Advancing High-Concentration mAb Processing Through Improved TFF Cassette Design

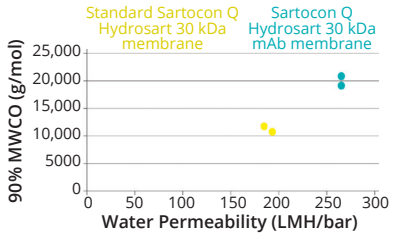
Anika Manzke and Katy McLaughlin

Monoclonal antibody (mAb) therapeutics are increasingly formulated at high concentrations, driven by escalating upstream titers, the shift toward personalized treatment, and growing use of subcutaneous administration (**1**). Thus, downstream concentration steps require scalable and robust tangential-flow filtration (TFF) solutions that can achieve high protein concentrations while maintaining product retention, flux, and operational stability.

As the only operation that simultaneously separates and concentrates target molecules, TFF's most critical application is the ultrafiltration and diafiltration (UF/DF) step before sterile filtration and filling. At that stage, mAbs are processed to a final target concentration, often with exchange into a formulation buffer. Yet UF/DF performance is challenging at high mAb concentrations. High solution viscosities reduce mass transfer; concentration polarization and gel-layer formation at the membrane surface can restrict operating windows. In practice, high-viscosity solutions can create operational challenges, including long process times, high pressures, and increased risk of performance drift during the final UF phase.

As a result, cassette design becomes a decisive factor in whether high-concentration targets can be reached efficiently without compromising scalability and operational stability. Wider channels can accommodate more viscous solutions but require increased pump capacity to maintain effective crossflow. Narrower channels require lower flow rates but can reach pressure limits sooner as viscosity increases. The selected cassette design must balance pressure, flow, processing time, and shear exposure.

Figure 1: The optimized Sartocon Q Hydrosart 30 kDa mAb membrane combines high water permeability with a retention profile ideal for high-yield mAb processing. (LMH = liters per square meter per hour, MWCO = molecular-weight cutoff)



Membrane selection is equally important. Although a 30 kDa molecular-weight cutoff (MWCO) is typical for processing standard mAbs, differences in membrane pore structure and permeability can affect product retention, flux stability, and overall process efficiency.

The Sartocon Q Hydrosart 30 kDa mAb cassette has been developed specifically to address those challenges. It is optimized for mAb concentration steps and designed to improve process efficiency while maintaining scalability and operational robustness. Here, we introduce key elements in the cassette's design and explain how those features apply in mAb processing workflows.

Optimized Membrane Design

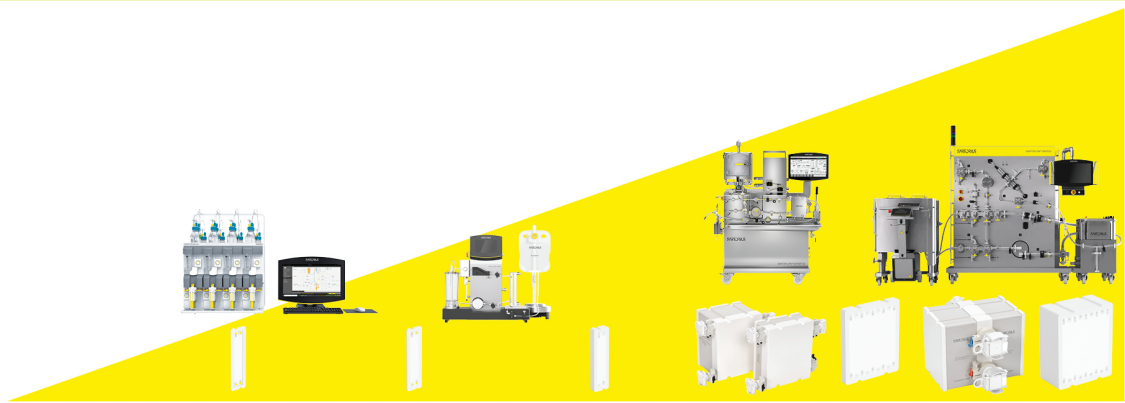
At the core of the Sartocon Q Hydrosart 30 kDa mAb cassette is a membrane optimized for mAb processing rather than general UF. Stabilized, cellulose-based Hydrosart membranes are well established in the biopharmaceutical industry. The membranes' high hydrophilicity and negligible protein adsorption make them virtually nonfouling, supporting high product recovery and sustained flux throughout processing. Hydrosart membranes are also stable across a broad pH range. Unlike other membranes on the market, they can withstand cleaning with up to 1 M NaOH, even at elevated temperatures, without loss of performance over repeated cleaning cycles. As mAb concentrations and protein loads increase, effective and reproducible cleaning becomes essential to maintaining consistent performance across multiple cycles. This combination of sustained filtration performance and efficient cleanability supports a long product life cycle.

The Sartocon Q Hydrosart 30 kDa mAb membrane was further optimized for mAb applications, combining higher water permeability with a retention profile suitable for mAb processing (Figure 1). That optimization provides 30–50% higher buffer flux than the standard Hydrosart 30 kDa membrane while maintaining mAb retention.

New Screen Design

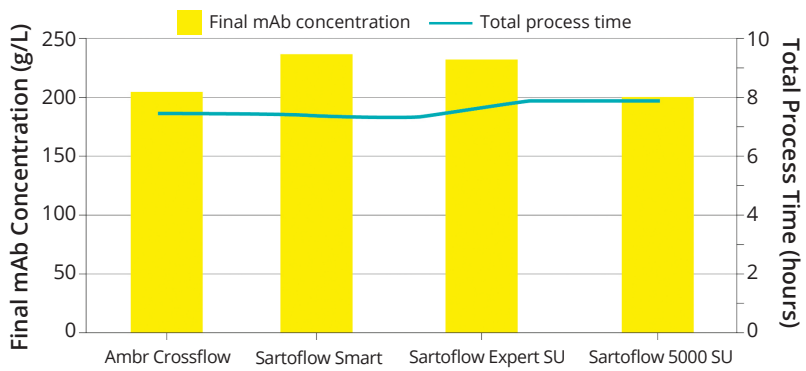
In addition to an optimized membrane, the cassette incorporates a new screen configuration intended to support viscous solutions. Compared with legacy systems, Q-Screen technology combines a fine-mesh design with a more open flow path, maintaining higher flux as solution viscosity increases. That feature supports high

Figure 2: Sartocon Q Hydrosart 30 kDa mAb modules for tangential-flow filtration (TFF) are available in five configurations offering different effective filtration areas and compatibility with multiple TFF systems.



Format	Sartocon Q Slice 100	Sartocon Q Slice 200	Sartocon Q Slice	Sartocon Q	Sartocube Q
Effective filtration area	86 cm²	172 cm²	0.13 m²	0.63 m²	3.09 m²
System	Ambr Crossflow	Sartoflow Smart		Sartoflow Expert SU	Sartoflow 5000 SU

Figure 3: Total process time and final monoclonal antibody (mAb) concentration achieved with Sartocon Q Hydrosart 30 kDa mAb cassettes at different scales



final mAb concentrations while limiting shear exposure, reducing the need for extended process times and operation close to pressure limits.

Scalability

The Sartocon Q Hydrosart 30 kDa mAb cassette is available in multiuse formats and self-contained units. Those offerings range in size from small-scale Sartocon Slice cassette formats, such as the Sartocon Slice 100 cassette (with an effective filtration area of 86 cm²), to conventional cassette formats up to 0.63 m² and larger Sartocube and self-contained single-use configurations of up to 6.18 m² (Figure 2). The small-scale Sartocon Slice 100 cassette enables process development and optimization using low volumes, which is critical in early phases, when material is limited.

The smaller devices are designed to scale to larger formats, so parameters established during development can be transferred to manufacturing without redefining a process. In a study performed using a customer's mAb feed, small configurations showed performance consistent with larger formats (Figure 3) (**2**). At a loading density of 1000 g/m², final mAb concentrations exceeded 230 g/L with 99% recovery. Results were largely unchanged across scales and comparable with those achieved using other filters on the market.

Process duration — encompassing initial UF, DF, and final UF steps — remained within an eight-hour production shift across all device sizes. Being able to finish an entire UF/DF process within a single shift helps to minimize the risk of product degradation and allows more batches to be processed within the available manufacturing schedule.

Facilitating TFF Workflows

Fast, reliable, and scalable TFF solutions are increasingly important as high-concentration mAb formulations become more common. The Sartocon Q Hydrosart 30 kDa mAb cassette offers a balanced solution that combines high performance with operational efficiency. Its optimized membrane, advanced screen design, and built-in scalability are intended to fit seamlessly into demanding mAb processing workflows without compromising development flexibility or operational consistency.

Learn more about the Sartorius TFF portfolio and request a sample at *https://www.sartorius.com/en/products/process-filtration/tangential-flow-filtration/tff-cassettes#id-1821194*.

References

1 Rathore AS, et al. Challenges and Developments in the Manufacturing of High-Concentration Biotherapeutic Monoclonal Antibodies. *Adv. Drug Deliv. Rev.* 232, 2026: 115812; https://doi.org/10.1016/j.addr.2026.115812.

2 Machava M, Jenke M, Manzke A. *Scalability of Sartocon Q Hydrosart 30 kDa mAb for Monoclonal Antibody Purification.* Sartorius: Göttingen, Germany, 2026; https://www.sartorius.com/en/application-note-scalability-of-sartocon-q-1839904.

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