Single-Use Technologies and Sustainability-by-Design in Biopharma Production

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Keywords: biopharmaceutical manufacturing, life cycle assessment, bioprocess intensification, process analytical technology, circularity

Introduction

Single-use technologies (SUT) have emerged as a flexible and cost-efficient alternative to traditional stainless steel systems in biopharmaceutical manufacturing. They offer faster changeovers, reduced contamination risks, and lower water, chemical, and energy consumption, leading to shorter setup times and reduced capital investments (Lalor et al., 2019; Pietrzykowski et al., 2013); however, these advantages come with environmental trade-offs, particularly relative to increased plastic waste, supply chain dependencies, and storage requirements for used components awaiting disposal under biosafety conditions (Ottinger et al., 2022; Whitford et al., 2021).

Climate change and environmental degradation are among the most pressing global challenges. The World Economic Forum (2025) lists steadily more extreme weather events, biodiversity loss, and disruption of good living conditions as top global risks in the coming decade. Although the healthcare sector itself contributes 4 – 5% to global greenhouse gas (GHG) emissions, many of these emissions are linked to supply chains (BioPhorum, 2023). The pharmaceutical industry has a disproportionately high environmental footprint, including CO_2 emissions, water and energy consumption, and plastic waste (Di Russo et al., 2023), with

significantly more emissions than the automotive industry in 2015 (49 vs. 31 Mt CO_2-eq emissions per million USD of revenues; Belkhir & Elmeligi, 2019, Jackson and Belkhir, 2018). The contribution of the total healthcare sector is naturally even more significant, contributing 6% or more to national GHG emissions in Europe and the US (Karliner et al, 2019, Bartolo et al., 2021). The impact of products on environmental pollution is often not included for most components, making the true effect difficult to assess. Furthermore, actions to reduce emissions are diverse and are impacted by national regulations, creating a lack of general strategies towards a substantial reduction in emissions (di Russo et al, 2023).

Within this broader environmental landscape, biopharmaceutical operations—in particular, the rise of SUT—introduce additional sustainability challenges. While focus is put on sterility and regulatory frameworks around product quality, biopharmaceutical manufacturing is inherently complex and resource-intensive, relying on energy- and water-demanding operations and generating significant amounts of process waste (Sarkis et al., 2025). The widespread adoption of SUT has improved operational flexibility and reduced cleaning-related downtime but has also raised concerns regarding increased plastic use and end-of-life (EoL) waste (Markarian, 2019; Frank, 2018). Although components such as connectors, tubing, and sensors are capable of withstanding multiple sterilization cycles, current consumption patterns show that these items are typically used for a single production batch and subsequently discarded (Ottinger et al., 2022). Additionally, 20 – 30% of single-use materials sold for biopharma production remain unused and are disposed of as waste, often due to overstocking, process safety margins, or changes in production scheduling, contributing significantly to the total plastic waste generated by biomanufacturing operations and underscoring the need for optimized procurement and waste management practices (Ottinger et al., 2022).

At the same time, updated net zero targets are pushing manufacturers to fundamentally rethink their supply chains and processes and to reduce their overall footprint across GHG emissions. Emissions can be categorized into three scopes as defined by the greenhouse gas protocol (GHG protocol 2025): Scope 1 includes direct emissions from company-owned/controlled sources, Scope 2 includes indirect emissions from purchased energy, and Scope 3 covers all other indirect emissions occuring in the value chain. While recent industrial initiatives have achieved moderate reductions of emissions categorized as Scope 1 and 2, Scope 3 emissions, which include raw material supply, remain the most difficult to

quantify and mitigate (Philpott, 2023; Fernandez & Perez, 2023; My Green Lab, 2024; GlobalData, 2024).

Sustainability implementation in bioproduction is further complicated by strict regulatory requirements, high quality standards, and the complexity of biological manufacturing systems (McGlinchey et al., 2025). Even small changes to materials or process configurations can trigger costly revalidations and extended approval timelines. Moreover, sustainable manufacturing requires the consideration of system-wide procedures across the full product lifecycle, including commercialization (Sarkis et al., 2025). Besides the quantification of upstream and downstream emissions, supply chain impacts, and the integration of process modeling to evaluate design and supply choices in silico before deployment at scale.

While industry commitments to sustainability-by-design (SbD) principles are generally increasing, progress remains uncertain across different regions and technologies (Pharma's Almanac, 2025). This review focuses on the recent reports and developments related to sustainability matters in biopharmaceutical production, and SbD in the context of single-use technologies (SUT). Technical and process-level advances that can support waste reduction and resource efficiency in bioproduction are highlighted:

- Process and equipment design choices and material selection under regulatory and quality constraints
- The role of life cycle assessment (LCA) in evaluating environmental impacts
- Process intensification strategies for improved efficiency
- Integration of process analytical technologies (PAT) and process models (e.g., for continuous processing)
- Potential for multi-use plastic options, waste reduction, and recycling.

Sustainability is a multidimensional concept encompassing technical and economic feasibility, environmental performance, and social aspects, as illustrated in Figure 1. This review aims to provide a structured overview of practical pathways to making single-use biomanufacturing more sustainable. The emphasis is on technical feasibility, process integration, and alignment between innovation, regulatory expectations, and environmental goals.

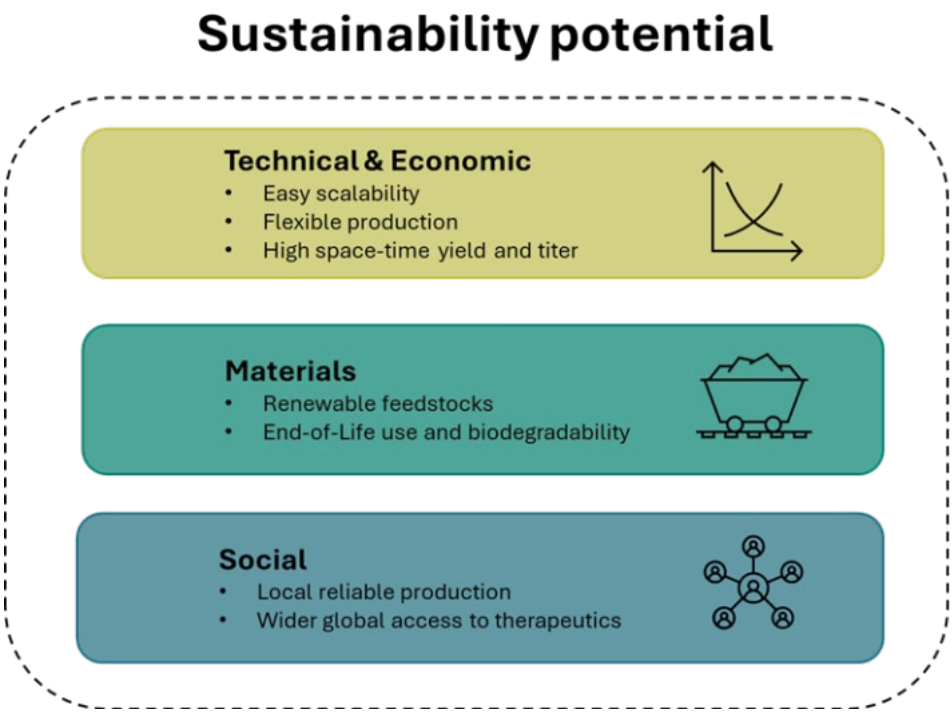


Figure 1. Categories of sustainability potential relevant to sustainability-by-design decisions in biopharmaceutical manufacturing.

References

Bartolo, N., Azzopardi, L. M., & Serracino-Inglott, A. (2021). *Pharmaceuticals and the environment*. Early Human Development, 155, 105218. https://doi.org/10.1016/j.earlhumdev.2020.105218

Belkhir, L., & Elmeligi, A. (2019). Carbon footprint of the global pharmaceutical industry and relative impact of its major players. *Journal of Cleaner Production, 214*, 185–194. https://doi.org/10.1016/j.jclepro.2018.11.204

BioPhorum. (2023). *Environmental Sustainability Roadmap*. https://www.biophorum.com/download/biophorum-environmental-sustainability-roadmap/

Calciolari, S., Cesarini, M., & Ruberti, M. (2024). Sustainability disclosure in the pharmaceutical and chemical industries: Results from bibliometric analysis and AI-based comparison of financial reports. *Journal of Cleaner Production, 447*, 141511. https://doi.org/10.1016/j.jclepro.2024.141511

Di Russo, M., Zjalic, D., Lombardi, G. S., Perilli, A., Congedo, G., Daugbjerg, S., & Cadeddu, C. (2023). Impact of the 50 biggest pharma companies: A review of environmental report aspiring to NetZero. *European Journal of Public Health. Impact of the 50 biggest pharma companies: a review of Environmental report aspiring to NetZero | European Journal of Public Health | Oxford Academic*

Etit, D., Meramo, S., Ögmundarson, Ó., Jensen, M. K., & Sukumara, S. (2024). Can biotechnology lead the way toward a sustainable pharmaceutical industry? *Current Opinion in Biotechnology, 85*, 103100. https://doi.org/10.1016/j.copbio.2024.103100

Fernandez, M., & Pérez, L. (2023, August 11). *Accelerating the transition to net zero in life sciences.* McKinsey & Company. https://www.mckinsey.com/industries/life-sciences/our-insights/accelerating-the-transition-to-net-zero-in-life-sciences

Frank, G. T. (2018). Transformation of biomanufacturing by single-use systems and technology. *Current opinion in chemical engineering*, *22*, 62-70. https://doi.org/10.1016/j.coche.2018.09.006

GlobalData. (2024, April). *Thematic Intelligence: Net Zero Strategies in the Pharmaceutical Sector – Reduction targets, data and strategies of 18 leading pharmaceutical companies* [Report]. https://www.globaldata.com/store/report/net-zero-strategies-in-pharmaceutical-theme-analysis/#:~:text=The%20%E2%80%9CNet%20Zero%20Strategies%20in%20The%20Pharmaceutical%20Sector%E2%80%9D,targets%20and%20performance%20of%2018%20leading%20pharmaceutical%20companies.

Greenhouse Gas Protocol. (n.d.). *The greenhouse gas protocol*. https://ghgprotocol.org/

Health Systems Task Force. (n.d.). *Sustainable Markets Initiative*. https://www.sustainable-markets.org/taskforces/health-systems-taskforce/

Jackson, J., & Belkhir, L. (2018). *Assigning firm-level greenhouse gas emission reductions based on national goals: Mathematical model and empirical evidence*. Journal of Cleaner Production, 170, 76–84. https://doi.org/10.1016/j.jclepro.2017.09.075

Karliner, J., Slotterback, J., Boyd, S., Ashby, B., & Steele, K. (2019). *Health care's climate footprint: How the health sector contributes to the global climate crisis*. Health Care Without

Harm. https://noharm-global.org/sites/default/files/documents-files/5961/HealthCaresClimateFootprint_092319.pdf

Markarian, J. (2019). Supply Chain Challenges for Single-Use Systems. Markarian, J. (2019). Supply Chain Challenges for Single-Use Systems | Pharmaceutical Technology

McGlinchey, Y., Iqbal, J., Trubetskaya, A., Thenarasu, M., & McDermott, O. (2025). Design for Green Lean Six Sigma to improve sustainability in the pharmaceutical industry – A case study. *Production & Manufacturing Research, 13*(1), 2461010. https://doi.org/10.1080/21693277.2025.2461010

My Green Lab. (2024). *The carbon impact of biotech & pharma*. https://mygreenlab.org/wp-content/uploads/2025/07/2024_carbon_impact_of_biotech_and_pharma_report.pdf

Ottinger, M., Wenk, I., Carvalho Pereira, J., John, G., & Junne, S. (2022). *Single-use technology in the biopharmaceutical industry and sustainability: A contradiction? Chemie Ingenieur Technik, 94*(12), 1883–1891. https://doi.org/10.1002/cite.202200105

Pharma's Almanac. (2025, January 31). How can pharma manufacturing align with green initiatives while maintaining efficiency and compliance? *Pharma's Almanac*. https://www.pharmasalmanac.com

Philpott, J. (2023, November 29). *Pharma's path to Net Zero: Targeting Scope 3 emissions.* Pharmaceutical Technology. https://www.pharmaceutical-technology.com/features/pharmas-path-to-net-zero-targeting-scope-3-emissions/

Sarkis, M., Monteiro, M., Bernardi, A., Chiplunkar, R., Kontoravdi, C., & Papathanasiou, M. M. (2025). Sustainable by design: A first attempt on bioprocessing. *Computers & Chemical Engineering*, 109454.

World Economic Forum. (2022, November 7). 3 ways healthcare systems can reduce their carbon footprint. https://www.weforum.org/agenda/2022/11/3-ways-healthcare-systems-carbon-footprint

World Economic Forum. (2025). These are the biggest risks we face now and in the next 10 years. *Global Risks Report 2025*. https://www.weforum.org/publications/global-risks-report-2025/

Regulatory Drivers Shaping Sustainability Practice in Biomanufacturing

Regulatory frameworks increasingly influence how sustainability considerations are integrated into biomanufacturing, shaping both strategic priorities and technical decision-making. In the European Union, the Corporate Sustainability Reporting Directive (CSRD) and the accompanying European Sustainability Reporting Standards (ESRS) significantly expand mandatory disclosure requirements, obliging companies to report detailed, auditable information on GHG emissions, resource consumption, waste streams, circularity indicators, and climate-transition plans (Hummel & Jobst, 2024). These reporting obligations reinforce the need for transparent, high-quality environmental data and directly increase the relevance of outcomes from life-cycle assessment (LCA), energy and mass consumption, and end-of-life scenarios within biopharma production.

Beyond corporate disclosure, the EU taxonomy regulation (European Commission, 2025) defines criteria for environmentally sustainable economic activities by focusing on climate mitigation, climate adaptation, pollution prevention, and circularity. This taxonomy encourages companies to adopt technologies and processes with lower carbon intensity, improved resource efficiency, and reduced environmental burden — characteristics closely tied to upstream and downstream bioprocess design (Hummel & Jobst, 2024). Additional EU instruments, such as the single-use plastics directive (European Parliament & Council, 2019) and the emerging Ecodesign for Sustainable Products Regulation (ESPR; European Commission, 2025), aim to reduce plastic pollution and promote circular product design. These policies aim to support recyclability, material efficiency, and improved waste management strategies in industrial production, all of which are relevant to the decision for using SUT in biopharmaceutical production.

At the global level, frameworks such as the UN sustainable development goals and growing plastics policies underscore international momentum toward resource-efficient and low-impact production systems (Knoblauch & Mederake, 2021; United Nations Environment Program, 2025). International disclosure frameworks complement these regional developments. The International Sustainability Standards Board (ISSB), established by the International Financial Reporting Standards (IFRS) Foundation, developed global baselines for environmental, social, and governance reporting (ESG; International Sustainability Standards Board, 2023). The IFRS S1 and IFRS S2 standards integrate sustainability-related risks and opportunities into mainstream financial reporting, thereby strengthening the

connection between environmental performance, governance, and financial materiality (Wagenhofer, 2024). Empirical evidence shows that such transparency mechanisms can influence organizational behaviour by increasing external pressure to demonstrate measurable progress in sustainability performance (Rusu et al., 2024). This requires the combination of process engineering-related data with an environmental assessment of decisions based on quantitative data (Stroehle et al., 2025).

Collectively, these regulatory and reporting frameworks position sustainability as an operational and design parameter in biomanufacturing rather than a purely corporate responsibility. They increasingly motivate the adoption of SbD principles, including material reduction, process intensification, digital monitoring, and improved end-of-life strategies. As a result, regulatory compliance and technical innovation become mutually reinforcing drivers in the transition toward more resource-efficient and environmentally friendly bioproduction.

Table 1. Overview of selected single-use plastic policy frameworks, motivated by global, areal, and national sustainability efforts.
Summary of a selection of global, areal, and national policies, laws, and regulatory frameworks addressing environmental protection, with a particular focus on single-use plastics across multiple industries. (Country selection is illustrative rather than comprehensive and does not represent a full inventory of all existing legal framework worldwide.)

Region	Regulation or Framework	Summary	Reference
Global			
	UN 2030 Agenda and Sustainable Development Goals, 2015	Global plan to end poverty sustainably 17 goals covering sustainability, climate, biodiversity, inequality	https://sdgs.un.org/2030agenda
	5/14. End plastic pollution: towards an international legally binding instrument, 2022	Mandates creating a global legally binding agreement on plastic pollution (in negotiation)	https://digitallibrary.un.org/record/3999257?v=pdf
Asia			
China	Administration of the Use and Reporting of Single-Use Plastics, 2023	Regulating single-use plastics in commercial fields	https://moef.gov.in/national-action-plan-on-climate-change
India	Plastic Waste Management Rules, 2022	Regulating use, collection, recycling, disposal of plastic waste	https://cpcb.nic.in/uploads/plasticwaste/2-amendment-pwmrules-2022.pdf

	Extended Producer Responsibility, 2022	Enforcing producer responsibility targets	https://cpcb.nic.in/uploads/plasticwaste/PWM-Amendment-Rules-2022.pdf
Europe			
EU	Directive (EU) 2019/904 – Single-Use Plastics, 2019	Banning selected single-use plastics, setting targets, promoting circular alternatives	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32019L0904&qid=1767367846267
	A new Circular Economy Action Plan, 2020	Plan for a cleaner and more competitive Europe	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex:52020DC0098
	Eco-design for Sustainable Products Regulation (ESPR), 2024	Circular design rules for all products, introducing a digital product passport	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32024R1781&qid=1719580391746

	European Climate Law Regulation (EU) 2021/1119, 2021	Legally binding EU to climate neutrality by 2050 with emissions-reduction targets and governance	https://eur-lex.europa.eu/eli/reg/2021/1119/oj/eng
	EU Supply Chain Due Diligence Directive, 2024	Requirements for companies to identify and mitigate environmental and human-rights risks	https://eur-lex.europa.eu/eli/dir/2024/1760/oj/eng
	CSRD – Corporate Sustainability Reporting Directive, 2023	Sustainability reporting of +50,000 companies introducing EU reporting and transition plan requirements	https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32022L2464
DE	Bundes-Klimaschutzgesetz (KSG), 2019	Legally binding Germany to climate neutrality by 2045 with sectoral emissions targets and monitoring	https://www.bmuv.de/fileadmin/Daten_BMU/Download_PDF/Gesetze/191118_ksg_lesefassung_bf.pdf
	Act on the Single-Use Plastic Fund, 2023	Funding plastic waste cleaning with extended producer responsibility	https://www.bundesumweltministerium.de/fileadmin/Daten_BMU/Download_PDF/Gesetze/ewkfondsg_en_bf.pdf

CH	Federal Act on Climate Protection Goals, Innovation and Strengthening Energy Security, 2022	Legally committing Switzerland to net-zero emissions by 2050, funding climate-friendly innovation	https://www.fedlex.admin.ch/eli/fga/2022/2403/
	Ordinance on Climate Disclosures, 2024	Mandating climate-related corporate disclosures and reporting with climate transparency standards	https://www.newsd.admin.ch/newsd/message/attachments/74006.pdf
North America			
USA	EPA National Strategy to Prevent Plastic Pollution, 2024	Producers are legally responsible for EOL management	https://www.epa.gov/system/files/documents/2024-11/final_national_strategy_to_prevent_plastic_pollution.pdf
	Inflation Reduction Act, 2022	US climate investment supporting clean energy and manufacturing	https://www.congress.gov/bill/117th-congress/house-bill/5376
Canada	*Single-use Plastics Prohibition Regulations,* SOR/2022-138, 2022	Banning manufacture and import of certain single-use plastics, reducing plastic waste generation	https://laws-lois.justice.gc.ca/PDF/SOR-2022-138.pdf
South America			

Brazil	National Solid Waste Policy, 2010	Establishing waste hierarchy: prevention, reuse, recycling, disposal; mandating producer responsibility	https://www.planalto.gov.br/ccivil_03/_ato2007-2010/2010/lei/l12305.htm
Colombia	Ley 2232 de 2022, 2022	Gradual reduction of single-use plastics, promoting sustainable alternatives and circular economy goals	https://www.minambiente.gov.co/documento-normativa/ley-2232-de-2022/
Chile	Single-Use Plastics Law, 2021	Banning single-use plastics in food services nationwide, promoting reusables and waste reduction	https://www.bcn.cl/leychile/navegar?idNorma=1163603
Africa			
African Union	Continental Circular Economy Action Plan 2024-2034, 2024	Includes plastics and circular economy actions	https://africacircular.org/continental-action-plan-for-circular-economy-in-africa-2024-2034/
South Africa	Carbon Tax Act 15, 2019	Carbon pricing mechanism; national framework for mitigation, adaptation and transition	https://www.gov.za/documents/acts/carbon-tax-act-15-2019-english-

			afrikaans-23-may-2019
	Extended Producer Responsibility for plastic packaging, 2021	Mandates extended producer responsibility for packaging including some single-use plastics	https://www.wwf.org.za/?34924%2FExtended-Producer-Responsibility-for-plastic-packaging-in-South-Africa
Oceania			
Australia	Climate Change Act, 2022	Legally binding a net-zero GHG emission goal by 2050, 43% reduction by 2030	https://www.legislation.gov.au/Details/C2022A00037
	National Plastics Plan, 2022	Plastic waste reduction and increased recycling rates	https://www.dcceew.gov.au/environment/protection/waste/plastics-and-packaging
New Zealand	Climate Change Response (Zero Carbon) Amendment Act, 2019	Net-zero GHG emission goal by 2050, carbon budgets and advisory commission	https://www.legislation.govt.nz/act/public/2019/0061/latest/LMS183736.html
	Waste Minimisation (Plastic and Related Products) Regulations, 2022	Ban for the manufacture and sale of certain products	https://legislation.govt.nz/regulat

			ion/public/2022/0069/13.0/LMS654282.html
Tuvalu	Climate Resilience Act and Constitutional Amendments, 2019	Constitutional amendment to preserve statehood despite sea-level rise	https://tuvalu-legislation.tv/cms/images/LEGISLATION/PRINCIPAL/2019/2019-0009/2019-0009.pdf?zoom_highlight=climate+change#search=%22climate%20change%22

References

European Commission. (2024). *Ecodesign for Sustainable Products Regulation*. European Commission. https://commission.europa.eu/energy-climate-change-environment/standards-tools-and-labels/products-labelling-rules-and-requirements/ecodesign-sustainable-products-regulation_en

European Commission. (2025, December 17). *EU taxonomy for sustainable activities*. European Commission. https://finance.ec.europa.eu/sustainable-finance/tools-and-standards/eu-taxonomy-sustainable-activities_en

European Parliament & Council of the European Union. (2019). *Directive (EU) 2019/904 of the European Parliament and of the Council of 5 June 2019 on the reduction of the impact of certain plastic products on the environment* (Single-Use Plastics Directive). *Official Journal of the European Union*, L155, 1–19. https://eur-lex.europa.eu/eli/dir/2019/904/oj EU

Hummel, K., & Jobst, D. (2024). *An overview of corporate sustainability reporting legislation in the European Union*. Accounting in Europe, 21(3), 317–356.

International Sustainability Standards Board. (2023). *IFRS S1 general requirements for disclosure of sustainability-related financial information*. IFRS Foundation. https://www.ifrs.org/issued-standards/ifrs-sustainability-standards-navigator/ifrs-s1-general-requirements/

Knoblauch, D., & Mederake, L. (2021). Government policies combatting plastic pollution. *Current Opinion in Environmental Science & Health, 22*, 100254. https://doi.org/10.1016/j.coesh.2021.100254

Rusu, T. M., Odagiu, A., Pop, H., & Paulette, L. (2024). Sustainability performance reporting. *Sustainability, 16*(8538), 1–12.

Stroehle, J. C., Gümüşay, A. A., Edinger-Schons, L. M., Vogel, A., Ebrahim, A., Rasche, A., King, A., Pucker, K., Barker, R., Reinecke, J., Michelon, G., Cooper, S., Etzion, D., Harji, K., Besharov, M., Mayer, C., Hsieh, N.-h., & van den Terrell, E. (2025). *A critical examination of corporate environmental and social impact measurement and valuation*. Journal of Management Inquiry, 35(1), 3–18.

United Nations Environment Program. (2025, August 5). *Resumed fifth session of negotiations on the global plastic pollution treaty takes stock of progress*. United Nations

Environment Programme. https://www.unep.org/news-and-stories/press-release/resumed-fifth-session-negotiations-global-plastic-pollution-treaty

United Nations Office of the Sustainable Development. (2025). *Sustainable Development Goals (SDGs)*. United Nations. https://unosd.un.org/content/sustainable-development-goals-sdgs

Wagenhofer, A. (2024). Sustainability reporting: A financial reporting perspective. *Accounting in Europe, 21*(1), 1–13.

Importance of Sustainability Awareness

Sustainability awareness is gaining overall importance in industry due to intense discussions about the consequences of climate change on daily life. To complement the growing body of evidence on sustainability awareness in biomanufacturing with respect to the application of SUT, a survey was conducted by the German Society for Chemical Engineering and Biotechnology (DECHEMA e.V., Frankfurt, Germany), a working group for SUT in bio-based applications. The survey targeted two groups: members of the working group itself (63%) and a broader group of bioprocess suppliers, end users, and academics.

Among the 115 participants, SUT was widely perceived as a preferred option for future biomanufacturing due to its operational flexibility, modularity, and process efficiency (Figure 2A). However, opinions diverged regarding its environmental impact. In the general biotech group, more than half of respondents viewed SUT as more environmentally harmful than stainless steel (multi-use), whereas perceptions among SUT experts were more balanced (Figure 2B). This reflects the ongoing debate about biomanufacturing: while SUT reduces water and energy consumption and cleaning-related downtime, it also increases plastic use and waste generation (ISPE, 2023; Sarkis et al., 2025), including waste material from irradiation. These trade-offs underscore the need for a holistic understanding of sustainability that covers all steps of biomanufacturing.

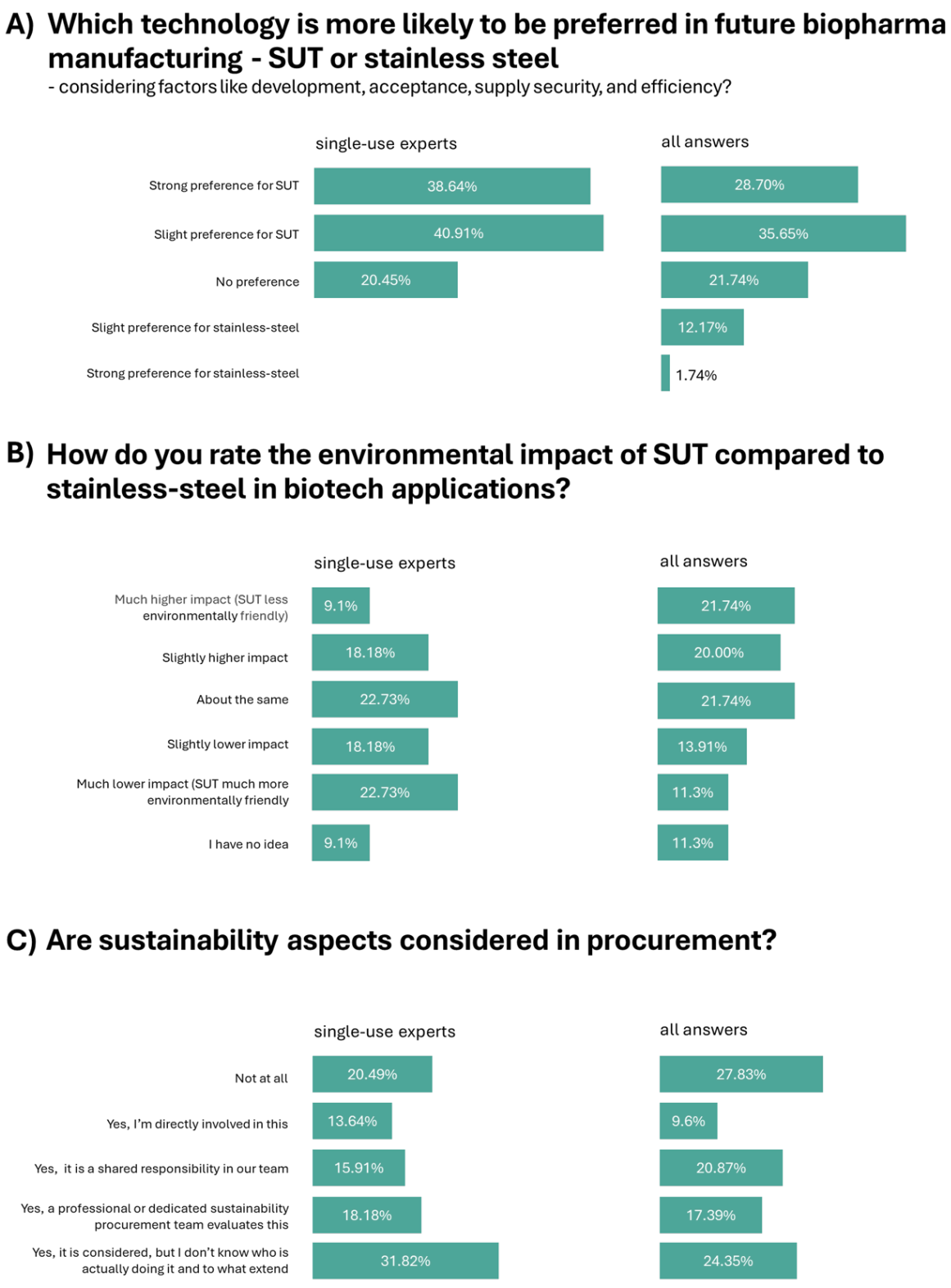
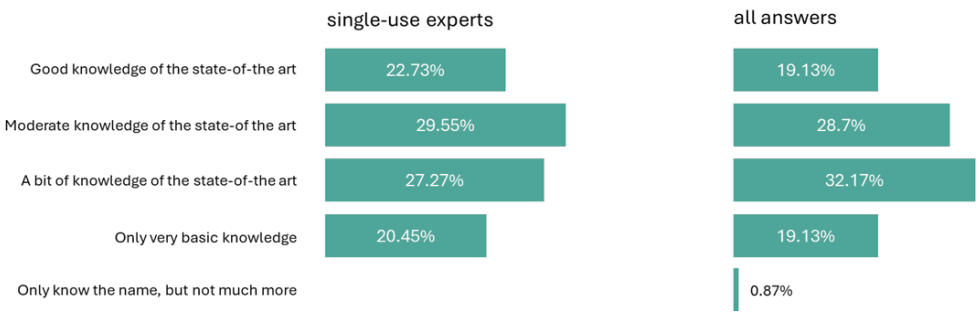


Figure 2. Outcome of a survey with about 115 participants, mainly from the biotech industry. A) Preferred future manufacturing technology in biopharmaceutical production. B) Perceived environmental impact among single-use and stainless steel technology. C) Consideration of sustainability in procurement.

Although sustainability is increasingly considered in procurement processes, only a minority of survey participants reported being directly involved in sustainability assessments or aware of clear accountability structures (Figure 2C). This highlights governance gaps and a lack of transparency along the value chain. According to Deloitte (2023), up to 70% of total GHG emissions in the biopharmaceutical sector originates from supply chain activities rather than direct manufacturing operations. Integrating environmental and social criteria into supplier selection and engagement frameworks is, therefore, critical to improving sustainability performance across scope 3 emissions.

The survey also revealed limited confidence and knowledge among stakeholders. Most respondents rated their sustainability knowledge as basic to moderate (Figure 3A), and more than 40% expressed neutral confidence in sustainability-related decision-making (Figure 3B), underlining the need for targeted training, shared best practices, and standardized tools. As Sarkis et al. (2024) emphasized, achieving sustainable biomanufacturing requires organizational learning, cross-functional collaboration, and the systematic inclusion of sustainability metrics into performance evaluations and process development.

A) How would you rate your own knowledge of sustainability practices in the biotech industry?



B) How confident are you in making decisions that involve sustainability considerations in your biotech work?

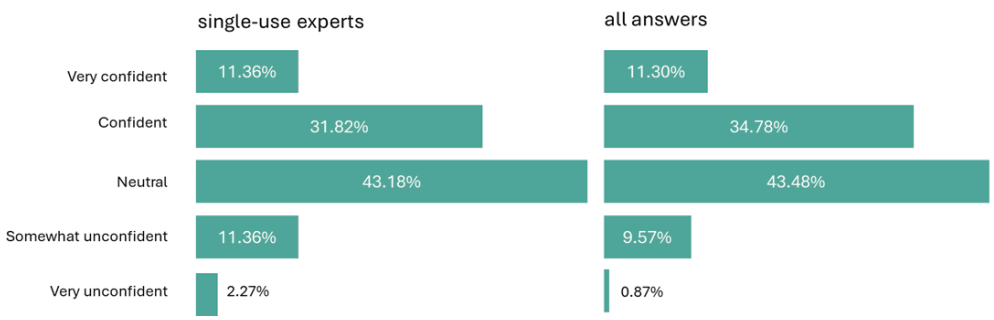


Figure 3. Expertise assessment among 115 survey participants about A) knowledge of sustainability practices in the biotech industry and B) self-reported confidence in sustainability-related decision-making.

Cost considerations, internal policies, and regulatory requirements emerged as the strongest drivers of sustainability action, while investor expectations and workforce engagement played a lesser role. This suggests that sustainability is still considered primarily a compliance and efficiency issue rather than as a strategic opportunity. Yet, economic and environmental goals can be mutually reinforced.

Overall, the survey results highlight both progress and persistent barriers in integrating sustainability into bioprocess engineering. While SUT adoption supports flexibility, efficiency, and process intensification, environmental trade-offs and knowledge gaps remain. Strengthening supplier collaboration, embedding sustainability metrics such as process mass intensity (PMI) and carbon intensity, and aligning innovation with circular economy principles are essential to meeting climate and resource goals. Integrating life cycle assessment, process intensification, and data-driven design as emphasized by others (ISPE 2023, Deloitte 2023, Sarkis et al. 2025) offers a realistic pathway toward low-carbon, resource-efficient, and economically resilient biomanufacturing.

References

Deloitte. (2023). *Making biopharma's supply chains more environmentally sustainable.* Deloitte Insights. https://www.deloitte.com/us/en/insights/industry/health-care/scaling-pharmaceutical-supply-chain-sustainability-efforts.html

International Society for Pharmaceutical Engineering (ISPE). (2023). *Environmental sustainability in biopharmaceutical facility design. Pharmaceutical Engineering,* March–April 2023. Environmental Sustainability in Biopharmaceutical Facility Design | Pharmaceutical Engineering

Partopour, B., & Pollard, D. (2025). *Advancing biopharmaceutical manufacturing: Economic and sustainability assessment of end-to-end continuous production of monoclonal antibodies. Trends in Biotechnology, 43*(2), 462–473. https://doi.org/10.1016/j.tibtech.2024.10.007

Sarkis, M., Fyfe, A. T., Kontoravdi, C., & Papathanasiou, M. M. (2024). *Towards a net zero, socially sustainable and eco-efficient biopharma industry: How far are we? Current Opinion in Chemical Engineering, 44,* 101027.

Quantifying and Comparing Environmental Impact in Biomanufacturing

Measuring the sustainability impact of biopharmaceutical manufacturing requires standardized and robust methodologies to assess environmental footprints across the full product life cycle. The LCA framework, standardized under ISO 14040/14044, examines and categorizes environmental impacts from raw material extraction to end-of-life disposal. Core indicators typically include GHG equivalent emissions determined, in part, by process mass intensity (PMI, illustrated in Figure 4), energy and water demand, and waste treatment. LCA is supported by databanks that have increasing amounts of biopharmaceutical production data and process simulation tools like BioSolve *Process*™ (Biopharm Services, 2025) that enables early-stage sustainability evaluations and scenario modeling (Alaria et al., 2023).

Comparative LCA studies consistently show that, despite generating more plastic waste, SUT often have a smaller overall environmental footprint than stainless steel systems due to the elimination of cleaning and sterilization efforts, which are major contributors to water, chemical, and energy consumption (Budzinski et al., 2022; Barbaroux et al., 2020). This advantage is especially relevant in multiproduct and early-phase facilities, where flexibility and rapid turnaround outweigh end-of-life burdens, and in the case of established processes like monoclonal antibody production. Conversely, stainless steel systems may achieve better performance in large-scale production with low requirements for flexible production, where cleaning and sterilization is in-place (CIP/SIP; Zürcher et al., 2020). Additionally, scale out remains the only option at SUT based production, as maximum working volumes of single-use bioreactors are restricted to several thousand liters. Then, logistics and on-site storage can contribute largely to the carbon footprint.

While energy and water consumption has a major impact on stainless steel-based systems, the local situation of energy generation and its carbon footprint play an important role as well as the availability of water and the impact of water utilization on the local environment. Hence, the true impact of choosing between multi-use stainless steel-based fabrication and SUT depends on factors that are often not easily available in databanks, as they are too specific for some local conditions. Another major impact factor is emissions related to logistics, where shipping may be across countries or continents. The outcomes of an LCA can, therefore, vary

significantly under these conditions, so that a general statement regarding the most environmentally friendly option is not possible (Whitford 2017). Additionally, the impact of waste from gamma irradiation is difficult to assess as there are no general procedures for treating or storing the radioactive residues. While gamma irradiation is commonly used as a standard for sterilization of SUT, X-ray irradiation that comes with no radioactive waste has proven to be a comparable option for filters (Budde et al., 2025) and for polyethylene/ethylene-vinyl alcohol/polyethylene (PE/EVOH/PE) multilayer films (Girard-Perier et al., 2021). X-ray and electron beam sterilization was proven to be a comparable and suitable option for ethylene vinyl acetate/ethylene vinyl alcohol/ethylene vinyl acetate (EVA/EVOH/EVA) films (Ni et al., 2023). It is likely that the penetration of those methods into the market will also change the burden of SUT concerning radioactive waste generation.

End-of-life management remains one of the central sustainability challenges for SUT. While the application of SUT reduces water and energy consumption by eliminating CIP/SIP, it increases solid waste volumes. The current literature identifies no validated large-scale reuse strategies for SU components; thus, concepts such as reuse or extended component lifetimes require cautious interpretation and robust empirical validation (Alaria et al., 2023; Lalor et al., 2019). Most systems are currently incinerated, which contributes to greenhouse gas emissions but can allow partial energy recovery. Recycling remains limited, constrained by material heterogeneity, validation requirements, and a lack of closed-loop logistics infrastructure. Moreover, the temporary storage of used bulky materials increases logistical complexity and facility space demands (Whitford et al., 2021; Barbaroux et al., 2021; Ottinger et al., 2022). To address these challenges, manufacturers are exploring design-for-recycling strategies, mono-material polymers, and regional take-back programs to enhance circularity and reduce storage-related burdens.

Table 2. Environmental assessments of single-use technology applications in biopharmaceutical production within the past 15 years and reviews thereof

Reference	Focus Area	Key Findings
J. Pollock et al. (2013)	Comparison of fed-batch and perfusion cell culture processes under environmental uncertainty	The fed-batch scenario performed better due to reduced water and consumables consumption
Pietrzykowski et al. (2013)	Monoclonal antibody production with single-use and stainless-steel equipment	Reduced environmental burden from the single-use process across a variety of operating scales
Ramasamy et al. (2015)	Life cycle analysis for decision-making	Discussion of limitations and challenges in applying LCA under regulatory constraints
Flanagan et al. (2014)	Life cycle analysis of single-use and stainless steel production systems at three scales	Environmental impacts across the full process train are lower for single-use variants.
Bunnak et al. (2016)	Monoclonal antibody in fed-batch and perfusion mode	The more environmentally friendly option depends on pooling intervals for purification.
Whitford, et al. (2019)	Life cycle assessment of monoclonal antibody and adenovirus production in single-use and stainless steel variants	Comparison favours single-use variants, but results strongly depend on location and energy generation.
Lalor et al. (2019)	Holistic sustainability in biopharma (Review)	Macroeconomic policies and pricing are examined beside technological aspects.

Budzinski et al. (2019)	Process mass intensity applied as a metric to evaluate process efficiency	Quantification for monoclonal antibody production, highlighting the large amount of water use
Zürcher et al. (2020)	Decision support for process design	Multi-objective modelling for cost-balancing, scalability, and environmental impact reduction
Barbaroux et al. (2020, 2021)	Industrial case studies and post-use management with the emphasis on circularity options	End-of-life waste is relevant; recycling, energy recovery, and closed-loop design required
Whitford et al. (2021)	Post-use and recycling strategies	Evaluating recycling and energy recovery options; technical and infrastructure barriers are noted.
Budzinski et al. (2022)	Cradle-to-gate life cycle assessment of single-use systems at the 2,000 L scale	Largest contribution to emissions was electricity; process efficiency increases most important factor
Ottinger et al. (2022)	Sustainability trade-offs	Contradictions between flexibility and waste; calls for improved LCA metrics and storage logistics
Luu et al. (2022)	Technical and comparative life cycle assessment for post-use plastic containers	Proposal for mechanical end-of-life recycling options based on a theoretical framework
Alaria et al. (2023)	Industrial sustainability metrics	Describes integration of LCA data and PMI indicators into digital process modelling tools.

Barbaroux et al. (2024)	Life cycle assessment of a closed-loop recycling concept for a small-scale bioreactor	Technical feasibility demonstration and summary of challenges for implementation
Goggin et al. (2025)	Review of the contradiction between single-use adoption and importance of circularity	Research required on sustainable materials, business models, and regulatory framework

The biopharmaceutical sector is increasingly shifting toward harmonized and transparent environmental assessment standards. The BioPhorum (2024) Product Carbon Footprint (PCF) Framework provides standardized methodologies and datasets for Scope 3 emissions, supporting carbon transparency across complex supply chains. Complementing this, the British Standards Institution (2025) PAS 2090 established product category rules (PCR) and standardized reporting criteria for LCAs of pharmaceutical products, encompassing manufacturing, packaging, distribution, patient use, and end-of-life disposal.

These initiatives build on decades of methodological evolution, from early eco-labeling efforts to modern, science-based, and sector-specific frameworks (Barle & Stärkle, 2024). They align closely with broader environmental reporting systems such as the Taskforce on Nature-related Financial Disclosures (TNFD), which promotes the integration of nature-related risk and impact metrics into sustainability governance (Taskforce on Nature-related Financial Disclosures, 2023, 2024). By harmonizing standards, improving data quality, and embedding LCA insights into strategic decision-making, such frameworks enable greener procurement, regulatory transparency, and more credible sustainability reporting. Ultimately, aligning technological innovation with harmonized life cycle methodologies will be essential for achieving circular, low-carbon, and resource-efficient biomanufacturing.

References

Alaria, M., Barbaroux, M., McLaughlin, K., Monge, M., & Tillmanns, K. (2023). *Driving environmental sustainability in the biopharmaceutical industry.* Sartorius. Driving Environmental Sustainability in the Biopharmaceutical Industry

Barbaroux, M., Horowski, B., Mokuolu, S., Petrich, M., & Whitford, W. (2020). The green imperative: Part One - Life-cycle assessment and sustainability for single-use technologies in the biopharmaceutical industry. *BioProcess International, 18*(6), 12–18.

Barbaroux, M., Rosskamp, A., Dippel, J., Rees-Manley, A., Garska, B., & Tosato, R. (2024). *Concept for recycling a small-scale plastic-based bioreactor in a close-loop – Technical approach*. Journal of Cleaner Production, 471, 143436. https://doi.org/10.1016/j.jclepro.2024.143436

Barle, E., & Stärkle, S. (2025). Future-proofing pharma and personal care: How life cycle assessments and carbon footprinting drive real change. *Pharmaceutical Engineering (ISPE).* https://ispe.org/pharmaceutical-engineering/ispeak/future-proofing-pharma-and-personal-care-how-life-cycle

Biopharm Services. (2025). *BioSolve Process™: In silico process design for biopharmaceutical production*. Biopharm Services. https://biopharmservices.com/biosolve-software/biosolve-process/

BioPhorum. (2024). *Product carbon footprint framework for biopharma manufacturing* [Position statement]. https://www.biophorum.com/news/biophorum-and-bsi-shaping-the-pas-2090-standard/

British Standards Institution. (2025). *PAS 2090: Pharmaceutical products – Product category rules for environmental lifecycle assessments – Specification* [Draft standard]. BSI Knowledge. https://standardsdevelopment.bsigroup.com/projects/9025-12045

Budde, D., Rothenberg, L., Hue, C., Roulin, C., Nellis, D., Chen, B., ... & Dorey, S. (2025). Impact of X-Ray Versus Gamma Irradiation of Single-Use System Filter Assemblies on CHO Cell Culture Growth. *GEN Biotechnology*, *4*(3), 119-126.

Budzinski, K., Blewis, M., Dahlin, P., D'Aquila, D., Esparza, J., Gavin, J., Ho, S. V., Hutchens, C., Kahn, D., Koenig, S. G., Kottmeier, R., Millard, J., Snyder, M., Stanard, B., & Sun, L. (2019). *Introduction of a process mass intensity metric for biologics*. New Biotechnology, 49, 37–42. https://doi.org/10.1016/j.nbt.2018.07.005

Budzinski, K., Constable, D., D'Aquila, D., Smith, P., Madabhushi, S. R., Whiting, A., Costelloe, T., & Collins, M. (2022). Streamlined life cycle assessment of single-use technologies in biopharmaceutical manufacture. *New Biotechnology, 68,* 28–36. https://doi.org/10.1016/j.nbt.2022.01.002

Bunnak, P., Allmendinger, R., Ramasamy, S. V., Lettieri, P., & Titchener-Hooker, N. J. (2016). *Life-cycle and cost of goods assessment of fed-batch and perfusion-based manufacturing processes for mAbs*. Biotechnology Progress, 32(5), 1324–1335. https://doi.org/10.1002/btpr.2323

Demling, P., Rosenthal, K., & Grünberger, A. (2025). Window of sustainable bioprocess operation: Towards merging environmental sustainability assessment and process operation at early-stage bioprocess development. *Current Opinion in Biotechnology, 93,* 103292. https://doi.org/10.1016/j.copbio.2025.103292

Flanagan, W., Brown, A., & Pietrzykowski, M. (2014). *An environmental lifecycle assessment of single-use and conventional process technology: Comprehensive environmental impacts*. *BioPharm International*. https://www.biopharminternational.com/view/environmental-lifecycle-assessment-single-use-and-conventional-process-technology-comprehensive-envi

Girard-Perier, N., Claeys-Bruno, M., Marque, S. R., Dupuy, N., Gaston, F., & Dorey, S. (2021). Effects of X-ray, electron beam and gamma irradiation on PE/EVOH/PE multilayer film properties. *Chemical Communications*, *57*(84), 11049-11051.

Goggin, M., Fleming, A. F. M., MacMahon, C., & Owende, P. (2025). *Exploring the sustainability of single use plastics in the biopharmaceuticals sector: A scoping review of challenges, opportunities, and impacts*. Frontiers in Sustainability, 6, Article 1536382. https://doi.org/10.3389/frsus.2025.1536382

Lalor, F., Fitzpatrick, J., Sage, C., & Byrne, E. (2019). Sustainability in the biopharmaceutical industry: Seeking a holistic perspective. *Biotechnology Advances, 37*(5), 698–707. https://doi.org/10.1016/j.biotechadv.2019.03.015

Luu, D.-N., Barbaroux, M., Dorez, G., Mignot, K., Doger, E., Laurent, A., Brossard, J.-M., & Maier, C.-J. (2022). *Recycling of post-use bioprocessing plastic containers — Mechanical recycling technical feasibility*. **Sustainability, 14**(23), 15557. https://doi.org/10.3390/su142315557

Ni, Y., Bisel, T. T., Hasan, M. K., Li, D., Fuchs, W. K., Cooley, S. K., ... & Fifield, L. S. (2023). Compatibility of ethylene vinyl acetate (EVA)/ethylene vinyl alcohol (EVOH)/EVA films with gamma, electron-beam, and X-ray irradiation. *npj Materials Degradation*, *7*(1), 93.

Ottinger, M., Wenk, I., Pereira, J. C., John, G., & Junne, S. (2022). Single-use technology in the biopharmaceutical industry and sustainability: A contradiction? *Chemie Ingenieur Technik, 94*(12), 1096–1110. https://doi.org/10.1002/cite.202200105

Pietrzykowski, M., Flanagan, W., Pizzi, V., Brown, A., Sinclair, A., & Monge, M. (2013). An environmental life cycle assessment comparison of single-use and conventional process technology for the production of monoclonal antibodies. *Journal of Cleaner Production, 41,* 150–162. https://doi.org/10.1016/j.jclepro.2012.09.048

Pollock, J., Ho, S. V., & Farid, S. S. (2013). *Fed-batch and perfusion culture processes: Economic, environmental, and operational feasibility under uncertainty*. Biotechnology and Bioengineering, 110(1), 206–219. https://doi.org/10.1002/bit.24608

Ramasamy, S. V., Titchener-Hooker, N. J., & Lettieri, P. (2015). Life cycle assessment as a tool to support decision making in the biopharmaceutical industry: Considerations and challenges. *Food and Bioproducts Processing, 94,* 297–305. https://doi.org/10.1016/j.fbp.2014.03.009

Taskforce on Nature-related Financial Disclosures. (2023). *Guidance on the identification and assessment of nature-related issues: The LEAP approach* (Version 1.1). https://tnfd.global/publication/recommendations-of-the-taskforce-on-nature-related-financial-disclosures/

Taskforce on Nature-related Financial Disclosures. (2024). *Additional sector guidance: Biotechnology and pharmaceuticals* (Version 1.0).

Whitford, W., Petrich, M., & Flanagan, W. (2019). Environmental impacts of single-use systems. In R. Eibl & D. Eibl (Eds.), *Single-use technology in biopharmaceutical manufacture* (2nd ed., pp. 271–285). John Wiley & Sons.

Whitford, W., Mokuolu, S., Barbaroux, M., Snyder, M., & Petrich, M. (2021). The green imperative: Part 3 – Postuse management of single-use bioprocessing materials, today and tomorrow. *BioProcess International, 19*(11–12), 12–18.

Zürcher, P., Shirahata, H., Badr, S., & Sugiyama, H. (2020). Multi-stage and multi-objective decision-support tool for biopharmaceutical drug product manufacturing: Equipment technology evaluation. *Chemical Engineering Research and Design*, *161*, 240-252.

Designing Sustainable Biomanufacturing Processes

Designing sustainable biomanufacturing processes increasingly relies on integrating environmental considerations early in product and process development. The concept of SbD builds on the principles established in Quality by Design (QbD) under ICH Q8(R2), extending structured, risk-based decision-making frameworks to include environmental performance, lifecycle thinking, and resource efficiency, alongside quality and cost objectives (International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use, 2009). In practice, sustainability by design requires an iterative and structured approach to identifying relevant environmental aspects, prioritizing impacts, and implementing improvement measures across material, energy, and emission flows, as illustrated in Figure 4.

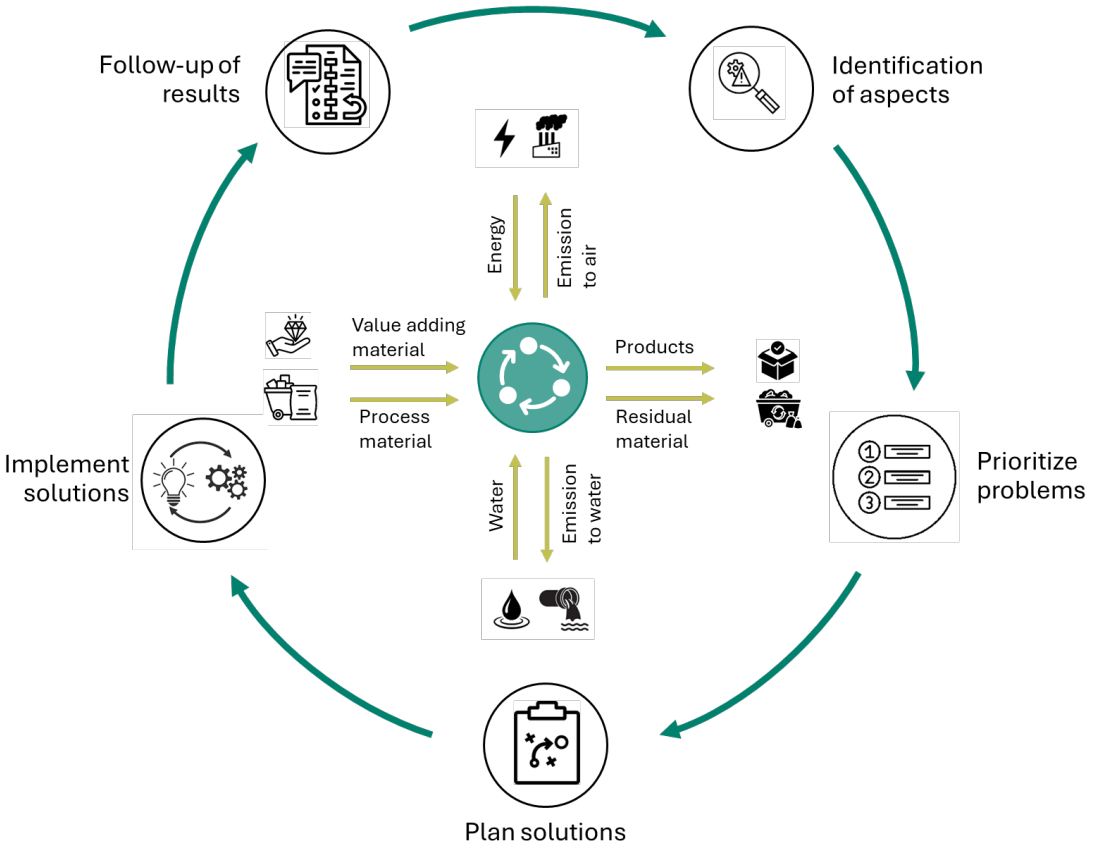


Figure 4. Iterative sustainability-by-design framework for early bioprocess and product development.

Recent research underscores that the most influential leverage points for improving the environmental footprint of pharmaceuticals occur during early R&D and clinical development. Luu et al. (2022) examined eco-design opportunities across the pharmaceutical R&D process and demonstrated that, although eco-design can be applied at multiple stages, the strongest opportunities for reducing downstream environmental impacts arise during activities conducted alongside clinical Phases IIa and IIb. At this transition point, critical product and process attributes, including the final dosage form, route of administration, manufacturing pathway, and key material selections, are consolidated, making this stage particularly decisive for long-term environmental performance.

Complementary work on recombinant protein therapeutics highlights how early product attributes, such as molecular format, formulation complexity, platform compatibility, and dosing requirements, shape the design space for biomanufacturing and affect energy usage, material demand, and cold-chain requirements throughout the lifecycle (Mastrangeli et al., 2025). Taken together, these findings position SbD as a strategic framework that embeds sustainability criteria directly into the product development lifecycle, rather than applying environmental optimizations post-hoc during late-stage engineering.

SbD requires transparent and quantitative sustainability metrics; however, the metrics traditionally used in bioprocess design have limitations. Sinclair et al. (2024) conducted a detailed evaluation of Process Mass Intensity (PMI), a widely used environmental indicator that quantifies material inputs per kilogram of biologic drug substance. PMI does not include energy consumption, particularly the substantial contribution of facility and cleanroom HVAC systems. Their process modelling showed that the application of SUT can reduce PMI significantly but may not proportionally reduce carbon emissions. This illustrates the disconnect between mass-based metrics and energy-driven environmental impacts. To address this gap, Sinclair and co-authors propose combining mass-based and facility-based indicators, such as the process facility index (PFI), which integrates PMI (including cleaning materials) with process intensity, thereby capturing both resource use and cleanroom efficiency (Sinclair et al., 2024). In parallel, they recommend incorporating a cradle-to-gate LCA for early-phase decision support. These approaches align with SbD by enabling earlier, data-driven evaluation of trade-offs across material use, energy demands, and facility configurations.

Integrating insights from eco-design frameworks (Luu et al., 2022) and quantitative sustainability metrics (Sinclair et al., 2024) strengthens the methodological foundation of

SbD. Together, they highlight that meaningful decarbonization and resource efficiency in biomanufacturing depend on (i) incorporating sustainability criteria during early product and process design, (ii) using appropriate metrics that reflect both material and energy drivers of environmental impact, and (iii) creating structured governance mechanisms that sustain these priorities through clinical development, scale-up, and commercialization.

References:

Barle, E., & Stärkle, S. (2025). Future-proofing pharma and personal care: How life cycle assessments and carbon footprinting drive real change. *Pharmaceutical Engineering (ISPE)*. https://ispe.org/pharmaceutical-engineering/ispeak/future-proofing-pharma-and-personal-care-how-life-cycle

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. (2009). *ICH Harmonised Tripartite Guideline Q8(R2): Pharmaceutical Development*. ICH. ICH Q8 (R2) Pharmaceutical development - Scientific guideline | European Medicines Agency (EMA)

Luu, D. N., Gachet, H., Maier, C. J., Maranzana, N., & Aoussat, A. (2022). Eco-design and medicine: Opportunities to implement eco-design in the pharmaceutical R&D process. *Journal of Cleaner Production*, *365*, 132785.

Mastrangeli, Renato, et al. "Sustainability by design for recombinant protein therapeutics." *Drug Discovery Today* (2025): 104393.

Sinclair, P., Dieringer, F., & Hill, C. (2024). *Bioprocess eco-design metrics: Evaluating the predictive power of PMI and alternatives for biologics manufacturing* (SSRN preprint). BioPharm Services. https://ssrn.com/abstract=4987282

Process Intensification and Continuous Biomanufacturing

The development of process intensification in biopharmaceutical manufacturing addresses the dual requirement of increasing productivity and improving sustainability performance. The shift from conventional fed-batch processing towards continuous and hybrid biomanufacturing is driven by advances in high-density cell culture, automation, and real-time analytics, which increasingly enable integrated upstream–downstream operations. These developments facilitate end-to-end intensified process trains that can reduce facility

footprints, increase volumetric productivity, and enhance cost efficiency (Mahal et al., 2021; Partopour & Pollard, 2025; Del Hierro et al., 2024).

Fed-batch processing (Figure 5A) remains the dominant platform for monoclonal antibody (mAb) production due to robustness, regulatory maturity, and high achievable titers (Pollock et al., 2013; Xu et al., 2020); however, the inherent start–stop mode limits equipment utilization and facility throughput. Continuous upstream processing, particularly perfusion (Figure 5B), maintains cells in a quasi-steady state for extended durations, enabling sustained productivity and reducing the need for extensive CIP and SIP operations typical of stainless steel facilities (Lee, 2022; Walther et al., 2015). Cell retention technologies, such as XCell® Alternating Tangential Flow (ATF) Technology (Repligen) and tangential flow filtration (TFF), enable the high cell densities required for intensified upstream operation and support integration with multi-column chromatography, continuous viral inactivation, and other intensified downstream steps (Pollock et al., 2013; Mahal et al., 2021; Cataldo et al., 2020).

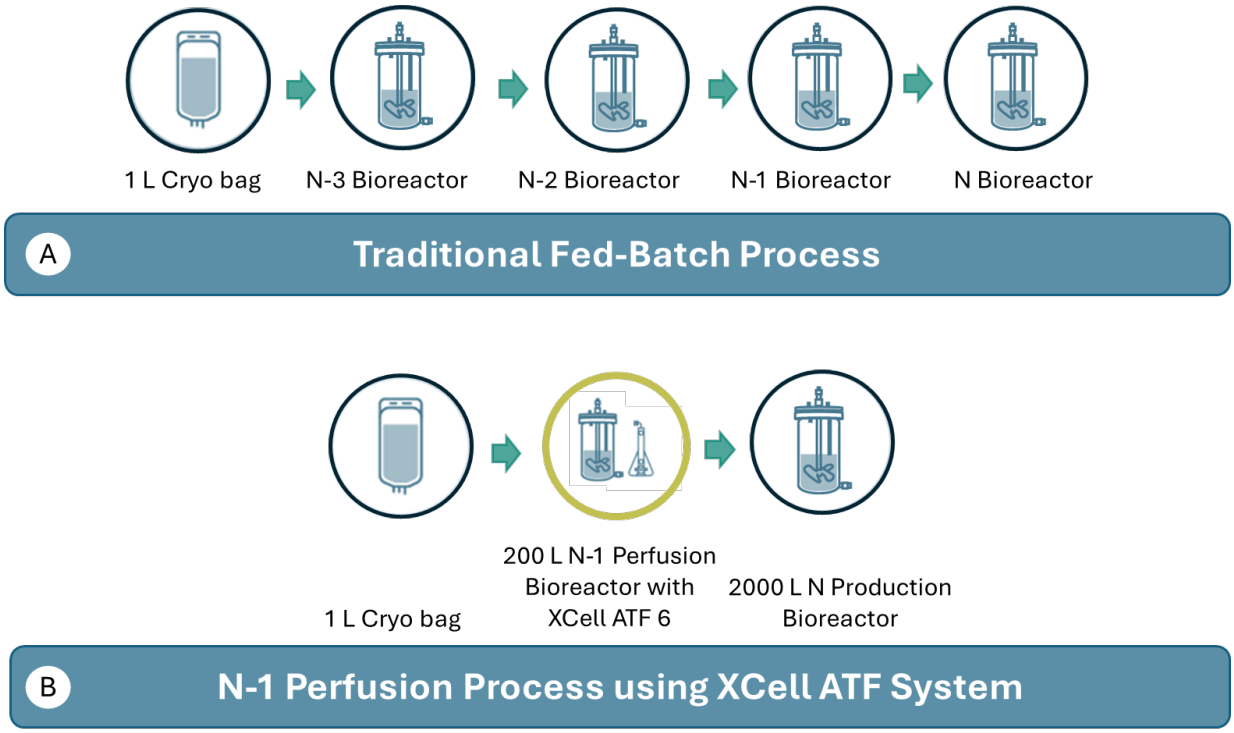


Figure 5. Comparison of A) a conventional fed-batch seed train, and B) an intensified N-1 perfusion-based upstream process.

Integrated continuous bioprocessing can reduce downtime, improve resin utilization, and minimize facility footprint, resulting in both operational and economic advantages (Klutz et

al., 2016; Cataldo et al., 2020). Continuous and intensified biomanufacturing processes, for instance, can reduce cost of goods (COGs) by up to 23%, plastic waste by 57%, and CO_2 emissions by 54% compared with optimized fed-batch processes (Partopour & Pollard, 2025). Similarly, sustainable facility design and modular, single-use-based systems can lower capital and operational expenditures by 30 – 50% while reducing energy and water demand through minimized cleaning and sterilization (ISPE, 2023). Continuous and intensified systems also support compact, modular facilities that enable distributed manufacturing, reduce supply-chain distances, and decrease transportation-related impacts — key elements of a sustainable bioeconomy (Del Hierro et al., 2024). These shifts align with broader industry goals around resource efficiency, climate mitigation, and circularity (Lalor et al., 2019); however, the environmental advantages of process intensification are highly dependent on specific process configurations. LCAs provide different outcomes depending on productivity, medium consumption, buffer volumes, and facility design. Bunnak et al. (2016) reported higher water and energy consumption in a standard perfusion process compared with fed-batch due to increased medium usage. In contrast, Amasawa et al. (2021) and Cataldo et al. (2020) demonstrated that intensified or continuous designs can reduce environmental impacts per gram of product, especially when they enable smaller equipment, lower buffer consumption, or improved resin utilization.

A hybrid design that combines perfusion-based upstream operations with intensified, semi-continuous, or batch downstream processes is regarded as a practical transitional model toward fully continuous manufacturing (Pleitt et al., 2019; Pollock et al., 2017). The hybrid process provides significant operational and economic benefits while remaining compatible with existing facility infrastructures and regulatory expectations. Multiple studies demonstrate reduced buffer requirements, resin consumption, and capital expenditures in hybrid intensified configurations (Klutz et al., 2016; Mahal et al., 2021).

Techno-economic analyses consistently show that intensified and continuous processes can reduce cost of goods (COGs), particularly in multiproduct or small-scale facilities where flexibility is critical (Yang et al., 2019; Klutz et al., 2016). Perfusion enables smaller bioreactors with high volumetric productivity, reducing capital expenditures and supporting scale-out production models suited for personalized medicines and rare-disease biologics (Farid et al., 2020; Partopour & Pollard, 2025; Xu et al., 2020). Achieving economic and environmental advantages requires demonstrable productivity gains and careful minimization

of medium and buffer consumption, as emphasized in sustainability-integrated techno-economic assessments (Amasawa et al., 2021).

Digitalization further enhances intensified manufacturing by enabling real-time monitoring and predictive control. Advanced process analytical technology (PAT), digital twins, and model-based control systems provide the data foundation required for continuous validation and lifecycle-based regulatory frameworks (Gadgil, 2024; Genzyme & Konstantinov, 2015).

Despite the benefits described, implementation barriers remain. End-to-end continuous processing requires synchronized control strategies, robust data management, and advanced automation to ensure consistent product quality (Pleitt et al., 2019; Jones & Gerogiorgis, 2022). Existing regulatory paradigms, which are built around batch definitions and discrete release testing, require continued collaboration between regulators and industry to establish continuous-compatible models (Del Hierro et al., 2024). Cultural and organizational factors also influence adoption, as continuous manufacturing requires different competencies, operational cultures, and cross-functional integration (Lalor et al., 2019).

Future progress will rely on hybrid validation strategies, improved digital integration, harmonized sustainability metrics, and strengthened cross-sector collaboration. Standardized LCA methodologies are essential for transparent comparison of SU, multi-use, and intensified biomanufacturing approaches (Amasawa et al., 2021; Alaria et al., 2023; Bunnak et al., 2016). Ultimately, process intensification represents not only a technological evolution but a systemic transformation toward more flexible, resilient, and sustainable biomanufacturing ecosystems.

References:

Alaria, M., Barbaroux, M., McLaughlin, K., Monge, M., & Tillmanns, K. (2023). *Driving environmental sustainability in the biopharmaceutical industry.* Sartorius.

Amasawa, E., Kuroda, H., Okamura, K., Badr, S., & Sugiyama, H. (2021). Cost–benefit analysis of monoclonal antibody cultivation scenarios in terms of life cycle environmental impact and operating cost. *ACS Sustainable Chemistry & Engineering*, *9*(42), 14012-14021.

Bunnak, P., Allmendinger, R., Ramasamy, S. V., Lettieri, P., & Titchener-Hooker, N. J. (2016). Life-cycle and cost of goods assessment of fed-batch and perfusion-based manufacturing processes for mAbs. *Biotechnology progress*, *32*(5), 1324-1335.

Cataldo, A. L., Burgstaller, D., Hribar, G., Jungbauer, A., & Satzer, P. (2020). Economics and ecology: Modelling of continuous primary recovery and capture scenarios for recombinant antibody production. *Journal of Biotechnology*, *308*, 87-95.

Del Hierro, A. G., Moreno-Cid, J. A., & Casey, E. (2024). Continuous biomanufacturing for sustainable bioeconomy applications. *EFB Bioeconomy Journal, 4*, 100071.

Farid, S. S., Baron, M., Stamatis, C., Nie, W., & Coffman, J. (2020). Benchmarking biopharmaceutical process development and manufacturing cost contributions to R&D. *mAbs, 12*(1), 1754999.

Gadgil, M. (2024). *Breaking the $40 per gram barrier for mAbs.* Conference presentation.

Genzyme, & Konstantinov, K. (2015). *The promise of continuous biomanufacturing.* Genzyme White Paper.

Hutchinson, D. (2022). *Continuous biomanufacturing: A flexible approach for CDMOs.* Evotec Just White Paper.

Jones, W., & Gerogiorgis, D. I. (2022). Dynamic simulation, optimisation and economic analysis of fed-batch vs. perfusion bioreactors for advanced mAb manufacturing. *Computers & Chemical Engineering*, *165*, 107855.

Klutz, S., Holtmann, L., Lobedann, M., & Schembecker, G. (2016). Cost evaluation of antibody production processes in different operation modes. *Chemical Engineering Science*, *141*, 63-74.

Lalor, F., Fitzpatrick, J., Sage, C., & Byrne, E. (2019). Sustainability in the biopharmaceutical industry: Seeking a holistic perspective. *Biotechnology advances*, *37*(5), 698-707.

Lee, S. (2022). *Large-scale continuous biomanufacturing: Utilizing N-1 technology for higher productivity and quality.* Samsung Biologics Technical Report.

Mahal, H., Branton, H., & Farid, S. S. (2021). End-to-end continuous bioprocessing: Impact on facility design, cost of goods, and cost of development for monoclonal antibodies. *Biotechnology and Bioengineering*, *118*(9), 3468-3485.

Partopour, B., & Pollard, D. (2025). Advancing biopharmaceutical manufacturing: Economic and sustainability assessment of end-to-end continuous production of monoclonal antibodies. *Trends in Biotechnology, 43*(2), 462–475.

Pleitt, K., Somasundaram, B., Johnson, B., Shave, E., & Lua, L. H. (2019). Evaluation of process simulation as a decisional tool for biopharmaceutical contract development and manufacturing organizations. *Biochemical Engineering Journal*, *150*, 107252.

Pollock, J., Ho, S. V., & Farid, S. S. (2013). Fed-batch and perfusion culture processes: Economic, environmental, and operational feasibility under uncertainty. *Biotechnology and bioengineering*, *110*(1), 206-219.

Pollock, J., Coffman, J., Ho, S. V., & Farid, S. S. (2017). Integrated continuous bioprocessing: Economic, operational, and environmental feasibility for clinical and commercial antibody manufacture. *Biotechnology progress*, *33*(4), 854-866.

Walther, J., Godawat, R., Hwang, C., Abe, Y., Sinclair, A., & Konstantinov, K. (2015). The business impact of an integrated continuous biomanufacturing platform for recombinant protein production. *Journal of biotechnology*, *213*, 3-12.

Xu, J., Xu, X., Huang, C., Angelo, J., Oliveira, C. L., Xu, M., ... & Li, Z. J. (2020, January). Biomanufacturing evolution from conventional to intensified processes for productivity improvement: a case study. In *MAbs* (Vol. 12, No. 1, p. 1770669). Taylor & Francis.

Yang, O., Prabhu, S., & Ierapetritou, M. (2019). Comparison between batch and continuous monoclonal antibody production and economic analysis. *Industrial & Engineering Chemistry Research*, *58*(15), 5851-5863.

Digital Bioprocessing in the Context of Sustainability

Digital manufacturing based on recent developments in monitoring and data analysis, including the frame of Bioprocessing 4.0, integrates advanced digital, analytical, and modelling techniques to enable more sustainable, efficient, and resilient biomanufacturing systems. Its foundation lies in connecting process analytical technology (PAT), real-time data, and mechanistic and hybrid models to enhance process understanding and support data-driven decision-making (Isoko et al., 2024; Babi et al., 2022). Recent work in bioprocess technology demonstrates that combining models with advanced monitoring and control strategies enables continuous optimization of critical process parameters, partly entirely in silico, and improves operational robustness (Shariatifar et al., 2025). Also, sustainability-oriented modelling approaches increasingly link process design with sustainability parameters. Meramo et al. (2022) show how coupling bioprocess simulation with life-cycle indicators guides early-stage design decisions by quantifying trade-offs in energy, water, and

material use, whereas Demling et al. (2025) introduce the window of sustainable bioprocess operation (SBO window), defining operational ranges where processes remain simultaneously robust, efficient, and environmentally favorable. Together, these frameworks follow the SbD paradigm by embedding ecological considerations into iterative optimization loops.

Digitalization also transforms how sustainability-relevant data are generated and exploited. A recent study by Simon et al. (2025) demonstrates that replacing offline sampling with, in this case, inline Raman spectroscopy can eliminate approximately 13 kg of single-use plastics and prevent more than 80 kg of CO_2 emissions per combined small- and large-scale operation. Complementary optical PAT tools like UV-VIS slope spectroscopy further support sustainable biopharma production enabling continuous, reagent-free quantification of biomolecules during purification, significantly reducing sample waste and chemical consumption (Chemistry for Sustainability, 2024; Eifert et al., 2024). Similarly, compact microfluidic analytical systems deliver high-frequency, data-rich profiling of nutrient dynamics with minimal sample volume, reduced consumables, and streamlined workflows. Compared with traditional LC-MS or UHPLC workflows, such microfluidic platforms lower resource demands and increase analytical throughput (Azer et al., 2023). This indirect reduction of consumption can reduce the carbon footprint during downstream processing.

At the early investment stage, efficient reactor design and resource use, optimized through pre-use modeling (Ramonet et al., 2023), form a critical foundation for any SbD strategy. In parallel, artificial intelligence can enhance predictive maintenance, production scheduling, and emissions tracking across manufacturing scenarios (Ullagaddi, 2024). Integrated digital infrastructure, such as electronic batch records and laboratory information systems, further improve data integrity, traceability, and transparency, supporting evolving regulatory and ESG expectations (Isoko et al., 2024).

Although these digital and analytical technologies significantly strengthen sustainability-oriented bioprocessing, persistent challenges, including interoperability, standardization, and accessibility for small and medium organizations, must be addressed to enable broad adoption (Isoko et al., 2024). Looking ahead, industry 5.0 extends the bioprocessing 4.0 paradigm by integrating human expertise, cognitive robotics, and ethical data use to improve resilience, societal value creation, and sustainability outcomes (Selvam et al., 2023). In this evolution, bioprocessing 4.0 can become not only a digital transformation framework, but

also a foundational enabler of comprehensive SbD strategies, although the true quantification of benefits is still lacking.

References

Azer, N., Bush, X., Kohnhorst, C., Trunfio, N., Berilla, E., & Powers, D. (2023). *Evaluating traditional mass spectrometry against the new generation of emerging analytical technology.* FDA/CDER/OPQ/OBP/DBRRII. Poster presented at the FDA Science Forum 2023.

Babi, D. K., Griesbach, J., Hunt, S., Insaidoo, F., Roush, D., Todd, R., ... & Wittkopp, F. (2022). Opportunities and challenges for model utilization in the biopharmaceutical industry: current versus future state. *Current Opinion in Chemical Engineering*, *36*, 100813.

Chemistry for Sustainability. (2024). *Innovative UV spectrophotometry: Sustainable drug analysis.* https://chemistryforsustainability.org/community-news/innovative-uv-spectrophotometry-sustainable-drug-analysis

Demling, P., Rosenthal, K., & Grünberger, A. (2025). Window of sustainable bioprocess operation: towards merging environmental sustainability assessment and process operation at early-stage bioprocess development. *Current Opinion in Biotechnology*, *93*, 103292.

Eifert, T., Gerlach, M., Dahlmann, K., Lendl, B., Rädle, M., & Jaeger, M. (2024). Prozessanalytische Technologien (PAT) im Recycling: Übersicht und Praxisbeispiele. *Process Technology Online (GDCh).* Übersicht und Praxisbeispiele: Prozessanalytische Technologien (PAT) im Recycling • WPT – Fachportal für alle prozessrelevanten Themen aus den Bereichen Chemie, Pharma, Reinraum und Lebensmittel

Isoko, K., Cordiner, J. L., Kis, Z., & Moghadam, P. Z. (2024). Bioprocessing 4.0: a pragmatic review and future perspectives. *Digital Discovery*, *3*(9), 1662-1681.

Meramo, S., González-Delgado, Á. D., Sukumara, S., Fajardo, W. S., & León-Pulido, J. (2021). Sustainable design approach for modeling bioprocesses from laboratory toward commercialization: optimizing chitosan production. *Polymers*, *14*(1), 25.

Ramonet, F., Kovacevic, M., Haddadi, B., Jordan, C., & Harasek, M. (2023). Bioreactor Mixing: a Comparison of Computational Fluid Dynamics and Experimental Approaches in the Pursuit of Sustainable Bioprocessing for the Bioeconomy. *Chemical Engineering Transactions*, *105*, 265-270.

Selvam, A., Aggarwal, T., Mukherjee, M., & Verma, Y. K. (2023). Humans and robots: Friends of the future? A bird's eye view of biomanufacturing industry 5.0. *Biotechnology advances*, *68*, 108237.

Shariatifar, M., Rizi, M. S., Sotudeh-Gharebagh, R., Zarghami, R., & Mostoufi, N. (2025). On Digital Twins in Bioprocessing: Opportunities and Limitations. *Process Biochemistry*.

Simon, S., Pugh, P., Boppana, P., Allen, Z., Lemons, J., & Padmanabhan, V. (2025). Sustainability impacts for converting to Raman spectroscopy inline monitoring from traditional offline manual sampling in small-scale and large-scale biomanufacturing. *Journal of Chemical Technology & Biotechnology*.

Ullagaddi, P. (2024). Digital transformation strategies to strengthen quality and data integrity in pharma. *International Journal of Business and Management*, *19*(5), 16-26.

Barriers to Circular End-of-Life Strategies for Single-Use Systems

The sustainability challenges associated with SUT are closely linked to end-of-life management and material circularity. Circular economy concepts have been published that emphasize reuse, recycling, and closed-loop material flows (Ellen MacArthur Foundation, 2023; Geissdoerfer et al., 2017). However, while advances have been made or are foreseen at the stage of use, circularity remains a challenge. The increasing adoption of SUT in biopharmaceutical manufacturing has generated heterogeneous plastic waste streams that include packaging materials, multilayer films, tubing sets, filters, and assemblies incorporating sensors or metal components. The material complexity and functional design, especially of those components other than packaging material, limit the possibilities of separation and constrain current recycling options (Luu et al., 2022; McMahon et al., 2025). In practice, most post-use SUT is treated as biohazard, requiring decontamination prior to downstream processing, which increases operational effort and cost and frequently results in incineration as the default disposal route (ISPE, 2023). Industry surveys indicate that approximately 60% of SUT waste is thermally treated and around 30% is landfilled, while material recycling remains marginal. This practice stands in direct contrast to corporate sustainability strategies and global expectations for circular material flows (ISPE, 2023).

Material heterogeneity remains a primary barrier to circularity. Process-contact components often combine polymers with incompatible thermal and mechanical properties, multilayer structures, additives, and pigments that impair both mechanical and chemical recyclability (Hahladakis et al., 2018; Hopewell et al., 2009). Even in assemblies dominated by a single polymer, such as low-density polyethylene-based media and culture bags, process residues can reduce recyclate purity. Regulatory constraints further restrict circular pathways. There are currently no established approval mechanisms for introducing recycled polymers into GMP-relevant components, and conservative interpretations of contamination risks often preclude recycling even where materials can be recovered (McMahon et al., 2025).

Infrastructure and logistics constitute an additional challenge. Waste volumes vary across sites and are often insufficient to feed economically viable recycling streams. Specialized facilities capable of processing high-purity technical plastics from controlled environments remain limited, and the transport of potentially contaminated materials adds logistical complexity and cost (Ragaert et al., 2017). In this context, thermal treatment remains the most predictable and least operationally burdensome option for many manufacturers.

Standardization gaps also impede progress. Design heterogeneity across connectors, tubing dimensions, film types, and bag assemblies complicates sorting, reduces economies of scale, and undermines the development of consistent, high-volume recycling streams. As highlighted by Schmidhalter et al. (2022), the absence of design rules and the proliferation of bespoke assemblies increase the number of stock-keeping units (SKUs), reduce the applicability of standardized workflows, and diminish the feasibility of alternative end-of-life solutions.

Taken together, these intertwined technical, regulatory, organizational, and economic barriers constrain the transition from linear disposal practices toward circular EoL strategies for SUT. Addressing them requires coordinated action across material design, process operation, and regulatory frameworks.

References

Ellen MacArthur Foundation. (2023). *What is the linear economy?*

What is the linear economy? | Ellen MacArthur Foundation

Geissdoerfer, M., Savaget, P., Bocken, N. M. P., & Hultink, E. J. (2017). The circular economy—A new sustainability paradigm? *Journal of Cleaner Production, 143*, 757–768. https://doi.org/10.1016/j.jclepro.2016.12.048

Hahladakis, J. N., Velis, C. A., Weber, R., Iacovidou, E., & Purnell, P. (2018). An overview of chemical additives present in plastics: Migration, release, fate, and environmental impact during their use, disposal, and recycling. *Journal of Hazardous Materials, 344*, 179–199. https://doi.org/10.1016/j.jhazmat.2017.10.014

Hopewell, J., Dvorak, R., & Kosior, E. (2009). Plastics recycling: Challenges and opportunities. *Philosophical Transactions of the Royal Society B: Biological Sciences, 364*(1526), 2115–2126. https://doi.org/10.1098/rstb.2008.0311

ISPE. (2023). *Industry survey on single-use technology waste management*. End-Of-Life Management for Single-Use Products in Bioproduction | Pharmaceutical Engineering

Luu, D.-N., Barbaroux, M., Dorez, G., Mignot, K., Doger, E., Laurent, A., Brossard, J.-M., & Maier, C.-J. (2022). Recycling of post-use bioprocessing plastic containers—Mechanical recycling technical feasibility. *Sustainability, 14*(23), 15557. https://doi.org/10.3390/su142315557

McMahon, J., Fleming, D., Owende, P., & Goggin, D. (2025). Exploring the sustainability of single-use plastics in the biopharmaceutical sector: A scoping review. *Frontiers in Sustainability*.

Ragaert, K., Delva, L., & Van Geem, K. (2017). Mechanical and chemical recycling of plastics: State of the art and challenges. *Waste Management, 69*, 24–58. https://doi.org/10.1016/j.wasman.2017.07.044

Schmidhalter, D. R., Schmidt, A. C., Beck, S., & Morgenstern-Egli, S. A. (2022). A strategic approach to the management of single-use technology. *Chemie Ingenieur Technik, 94*(12), 1902–1913. https://doi.org/10.1002/cite.202200146

Current End-of-Life Options and Perspectives

Packaging material is a high share of the whole material, in particular plastic material wrapped around plastic bags. To recycle this material is a matter of collection, and recycling routes are not different from any other packaging waste. This is, therefore, not further

described. The focus is on material that was in contact with any process-related matter, biological material, intermediates, or products.

Mechanical recycling remains the most immediately feasible end-of-life pathway for selected components, particularly low-density polyethylene (LDPE) bioprocess containers, if pre-sorting, disassembly, and decontamination routines are implemented. Recent LCAs confirm environmental benefits over incineration when material purity and sufficient volumes can be achieved (Luu et al., 2022; Walker & Rothman, 2020). However, contamination risks, polymer heterogeneity, and fragmented waste streams restrict mechanical recycling to a limited subset of SUT components.

Chemical recycling expands the range of recoverable plastics, particularly for complex, multilayer, or additive-rich structures that are not amenable to mechanical processing. The STRAP™ (solvent-targeted recovery and precipitation) process is a dissolution-based approach guided by thermodynamic solubility modelling and sequential solvent/antisolvent selection, enabling selective polymer dissolution and controlled precipitation without polymer chain degradation. Walker et al. (2020) demonstrated near-complete deconstruction of a commercial multilayer film into PE, EVOH, and polyethylene terephthalate (PET) with high material efficiency and provided techno-economic evidence for potential cost-competitive recycled resins under defined feed scenarios. More recently, Sanchez-Rivera et al. (2025) extended STRAP to complex post-industrial mixed plastic waste streams, reporting recovery of up to ten polymers (e.g., LDPE, high-density polyethylene (HDPE), polypropylene (PP), EVOH, PET, polyvinyl chloride (PVC), and polyamides) with polymer-specific recovery yields exceeding 89%. Together, these studies indicate that STRAP can enable high-value recycling routes for multilayer films relevant to biomanufacturing if material compositions are sufficiently standardized and contamination is effectively controlled.

Beyond technological development, operational recycling programs across the life-science sector demonstrate that regulated environments can support material recovery when waste streams are well characterized and logistics are coordinated. Established take-back and recycling schemes for injection devices and PVC-based consumables illustrate how product-specific massification, source segregation, and centralized processing enable recycling under strict hygiene and safety requirements (Vinyl Council of Australia, 2020; Pharmaceutical

Journal, 2023). These approaches are conceptually transferable to rigid SUT components in biopharmaceutical manufacturing, such as connectors, housings, and caps.

Laboratory recycling programs provide a further relevant analogue. Initiatives targeting pipette tip racks, tubes, microplates, personal protective equipment, and mono-material packaging demonstrate that controlled laboratory environments can generate sufficiently homogeneous and traceable waste streams to support recycling despite contamination-sensitive conditions (TerraCycle, 2024; Eppendorf SE, 2023; Kimberly-Clark Professional, 2022). Key enabling factors include source segregation, documentation of material specifications, and supplier-led or centralized logistics, conditions that closely resemble those in biopharmaceutical production.

Within biopharmaceutical manufacturing itself, early pilot projects indicate that recycling of SUT materials is technically feasible under GMP-related constraints. Mechanical recycling studies on post-use bioprocess containers show that LDPE-dominant materials can retain adequate properties for non-critical applications following appropriate sorting and decontamination, with favorable life-cycle performance compared to incineration (Luu et al., 2022). In addition, closed-loop initiatives for high-specification polymers, such as polycarbonate components used in small-scale bioreactors, suggest that even demanding SUT materials can be reintegrated into new products when traceability, controlled decontamination, and polymer characterization are ensured (Sartorius & Covestro, 2024).

In summary, current end-of-life approaches demonstrate that technical solutions for improving the circularity of single-use technologies are emerging but remain constrained by system-level factors. While both mechanical and chemical recycling pathways show technical feasibility under defined conditions, their broader deployment is limited by material heterogeneity, fragmented waste streams, regulatory requirements, and economic viability. Consequently, effective end-of-life strategies for biopharmaceutical SUT cannot be addressed in isolation but require alignment with upstream design choices, material standardization, and coordinated logistics across the value chain (Luu et al., 2022; Walker & Rothman, 2020).

References

Luu, D.-N., Barbaroux, M., Dorez, G., Mignot, K., Doger, E., Laurent, A., Brossard, J.-M., & Maier, C.-J. (2022). Recycling of post-use bioprocessing plastic containers - Mechanical recycling technical feasibility. *Sustainability, 14*(23), 15557. https://doi.org/10.3390/su142315557

Sanchez-Rivera, K. L., Zhou, P., Radkevich, E., Sharma, A., Bar-Ziv, E., Van Lehn, R. C., & Huber, G. W. (2025). A solvent-targeted recovery and precipitation scheme for the recycling of up to ten polymers from post-industrial mixed plastic waste. *Waste Management, 194*, 290–297. https://doi.org/10.1016/j.wasman.2025.01.022

Walker, T. W., Frelka, N., Shen, Z., Chew, A. K., Banick, J., Grey, S., Kim, M. S., Dumesic, J. A., Van Lehn, R. C., & Huber, G. W. (2020). Recycling of multilayer plastic packaging materials by solvent-targeted recovery and precipitation. *Science Advances*, *6*(47), eaba7599. https://doi.org/10.1126/sciadv.aba7599

Walker, S., & Rothman, R. (2020). Life cycle assessment of bio-based and fossil-based plastic: A review. Journal of Cleaner Production, 261, 121158. https://doi.org/10.1016/j.jclepro.2020.121158

Eppendorf SE. (2025). Recycling of used lab consumables? . https://www.eppendorf.com/ch-de/company-careers/sustainability/environment/plastics/recycling-used-plastics/

Kimberly-Clark Professional. (2025). *Kimberly-Clark Professional™ ICON™-Kollektion und RightCycle™*. https://www.kcprofessional.com/en-us/solutions/kimberly-clark-professional-icon-dispenser-collection

Pharmaceutical Journal. (2023). *Patients return 200,000 injection pens through recycling scheme*. https://pharmaceutical-journal.com/article/news/patients-return-200000-injection-pens-through-recycling-scheme

Sartorius & Covestro. (2024). *On the Path to Circularity: Sartorius and Covestro Prove the Recycling Potential of Small-Scale Bioreactors*. https://www.sartorius.com/en/company/newsroom/blog/working-on-the-future-of-plastics-recycling-in-biopharma-1652138

TerraCycle. (2024). *Laboratory plastics recycling programmes*. https://shop.terracycle.com/en-US/pages/sciencecycle

Vinyl Council of Australia. (2025). *PVC recycling in hospitals.* https://www.vinyl.org.au/pvc-recycling-in-hospital

Short-Term Implementable Measures and Integration into Sustainability-by-Design

Short-term measures with immediate applicability in GMP-regulated environments primarily address waste stream simplification, design rationalization, and logistical optimization. Industry surveys consistently identify manual or semi-automated disassembly and mono-material separation as the most practical initial steps to improve recyclability of SUT assemblies, as they enable removal of non-recyclable components and targeted routing of dominant polymer fractions (ISPE, 2023).

Design standardization represents a particularly high-impact lever. Harmonizing connectors, tubing dimensions, and film types across product lines and sites reduces sorting complexity, supports material massification, and increases the feasibility of both mechanical and chemical recycling pathways. This aligns with strategic assessments showing that uncontrolled design variability constitutes a structural barrier to end-of-life innovation and supply-chain efficiency (Schmidhalter et al., 2022).

Additional short-term options include selective reuse of non-contaminated auxiliary components, predefined recycling partnerships for specific polymers (e.g., PE or PP), and structured routing of materials requiring thermal treatment, where energy recovery remains necessary. While these measures do not eliminate the need for incineration, they can reduce overall environmental impact when embedded in broader footprint-reduction strategies.

Integrating end-of-life considerations into SbD frameworks requires shifting key decisions upstream, including prioritizing mono-material construction where feasible, reducing sensor and component diversity, enabling modular assembly concepts, and ensuring traceability of material composition across the lifecycle. Emerging chemical recycling approaches such as STRAP further illustrate how material and film design choices made today can determine future eligibility for high-value recycling, reinforcing the link between SbD principles and long-term circularity of biopharmaceutical SUT.

References:

ISPE. (2023). *Industry survey on single-use technology waste management*. End-Of-Life Management for Single-Use Products in Bioproduction | Pharmaceutical Engineering

Schmidhalter, D. R., Schmidt, A. C., Beck, S., & Morgenstern-Egli, S. A. (2022). A strategic approach to the management of single-use technology. *Chemie Ingenieur Technik, 94*(12), 1902–1913. https://doi.org/10.1002/cite.202200146

Conclusion

Sustainability in biopharmaceutical manufacturing is increasingly determined by the integration of regulatory frameworks, process design choices, and data-driven engineering. The growing use of SUT has intensified the need to address environmental impacts across the full lifecycle, particularly regarding material use, waste generation, and supply-chain-related emissions. Current evidence shows that sustainability challenges in biomanufacturing cannot be resolved through isolated technical measures. Addressing these challenges requires coordinated governance mechanisms across biopharmaceutical supply chains, combining collaborative, behavioral, operational, and authoritative approaches, as summarized in Figure 6.

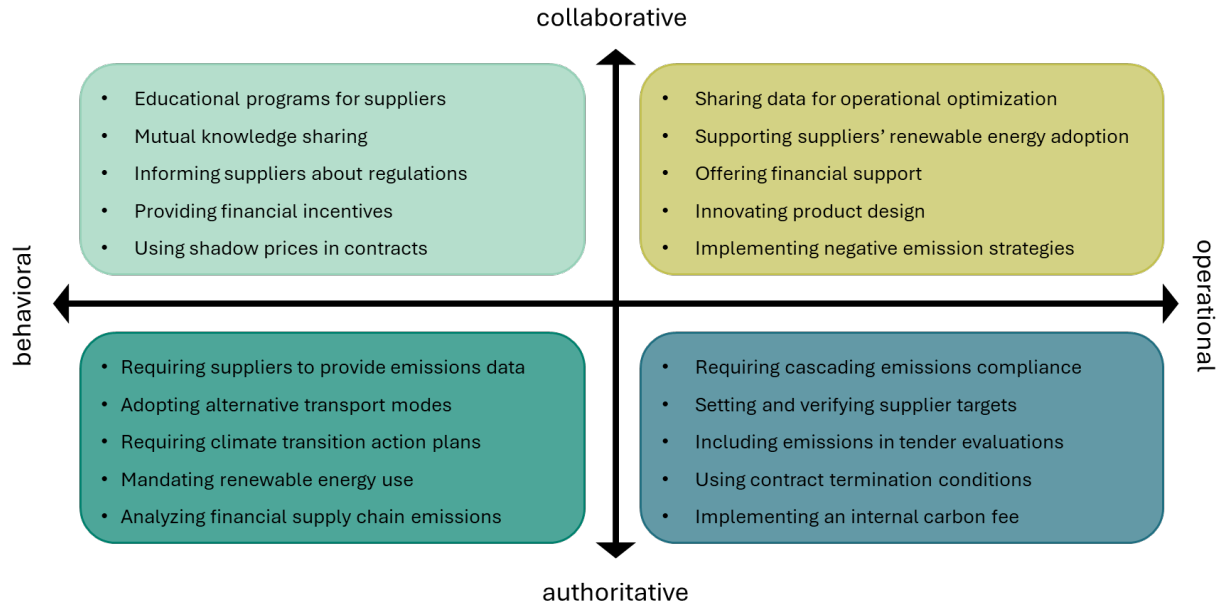


Figure 6: Governance mechanisms for implementing sustainability across biopharmaceutical supply chains.

End-of-life solutions for SUT remain constrained by material complexity, regulatory uncertainty, and fragmented infrastructure, limiting their scalability. As a result, downstream waste management options alone are insufficient to achieve meaningful environmental improvements. Although overall material use in biopharmaceutical production is low in comparison to global plastics use—and SUT contribution to high-value products and to avoid GHG relevant emissions in other sectors is evident—the biopharmaceutical industry is nevertheless expected to contribute to sustainable manufacturing. As a sector dedicated to improving human health, it is both logical and imperative that the industry also prioritizes minimizing environmental impacts and mitigating GHG emissions across its value chain.

SbD, therefore, emerges as a central organizing principle, shifting decision-making upstream to stages where material selection, process architecture, and equipment design exert the greatest influence on lifecycle emissions. Process intensification, continuous manufacturing, and digitalization enable more efficient resource use and support earlier identification of environmental trade-offs. Their effectiveness depends on the application of sustainability metrics that adequately reflect both material and energy drivers rather than single, isolated indicators.

Overall, progress toward sustainable biomanufacturing requires coordinated, system-level action across development, manufacturing, and supply chains. Embedding SbD principles early, aligning process innovation with regulatory expectations, and strengthening methodological consistency in sustainability assessment are essential to translating environmental ambition into operational practice. To achieve substantial progress from current practices, particularly in terms of data generation and analysis, reducing material and design variability in SUT is essential to supporting scalable lifecycle management. The definition and application of harmonized sustainability metrics that capture both material- and energy-related impacts at the design and operation stage is required. Furthermore, end-of-life strategies must be better integrated into upstream design decisions rather than treating waste management as a standalone optimization problem.

Author contributions

All authors contributed equally to writing and reviewing the manuscript.

Conflict of Interest

All authors declare to have no conflict of interest.

Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Data availability statement

Not applicable.