalt proteins, peptides, nucleic acids (DNA, RNA, oligonucleotides)
- ◆ Separate and purify biopharmaceuticals
- ◆ Recover and purify antibodies or recombinant proteins from cell culture media
- ◆ Fractionate diluted protein mixtures
- ◆ Remove pyrogens from water, buffers and media solutions
- ◆ Sample preparation prior to chromatography

Quality & Membrane Physical Properties and Chemical Compatibility

Manufacturing & Quality:

Sius™ cassettes are manufactured and quality controlled in a facility modeled for cGMP compliance. Each cassette undergoes rigorous preparation and QA lot release testing to verify it meets specification. Quality Control (QC) performance testing includes hydrodynamic (pressure drop) and air integrity measurements. Each cassette is flushed with purified water and sanitized after completing QC testing. Stringent testing ensures cassette-to-cassette consistency, resulting in scalable process development and reproducible manufacturing. Each Sius™ device is sanitized and individually sealed in a foil-lined vapor barrier bag, then packaged in an outer cardboard carton. Sodium hydroxide at 0.2 M concentration is used as a sanitizing agent and to prevent membrane drying and loss of performance.

Specifications:

Materials of Construction*	
Membrane	Polyethersulfone
Membrane support	Polypropylene/Polyethylene
Screens	Polypropylene
Channel spacer	Polyethylene (HDPE)**
Encapsulant	1) Polyurethane** 2) Silicone***
Gasket	White EPDM**
Preservative	0.2 M NaOH****

Dimensions (Sius™)	
Length	21.1 cm (8.3 inch)
Width	20.1 cm (7.9 inch)
Thickness	1.3 - 20.3 cm (0.5 - 8 inch)
Membrane Area	0.5, 1.5, 2.5 m ² (5.4, 16.2, 26.9 ft ²)

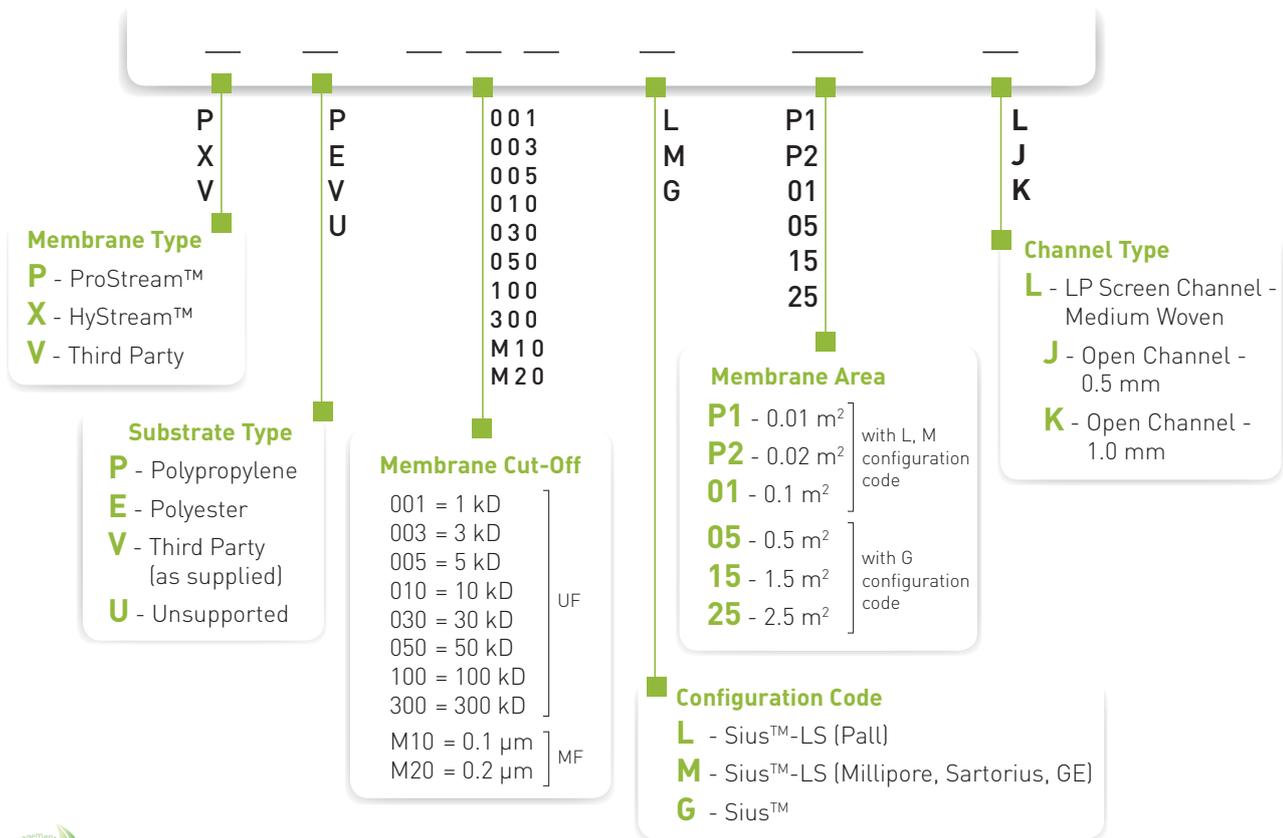
NOTES:

- * Apply for Sius™-LS also
- ** From FDA Approved material and Class VI Tested
- *** Class VI Tested
- **** To remove preservative - equilibrate with buffer and process, no flushing required.

Channel Type	Max Pressure (bar) at 30°C	Cross-Flow (L/min/m ²)	Air Diffusion		
"LP" Screen	Forward 4.1 (60 psi)	5-8 at 0.7 bar (10 psi)	"LP" Screen "J" Channel "K" Channel	Ultrafiltration 1 kD - 5 kD	≤ 323 ccm/m ² at 1 bar (≤30 ccm/ft ² at 15 psi)
	Reverse 0.48 (7 psi)			Ultrafiltration 10 kD - 300 kD	≤ 323 ccm/m ² at 0.5 bar (≤30 ccm/ft ² at 7.3 psi)
"J" Open Channel (0.5 mm)	Forward 4.1 (60 psi)	12 at 0.07 bar (< 1 psi)		Microfiltration ≥ 0.1 µm	≤ 323 ccm/m ² at 0.2 bar (≤30 ccm/ft ² at 3 psi)
	Reverse NOT RECOMMENDED				
"K" Open Channel (1.0 mm)	Forward 4.1 (60 psi)	24 at 0.07 bar (< 1 psi)			
	Reverse NOT RECOMMENDED				

NOTE: Reverse pressure is not recommended for "J" or "K" channel

Ordering & Specifications



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