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Sartoflow® 5000 SU: A Single-Use Tangential Flow Filtration Platform for Flexible, Large-Scale Downstream Processing

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Abstract

Modern biomanufacturing is evolving toward multi-product, multi-modality operations handling monoclonal antibodies, antibody-drug conjugates, vaccines | viral vectors, and nucleic acids within the same facility. Traditional stainless-steel tangential flow filtration skids — often dedicated to a single process — struggle to deliver the flexibility, speed, and containment such environments demand.

The Sartoflow® 5000 SU provides a large-scale, fully single-use tangential flow filtration platform designed to address these challenges. It combines high-capacity pumping, a low hold-up single-use flow path, and integrated Biobrain® automation to deliver efficient ultrafiltration, diafiltration, and microfiltration across a wide range of molecule types. The system eliminates cleaning and cross-contamination risks, reduces turnaround time, and supports standardized, recipe-driven processing in GMP environments.

In this white paper, we outline the design and capabilities of the Sartoflow® 5000 SU, showcase its performance in a case study using high-concentration monoclonal antibodies, and discuss how the platform can be deployed across modalities to streamline downstream operations in multi-product facilities.

Introduction

Biopharmaceutical manufacturers face mounting pressure to accelerate production, reduce costs, and maintain quality across multiple molecule types. Facilities today handle a spectrum of modalities—from large proteins like monoclonal antibodies (mAbs) to complex bioconjugates (antibody-drug conjugates [ADCs]), viruses for gene therapy, and mRNA | DNA-based drugs—each with distinct process requirements. Traditional downstream setups often require dedicated equipment for each product, which inflates capital expenditure and cleaning downtime.

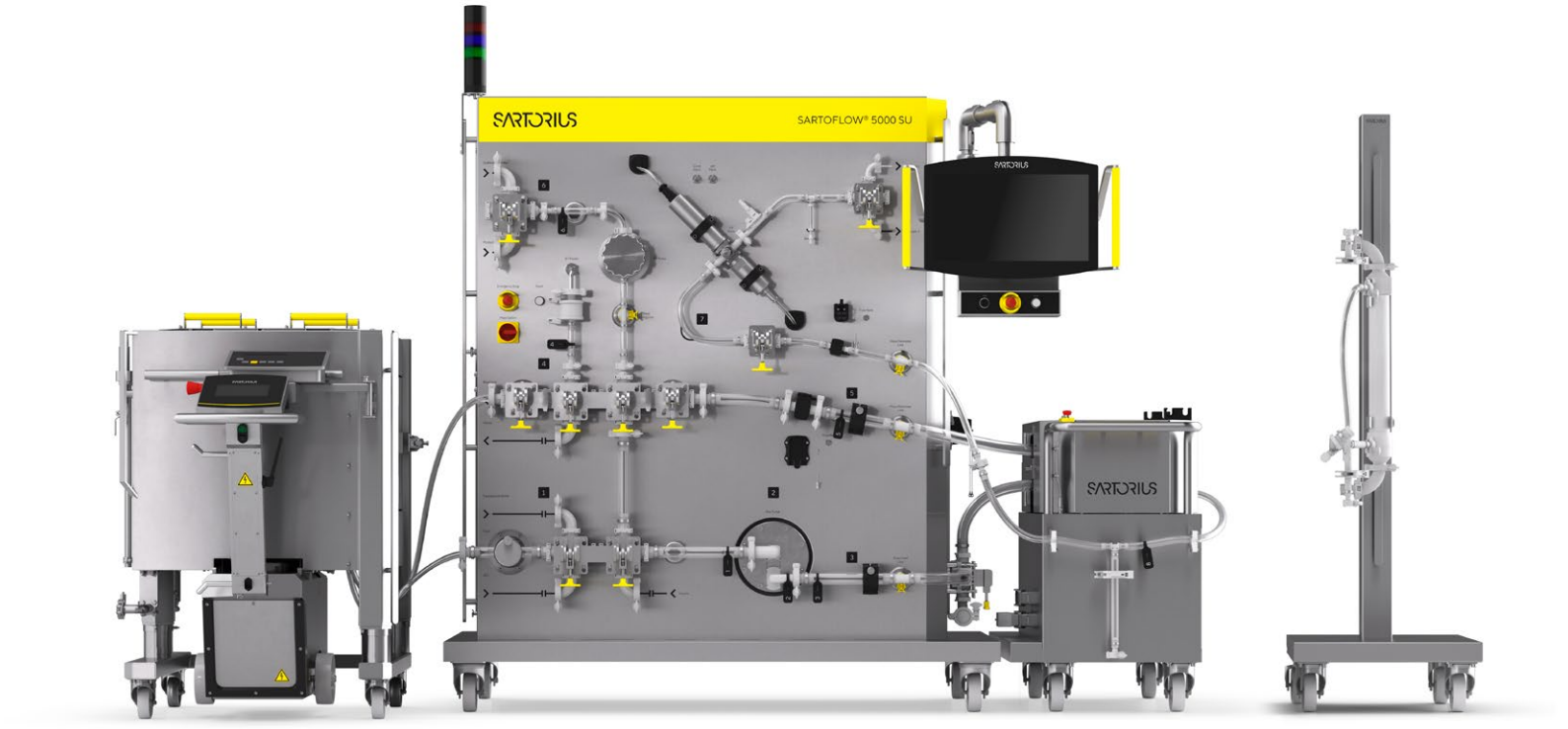
Batch ultrafiltration | diafiltration (UF | DF) steps have emerged as significant bottlenecks as upstream titers increase and final formulations demand higher protein concentrations.[1] Manufacturers must often achieve antibody concentrations of more than 150 g/L for subcutaneous formulations without introducing aggregation or viscosity issues, and must quickly switch between campaigns while adhering to strict GMP and data logging standards.

Conventional stainless-steel tangential flow filtration (TFF) skids, although robust, require time-consuming clean-in-place (CIP) | steam-in-place (SIP) cycles and extensive validation for each use.

In multi-product facilities, using separate stainless systems for different modalities or scales is impractical, as it increases footprint, validation burden, and cross-contamination risk. Even single-use TFF units are reaching their capacity limits, as they typically accommodate only lower volumes and flow rates.

As batch sizes grow into the thousands of liters and new therapies proliferate, downstream teams need a single platform that is scalable, agile, and universally applicable. In short, the industry requires a fully single-use, large-scale TFF system that can intensify UF | DF steps—achieving higher concentration factors and faster diafiltration while minimizing downtime between productions.

Sartorius developed the Sartoflow® 5000 SU to meet these needs, building on experience from earlier systems such as the Sartoflow® 4500 and incorporating advances in flow-kit design, system performance, and automation. This white paper describes how the features of the Sartoflow® 5000 SU, supported by the automation capabilities of Biobrain® software, solve modern bioprocessing challenges.



Overview

Key features of the Sartoflow® 5000 SU system
The Sartoflow® 5000 SU is a commercial-scale, single-use TFF system engineered for fully automated UF, DF, and microfiltration (MF) operations from 200 – 2,000 L batch volume.[2] It extends the single-use TFF range beyond its predecessors (Sartoflow® 4500) with roughly 10% higher flow capacity and 40% greater filter area, filling the gap for large-scale processing. Table 1 summarizes key technical specifications of the system.

Table 1: Sartoflow® 5000 SU specifications

Feature	Specification
Membrane area – cassettes	4.2 – 14 m^2 (optional 21 m^2 available upon request)
Membrane area – hollow-fiber modules	1.3 – 5 m^2 WaterSep® Modules
Tube inner diameter (ID)	1"
Recirculation vessel volumes	50, 200, 400 L
Minimum recirculation volume	7 – 33 L dependent on the retentate flow rate (7 L with bypass)
Recirculation pump	4-piston single-use diaphragm pump (up to 5,000 L/h)
Media addition pumps	4-piston single-use diaphragm pump (up to 1,000 L/h)
Process analytics	UV (permeate), conductivity (recirculation bag and permeate), pH (recirculation bag and permeate), flow and pressure (permeate, retentate, and feed), and weight (recirculation vessel)
Temperature control unit (TCU)	Operating range: 10 – 40 °C

At the heart of the system is a 4-piston diaphragm pump capable of delivering up to 5,000 L/h flow with low shear. In addition, the redesigned pump head reduces residual volume by up to 92% and improves ventability (compared to the Sartoflow® 4500). This pump provides gentle, high-flow recirculation across up to 14 m^2 of TFF flat sheet membrane or 5 m^2 of hollow fibers.

The multi-purpose solution design accommodates both flat-sheet cassettes (including self-contained units, multi-use cassettes, and single-use cassettes) and hollow-fiber modules interchangeably, allowing operators to use the optimal membrane format for individual products without changing the hardware. Importantly, the flow path and holders are pressure drop-optimized and volume-minimized; the system's hold-up volume is only 3.3 L, so even in a large 2,000 L batch, product loss is negligible, with >99% recovery in a completely evacuated bag during final concentration.

Sartoflow® 5000 SU employs gamma-irradiated single-use flow kits that include all wetted components—pump heads, tubing, valves (integrated multi-block valve manifolds), and sensors—with an option for a sterile, validated package.

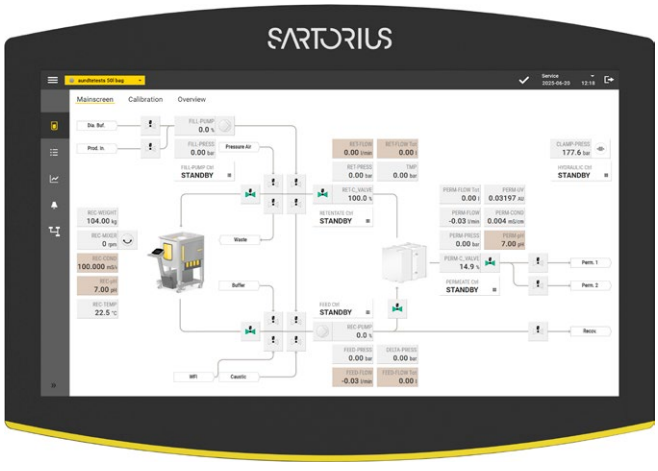
Upon setup, the operator simply mounts the disposable flow kit and connects it to the unit's feed vessel and retentate bag to establish a closed, aseptic loop. This design eliminates the need for CIP | SIP; after a run, the entire product-contact assembly is discarded, and a new kit is installed for the next run, virtually eliminating cross-contamination risk and cleaning downtime.

The multi-valve blocks in the flowkit reduce the number of valve installation steps by >50%, simplifying setup. Additionally, Flexsafe® Pro Mixer bags (50, 200, or 400 L) serve as single-use recirculation tanks; these bags feature a magnetically levitated impeller for low-shear mixing that automatically adjusts speed with fill level to prevent vortexing and shortcuts between retentate and feed. During diafiltration, the integrated mixer ensures excellent homogeneity, contributing to efficient buffer exchange.

The single-use flow path concept of Sartoflow® 5000 SU ensures that no product comes into contact with metal or reusable surfaces, which is especially crucial for high-potency or shear-sensitive products, such as bioconjugates and viral vectors.

Performance and Efficiency

Intelligent automation with Biobrain®
To enable consistent, scalable performance, the Sartoflow® 5000 SU uses the Biobrain® local control platform, a GMP-ready automation system developed by Sartorius. Biobrain® features a graphical recipe editor following ISA-88 batch structuring, allowing MSAT engineers to configure multi-step UF | DF sequences (concentration phases, diafiltration cycles, flushes, etc.) via an intuitive interface.



All critical process parameters are programmable with precise control loops (e.g., switching from flow control to pressure control when adjustable maximum process pressure is reached), and the system can respond to sensor feedback in real time, such as by pausing diafiltration when UV absorbance indicates product breakthrough. Data integrity and compliance are built in: Biobrain® records process data and audit trails in a 21 CFR Part 11-compliant manner, and it offers OPC Unified Architecture (OPC UA) connectivity for integration with plant historians, MES, or DCS supervision. This means Sartoflow® 5000 SU can seamlessly slot into digital manufacturing environments, enabling remote monitoring, batch reporting, and advanced process control strategies (e.g., linking with process analytical technologies). Automation not only reduces operator intervention and error, but also ensures reproducible performance across runs and sites, a key requirement for multi-product facilities.

By combining a high-performance pump, optimized flow path, and smart automation, Sartoflow® 5000 SU streamlines UF | DF operations that were previously time- and labor-intensive: System setup is typically completed in under 25 minutes, as single-use components are simply unwrapped and connected. In contrast to multi-use skids, there is no lengthy cleaning or sterilization between batches, which can save hours to days of downtime. The closed design and sterile connectors also eliminate the need for aseptic handling or cleanroom storage of intermediate products, further accelerating batch turnover.

The system's yield maximization features (including the low hold-up volume and product recovery via air blow-down) ensure optimal harvest. After UF | DF, the Sartoflow® 5000 SU can execute an automated product recovery sequence: it hydrostatically empties the recirculation loop using the diaphragm pump, then performs an air blow-down to push residual liquid from the cassette and tubing, and finally runs a low-volume buffer flush through a dedicated bypass line to recover remaining protein from the membrane. This approach was shown to achieve 99% recovery in practice, meaning almost no high-value product is left behind in the system.

Sustainability
From a sustainability perspective, eliminating CIP | SIP and cleaning validation translates to significant reductions in water and chemical usage. A single large-scale stainless-steel TFF run can require thousands of liters of purified water and caustic for cleaning, whereas the single-use approach eliminates these demands entirely. Moving to single-use process equipment can cut water and energy use by up to 80% for the TFF step and reduce the overall carbon footprint of downstream processing. The disposable flow kits are made of largely plastic components; while this introduces waste, Sartorius has optimized the design to minimize material volume, e.g., with shorter tubing lengths and right-sized connectors.

In summary, Sartoflow® 5000 SU delivers tangible operational advantages: faster batch completion, less idle time, lower consumable usage per batch, and maximum product yield—all critical drivers for lowering cost of goods in commercial manufacturing.

Case Study: High-Concentration mAb UF | DF

To demonstrate the capabilities of Sartoflow® 5000 SU, Sartorius performed an internal evaluation using a challenging high-viscosity mAb process. In this study, a purified mAb feed (15 g/L, 410 L) was ultrafiltered and diafiltered to achieve a target final concentration of ~200 g/L. The TFF setup included a 6.18 m^2 Sartocon® Q Hydrosart® 30 kDa mAb cassette (SCU format)—a new high-flux, mAb-optimized membrane—integrated with the Sartoflow® 5000 SU. After

Figure 1: Sartocon® Q Hydrosart® 30 kDa.

This case study highlights how Sartoflow® 5000 SU maintains performance under demanding conditions. During the UF, the system's pump supported a high crossflow (~3,050 L/h, 500 LMH) to concentrate the mAb, initially by 5-fold. The transmembrane pressure (TMP) was held at ~0.7 bar throughout, and the built-in automation seamlessly switched from flow control to pressure control mode as the retentate became more viscous (at ~75 g/L). Under pressure control (with retentate pressure ~1.4 bar), the system also activated its bypass loop to recirculate a portion of retentate directly at low volume. This advanced control strategy maintained process stability even as the mAb concentration reached 220 g/L at a viscosity of 40 cP, with no signs of membrane fouling or gel-layer formation.

Diafiltration was executed at a constant 500 LMH crossflow; notably, only ~5 diavolumes (out of 7 planned) were needed to achieve buffer exchange endpoints, owing to the pre-mix in the flow path, effective mixing in the recirculation bag, and the optimized dead-leg design.

concentration, the system's product recovery sequence left less than 3% of product unrecovered. The main fraction (pump-out and blow-down) yielded 24.8 L of mAb at ~220 g/L (~90% of the loaded protein), and a subsequent final flush added 4.6 L at ~110 g/L (~7%), which were pooled. The final combined pool (~29.4 L of solution at ~201 g/L mAb) represented 97% mAb yield. Crucially, analytical tests showed monomer purity remained unchanged: the high-concentration UF did not generate aggregates or fragments.[3]

From an operational standpoint, this case study underscores the time savings enabled by the Sartoflow® 5000 SU: the entire setup was completed in less than 1 hour (including automated sensor calibrations) and teardown in under 15 minutes. All process phases were automated via Biobrain®, allowing essentially walk-away operation once the recipe was started. In a traditional setup, achieving a 15× concentration with such recovery would likely require manual interventions or multiple systems; here, it was achieved in a single process sequence on one platform within a standard shift.

This demonstrates how Sartoflow® 5000 SU enables high-titer biologics manufacturing—e.g., producing a mAb drug substance at >200 g/L for syringe delivery—in a process that is efficient, reproducible, and production-ready.

Multi-Modality Applications

While the above example focused on a mAb, Sartoflow® 5000 SU is designed as a universal TFF solution across modalities. Its configurable hardware and control can accommodate the different needs of various biotherapeutics.

mAbs
mAbs often require high-volume processes that include UF to concentrations above 150 g/L, followed by diafiltration for formulation. The system's robust pumping and low hold-up ensure fast concentration and high yield, even for high-viscosity mAbs. Pre-loaded recipe templates can standardize UF | DF steps, simplifying tech transfer to production.

ADCs and other bioconjugates
ADCs are potent molecules requiring closed processing to protect operators from cytotoxic payloads.
The single-use, sealed flow path of Sartoflow® 5000 SU enables fully closed UF | DF for ADC conjugation mixtures (e.g., removing solvents or unbound toxin). All wetted materials are non-metal and compatible with commonly used solvents applied in conjugation processes. The system can integrate with containment isolators as needed, supporting a safe and GMP-compliant solution for ADC manufacturing.

Vaccines and viral vectors
Often produced in large volumes (hundreds of liters) but at relatively low product concentrations, vaccines benefit from the high throughput (5,000 L/h) capabilities of Sartoflow® 5000 SU. For example, in viral vector purification, the unit can perform gentle UF to concentrate vectors while maintaining infectivity, thanks to low-shear pumping and the ability to precisely control TMP to avoid shear stress on virus particles. The system's sterile single-use flow kits also align with the aseptic processing requirements of vaccine production, minimizing contamination risks in multi-product facilities.

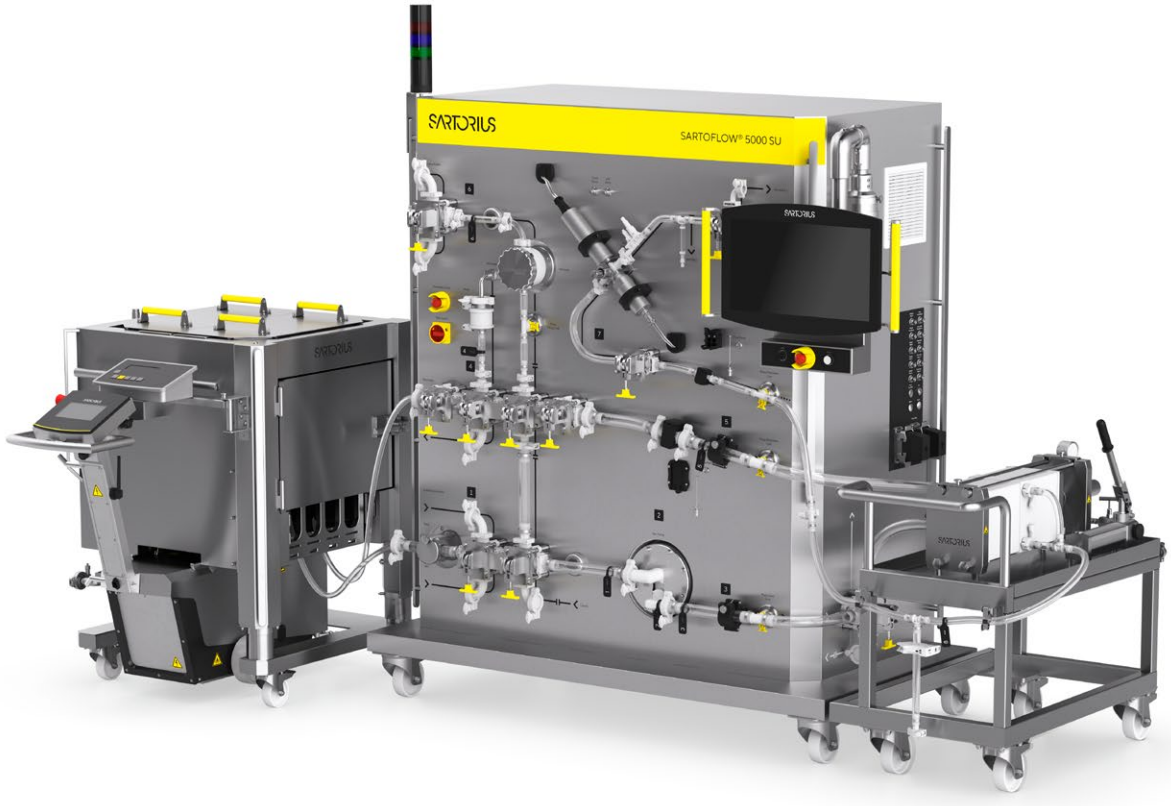
Nucleic acids (mRNA, pDNA)
New genetic therapies rely on processing large DNA plasmids or mRNA strands, which can be shear-sensitive. The Sartoflow® 5000 SU can handle these with specialized hollow-fiber modules (which may be preferred for shear-sensitive filtrations) or cassettes, and its digital automation ensures tight control of TMP to protect product integrity.
For instance, mRNA UF | DF might be run at lower pressures with in-line monitoring; the system's BioPAT® conductivity and UV sensors help confirm the removal of impurities (e.g., solvent, caps) in real time. Moreover, the low hold-up design is advantageous given the high value of nucleic acid products—nearly all mRNA can be recovered from the system. The ability to rapidly switch out flow paths also means the same system can be used in a facility's mAb campaign one week and an mRNA campaign the next, simply by changing the disposable kit and recipe.

In all these cases, having a single platform that can be adapted to various filters and processes reduces the training burden and validation effort. The common control software and interface mean that operators only learn one system, and a single qualification can cover TFF for multiple product lines. This standardization is a significant advantage for MSAT teams aiming to implement best practices and achieve global harmonization across a facility or multiple production sites.

Table 2 summarizes the expanded application envelope of the Sartoflow® 5000 SU across therapeutic modalities. By supporting UF, DF, and MF, the Sartoflow® 5000 SU provides a single scalable platform for downstream processes across the bioprocess spectrum. This allows organizations to intensify their processes (as it can support higher concentrations and continuous processing) and future-proof their facilities for new therapeutics without requiring a new TFF system for each product. In essence, Sartoflow® 5000 SU transforms TFF from a specialized unit operation into a flexible, facility-wide platform that aligns with Industry 4.0 and lean manufacturing goals.

Table 2: Capabilities of traditional TFF systems versus the Sartoflow® 5000 SU

Traditional TFF	Sartoflow® 5000 SU
Dedicated to one molecule or process	Configurable for mAbs, ADCs, viral vectors, mRNA, pDNA, and nucleic acids
Fixed range (1–2 batch sizes)	Scalable 450 – 5,000 L/h with configurable flow kits
Fixed flow path	Holder designs for cassettes (up to 14 m²) and hollow-fiber modules (up to 5 m²)
Manual or semi-automated control	Fully automated Biobrain® recipe execution (ISA-88 recipes, 21 CFR Part 11)
Stand-alone instrumentation	Seamless connectivity via OPC UA or MTP to SCADA, MES, and DCS
Cleaning validation required	Single-use flow kits eliminate CIP | SIP, minimizing water | chemical use
Separate validation per product	One system validated across modalities



Conclusion

Sartoflow® 5000 SU represents a new standard for large-scale TFF, combining single-use flexibility with the performance and automation of stainless-steel systems. Its modular design and dual membrane compatibility allow one platform to handle multiple modalities—mAbs, ADCs, vaccines, and nucleic acids—without hardware changes. This consolidation reduces complexity, accelerates tech transfer, and minimizes downtime, while Biobrain® automation ensures recipe-driven control and reproducible results across sites.

With a flow kit setup completed in under 25 minutes, no cleaning validation required, and automated batch reporting, the system streamlines GMP operations and shortens turnaround times. High-performance yet gentle pumping maintains yield and product quality—even at extreme concentrations—while the closed, disposable flow path lowers contamination risk.

Strategically, Sartoflow® 5000 SU enables seamless scale-up from development to commercial manufacturing thanks to consistent geometries and control logic across Sartoflow® platforms. Digital connectivity (OPC UA, ISA-88) supports MES | DCS integration for full regulatory alignment. Future-ready flexibility means the same system can be reconfigured for the next product campaign (for example, pivoting from an antibody process to a gene therapy process) with minimal investment.

In summary, Sartoflow® 5000 SU delivers flexibility, automation, and scalability—empowering MSAT and process engineering teams to streamline processes, reduce complexity, and confidently adapt to evolving portfolio needs.

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