# Exploring Today's Process Intensification Landscape

Industry leaders share their perspectives on how process intensification (PI) is transforming biomanufacturing — and why the time for implementation is now.

**Miriam Monge, Priyanka Gupta, Gerben Zijlstra, Bettina Renker, Lara Cobacho Lluesma, and Ann Ablavskaya**

The 2025 Sartorius PI Forum in Boston, MA, brought together a global community of biomanufacturing experts to address the critical turning point faced by the industry today: an urgent need to accelerate productivity while reducing cost, complexity, and carbon footprint. As Sartorius North America President Maurice Phelan noted in his introduction, "There is no more fitting place than Boston to talk about process intensification. The city has hosted countless breakthroughs, from the first use of anesthesia to the first organ transplant to the next evolution in bioprocessing."

Emphasizing urgency, Miriam Monge (Head of Customer & Industry Advocacy Strategy, Sartorius Bioprocess Solutions) added that although process intensification has been discussed for 15+ years, now it is no longer optional. "The industry is facing critical demand for higher productivity at lower cost of goods (CoG)." Today, companies that integrate PI into their workflows stand to win the new race to shorten timelines, increase facility output, and lower CoG, while leveraging additional benefits such as greatly reduced environmental impact.

Biomanufacturing is experiencing a complex and rapidly evolving landscape. As Phelan put it, "If you're not working on productivity, cost per dose, robustness, and predictability, [then] you're working on the wrong things." This reality is being felt across the industry, from blockbuster biologics facing unprecedented competition — e.g., adalimumab (AbbVie's Humira), which will be manufactured by more than 30 companies following its patent cliff — to the explosion of complex modalities requiring agile and adaptable production systems.

Maurice Phelan (Sartorius)

Miriam Monge (Sartorius)

## Key Market Aspects Driving the Shift to PI

**The need to stay competitive:** Facing increasing costs and higher demands for efficiency, manufacturers must adapt to survive.

**New therapeutic challenges:** Less stable and more complex molecules are becoming more common and placing more strain on today's processes.

**Rising demand for local, niche manufacturing:** Especially for biosimilars and regionalized supply models, smaller and more variable batch sizes require more flexible operations.

**Escalating costs:** From labor and materials to facility operations and construction, a combination of factors is driving the need for therapies to reach a manufacturing cost below $50 per gram.



Alongside all of those challenges is growing recognition in the industry — by regulators, industry groups, and manufacturers — that PI is the key to long-term sustainability. Regulatory agencies such as the US Food and Drug Administration (FDA) have started not just supporting the shift to continuous processing, but also actively asking biomanufacturers how they can achieve that transition together.

Upstream innovations such as high-efficiency bioreactors and advanced cell lines have come far, but downstream technologies have lagged behind. The result is a widening gap in productivity. Today, facilities face hurdles such as underused chromatography resins, manual column handling, time-consuming setup times, and long validation cycles — bottlenecks that need to be resolved to make end-to-end intensification a reality.

PI Forum presenters highlighted new tools for flexible automation and digitalization, showcasing their effects on connected and intensified upstream unit operations. Across tracks, applications, and modalities, speakers emphasized the pivotal roles that digital technologies — including data analytics, digital twins, and advanced process controls — play in advancing process understanding and fostering innovation.

## Increasing Pressure To Intensify Bioprocessing

New PI technologies are delivering unprecedented results and transformative gains. Although only 14% of organizations reported achieving connectivity in a 2024 BioPhorum survey (**1**), those early adopters are already seeing unprecedented performance across development. Some of the most dramatic results are accelerated processing, extreme gains in productivity and yield, and robust cost savings — along with additional efficiency benefits driven by in-parallel development, real-time monitoring, and subsequently optimized control strategies. And many early adopters have intensified only one or two parts of their processes, so their results are merely the tip of the iceberg in what's possible. Companies are moving on to expand overarching automation in their progress toward fully continuous processes.

**Joseph Shultz (Ottimo Pharma)** described PI as "born into the modern age" in his opening keynote presentation. Speaking from his experience implementing end-to-end PI technologies at commercial scale with his teams, he explained that despite nearly two decades of progress, many biomanufacturers are struggling to take the final steps toward implementation. "What's important to remember," he said, "is that the objective isn't the implementation of process intensification itself — it's aligning your organization to use it strategically."

Shultz explained how implementing commercial-stage continuous biomanufacturing demonstrated a clear model of what's possible when teams integrate PI and single-use technologies into their facilities, processes, and business strategies. Goals of speed, flexibility, and reduced cost are familiar across the industry, but what's changed now is the ability to address them all at once.

Key enablers include $N - 1$ perfusion, dynamic/continuous perfusion in the production bioreactors, and connected polishing to facilitate capital and labor cost reductions while supporting rapid process reconfiguration. By using modular automation and distributed control technologies such as the DeltaV system, manufacturers can remove downstream bottlenecks by dynamically adjusting unit operations in response to upstream changes. Connected downstream processes, typically considered to be "the hard part," have proven to be remarkably robust.

Even so, Shultz cautioned against overdesigning for flexibility. His advice for those getting started: Focus on the problem that you want to solve — then align your organization and budget around that goal. "We all want to see this happen," he said. "It's been 15–20 years. The examples are out there, but we're all just hesitating to make the transition."

**Weichang Zhou (WuXi Biologics)** presented a deep dive into the upstream PI technologies developed and implemented at his company and showcased what's possible when intensification meets thoughtful and systematic execution. WuXi Biologics has spent the past decade investing in platform fed-batch and perfusion processes, achieving breakthrough productivity gains with up to sixfold increases in intensified fed-batch titers, and reaching up to 85 g/L in intensified perfusion approaches.

The company's ultraintensified fed-batch WuXiUI platform (Figure 1) combines *N* – 1 perfusion and high-inoculation intermittent perfusion with traditional fed-batch culture, delivering a 407% increase in one case and a sixfold boost in another when coupled with in-house media and the MagniCHO cell line and media platform. In a study involving 32 different biomolecules, productivity increased by, on average, around 3× and up to 6×, with further gains enabled by real-time process analytical technology (PAT) tools such as Raman spectroscopy.

"We can now allocate many cell culture parameters with a single measurement," Zhou said. "That lets us control things like temperature shift, which is critical

**Figure 1:** Schematic comparison of three process options: a regular fed-batch process with a batch *N* – 1 seed step, an intensified fed batch process with *N* – 1 perfusion step, and the WuXiUI ultra-intensified fed-batch process (using *N* – 1 perfusion followed by *N* – 1 cell concentration to achieve ultrahigh inocculation cell densities (20–80 million cells/mL) into the final *N*-stage fed-batch culture; subsequently in the latter, one to three perfusion cycles are used to replenish key nutrients, remove toxic waste components, and sustain productivity in extended culture duration. That enables titers of ≤35 g/L. Figure is adapted from Weichang Zhou at WuXi Biologics.

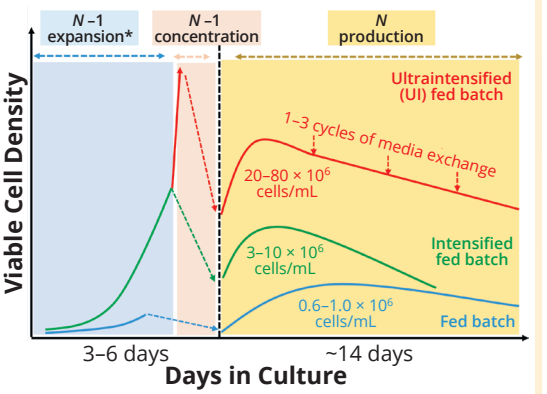
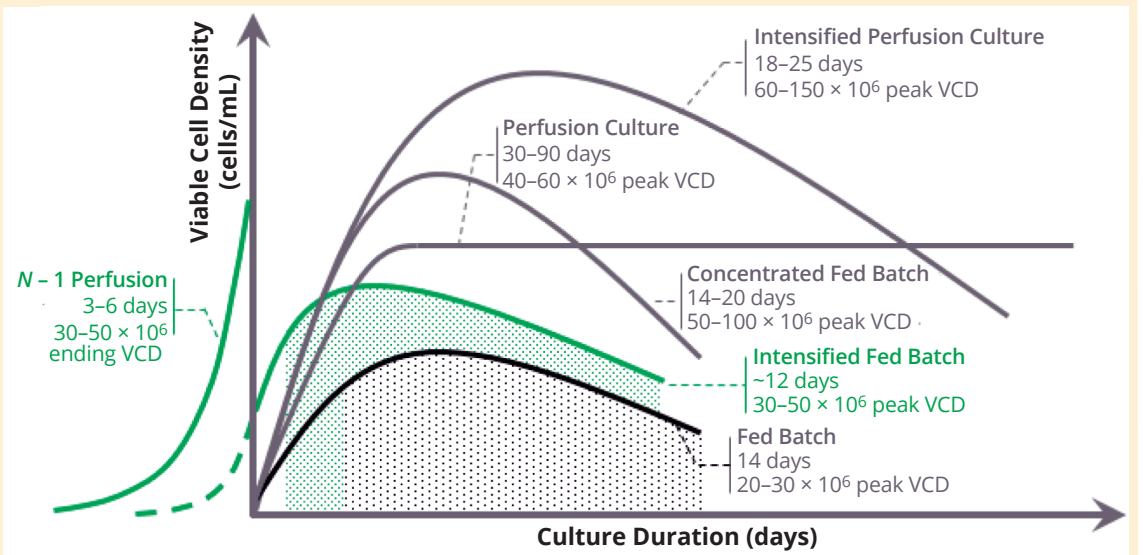



**Figure 2:** Schematic comparison of five process options: a regular fed-batch culture with a batch *N* – 1 seed step; an intensified fed-batch culture with *N* – 1 perfusion step; a concentrated fed-batch culture using an ultrafilter to perfuse the main bioreactor (supplying nutrients and removing toxic and inhibitory waste while accumulating product and cells inside the bioreactor); continuous perfusion using both a microfilter to perfuse the main bioreactor (supplying nutrients and removing toxic waste) and a cell bleed to maintain constant cell density and stable product quality; and the WuXiUP intensified dynamic perfusion process, which uses perfusion to replenish key nutrients, remove toxic waste components, and sustain productivity in extended culture duration without a cell bleed, enabling cumulative titers of >85 g/L. *N* – 1 perfusion can be used to achieve ultra-high inoculation cell densities into the final *N*-stage dynamic perfusion culture to reduce the culture duration. Figure is adapted from Weichang Zhou at WuXi Biologics. VCD = viable cell density.



Ron Gillespie (Just–Evotec Biologics)

Nuno Pinto (Merck & Co.)

to performance." With PAT and automation combined, WuXi Biologics has scaled performance gains from pilot- to 2,000-L bioreactors and now is applying the WuXiUI platform to commercial manufacturing with titers from 10–35 g/L after about 17 days in intensified fed-batch culture.

Using the WuXiUP intensified perfusion technology, with bioreactors continuously perfused for nutrient replenishment and inhibitory metabolite removal, the company increased outputs even further (Figure 2): Zhou shared examples with accumulated titers of 51 g/L in 21 days and 85 g/L in 27 days. He highlighted that the future lies in manufacturers' ability to start at small scale and scale up with precision. "With PAT, we're leveraging 30 years of cell culture knowledge and applying it to development of the next molecule. That's a major breakthrough, and I'm excited even after 35 years in this field."

**Kevin Brower (Sanofi)** explained that, in addition to performance, Sanofi has experienced equally transformative gains in agility. His team has been developing flexible, modular purification trains that adapt to each molecule, modality, and scale of production without compromising regulatory readiness. "Don't wait for the perfect moment or the perfect technology," he advised. "You're better off practicing. You'll learn more by trying."

His company's proposed approach uses interoperable equipment and automation to transition downstream processes from fed batch to continuous, or even to run them in either mode depending on what's needed. Brower underscored the potential real-world value of such flexibility: "With continuous downstream processing, you can serve a portfolio of biologics and macromolecules from a single suite." His case studies showed that automation, ultrafiltration/diafiltration (UF/DF) integration, and smart pooling strategies can make downstream processing scalable and sustainable — capable of operating at throughputs of 200–4,000 L/day with effective control.

In a keynote address, **Ron Gillespie (Just–Evotec Biologics)** offered another compelling look at platform-driven intensification. He showed how modular facility design and intensification-based process development (PD) allowed Just–Evotec teams to reduce process footprints while scaling productivity. Ron said that with tools such as its J.MD molecular design platform, J.CHO expression system, and J.P3 process and product design platform, the company has driven media costs down to "single-digit dollars" per liter, while increasing productivity up to 10-fold using hybrid and fully continuous formats. The commercial-scale facilities already are ready for good manufacturing practice (GMP) operations in the United States and Europe, where they are designed to enable rapid process transfer for flexible, integrated manufacturing for high mass and low CoG.

**Ashley Baltes (Just–Evotec Biologics)** presented an evaluation of PI tools in the PD environment. She highlighted a collaboration with Sartorius to transfer a process to an Ambr 250 perfusion system. Results demonstrated the utility of its fully automated small-scale bioreactor design to enhance PD throughput and reduce reactor-to-reactor variability while aligning with larger-scale continuous perfusion cultures.

**Nuno Pinto (Merck & Co.)** discussed the limitations of current hollow-fiber membranes for enabling large-scale perfusion bioreactors. He highlighted how membrane-design improvements are helping companies partially mitigate the resulting bottlenecks, but suggested that further improvements in tangential-flow filtration (TFF) cell-retention technology will be needed to advance PI implementation at scale.

**Susan Dexter (Sonnet Biotherapeutics)** shared a case study (Figure 3) on implementing perfusion processes during cell-line development to improve screening, selection, and scale-up of highly potent but challenging molecules. She emphasized how cell-line development services and bioreactor



technologies from Sartorius enabled the shift from fed-batch mode to continuous perfusion for increased productivity and product quality.

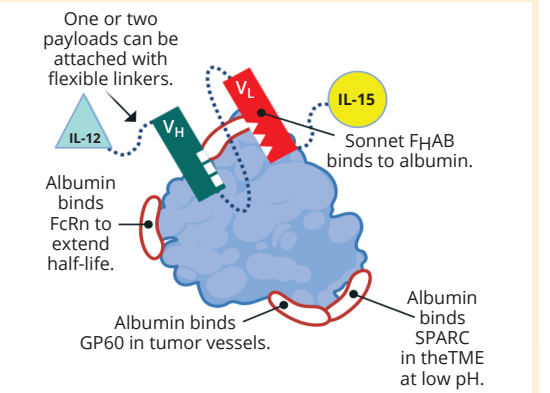
As **Amine Djeffal (Sartorius)** explained, the regulatory framework is no longer a barrier but rather a strategic enabler. "If you're risk averse, I don't think PI is for you," he said. "But if you understand your process, regulators will support you." With the FDA and other agencies now offering clear guidance and streamlined review pathways, the industry is finally equipped to scale what has been in development for some time: a connected, continuous, and collaborative way to make biologics.

## Enabling Flexibility by Design

Modular platforms and continuous-flow processes are reshaping the economics and agility of biomanufacturing. At the PI Forum, industry leaders demonstrated how intensified and fully connected processes can unlock new levels of responsiveness, cost efficiency, and scalability.

**Himanshu Gadgil (Enzene Biosciences)** described his company's next-generation, fully connected EnzeneX 2.0 continuous-manufacturing platform. Positioned as a fully connected process from upstream through downstream processing, the platform is already on the way to producing therapeutic monoclonal antibodies (mAbs) at a cost below $40/g, a milestone that once seemed out of reach.

**Figure 3:** Sonnet Biotherapeutics is producing highly potent recombinant proteins that include cytokine and antigen-binding fragment (Fab) elements. Due to product cleaving and instability under cell culture conditions, perfusion cell culture (with much reduced product residence time in the bioreactor) allows for yields that are larger by an order of magnitude. Therefore, Sonnet has decided to transition fully to perfusion cell culture for its biomolecule pipeline.




**IL** = interleukin; **FcRN** = neonatal Fc receptor; **$F_H$AB** = fully human albumin-binding protein; **GP60** = mammalian albumin-binding receptor protein; **SPARC** = secreted protein, acidic and rich in cysteine; **TME** = tumor microenvironment; **$V_L$** = variable light chain; **$V_H$** = variable heavy chain


"Biosimilars are a low-volume business," he said. "When you go down in volume, fixed costs matter more, and the best way to reduce them is by shrinking your footprint." The EnzeneX 2.0 platform demonstrates that principle by minimizing hold steps and boosting cell viability through continuous perfusion. For complex or unstable molecules, where maintaining cell health and rapid harvest are critical, the Enzene process provides a distinct advantage over fed-batch or semicontinuous approaches.

Gadgil highlighted the stark contrast between traditional facilities and his company's modular, adaptable approach. The team has launched eight successful biosimilars in India and can scale new operations within six to eight months.

Flexibility isn't only about reducing costs; it's expanding what's possible and shaping the future of

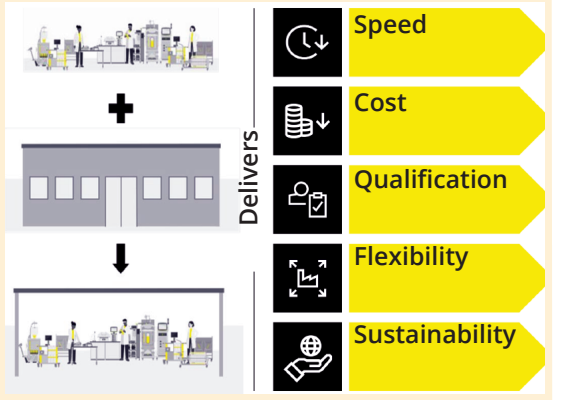

intensified manufacturing. To that end, G-CON and Sartorius are collaborating to deliver another dimension of manufacturing flexibility: modular, rapidly deployable cleanrooms designed for intensified processing from day one.

In a joint presentation, **Dennis Powers (G-CON) and Miriam Monge (Sartorius)** shared the transformative potential of POD cleanroom systems for intensified bioprocessing, most notably for upstream operations. Upstream PI leverages relatively small, single-use bioreactors that fit easily in POD cleanrooms to match the productivity of larger, traditional facilities. The combination (Figure 4) also enables rapid implementation of end-to-end PI and continuous processes with compact perfusion-based bioreactors, flexible seed trains, and matching PI-based downstream technologies. Those come with additional benefits — for example, in regional manufacturing.

Rapid implementation and care-free commissioning result when manufacturers use a preengineered, end-to-end process matching the needs of a typical molecule (e.g., mAb) as a starting point. That substantially reduces custom process-engineering timelines by providing a fit-for-purpose standard process and automation solutions — which is instrumental for accelerating and scaling PI and continuous upstream and downstream platforms. One example of a preengineered PI process is the Sartorius ProcessGo manufacturing and advanced-control platform, which integrates easily within POD cleanrooms to enable state-of-the-art cleanroom conditions, centralized cleanroom and process monitoring with real-time analytics, and seamless orchestration of PI processes across modular equipment and POD units.

"One of the key benefits is rapid deployment," said Monge. "The beauty is that you're separating the engineering schedules of the cleanroom from the process so you can do everything in parallel, which greatly reduces the timeline. You accelerate time to clinic, which is the goal."

**Figure 4:** Concept of Sartorius ProcessGo manufacturing platforms and G-CON POD cleanrooms




Powers agreed. "Traditional construction always happens consecutively. The parallel approach really allows us to compress the schedules." In addition, companies leveraging POD systems experience enhanced efficiency with access to direct collaboration. "In traditional models, there's always an intermediary, someone who translates a process into cleanroom requirements. It works much better when we can work directly with process engineers."

## Upstream Innovations: Scaling Smarter and Faster

From scale-down models to PAT-enabled perfusion, upstream platforms are providing the PD speed, productivity, advanced control, and connectivity needed to support commercial-scale intensified manufacturing. As intensification is integrated across the industry, upstream PD and scale-up are transforming into a high-speed operation. No longer limited to use of time-consuming, largely manual benchtop processes with basic inline sensors, biomanufacturers need fully automated upstream platforms that are responsive and precise. That requires access to real-time in-, at-, or on-line sensor data as well as advanced model-based process control and robust model-based scale-up strategies, from PD to commercial scale.

At the Sartorius PI Forum, several upstream-track sessions emphasized the intersection of PI with high-throughput PD tools and PAT. Upstream intensification has led to faster cell growth, higher densities, and highly increased volumetric bioreactor outputs. Dynamic/continuous perfusion with continuous product outflow from a bioreactor increases demand for additional layers of visibility and control. For biomanufacturers, noninvasive and multiparameter sensors such as Raman spectroscopy

— along with others such as capacitance sensors for real-time critical process parameter (CPP) or critical quality attribute (CQA) monitoring — are becoming essential tools for derisking complex processes.

**Kate Harvey (AstraZeneca)** gave a strong example of a successful upstream transformation when she shared results from converting a high-volume, fed-batch mAb process to an integrated, dynamic, continuous-manufacturing format developed at AstraZeneca (Figure 5). Her team wanted to reduce CoG while maintaining product quality during scale-up, and intensification delivered on both fronts.

The team performed a two-week dynamic-perfusion culture and used direct capture to harvest product from day zero during the growth phase rather than only during the high–cell-density steady-state phase. Using cell bleeding, they kept cell density within 100–120 million cells/mL. Although the approach led to some changes in product quality during the run, AstraZeneca achieved a 6.3× improvement in space-time yield while keeping all CQAs within acceptable ranges (similar to the fed-batch reference process).

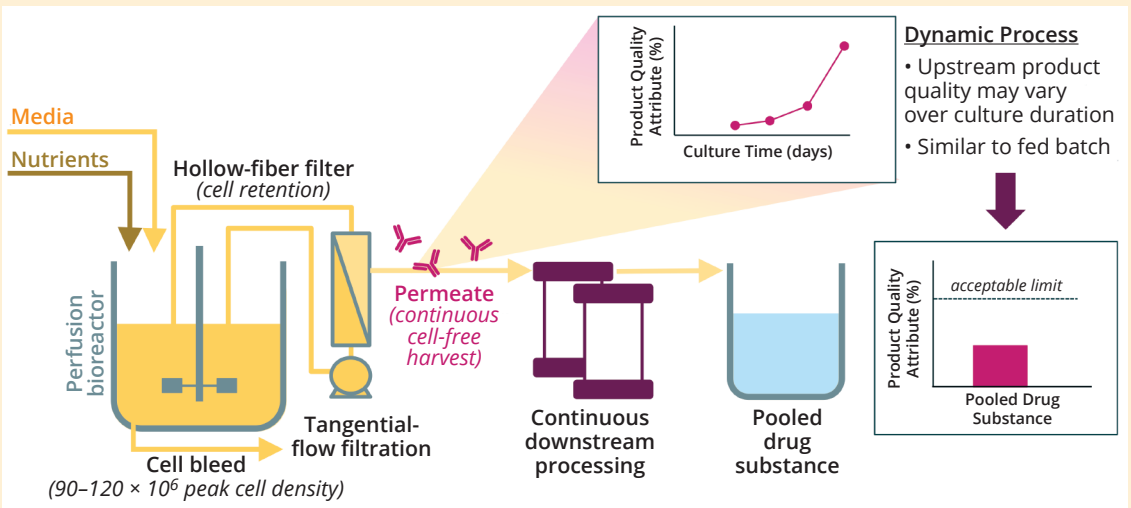
"Our CoG was reduced by 64.4% compared with the fed-batch process, which was very exciting," Harvey said. The data also revealed consistent performance from small to large scale (250 mL to 230 L), demonstrating the scalability of the platform as well as its potential to be applied across other commercial products.

**Andrew Brown (Lonza)** focused on the way his company has enhanced its global single-use and large-scale (up to 20 kL) stainless-steel commercial-manufacturing facility's throughput with the rollout of $N - 1$ perfusion, using PAT tools to optimize that step for improved outputs in fed-batch manufacturing. Brown acknowledged that today's industry feels comfortable with traditional fed-batch approaches, but he emphasized that intensifying the $N - 1$ step can reduce main bioreactor culture duration, allowing for more runs per facility each year. That can raise overall productivity by 80%, with titers >10.5 g/L, representing a CoG reduction of 30–40% at 1,000-L single-use scale with further potential at larger scale. Lonza considered fully automated Raman-based feed-rate control to be a key technology for enabling robust PI implementation.

One key takeaway, Brown said, was that customers increasingly are considering PI even for commercially approved processes — not just to enhance time to clinic, but also to improve CoG during scale-up. He also shared that Lonza integrated advanced sensors and Raman spectroscopy into its platform, underscoring how PAT is providing proactive control in development and manufacturing.

**Stephen Hsu (GenVivo)** introduced a new upstream strategy for enveloped retrovirus production that leveraged low-shear rocking-motion bioreactors with integrated perfusion membranes or stirred-tank bioreactors with large-pore (5-µm) TFF

**Figure 5:** Schematic depicts AstraZeneca's integrated dynamic bioprocess (IDB), which includes a dynamic high–cell-density perfusion bioreactor with tangential-flow filtration (TFF) cell retention, direct capture of a monoclonal antibody (mAb) product from the permeate stream by continuous capture, and further continuous downstream processing into a single batch for each bioreactor. The process also uses a cell bleed to maintain a target peak cell density. The upstream process is dynamic, so product quality can vary over the culture duration similar to how it can vary in a traditional fed-batch.




Stephen Hsu (GenVivo)

filters. This is a growing area of interest for companies involved in viral vector manufacturing. The GenVivo approach aligns with broader industry trends of boosting productivity, simplifying process design, improving scalability, and reducing footprint.

Throughout the forum, **experts from Sartorius** held multiple sessions featuring live demonstrations of powerful upstream technologies such as Ambr 250HT, Ambr 15, and Biostat STR systems combined with alternating tangential flow (Xcell ATF).

**Ambr 250 and 15 scalable, automated bioreactors** support early screening, design-of-experiments (DoE) optimization, and predictive modeling. The recently launched Ambr 250 HT Generation 2 system features advanced sensors for measuring parameters such as capacitance for accurate perfusion flow control during the growth phase and accurate cell-bleeding control during production. Such features enable high-throughput, intensified upstream processing, especially when strategies require rapid iteration and accurate scale-up.

The **Biostat STR stirred-tank reactor** integrates ATF cell retention to drive robust, high-density perfusion processes. Demonstrations emphasized real-time digital integration, showing how inline analytics and Biobrain Supervise control capabilities enable operators to automate management of cell density, nutrient feed, and waste removal. Such control helps to unlock the full potential of continuous upstream processing.

Across all presentations on upstream processing, one key theme emerged: Automation is critical to accessing the benefits of intensification. As processing speeds increase, manual operation can become a bottleneck quickly. Real-time capture, model-based control, and closed-loop automation are no longer tools for optimization, but rather necessities for scalable intensification.

## Downstream Processing: From Bottleneck to Competitive Advantage

Innovations in PAT, membrane chromatography, modular skid platforms, and extractables and leachables (E&Ls) approaches are reinventing

Ambr 250 automated bioreactor

Ashley Reeder (Merck & Co.)

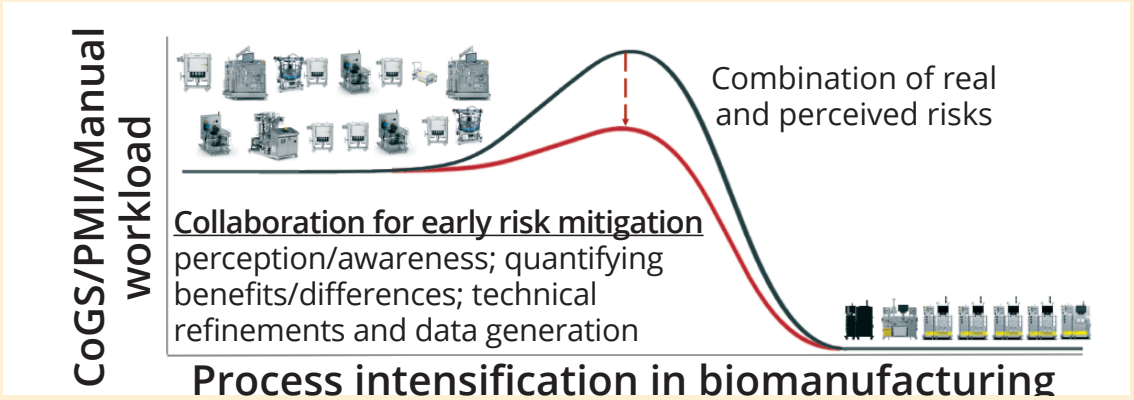
downstream processing into a driving force for efficiency. In the past, separation and purification constituted a growing bottleneck that lagged behind upstream innovations — but through PI technologies, that gap is narrowing fast.

As **Ashley Reeder (Merck & Co.)** emphasized in her presentation, "Most development has focused on upstream, but new tools are enhancing how we evaluate downstream steps, which are critical to both process understanding and overall efficiency." PAT is one area where she's seen strong gains.

Reeder's team leveraged biolayer interferometry (BLI) and localized surface plasmon resonance (SPR) to detect breakthrough events in real time, enabling her team to prevent column overloading, automate switch triggers, and ensure maximum resin use. In collaboration with Sartorius, Merck & Co. piloted a FlowBLI prototype that captures real-time analyte shifts in just 60 seconds with a sample volume of only 300 µL.

"With an upstream Raman monitor already in place, we were able to pivot quickly to measuring perfusate concentration," Reeder explained.

**Figure 6:** Lowering the implementation energy for continuous downstream processing; PMI = process mass intensity.; CoGS = cost of goods sold, PMI = process mass intensity




"Coupling this with BLI and localized SPR in capture chromatography is helping us move toward a full picture of performance."

According to **Chad Varner (Sanofi),** the future of intensified downstream processing lies in modularity, flexibility, and real-world implementation. His team's collaboration with Sartorius using the Pionic platform already is demonstrating significant results (Figure 6). "We don't need a skid that does everything," he said. "We need targeted entry points that lower the energy barrier for implementation." Instead of overdesigned, fixed systems, the Pionic platform provides modular configurations that adapt to site constraints for solving specific pain points.

Pilot-scale success at Sanofi leveraged a prototype skid capable of executing four operations: continuous chromatography, continuous viral inactivation, normal-flow filtration, and single-pass tangential flow filtration (SPTFF). Those evolved into a compact, interconnected set of skids with modular process automation. Varner emphasized that his team used real process conditions, not ideal simulations, to engineer and validate the system's performance.

"I believe the Pionic platform is a commercial solution that can be applied across the industry for


intensifying downstream operations," he said. "Through our collaboration with Sartorius, it was developed to be a robust solution that can be trusted and implemented in a flexible way to meet customer needs."

**David Brown (KBI Biopharma)** demonstrated how membrane-based capture and polishing steps are another major area of innovation streamlining downstream processing (Figure 7). In his talk, Brown discussed how rapid-cycling membrane chromatography (RCMC) is replacing traditional protein A resins to accelerate results without sacrificing quality in early phase mAb manufacturing.

"Being able to complete a full lifetime study in just two days amazed me," Brown said. "We

**Figure 7:** Cost savings with implementation of membrane-based chromatography process

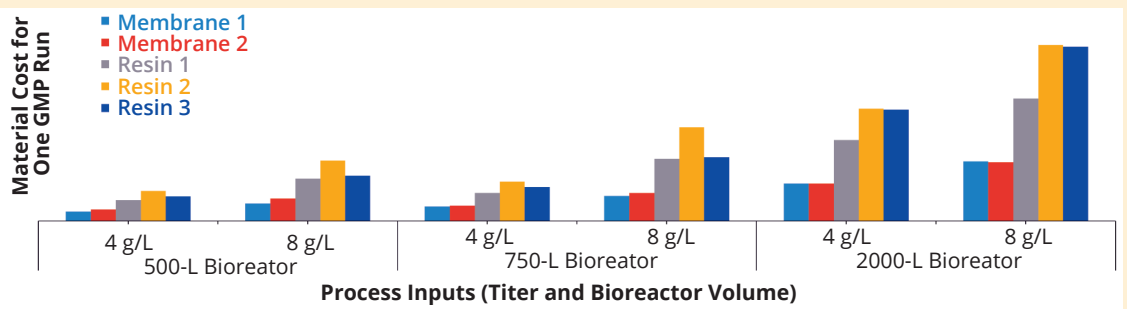
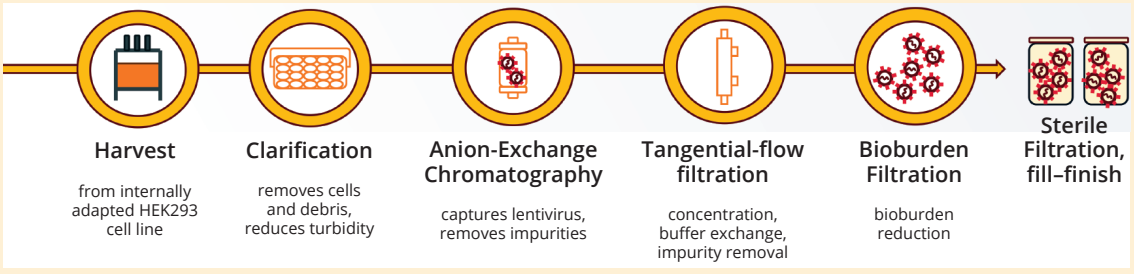


**Figure 8:** Overview of SK pharmteco's lentivirus suspension DSP platform






maintained over 97% yield through 150 cycles with no increase in pressure or fouling."

The benefits of RCMC extend not only to performance, but also cost. With no capital expenditure or facility modifications required, membranes reduce CoG for clinical batches, eliminate storage and contamination concerns, and enable quick adoption. "The cost savings were substantial," noted Brown.

**Jae Hwang (SK pharmteco)** shared a similar success story of intensification, but in lentiviral vector manufacturing, for which downstream processing is slow and yields are extremely low. "In the lentiviral world, we expect 10% recovery," Hwang said. "By adopting Sartobind Q membranes, we achieved fourfold higher yield and functional titers up to 110% within 20 minutes" (Figure 8).

His team optimized residence time to under six seconds, achieving up to 77% recovery at 50-L scale with a process that cost under $20,000. "You get everything done in one hour, then go home and take a break," he said. "These results are not something you'll see in any lentiviral vector literature."

As processes become more intensified, concerns about extractables and leachables grow, especially for single-use systems that can remain in operation for weeks at a time. **Nelly Montenay (Sartorius)** addressed such questions head-on with a dynamic modeling approach that estimates E&L exposure in continuous bioprocessing. Her work demonstrated how real-time migration equations accurately predict exposure curves, and she showed that dynamic steady-state conditions result in lower risk than static models. "Our calculated process-equipment–related leachables (PERL) curves matched the experimental data perfectly," she explained (Figure 9). "We can now assess long-term E&L risks for up to 60 days of continuous processing and show that exposure stays well below thresholds."

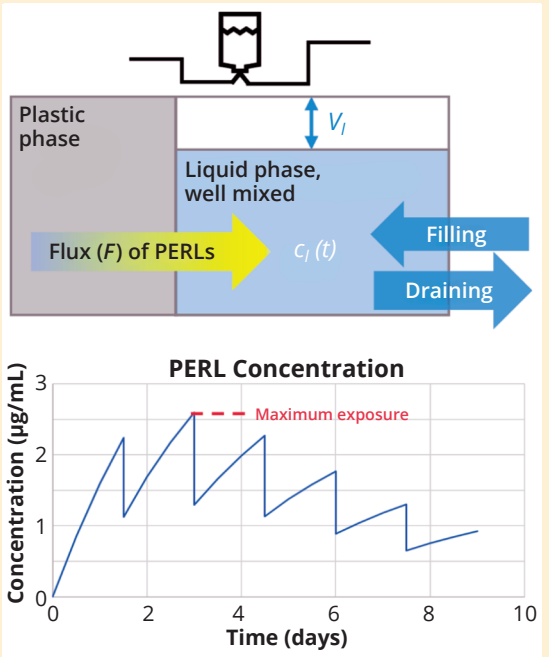
## Digital and Automated Solutions: Enabling the Next Phase of PI

Real-time insight, intelligent control, and seamless system integration are redefining biomanufacturing. As emphasized by presenters in the upstream and downstream tracks, digital and automated solutions have become critical to PI integration.

In a Deloitte survey shared by **Steve Miller (Sartorius),** 80% of pharmaceutical executives agreed that digitalization is essential to stay competitive (**2**). But digital transformation isn't just about software upgrades; it's a fundamentally different way of working that is predictive, interconnected, and resilient.

One of the most discussed topics at the Sartorius PI Forum was *interoperability*: the capability for diverse systems, platforms, and equipment to speak the same language. During his presentation, Miller asked attendees how confident they were in their ability to integrate across vendors. The results reflected how the industry still is working toward digital cohesion. "Today, fewer than 5% of sites operate at level-two digital maturity," he said. "But

**Figure 9:** Process-equipment–related leachables (PERLs) concentration in a surge tank follows the filling–draining scenario so that maximum PERL concentration can be calculated and the wash-out effect dominates; $V_L$ = liquid volume, $c_L$ = concentration, $t$ = temperature.





interoperability is no longer optional; it's the foundation for an autonomous facility."

Today, success requires proactive alignment across vendors, process engineers, and information technology (IT) groups. "We need to work together on standards," Miller emphasized, highlighting Discover Negotiate Pair (DNP) technology being developed through the National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL). "That's how we build fully integrated and intensified processes that are scalable, flexible, and future proof."

**Courtney Hazelton-Harrington (Lonza)** shared a strong example of how a digital vision translates to action. Her team implemented inline Raman spectroscopy with single-use flow cells to monitor protein and excipient concentrations during ultrafiltration and diafiltration in real time.

Traditionally, UF/DF steps include sample collection, laboratory analysis, and hours of waiting while material is held in tanks. A new system enables Lonza to identify and correct deviations in real time, enabling operators to act immediately and maintain product quality while allowing product to flow downstream.

"The biggest advantage is to avoid having product sitting still," she said. "If there's a deviation, we can address it in real time instead of being forced to wait for lab results." Combining data analytics and real-time sensing capabilities with the ability to generalize models across products demonstrates the kind of ready-to-use solutions that are needed to ensure quality and sustainable PI.

**Peter Graham (BioMarin)** presented a different challenge. What happens after capturing data? For perfusion processes that run up to 90 days, data volumes can be massive. Without structure and contextualization, noise can dominate. To change that, Graham's team uses multivariate data analysis to extract actionable insights and build fit-for-purpose models.

"You have to know what you're trying to achieve and who the model is for," he advised. "You can't just throw everything in, shake the box, and hope for a valuable outcome." Graham stressed the importance of collaboration. "The only way we can effectively use data analytics is by breaking down silos and getting data scientists and end users to work together." That point was echoed repeatedly in discussions after the session.

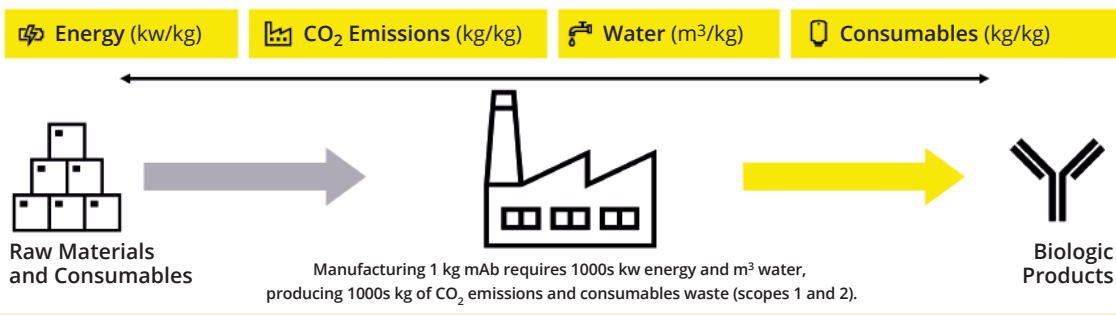
**Chris McCready (Sartorius)** expanded on that with a presentation on the Cell Insights by Umetrics Studio hybrid modeling tool. It was designed to reduce the number of scaling runs by predicting how a small-scale process (250 mL) will behave at 2,000 L.

"Usually, we make decisions before we have data," he said. "Artificial intelligence flips that. Instead, we need data first, and then we build the model." McCready highlighted that scientists tend to overestimate the volume of the data required for that purpose. Using an iterative approach with only a small number of batches is typically still very insightful, he said.

McCready's approach uses engineering and artificial intelligence to build supervisory systems for both upstream and downstream processing. That establishes a foundation for rapid, smart process control — and a future when automation and intensification work hand in hand.



**Figure 10:** Environmental impacts of biomanufacturing




## Sustainability: A Shared Imperative and Collaborative Effort

From materials to process modeling and recycling opportunities, the road to sustainable biomanufacturing is being paved through collaboration. Sustainability was another central theme throughout the Sartorius PI Forum. Across multiple presentations, speakers shared concrete tools, data-driven models, and pilot projects meant to reduce the environmental impact of biologics manufacturing. The clearest takeaway was the idea that no single player or technology can solve this challenge alone.

**Pierre Moulinié (Covestro)** opened the track with a materials-focused perspective. His company is committed to sustainability, focusing on climate neutrality and circularity. This effort is driven by integrating ISCC PLUS-certified biocircular polycarbonate into their products. Covestro also advocates for enhanced designed-for-recycling products that could help make future bioprocessing components more compatible with circular-economy goals.

**Behnam Partopour (Sartorius)** presented on bioprocess simulations using the BioSolve tool, which demonstrated that switching from fed-batch to continuous processing significantly reduces processing area, plastic waste, energy consumption, and overall operating costs. The results clarify future pathways to further reducing environmental impacts by moving away from high-volume buffer preparation toward more efficient inline procedures (Figure 10).

In a related talk, **Priyanka Gupta (Sartorius)** shared early outcomes from the NIIMBL sustainability workstream, by which a lifecycle assessment tool was developed to evaluate environmental impacts across the mAb production lifecycle. Preliminary models indicate that continuous processes offer notable carbon reductions driven largely by lowered energy consumption (the primary cause of carbon emissions) with relatively small facilities. However, Gupta noted in her presentation that the tool was based on very basic process models that were developed to build it. The NIIMBL workstream now is incorporating realistic manufacturing processes and facilities to further fine-tune that model.

Data analyst **Bob Davis (Sartorius)** presented on the data-driven aspects of sustainability, showing how software tools such as SIMCA software can



support it across scopes one (direct energy), two (purchased power), and three (indirect emissions). By improving process efficiency, the software delivers dual benefits of lower environmental impact and reduced operational costs. As Davis emphasized, *operational sustainability* doesn't have to mean *operational compromise*.

**Eric Sorge (Merck & Co.)** presented one of the most intriguing initiatives: his company's Circular Ambr Project collaboration with Sartorius and Covestro. Together, the three have explored recovering plastic from used Ambr vessels for reuse in the molding of new Ambr reactors. Laboratory-scale cell-culture tests were performed using both traditional mAb- and nontraditional bsAb-producing cell lines in reactors made from either virgin or recycled polycarbonate. Process performance was consistent across reactor types.

Sorting used vessels would be a critical success factor for recycled plastic quality, and the relatively small volume of plastic recovered so far posed a practical challenge. A pilot-scale trial will help the companies assess feasibility at industry scale, but the project sets a clear precedent for what collaborative circularity could look like in practice.

Altogether, such efforts demonstrate that sustainability in biomanufacturing is measurable, practical, and increasingly collaborative. From materials sourcing and energy modeling to analytics, process design, and recycling, progress is being made across the industry through collaboration. No solution exists in a silo.


## Intensifying New Modalities To Broaden Their Impact

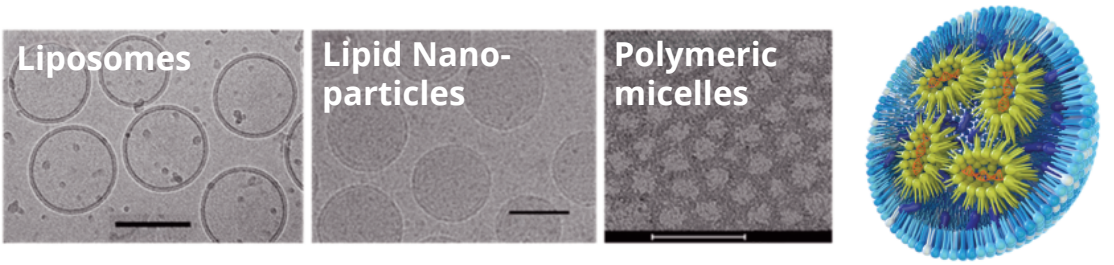
From mRNA and lipid nanoparticles (LNPs) to chimeric antigen receptor (CAR) T cells, PI is enabling the future of advanced therapeutics. The biopharmaceutical industry is expanding, and traditional fed-batch culture methods are proving to be insufficient for meeting the demands of scalable, cost-effective, and quality-driven biomanufacturing. At the Sartorius PI Forum, multiple speakers tackled that challenge with different innovations.

**Antonio Costa (DIANT Pharma)** is reimagining mRNA–LNP manufacturing for scale and control using continuous nanoparticle manufacturing. He highlighted the inefficiencies of current batch approaches: large facility footprints, long timelines, and limited control over particle characteristics such as size and polydispersity. A lack of inline process analytics can delay lot release and hinder quality assurance.

In response, his company developed a continuous platform integrating PAT, single-use components, and modular flow systems for scalability from research and development (R&D) to commercial manufacturing. The DIANT LARU Discovery system combines nanoparticle formulation and SPTFF into one streamlined tool (Figure 11). Pilot and clinical-scale skids were built using Sartorius technologies including Sartocon cassettes and Flexsafe bags, then validated in a case study producing mRNA–LNPs with >95% encapsulation efficiency and in vivo functionality. In collaboration with Sartorius, DIANT Pharma is showcasing a clear path for intensifying nanoparticle production and paving the way toward consistent, scalable vaccines and RNA therapeutics.

**Pierre Springuel (University College London)** presented an equally ambitious transformation for

**Figure 11:** Continuous manufacturing approach of nanoparticle therapeutics and vaccines




autologous and allogeneic CAR-T manufacturing. Today's CAR-T processes often are constrained by patient variability, small-scale manual workflows, and prohibitively high costs. Springuel's work overcomes those challenges by leveraging stirred-tank bioreactors and intensification strategies including perfusion and automation.

Using an Ambr 250 HT system from Sartorius, he developed a perfusion-based protocol that reduced the time to dose by >50% for autologous therapies and increased cell yield 4.5-fold for allogeneics (Figure 12). He identified important process parameters including perfusion start time and rate as key variables driving both productivity and efficiency. Springuel successfully scaled the process to a Univessel system from Sartorius and produced >100 CAR-T doses per batch while maintaining consistent phenotype and functionality. Downstream, a Ksep 400 system enabled fully automated, low-shear harvest and buffer exchange, preserving product quality with >90% recovery. Springuel's journey illustrates how intensified platforms enable the scalability, monitoring, and automation needed to help CAR-T therapies become an accessible standard of care.



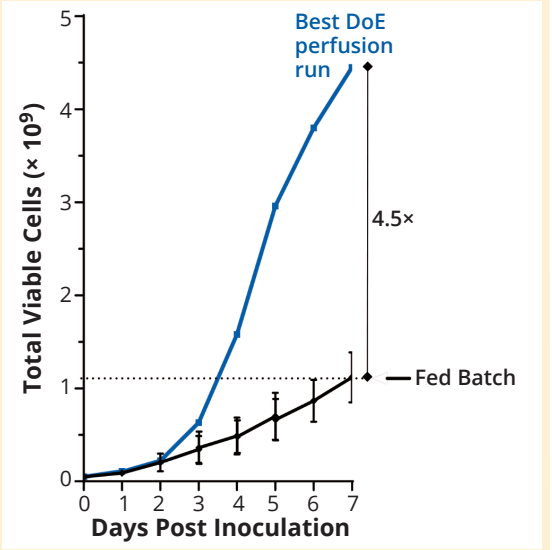
## Sartorius Center for Bioprocess Innovation: Enabling the Future of PI

Located in Marlborough, MA, the newly opened Sartorius Center for Bioprocess Innovation is hosting and developing tools for next-generation bioprocessing. Another common theme at the PI Forum was the company's continued investment in implementation-ready technologies for intensified biomanufacturing. The 12,000-ft$^2$ facility is home to new solutions for RNA and LNP manufacturing, viral-vector production, and PI across advanced modalities.

**Sunandan Saha (Sartorius)** introduced new PD services for advanced therapies available through the center. Designed for early phase programs involving stem cells, immune cells, extracellular vesicles, viral vectors, or RNA–LNP therapeutics, the center combines state-of-the-art tools with hands-on collaboration. Workflows span from clone and media screening in Ambr systems to perfusion process optimization — all the way through formulation, cryopreservation, and clinical production. The result is a practical, modular environment where customers can explore accelerated and intensified ATMP workflows using real-world constraints, fast-tracking PD and smoothing transitions during technology transfer.

**Samin Akbari (Sartorius)** described miniature solutions, notably the comprehensive Pipette-to-Process Toolbox offering now accessible in Marlborough for scalable RNA and LNP manufacturing. Designed to address a critical bottleneck for developers, the toolkit includes high-throughput screening, hydrodynamic chip-based mixers, and analytics for load, size, and stability.

**Figure 12:** Clinical relevance of perfusion-driven process intensification




The Pionic Spin platform also was introduced in a series of demonstrations at the Sartorius PI Forum. Chad Varner (Sanofi) reported on his team's success using the platform, which Sartorius designed for continuous low-pH viral inactivation. The system integrates homogenization, acidification, incubation, and neutralization into a modular, single-use platform offering key advantages such as a recirculation mixing loop, scalable performance, and automation-ready operation. The system design is aligned with real-world downstream processing workflows, enabling consistent residence-time distribution and easy readjustment in response to process deviations without product loss.

That is another clear example of how Sartorius is integrating automation, modularity, and continuous processing principles into smoothly implementable hardware. Whether accelerating early phase RNA vaccines, refining viral-vector platforms, or enabling continuous virus inactivation, the tools showcased at the Sartorius PI Forum exemplify how the company is driving PI across applications and modalities.

## Addressing Today's Challenges: Lessons for the Road Ahead

How can we apply lessons learned by early adopters to streamline today's PI challenges? As PI evolves from a distant vision to standard practice, one message from this year's Sartorius PI Forum was clear: The remaining barriers are no longer technical, but rather strategic and organizational.

Steve Miller (Sartorius)

"You should try and do things without waiting to be perfect," urged Kate Harvey (AstraZeneca) in speaking to the hesitation many people feel when considering transition to a new process.

For those just getting started, Joseph Shultz (Ottimo Pharma) offered advice for getting the members of a team onboard: "Start with the problem you want to solve," he said. "The key isn't only the science or the technology; it's getting your company and management to integrate PI into your pipeline and release the capital needed. You need a problem worth solving — and to leverage the experience of those who integrated it early. We all want to see this happen. It's been 15–20 years since we started this journey, and we seem to be stuck just before the finish line when it comes to implementing."

Early PI adopters have learned this through experience, and their message to the rest of the industry is to start small, but start now. In moving projects rapidly into clinical testing, reducing footprint and cost, or enabling sustainability, the benefits are already being felt — and delaying intensification can hamper competitiveness for manufacturers. But adoption requires organizational buy-in, especially in early development phases when speed and risk-avoidance dominate decision-making.

"People are very comfortable with the traditional fed-batch approach," said Andrew Brown (Lonza). "Transitioning takes convincing. At early stages, decision makers want speed and low risk. Productivity and CoG come into play only once [a product] succeeds in clinic."

Data, precedent, and collaboration matter. Sharing outcomes from pilot projects — especially those that show reductions in facility costs, environmental impact, or time to market — can help teams make the case internally. By combining the experience of others with existing tools and expertise, you can start making the case for transition at your company, and you don't need to go at it alone.

As Steve Miller (Sartorius) put it, "Do you want to stick to what's possible today, or do you want to go beyond that? The goal isn't just digitalization — it's a fully autonomous plant."

Ultimately, the most powerful insight from the Sartorius PI Forum could be that the industry is no longer proving whether PI can work. Companies are learning how to make it work more efficiently, faster, and at scale. And today, with open collaboration and shared experience, the finish line is finally within reach.


## Acknowledgment

Sartorius thanks all the expert speakers for their great insights.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## Further Reading


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