Continuous Bioprocessing

Reducing the Cost and Environmental Impact of Monoclonal Antibody Manufacturing

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Monoclonal antibodies (mAbs) are valuable therapeutics that address a wide array of diseases and global healthcare needs. As clinical and commercial demand grows, mAb manufacturers must ensure robust, cost-effective, and sustainable production. Traditionally, they have relied heavily on batch-processing methods. Now, high costs of goods (CoG) and increasing pressure to reduce environmental impact present significant barriers to universal access and equitable distribution of these therapies. Here, we examine the potential for end-to-end continuous bioprocessing as a key innovation to address those challenges.

Sartorius Biostat STR with alternating tagential-flow (ATF) filtration system

Purpose and Scope

As detailed elsewhere, we performed a rigorous economic-efficiency assessment and sustainability evaluation comparing an optimized, best-in-class fed-batch (IO-FB) process with end-to-end continuous bioprocessing for mAb production (**1**). We focused particularly on multiproduct facilities handling a mix of clinical and commercial supply demands. The results quantified economic and environmental impacts while demonstrating scalability, operational adaptability, and flexibility in responding to demand fluctuations.

Our analysis leveraged advanced bioprocessing concepts such as perfusion bioreactors, multicolumn chromatography, and automation. Single-use (SU) technologies are prominent in both IO-FB and continuous scenarios, through which we evaluated both sustainability metrics and mixed production lines. Insight from those results can help to inform strategic decision-making and accelerate adoption of continuous processes.

Methodology Overview

Incorporating detailed process descriptions, productivity metrics, yield profiles, material bills, facility details, capital assumptions, and cost data, we used BioSolve Software (version 9) for deterministic cost analysis. Sustainability calculations were based on a greenfield facility in the northeastern United States. CO_2 emissions were estimated based on energy consumption — utilities, equipment; heating, ventilation and air conditioning (HVAC); and lighting — and plastic waste from SU consumables. To assess the robustness of each platform, we ran an uncertainty analysis using Monte Carlo simulations (100,000 scenarios) based on a mixed normal-distribution model for demand fluctuations, mirroring a previously published profile (**2**).

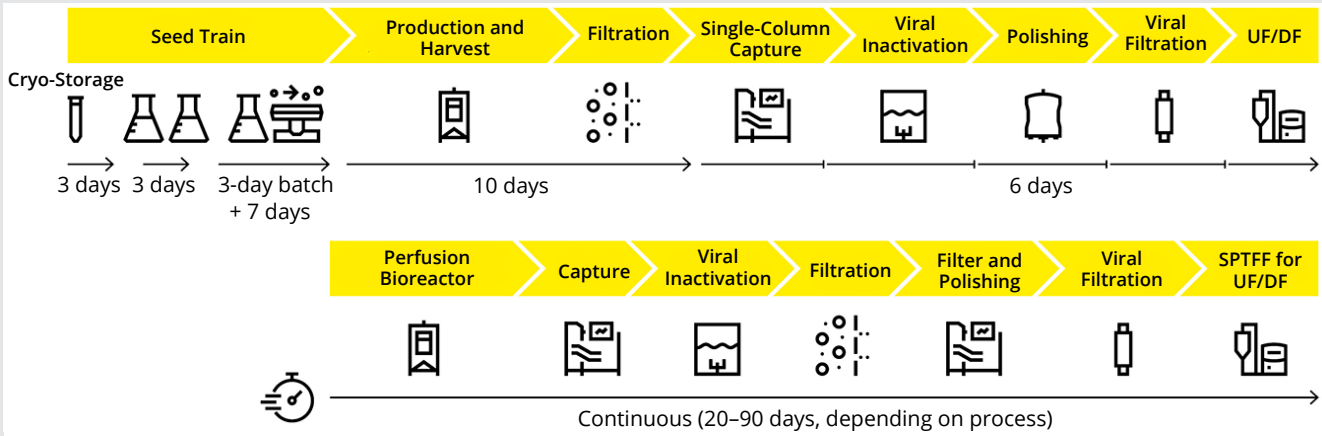
The analysis compared IO-FB and continuous production modes in mixed-product facilities across different production ranges (clinical to commercial) and optimized facility configurations at 90% use rates. Process-only costs were analyzed before incorporating facility-associated costs for a multiproduct facility case.

Key Findings

Economic Advantages: Our comparison between IO-FB and end-to-end continuous processing revealed clear economic advantages for continuous production in multiproduct facilities. On average, the total annual cost for IO-FB was 12–23% higher than for continuous processing. Operational expenses (OpEx) also were reduced by about 8% with continuous processing, largely due to the greater number of batches and higher consumables turnover associated with IO-FB.

Capital expenditure (CapEx) further underscores the economic benefits of continuous processing. Upfront

Figure 1: Intensified optimized fed-batch (IO-FB) and continuous process descriptions



IO-FB process with 15 g/L and 70% DSP recovery (TOP); continuous process with 3–5 g/L/day and 75% DSP recovery (BOTTOM)

DF = diafiltration; SPTFF = single-pass tangential-flow filtration; UF = ultrafiltration

investment for the IO-FB process was 15–38% higher than for the continuous process, driven primarily by equipment costs (9–28% more) and increased process area requirements.

The greatest savings potential lies in CoG, with end-to-end continuous processing reducing costs by up to 23% in a multiproduct facility. Although batch processes can be more cost-effective at very low production volumes (<20 kg/year) due to lower initial capital investment, continuous processes quickly become more economical as annual throughput increases. At production scales >150 kg/year — and especially beyond 350 kg/year — and for extended run durations (>30 days) at high productivity (5 g/L/day), continuous processing delivers substantial cost advantages.

Sustainability Gains: Continuous processing also offers significant sustainability gains over IO-FB. It uses 57% less plastic, with smaller and fewer bags and less frequent consumables changes over longer runs. The continuous process also generates 54% lower CO_2 emissions, which is primarily the result of its smaller equipment size and facility footprint requiring less energy for the process and for HVAC.

Flexibility and Robustness Under Uncertainty: Continuous processing is more flexible than IO-FB, which is especially important with fluctuating market demands. End-to-end continuous manufacturing supports adjustable run durations for fixed bioreactor volumes, enabling facilities to adapt capacity easily without frequent turnover.

In simulating 100,000 different demand scenarios, our uncertainty analysis revealed that the continuous process becomes even more cost-effective when demand deviates from what is planned. Whereas deterministic modeling under optimal use rates predicted cost savings of US$29 million annually, the uncertainty analysis revealed that those savings could climb to US$50 million when demand deviates from the plan. That highlights the increased robustness of a continuous platform under market volatility.

Operational Benefits: In addition to the economic, sustainability, and flexibility advantages, continuous bioprocessing delivers several important operational benefits. It provides for a more homogeneous output and more consistent product quality than IO-FB can, minimizing the variability often introduced by discrete batch operations.

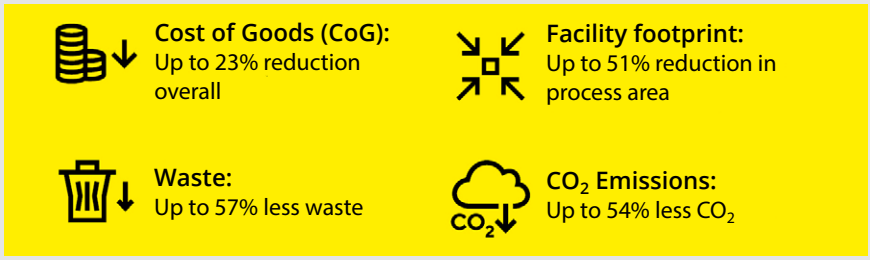
Real-time monitoring and control also support early defect detection in continuous manufacturing, allowing for corrective actions to be taken during production. By contrast, defects in batch processes often are found only after an entire batch is complete, leading to material losses and delays. Finally, because continuous processes require more automation, they are less reliant on operators than batch processes are, thus reducing the potential for human error.

Implementation Challenges: Despite the advantages, industry

Key Assumptions of the Study

- Single-use (SU) intensified fed-batch processes (15 g/L titer, 15 days); SU end-to-end continuous processing (3–5 g/L/day productivity, 30- to 90-day runs)
- Multiproduct facilities covering specified clinical (3–50 kg) and commercial (250–750 kg) throughput ranges
- Facility and labor costs included in a deterministic mixed-product facility case study (90% use for both platforms)
- Total annual cost calculation with a 15% capital charge and an eight-year overall facility life span for both platforms
- Sustainability calculations based on publicly available US energy-generation data for CO_2 equivalents
- Uncertainty analysis based on a specific demand-fluctuation model with defined probabilities for matching projection (70%), with 50% increase (15%), and 20% reduction (15%) approximated by a mixed normal distribution
- Input values (e.g., titers and yields) based on highly optimized processes supported by internal data, unless cited otherwise
- Detailed, proprietary process descriptions (flow rates, configurations, and price) not included

Figure 2: Benefits of moving from fed batch to continuous processing



adoption of end-to-end continuous processing has been slow. The two main obstacles involve regulatory compliance and finances.

Compliance Caution: Biomanufacturers often hesitate to adopt emerging technologies because the biopharmaceutical industry is highly regulated. Implementing new platforms can require changes to validated processes and regulatory filings, creating implementation hurdles even when the long-term benefits are clear.

Capital Investment: Although our study shows that the total CapEx is lower for continuous facilities than for IO-FB, implementing new technologies does require significant upfront capital investment. That can be difficult to justify to partners and shareholders, particularly in the absence of immediate returns or when infrastructure is already in place.

A Clear Choice

Our findings clearly demonstrate that implementing end-to-end continuous bioprocessing offers substantial advantages over best-in-class IO-FB methods for mAb manufacturing, particularly in multiproduct facilities. The economic benefits (significant savings in CapEx, OpEx, CoG, and total annual costs) and dramatic improvements in environmental metrics (reduced plastic waste and CO_2 emissions) align strongly with industry goals for cost reduction, sustainability, and equitable therapeutic access.

Furthermore, the inherent flexibility of continuous processing improves process robustness against uncertainties in global supply chains and demand fluctuations. Although challenges remain, the quantifiable benefits detailed in our study provide a strong, data-driven foundation for manufacturers and regulatory agencies to accelerate the transition toward continuous processing methodologies (**1**). It's time to intensify.

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Sartorius Corporate Research principal scientist ***Behnam Partopour*** *led the conceptualization, implementation, modeling, simulation, and original writing of the article. Sartorius sustainability marketing expert* ***Lara Cobacho Lluesma*** *contributed to the strategic framing of the article, with a focus on summarization and aligning the content with industry and sustainability trends. As head of advanced bioprocessing, Corporate Research, at Sartorius,* ***David Pollard*** *provided supervision and contributed to the article through conceptual input, critical review, and editorial guidance. All authors reviewed, edited, and approved the final manuscript. See the Sartorius website at https://www.sartorius.com/process-intensification for more information.*