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Comparative life cycle assessment of stainless steel and single-use bioreactor units: A laboratory scale case study

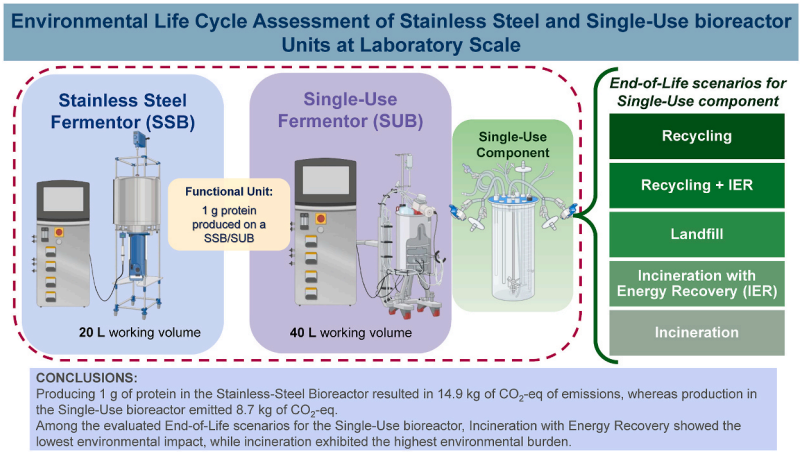
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HIGHLIGHTS

- Life Cycle Assessment comparing stainless-steel and single-use bioreactors.
- Study based on primary industrial data from a GSK biomanufacturing facility.
- Single-use system shows lower CO_2 emissions under baseline conditions.
- End-of-life scenarios strongly affect single-use technology sustainability.
- Provides insights to guide sustainable biopharmaceutical manufacturing.

GRAPHICAL ABSTRACT



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ABSTRACT

In recent years, the biopharmaceutical industry has witnessed a surge in the adoption of Single-Use technologies; however, concerns about environmental sustainability have arisen due to the substantial amount of solid plastic waste generated by implementing such technologies. This study presents a comparative Life Cycle Assessment grounded in an industrially applied case study at a pharmaceutical facility in Italy, using primary operational data. The assessment evaluates two distinct laboratory scale bioreactor units reflecting the actual equipment configuration at the facility: a conventional stainless-steel bioreactor (SSB) and a single-use bioreactor (SUB). The assessment followed a cradle-to-grave approach over a 20-year operational horizon, normalising the results to the functional unit of 1 g of protein produced in a bioreactor. Five end-of-life scenarios for the single-use bioreactor were explored: landfill, incineration, incineration with energy recovery (IER), recycling and a combined recycling with IER scenario. Results across all 16 evaluated impact categories consistently show that the

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SSB exhibits a higher environmental burden than the SUB. In the Climate Change impact category, producing 1 g of protein in the SSB emitted 14.9 kg of CO_2-eq., whereas the SUB emitted 8.7 kg of CO_2-eq, assuming landfill as the base case disposal method. Electricity consumption was identified as the dominant environmental driver for both systems. The study also demonstrates that end-of-life management is not a marginal factor. The environmental profile of the SUB varied across disposal scenarios, with IER providing the most ecological benefits. These findings confirm that the disposal of plastic components emerges as a critical factor in assessing the environmental sustainability of single-use technologies.

1. Introduction

The 2030 Agenda for Sustainable Development and its environmental goals, particularly those targeting reductions in greenhouse gas (GHG) emissions and mitigating global warming, have brought together all sectors of society. Political, economic, industrial, cultural, and educational stakeholders are increasingly engaged in conversations about climate change and sustainability. A central theme in these discussions is the development of environmentally responsible technologies and processes that minimise environmental and human health impacts. While often perceived as a non-pollutant industry, the global pharmaceutical sector is responsible for approximately 5% of the global GHG emissions (Darley, 2025). The environmental footprint of the pharmaceutical sector is driven by energy intensive manufacturing processes, resource-heavy supply chains and pharmaceutical waste disposal. To address environmental concerns, the World Business Council for Sustainable Development (WBCSD) published the 'Roadmap to Nature Positive: Foundations for the Pharmaceutical Sector,' which establishes five critical pillars for environmental mitigation: i) reducing water use, ii) addressing pollution risks from Active Pharmaceutical Ingredients (APIs), iii) mitigating GHG emissions across the value chain, iv) improving supply chain transparency, and v) reduce solid waste across the value chain (World Business Council for Sustainable Development (WBCSD), 2025).

Driven by strong international competition and growing financial pressures in the healthcare sector, the pharmaceutical industry has undergone a significant shift in its manufacturing practices, transitioning from conventional Stainless Steel (SS) equipment to the adoption of Single-Use Technologies (SUTs). Also referred to as disposable technologies, SUTs encompass a range of plastic-based manufacturing tools, equipment and components intended for one-time use (Eibl and Eibl, 2019). Unlike SS systems, which require cleaning and sterilisation between batches, SUTs are pre-sterilised and discarded after use, eliminating the need for cleaning-in-place (CIP) and sterilisation-in-place (SIP) procedures.

Shifting to SUTs offers several advantages, including increased process and product flexibility, reduced cross-contamination risks, reduced down-time and material consumption associated with cleaning and sterilisation tasks, and lower capital investment and infrastructure costs. However, SUTs also present limitations, such as the potential migration of leachables and extractables from the plastic into the product, limited scalability, and, remarkably, the generation of plastic solid waste (Eibl and Eibl, 2019), (Pietrzykowski et al., 2013). In 2019, it was estimated that annually around 30,000 tonnes of biopharma single-use products were disposed of via landfill or incineration (MacDonald, 2019). Nevertheless, the operational benefits of single-use platforms often outweigh the waste management burden, a trend accelerated by the COVID-19 pandemic's demand for rapid, flexible biomanufacturing (Langer, 2022). Nonetheless, concerns regarding the sustainability of these technologies persist. This paradigm shift raises a fundamental question: which technology offers a more sustainable path: one that avoids plastic waste but relies heavily on utilities such as water and steam, or one that relies on disposable plastic components?

To address this question, the internationally recognized Life Cycle Assessment (LCA) methodology for evaluating environmental consequences throughout a product's entire life cycle represents a robust analytical tool (Sphera). Several studies have applied LCA to pharmaceutical manufacturing to compare SS and Single-Use (SU) systems (Pietrzykowski et al., 2013;Barbaroux et al., 2020;GE Healthcare, 2020a;Budzinski et al., 2022), generally concluding that SUTs offer a more environmentally favourable profile than traditional SS technologies. For instance, Pietrzykowski et al. (2013) identified the bioreactor and the CIP/SIP systems as key units and major contributors to environmental impacts, highlighting their importance in LCA studies. (Budzinski et al., 2022) conducted an LCA on a 2000 L scale single-use process train for bulk drug substance production and found that upstream operations accounted for almost 80% of the total impact for every single impact category, with electricity consumption emerging as the dominant contributor across all impact categories.

As the pharmaceutical industry continues to evolve, SUTs appear to be emerging as the preferred technology for manufacturing pharmaceutical products. However, it is imperative not to overlook the associated environmental consequences. Addressing these issues is crucial for driving sustainability in the biopharmaceutical industry and guiding responsible innovation and technological advancements.

In the present study, we conduct a case study LCA comparing two specific process units at laboratory scale: a conventional 20 L Stainless-Steel Bioreactor (SSB) and a 40 L Single-Use Bioreactor (SUB). The study focuses on the production of a protein of interest through a laboratory-scale fermentation process over a 20 year-operation and a production target of 30 kg of protein.

The article is structured as follows: Section 2 details the four phases of the LCA, beginning with the goal and scope definition and a discussion of the study's assumptions and limitations; this is followed by the development of the Life Cycle Inventory (LCI) and a description of the Life Cycle Impact Assessment (LCIA) method. Section 3 presents the study's results, providing a cradle-to-grave analysis and evaluating five end-of-life (EoL) scenarios for the SUB plastic components: landfill, incineration, incineration with energy recovery, and a combined recycling and energy recovery model. Finally, Section 4 concludes the study by integrating the findings with existing literature, offering a comprehensive discussion on the environmental implications of adopting single-use technologies in pharmaceutical manufacturing.

2. LCA methodology

2.1. Goal and scope

This study was carried out in accordance with the ISO 14040 and ISO 14044 standards for Life Cycle Assessment (International Standards Organization (ISO), 2021), (International Standards Organization (ISO), 2020). The primary objective of this study is to compare the environmental footprint of two specific bioreactor technologies: a conventional technology based on SS and an alternative technology based on SU components, within the context of a laboratory scale biopharmaceutical process.

This work represents a case study for a pharmaceutical facility of GSK in Italy. The study specifically aims to provide insights for pharmaceutical companies and stakeholders currently evaluating a transition from conventional stainless-steel equipment to single-use technologies. In many industrial contexts, companies do not immediately adopt a full production train of single-use components; instead,

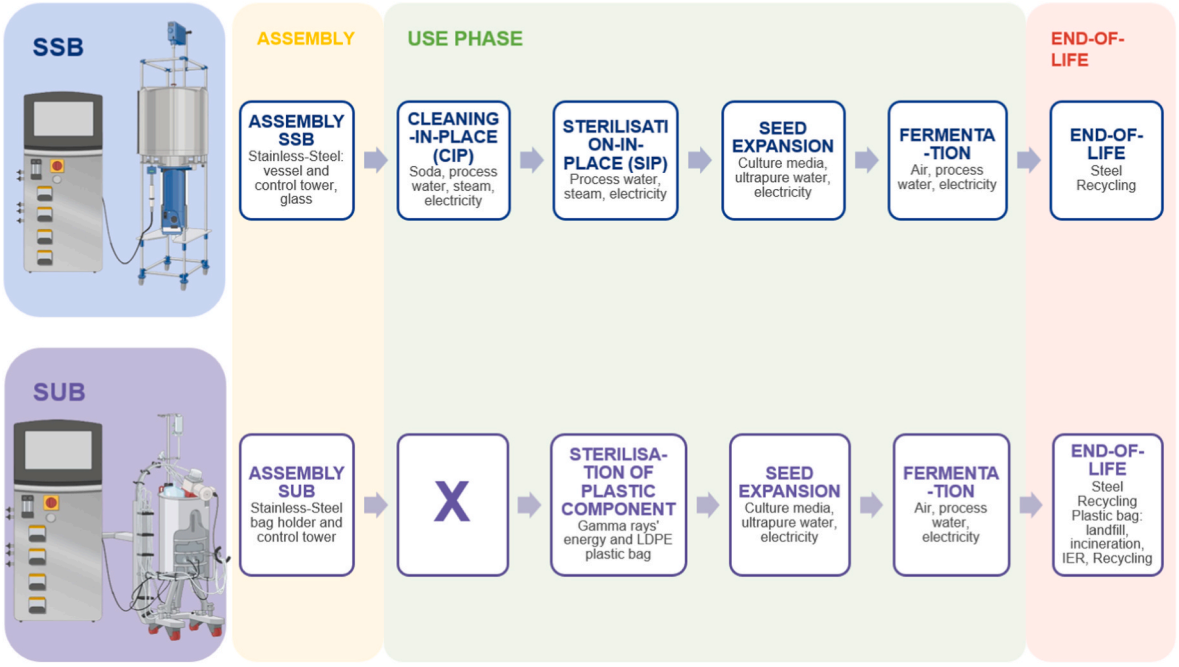


Fig. 1. Processes and life cycle stages considered for each technology, upper part: SSB, lower part: SUB.

they often begin by transitioning specific stages, such as upstream operations. Consequently, this case study provides a critical baseline for understanding environmental trade-offs by the technologies analysed. We believe that providing this level of detail for specific commercial units offers necessary information that reflects the current state of the industry and supports data-driven decision-making within the pharmaceutical sector.

2.1.1. System boundaries

The study considers a cradle-to-grave approach, encompassing all life cycle stages from the extraction of raw materials and manufacturing equipment to the operational use phase and the final end-of-life treatment. A graphical representation of the system boundaries can be seen in Fig. 1.

- **Assembly of the Bioreactor:** it includes the extraction of raw materials and the production of components such as stainless steel, glass, and copper wire. However, energy consumption associated with the assembly or welding of the bioreactor was excluded due to a lack of primary data from the original equipment manufacturers regarding specific assembly techniques and energy intensities.
- **Operational Use Phase:** this stage accounts for the utilities required for each bioreactor when a batch is carried out, including steam, process water, and chemicals, alongside electricity consumption. For the SSB, the use phase encompasses Cleaning-In-Place (CIP), Sterilisation-In-Place (SIP), Inoculum Preparation, and Fermentation. Conversely, the SUB considers Sterilisation of the plastic component, Inoculum Preparation and Fermentation.
- **End-of-Life:** this stage considers the final disposal of the equipment. For the SSB, the model includes the recycling of the stainless-steel parts. For the SUB, the recycling of durable steel parts is included, alongside five different scenarios for the single-use plastic component: Landfill, Incineration, Incineration with Energy Recovery (IER), Recycling and a combined scenario of Recycling with IER.

2.1.2. Functional unit

The Functional Unit (FU) for this study is defined as the **production of 1 g of protein in a bioreactor (SSB or SUB).** This FU allows for a direct comparison between the two technology platforms. To relate the FU to the processes of each system, a reference flow was established based on the production yield of this specific biological process.

The yield was considered equal for both technologies and set to 0.75 g of protein per Litre, for a single batch. Reflecting the specific infrastructure and equipment utilised in this case study, the SSB operated at a 20 L working volume, while the SUB operated at a 40 L working volume. The technical justifications and methodological implications of this choice are detailed in the Assumptions and Limitations section.

2.1.3. Assumptions and limitations

The assumptions of the study are listed next:

- The lifetime for all stainless-steel components (the SSB unit and the durable components for the SUB) is assumed to be 20 years (Haigney, 2019), a typical lifetime of SS equipment used in pharmaceutical production.
- Energy and related emissions from the assembly and welding of the bioreactors were excluded with regards to specific manufacturer assembly techniques and energy intensities.
- Specific minor components of the SSB and SUB were excluded from the inventory founded on a mass-based approach, as their individual contributions were negligible relative to the main SS structure. (See Section 1.1.1 and 1.2.1 from the Supplementary Information).
- Fermentation parameters (pH, temperature, dissolved oxygen) and protein yield (0.75 g/L) were assumed identical for both systems.
- A transport distance of 1200 km was assumed for the delivery of bioreactor units and single-use components from the manufacturing site (Germany) to the GSK facility (Italy).
- An average transport distance of 500 km was assumed for the transport of waste from the GSK facility to the waste treatment and recycling centres.

The authors acknowledge the difference in working volumes between the two analysed technologies. As noted in literature, single-use cultivation containers are not standardised across manufacturers, and not all sizes of cultivation containers are available for every SUB type and scale (Jossen et al., 2019); specifically, a smaller cultivation bag for the specific SUB model was not commercially available at the time of the study. The comparison of these two scales reflects the actual equipment configuration at the GSK facility: a stainless-steel unit, (geometrical volume of 31 L and working volume of 20 L), and an acquired single-use system, (geometrical volume of 68L; and a working volume of 40 L).

The authors acknowledge that operating the SUB at a reduced working volume (e.g., 20 L instead of 40 L) would materially affect the environmental results by increasing the impact per functional unit, as the fixed burdens of plastic production and sterilisation would be amortised over a smaller protein yield. However, given that the specific SUB model utilised in this study features a total geometric volume of 68 L, operating the unit at only 20 L would represent a significant insufficient use of the bioreactor unit and its disposable components. Consequently, the decision to utilise a 40 L working volume was driven by a commitment to process efficiency. The study reflects an industrial strategy aimed at minimizing the relative environmental footprint of single-use components through increased production throughput.

The selection of the single-use system was based on a careful consideration of key technical factors, including the design parameters of the bioreactor, the scale of operation, and the production organism's requirements (Jossen et al., 2019). In this case study, the GSK team chose the single-use equipment that most effectively aligned with the biological process requirements. This approach reflects common industry practice, where teams experienced in stirred stainless-steel systems select the most suitable plastic-based equivalent available.

Regarding the implications of comparing different scales, it must be emphasized that scaling biopharmaceutical processes is neither linear nor uniform across different process volumes (Jossen et al., 2019). Scaling up also changes the cell culture environment, directly impacting in product quality and process characteristics, such as production yield. Because yields at larger scales (e.g., 200 L or 500 L) cannot be accurately predicted without extensive empirical pilot data, the authors chose to maintain the integrity of primary data collected at the 20 L and 40 L scales. Consequently, the results described in this study are highly specific to this particular protein production and laboratory scale. Furthermore, moving to a larger scale would require speculative data regarding the mass of stainless-steel parts and single-use components, which would undermine the transparency and accuracy of the life cycle inventory.

2.2. Life cycle inventory (LCI)

The LCI was developed using primary data from the GSK biopharmaceutical facility located in Italy, supplemented by the Ecoinvent 3.10 (Cut-off) database for background processes. The preferred geography was selected as Europe (RER), specifically utilizing the Italian national grid mix for electricity. Where regional data were unavailable, global (GLO) datasets were employed. A detailed breakdown of the inventory, including all inputs, outputs and waste streams, is provided in Section 1 of the Supplementary Information (SI).

2.2.1. Bioreactors materials of construction

The inventory for the bioreactor systems was compiled using data from the technical datasheets of the manufacturers. The SSB inventory includes the vessel, supply unit, and control tower, accounting for stainless steel, glass, electronic components, and copper wiring (SI Section 1.1.1). The SUB inventory encompasses the durable stainless-steel bag holder, control tower, electronic components, and copper wiring (SI Section 1.2.1). The environmental impacts of these durable stainless-steel parts were amortised over a 20-year operational lifetime, normalised in terms of the total protein produced during this period (refer to Section 2.2.3 of this article).

2.2.2. Bioreactors operation

Utility and electricity consumption during the use phase were calculated using primary data from the facility monitoring systems and heat-transfer equations.

Stainless Steel Bioreactor (SSB): The use phase includes Cleaning-In-Place (CIP) and Sterilisation-In-Place (SIP) operations, accounting for process water, sodium hydroxide (soda), steam, and electricity. The seed expansion and fermentation stages include culture media and electricity for agitation and aeration for fermentation. Additionally, process water required for cooling the vessel to fermentation temperature was calculated using heat-transfer equations. The fermentation phase lasted 72 h. For the detailed LCI of the SSB, refer to the Supplementary Information Section 1.1, in which the specific amounts of utilities and energy are displayed for each operation (Table S3–S10).

Single-Use Bioreactor (SUB): The SUB model includes the mandatory gamma-ray sterilisation of the plastic component (11.2 kg of Low-Density Polyethylene, LDPE) prior to use, with energy requirements derived from literature (Rawlings and Pora, 2009). Transport of the disposable bag (1200 km) was accounted for each time that a single-use component has to be acquired. The seed expansion and fermentation stages include culture media and electricity for agitation, specifically for fermentation aeration and cooling water are considered. For cooling water, heat transfer was modelled by accounting the thickness of the two material layers (the stainless-steel jacket and the plastic liner). Electricity was computed for a 72-h operational window. Detailed utility and energy data is provided in SI Tables S12–S15.

2.2.3. Operational horizon and total production

To assess the long-term environmental performance of both technologies, the study assumes an operational horizon of 20 years, representing the typical life of stainless-steel pharmaceutical equipment. Over this period, a production target of 30 kg of protein was established as the basis of calculation. To reach this target, the SSB (with a 20 L working volume) needs to perform a total of 2000 batches, whereas the SUB (40 L working volume) requires 1000 batches, assuming the constant yield of production.

This approach accounts for the recurring impacts of the SUB system, specifically the production, sterilisation and transportation of 1000 disposable plastic bags, and the end-of-life treatment of plastic residue. It contrasts them against the utility demands (water, steam, and chemicals) required for the 2000 CIP and SIP cycles of the SSB system.

2.2.4. End-of-life (EoL)

End-of-Life scenarios were modelled using the Circular Footprint Formula (CFF), developed by the Joint Research Centre (JRC) of the European Commission's science and knowledge service (Zampori and Pant, 2019). The CFF integrates material recovery, energy recovery, and final disposal. Parameters for stainless steel and plastic materials from the CFF formula were taken from Annex C of the CFF guidelines (European Platform on LCA et al., 2020) (Supplementary Information Section 2; Table S16).

Stainless steel components given the significant economic value of stainless steel, and its capacity of being recycled without quality loss (Team Stainless Org, 2019), a recycling rate of 85% was applied for the stainless-steel components of both systems (Haigney, 2019), (Team Stainless Org, 2019). This EoL scenario accounts for the avoided burden of steel production coming from virgin raw materials.

Plastic Component: five different scenarios were modelled for the waste treatment of the LDPE bags.

- Landfill: accounts for the collection and disposal in a sanitary landfill.
- Incineration: accounts for the complete incineration of the plastic component.
- Incineration with Energy Recovery (IER): modelled with the parameters from the CFF Annex C (European Platform on LCA et al.,

2020), and energy recovery efficiencies of 22.5% for electricity and 27.8% for heat (Dong et al., 2020).
- Recycling: based on Polyethylene (PE) recycling data (Arena et al., 2003), (Hoffmann et al., 2025), assuming that 60% is efficiently recycled and the rest 40% goes to incineration.
- Recycling + IER: a combined scenario assuming 60% of the plastic component goes to recycling and 40% goes to IER (Budzinski et al., 2022). This combined scenario could reflect a realistic limitation: only the portions of plastic not in contact with the biological product can be recycled, while contaminated portions or parts of the material with direct contact require incineration (MacDonald, 2019).

None of the modelled scenarios considered disassembly or decontamination of the single-use component. Detailed modelling and CFF implementation, is provided in SI Section 2.2 (Table S19–S23).

2.3. Data quality

A semi-quantitative assessment of data quality was performed using the Pedigree Matrix approach by Weidema and Wesnæs (Pedersen Weidema and Suhr Wesnaes, 1996). The data sources were evaluated against six data quality indicators: reliability, completeness, temporal correlation, geographic correlation, further technological correlation, and sample size. Each indicator was assigned a score from 1 to 5 based on quality levels. These scores were then translated into uncertainty factors, which were aggregated to calculate the square of the geometric standard deviation. This value represents the 95% confidence interval and was used to characterize the uncertainty of the inventory data within the life cycle model. The LCI inventories are provided in the SI along with their corresponding scores (Table S1–S23). The resulting uncertainty ranges for the primary impact categories, derived from the Pedigree Matrix scores, are illustrated in Figure S.1 and Figure S.2 of the SI.

2.4. Life Cycle Impact Assessment

The openLCA software and the Ecoinvent 3.10 (Cut-off) database were used to conduct the study. The impact assessment was performed using the Environmental Footprint (EF) 3.1 method. This method consists of 16 midpoint characterized impact categories, which translate the inputs and outputs from the life cycle inventory into potential environmental impacts. The 16 impact categories analysed, including their indicators and units are summarized in Table 1.

3. Results and discussion

The primary focus of this study was the assessment of Climate Change and Water Use, impact categories. The cradle-to-grave analysis encompasses the encompasses the manufacturing of the equipment, the operational use phase, and the base case EoL scenario, defined as SS recycling and Landfilling for the SU plastic component.

3.1. Cradle-to-grave analysis

The characterised results across all 16 evaluated impact categories demonstrate that the SSB exhibits a higher environmental impact than the SUB. As illustrated in the radar chart (Fig. 2), the SSB (represented by the blue outer line) defines the 100% threshold, while the SUB (represented by the purple inner line) presents lower impacts. The relative values of the SUB remain above 50% in all impact categories. Detailed results for the 16 impact categories are provided in the SI – Section 3.

The most pronounced differences between the two systems are observed in Climate Change and Water Use. The inferior environmental performance of the SSB in these categories is primarily attributed to the high electricity demand alongside steam for sterilisation. In the Water

Table 1
Impact categories of the Environmental Footprint (EF) 3.1 Method (Bassi et al., 2023).

Impact category	Indicator/ Abbreviation	Unit	Environmental Significance
Acidification	Accumulated Exceedance (AE)	*mol H^+ $^-$eq*	Measures the potential for acidifying substances to increase the acidity of soil and water bodies.
Climate Change	Radiative forcing as Global Warming Potential (GWP100)	*kg CO_2-eq*	Measures the potential of greenhouse gas emissions to trap heat in the atmosphere over a 100-year horizon.
Ecotoxicity, freshwater	Comparative Toxic Unit for Ecosystems (CTUe)	*CTUe*	Estimates the potential for toxic substances to harm freshwater aquatic species.
Eutrophication, freshwater	Fraction of nutrients reaching freshwater end compartment	*kg P-eq*	Evaluates the potential for excessive phosphorus enrichment in freshwater, leading to oxygen depletion and biodiversity loss
Eutrophication, marine	Fraction of nutrients reaching marine end compartment	*kg N-eq*	Evaluates the potential for excessive nitrogen enrichment in marine ecosystems.
Eutrophication, terrestrial	Accumulated Exceedance (AE)	*mol N-eq*	Assesses the potential for excessive nutrient (nitrogen) enrichment in terrestrial ecosystems.
Human toxicity cancer	Comparative Toxic Unit for humans (CTUh)	*CTUh*	Estimates the increase in morbidity of cancer in the human population per unit of mass of a substance emitted.
Human toxicity non-cancer	Comparative Toxic Unit for humans (CTUh)	*CTUh*	Estimates the increase in morbidity of non-cancer in the human population per unit of mass of a substance emitted.
Ionising radiation, human health	Human exposure efficiency relative to U^{235}	*kBq U^{235}*	Measures the potential human health effects from exposure to radioactive releases.
Land use	Soil Quality Index	*Dimensionless (pt)*	Measures the potential impact on soil quality and ecosystem services based on changes in land use.
Ozone Depletion	Ozone Depletion Potential (ODP)	*kg CFC-11 eq*	Assesses the potential for substances to degrade the stratospheric ozone layer over an infinite time horizon.

(*continued on next page*)

Table 1 (*continued*)

Impact category	Indicator/ Abbreviation	Unit	Environmental Significance
Particulate matter	Human health effects associated with exposure to PM2.5	*Disease incidences*	Quantifies the potential human health impact (e.g., respiratory disease) associated with the inhalation of fine particulate matter.
Photochemical ozone formation, human health	Tropospheric ozone concentration increase	*kg NMVOC-eq*	Assesses the potential for the formation of summer smog (ground-level ozone) which can harm human health and vegetation.
Resource use, fossil	Abiotic resource depletion – fossil fuels (ADP-fossil)	*MJ*	Evaluates the depletion of non-renewable fossil fuel resources.
Resource use, minerals and metals	Abiotic resource depletion (ADP ultimate reserves)	*kg Sb-eq*	Evaluates the depletion of non-renewable mineral and metal resources.
Water use	User deprivation potential (deprivation-weighted water consumption)	*m^3 world eq. deprived water*	Assesses the potential for water scarcity by evaluating available water remaining in a region.

kBq U^{235}: kilobecquerels of Uranium-235, NMVOC: Non-Methane Volatile Organic Compounds, P: Phosphorus, N: nitrogen, Sb: antimony.

Use category specifically, the SUB represents 62% of the impact exhibited by the SSB. For the SSB, water impacts are driven by electricity consumption (86%) and enzyme production (12%). Conversely, the SUB water use impacts are distributed between electricity (67%), enzyme production (19%), and the production of the plastic SU component (11%).

An impact category where SUB almost reaches the value presented by the SSB is Resource Use Minerals and Metals. In this impact category SUB reaches 87% of the impacts presented by the SSB. The environmental burden of the SUB comes from the assembly of the SS parts of the bioreactor (14.2%), plastic production (28.6%), and electricity consumption (30%), whereas the SSB impact comes from assembling the bioreactor (10.3%) and electricity use (69%). Although the SUB consistently performs better than the SSB, its environmental profile is affected by the manufacturing of the disposable plastic component.

Going into detail in the Climate Change impact category, the SSB impact was 14.9 kg of CO_2 eq. per gram of protein produced. Within the life cycle, the equipment assembly accounted for 0.6%, the use phase represented the vast majority 99.4%, and the EoL treatment contributed with 0.1%. In comparison, the SUB resulted in a value of total emissions of 8.7 kg of CO_2 eq. per gram of protein produced. For the SU platform, equipment assembly accounted for 1.1%, the use phase represented 97.7% and the EoL treatment (landfill) contributed 1.1%. The contribution by process to Climate Change are illustrated in Fig. 3. In the following sections, each stage of the life cycle will be explained in detail.

3.1.1. *Assembly of the bioreactor*

The construction of the SSB resulted in total emissions of 2466 kg of CO_2 eq. A breakdown of the manufacturing impacts reveals the following: Stainless Steel production accounted for the vast majority of the burden with 2262 kg of CO_2 eq., corresponding to the 475 kg of stainless steel required for the vessel, supply unit and control tower. Electronic components contributed with 108 kg of CO_2 eq., while copper wire and borosilicate glass production added 28 kg and 0.35 kg of CO_2 eq., respectively. The transportation of the complete SSB unit accounted for 68 kg of CO_2 eq.

In comparison, the assembly of the durable components for the SUB emitted a total of 2980 kg of CO_2 eq. This higher footprint is attributed to the larger mass of the durable components required for the bag holder and the Temperature Control Unit (TCU). Steel production emitted 2738 kg of CO_2 eq., reflecting the 575 kg of stainless steel used for the aforementioned components. The production of electronic components

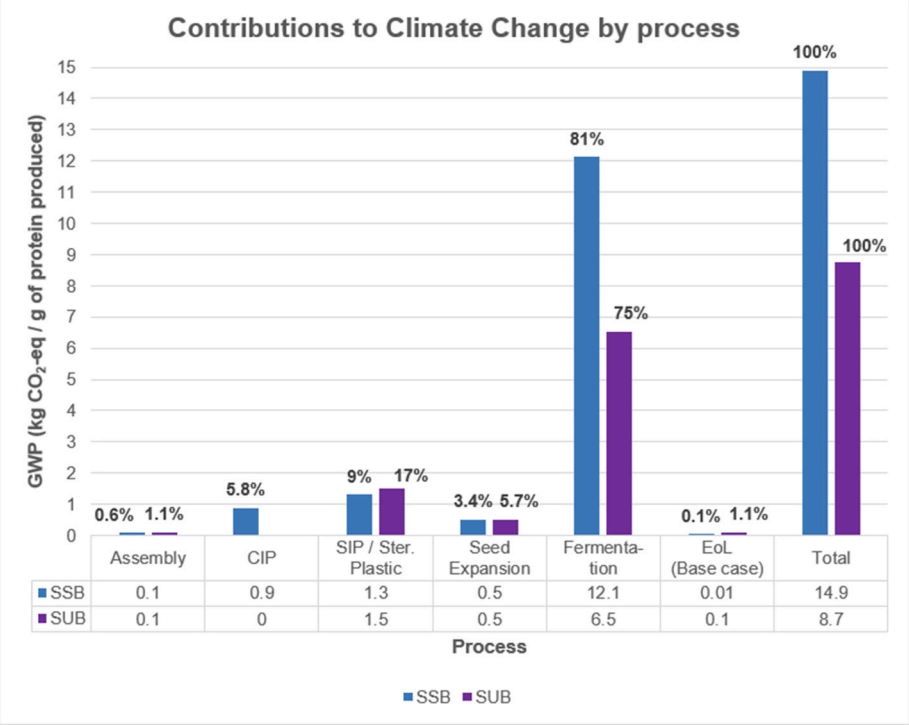


Fig. 2. Contributions to climate change by process, SSB and SUB.

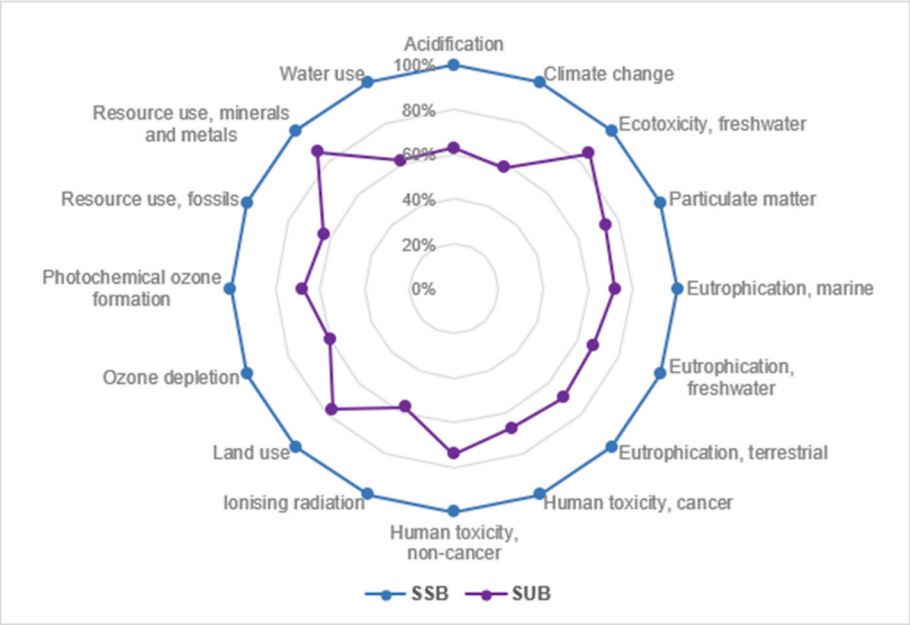


Fig. 3. Relative Environmental Profile of SSB and SUB across the 16 impact categories.

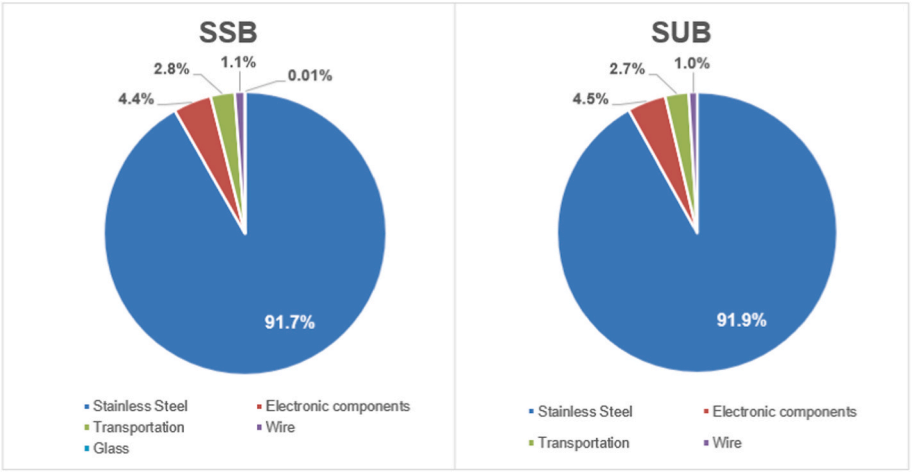


Fig. 4. Contributions to Climate Change by material and transportation of the SSB and SUB.

and copper wire accounted for 133 kg and 28 kg of CO_2 eq., respectively. Transportation of the SUB equipment accounted for 81 kg of CO_2 eq. Fig. 4 presents the contribution by material and transportation for the assembly of the SSB and SUB.

For both systems, stainless steel is identified as the material with the highest environmental burden due to the significant quantities required for construction. However, when these assembly emissions are normalised to the functional unit over the 20 years of operation, they contribute only 0.6% (SSB) and 1.1% (SUB) to the total climate change impact per gram of protein. This underscores the importance of the 20-year amortisation period in reflecting the true life cycle performance of durable pharmaceutical infrastructure.

3.1.2. *Use phase of bioreactors*

The operational use phase represents the most significant portion of the life cycle impact for both systems, accounting for 99.4% of the SSB and 97.7% of the SUB total climate change potential. Over the 20-year operational horizon the SSB must perform 2000 batches (at 15 g of protein per batch) to reach the production target of 30 kg. Whereas the SUB requires 1000 batches (at 30 g of protein per batch). The cumulative quantities of utilities and associated emissions required to meet the production target are summarized in Table 2.

The SSB impacts are primarily driven by utility and electricity consumption across the 2000 required batches. The primary environmental drivers for the CIP and SIP operations are steam accounting for 5.9% of the total emissions (CIP: 1.5%, SIP: 4.4%) and electricity consumption 8.6% (CIP and SIP: 4.3% each). Within the stages of seed expansion and fermentation, enzymes contribute 2.9% to the total emissions (Seed Expansion: 0.6%; Fermentation: 2.3%), and compressed air accounts for 1.5%. Electricity represents the dominant driver of environmental burdens, accounting for 80.4% of the total CO_2 emissions (Seed Expansion: 2.7% and Fermentation: 77.7%). Chemicals (soda), water production, and wastewater treatment accounted for less than 1% of the total CO_2 emissions.

While the SUB eliminates on-site CIP and SIP procedures through pre-sterilised components, the environmental burdens of plastic production, gamma-ray sterilisation, and transportation must be accounted for in every batch. Regarding the SU component, the most significant

Table 2
Cumulative utilities consumption and CO_2 emissions for SSB and SUB operations for the operational horizon of 20 years and production target of 30 kg.

SSB: Use Phase			SUB: Use Phase		
CIP	Quantity	kg CO_2-eq			
Steam (MJ)	5.8E+04	6.5E+03			
Process Water (kg)	1.4E+05	5.6E+01			
Electricity (kWh)	5.2E+04	1.9E+04			
Total emissions CIP		**2.6E+04**			
SIP	**Quantity**	**kg CO_2-eq**	**Sterilisation Plastic Comp.**	**Quantity**	**kg CO_2-eq**
Steam (MJ)	1.8E+05	2.0E+04	Plastic Production (kg)	1.1E+04	4.1E+04
Process Water (kg)	7.7E+04	5.6E+01	Electricity for Gamma Ster. (kWh)	1.3E+04	3.2E+03
Electricity (kWh)	5.2E+04	1.9E+04	Transportation (ton*km)	1.6E+03	5.9E+02
Total emissions SIP		**3.9E+04**	**Total emissions Sterilisation Plastic Comp.**		**4.5E+04**
Seed Expansion	**Quantity**	**kg CO_2-eq**	**Seed Expansion**	**Quantity**	**kg CO_2-eq**
Ultrapure water (kg)	4.0E+03	9.8E+00	Ultrapure water (kg)	4.0E+03	9.8E+00
Enzymes (kg)	2.8E+02	2.9E+03	Enzymes (kg)	2.8E+02	2.9E+03
Electricity (kWh)	3.3E+04	1.2E+04	Electricity (kWh)	3.3E+04	1.2E+04
Total emissions Seed Expan.		**1.5E+04**	**Total emissions Seed Expan.**		**1.5E+04**
Fermentation	**Quantity**	**kg CO_2-eq**	**Fermentation**	**Quantity**	**kg CO_2-eq**
Ultrapure water (kg)	3.6E+04	8.9E+01	Ultrapure water (kg)	3.6E+04	8.9E+01
Process Water (kg)	1.0E+05	4.2E+01	Process Water (kg)	1.2E+05	4.9E+01
Enzymes (kg)	1.0E+03	1.0E+04	Enzymes (kg)	1.0E+03	1.0E+04
Compressed air (m^3)	1.3E+05	6.6E+03	Compressed air (m^3)	6.6E+04	3.3E+03
Electricity (kWh)	9.3E+05	3.5E+05	Electricity (kWh)	4.9E+05	1.8E+05
Total emissions Fermentation		**3.6E+05**	**Total emissions Fermentation**		**2.0E+05**
Total Emissions of Use Phase SSB		**4.3E+05**	**Total Emissions of Use Phase SUB**		**2.6E+05**

burden is the production of LDPE plastic, accounting for 15.8% of emissions, while transportation and electricity for gamma sterilisation accounts for 1.2% and 0.2%, respectively. For the seed expansion and fermentation stages, enzymes production represents 5.0% of the CO_2 burden (Seed Expansion: 1.1%; Fermentation: 3.9%), and compressed air accounts for 1.3%. Similar to the SSB, electricity remains the largest contributor, representing 74.2% of the total CO_2 emissions (Seed Expansion: 4.6% and Fermentation: 69.6%). Water production, and wastewater treatment accounted for less than 1% of the total CO_2 emissions.

A direct comparison between the CIP and SIP operations against the production and sterilisation of the SU component reveals that the CIP and SIP operations emit a total of 6.5E+04 kg of CO_2 eq. In contrast, the operations related to the SU component emit 4.5E+04 kg of CO_2 eq. This transition to a single-use platform results in an approximately 30% reduction in emissions specifically related to sterilisation and preparation activities.

The SUB system showed a 42% reduction in total emissions compared to the SSB system in the Climate Change impact category. This reduction is primarily due to the larger working volume utilised by the SUB; because it can operate with higher volumes, the number of batches required to produce the same amount of protein is doubled for the SSB. This results in some of the advantages previously mentioned, such as production flexibility and reduced down-time. Specifically, performing CIP and SIP operations in the SSB takes a total of 8 h, which increases both electricity and utility consumption. Electricity was by far the biggest contributor to Climate Change in both systems. Given the energy-intensive nature of fermentation processes, improvements in energy efficiency and overall process optimization could significantly enhance the environmental performance of both technologies.

When comparing water consumption between the two technologies, the SSB system required 11.9 kg of water to produce 1 g of protein, primarily for CIP, SIP, and fermentation. In contrast, the SUB used only 5.3 kg of water per gram of protein, mainly to achieve and maintain the fermentation temperature. Eliminating CIP and SIP operations in the SUB system significantly reduces direct water use, a benefit previously addressed in literature (GE Healthcare, 2020a). However, the production of single-use plastic components accounted for an important share of CO_2 emissions in the SUB system. Additionally, the environmental management of the polyethylene waste remains a critical factor, which will be addressed in detail in the following section regarding End-of-Life scenarios.

3.1.3. *End-of-life (EoL) scenario analysis for the single-use component*

While the use phase remains the dominant lifecycle stage, the disposal of plastic solid waste is a critical consideration during the transition to single-use technologies. Post-use treatment is a major concern because single-use components often feature a complex plastic matrix and potential biological contamination, posing significant barriers to traditional recycling efforts (Whitford et al., 2019;Ottinger et al., 2022;Sinclair et al., 2008;Jobin and Krishnan, 2012).

Currently, several pathways exist for managing residues of the pharmaceutical industry. Landfill deposition is one of the most common methods for managing post-use of plastics (Jobin and Krishnan, 2012; Whitford et al., 2021). However, this approach presents several environmental and health-related drawbacks. As a result, environmental regulations and public policy discourage landfill disposal as a means of managing plastic residues. Moreover, in the pharmaceutical industry, landfill disposal is avoided due to the classification of residues as biohazardous waste, which requires specialised handling and procedures; therefore, they are managed differently (Pietrzykowski et al., 2013). Nowadays, the preferred waste management method among biopharmaceutical manufacturers is incineration with energy recovery (Whitford et al., 2021), also known as Waste-to-Energy (WtE). This method involves the combustion of plastic waste to generate energy, thereby partially offsetting fossil fuel use.

In light of these considerations, different EoL scenarios for the SU plastic bag were proposed and evaluated: Landfill disposal, Incineration, Incineration with Energy Recovery (IER). Despite technical challenges, recycling scenarios for Polyethylene (PE) and a combined scenario (Recycling + IER) were evaluated to assess the potential for circularity.

Table 3 summarizes the results for Climate Change and Water Use across all evaluated scenarios for the SUB with the SSB results included for comparison. The data in Table 3 demonstrates that regardless of the chosen disposal method, the SUB platform consistently results in lower absolute impacts compared to the SSB. For example, the highest SUB

Table 3
Climate Change and Water Use results for the different EoL scenarios normalised in terms of the FU.

Scenario	SSB	Landfill	Incineration	IER	Recycling PE	Recycling PE + IER
Climate Change (kg CO_2-eq/g of protein)	14.9	8.73	9.45	8.74	9.23	8.82
Water Use (m^3 deprived/g of protein)	11.1	6.88	6.94	6.68	6.98	6.80

carbon footprint (9.45 kg CO_2-eq in the incineration scenario) is still significantly lower than the 14.9 9.45 kg CO_2-eq produced by the SSB. Similarly, water deprivation for the SUB remains between 6.68 and 6.98 m^3, whereas the SSB requires 11.1 m^3. These figures highlight that the operational efficiencies of single-use technology outweigh the environmental burdens of its waste management.

The analysis of five key impact categories, namely, Climate Change, Freshwater Ecotoxicity, Human Carcinogenic Toxicity, Resource use, fossils, and Water Use, are presented in Fig. 5. In the Climate Change Impact category, Incineration presents the highest impact among the SUB scenarios at 108% relative to landfill base case, reaching 9.45 kg CO_2-eq. Conversely, landfilling and IER provide the lowest Climate Change impacts for the SUB, with 8.73 and 8.74 kg CO_2-eq, respectively. Interestingly, the recycling scenario showed higher relative impacts across the other analysed categories. These results can be attributed to the energy and utilities requirements of the recycling process, in addition to the operational burdens of collection and sorting. A decisive factor in this performance is the recycling efficiency of 60% as the remaining 40% of the material must be incinerated. When comparing these results to the combined scenario (Recycling + IER), in which the 40% residue is incinerated with energy recovery, the system demonstrates greater environmental benefits.

The EoL scenarios analysed were not marginal with respect to the entire life cycle, as shown in Table 4. While the Use Phase remains the dominant stage, the EoL stage can contribute significantly to total emissions depending on the chosen treatment pathway. The EoL contribution is most substantial in the Incineration scenario, where it accounts for 8.7% of total lifecycle emissions, primarily due to direct incineration impacts (8.2%). However, in the IER scenario, these impacts are effectively mitigated; the direct emissions from incineration (8.82%) are significantly outweighed by the environmental credits earned from electricity recovery (4.13%) and heat recovery (3.81%), resulting in a net EoL contribution of only 1.2%.

The Recycling scenario contributes approximately 6.5% to the total CO_2 emissions. While the recycling process accounts for 4.8% and provides environmental benefits through material recovery credits (2.19%), these are partially offset by the incineration of non-recoverable materials, which adds a burden of 3.34%. The Recycling + IER scenario represents a better approach, with a total EoL contribution of 2.1%. This scenario captures the benefits of material recycling (providing a 2.3% credit) while utilizing IER to process the non-recyclable 40% fraction, where electricity and heat recovery provide additional credits of 1.64% and 1.51%, respectively. These findings emphasize that optimizing the EoL phase through energy and material recovery is essential for further improving the environmental performance of single-use technologies.

3.2. Discussion

The cradle-to-grave analysis demonstrated that the environmental impacts of the manufacturing and assembly stages were relatively minor compared to the operational Use Phase. While the impacts of constructing the SS structure of the bioreactors are not negligible, they become relatively small when amortised over the equipment's lifetime compared to cumulative energy consumption.

Multiple studies analysing supply chain, use-phase, and end-of-life stages agreed that the operational use-phase contributes most significantly to overall environmental impacts (Pietrzykowski et al., 2013), (GE Healthcare, 2020a), (Budzinski et al., 2022). In this study, the use phase represented more than 90% of the total environmental impacts, with electricity consumption being the principal contributor for both the SSB and SUB technologies. These findings align with those of Pietrzykowski et al. (2013), who identified energy consumption and

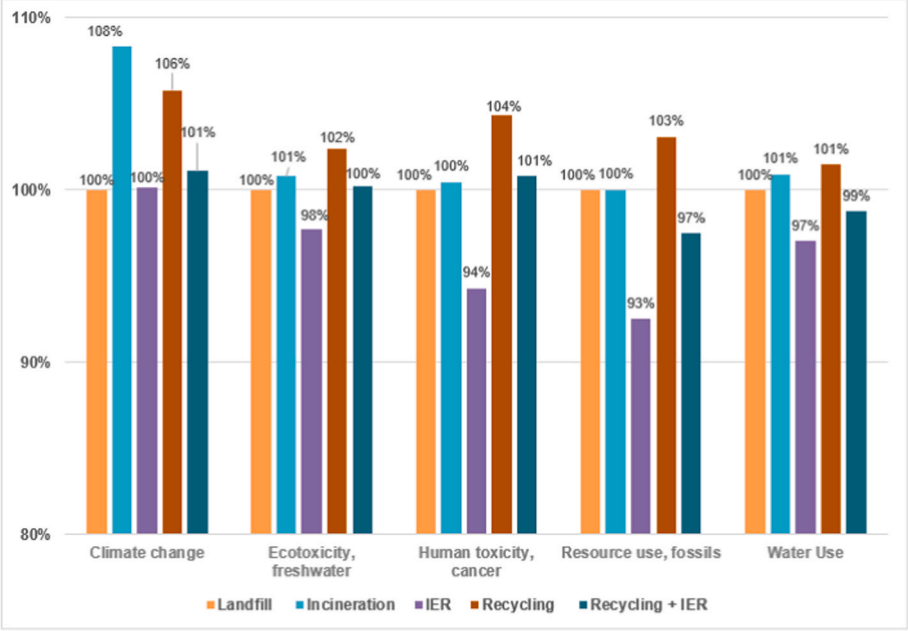


Fig. 5. Results for the different EoL scenarios for the SU plastic component. Landfill represents the base case (100%).

Table 4
Detailed process contribution to SUB EoL Scenarios for the Climate Change impact category.

Contribution to Climate Change by Life Cycle Stage			
Scenario	Assembly	Use Phase	EoL
Landfill	1.1%	97.8%	**1.1%** - **Landfill: 0.5%** - Transport: 0.4% - Steel Recycling: 0.1% - Other components: 0.05%
Incineration	1.0%	90.3%	**8.7%** - **Incineration: 8.2%** - Transport: 0.4% - Steel Recycling: 0.07% - Other components: 0.03%
IER	1.1%	97.6%	**1.2%** - **IER: 0.88%** Incineration: 8.82% *Environmental credits:* *Electricity recovery: 4.13%* *Heat recovery: 3.81%* - Transport: 0.24% - Steel Recycling: 0.07% - Other components: 0.03%
Recycling	1.0%	92.5%	**6.5%** - **Recycling: 5.95%** Recycling process: 4.8% Incineration of material that could not be recycled: 3.34% *Environmental credits:* *Material recycling: 2.19%* - Transport: 0.4% - Steel Recycling: 0.07% - Other components: 0.03%
Recycling + IER	1.1%	96.8%	**2.1%** - **Recycling: 1.2%** Recycling process: 3.5% *Environmental credits:* *Material recycling: 2.3%* - **IER: 0.35%** Incineration: 3.5% *Environmental credits:* *Electricity recovery: 1.64%* *Heat recovery: 1.51%* - Transport: 0.4% - Steel Recycling: 0.07% - Other components: 0.03%

steam as dominant contributors to environmental damage. Specifically, steam stands out as one of the principal contributors to the environmental footprint of the SSB in this analysis.

Furthermore, studies by GE Healthcare (GE Healthcare, 2020b) and Budzinski et al. (2022), emphasized that the primary energy sources within a specific geography electricity grid mix heavily influence environmental outcomes. While this study did not evaluate the specific electricity grid mix, a reduction in CO_2 emissions would be expected if a higher share of renewable energy is present in the electricity mix.

Overall, the findings from this study, in which the SSB has a greater environmental impact than the SUB in the Climate Change category (14.9 vs 8.7 kg CO_2-eq) is consistent with previous studies from literature (Pietrzykowski et al., 2013), (Rawlings and Pora, 2009), (GE Healthcare, 2020b), despite differences within the system boundaries (e.g. considering the entire production process train) and production scales. Regarding scale, Pietrzykowski et al. (2013) observed that environmental impacts per functional unit tend to decrease when moving from a smaller scale to a larger one; thus, assessing a larger production scale in future studies could potentially result in lower environmental impacts for both technologies.

Regarding the different EoL scenarios, various studies have assessed the environmental impacts related to the disposal of single-use components. Pietrzykowski et al. (Pietrzykowski et al., 2013) concluded that while the EoL phase of single-use systems had a higher environmental burden than that of traditional stainless-steel systems, it accounted for less than 1% of the overall life cycle impacts. Similarly, a second study performed by GE Healthcare (GE Healthcare, 2020b) evaluated five EoL scenarios: autoclave-landfill, shred-autoclave-landfill, incineration, incineration with energy recovery, and recycling, at 200 L and 2 × 2000 L mAbs production scales. As a result, EoL impacts were negligible regardless of the scenario or scale considered. Budzinski et al. (2022), reported that shifting from a baseline EoL scenario (in which 60% of single-use materials are recycled and 40% incinerated with ER) to full incineration without energy recovery led to an 8% increase in CO_2 emissions, while full recycling resulted in a 10% decrease compared to full incineration.

In the present study, however, EoL scenarios were not negligible at the analysed production scale. For example, in the Incineration scenario, the EoL phase contributed 8.7% of the total lifecycle emissions. Our results demonstrate that the IER scenario significantly improves environmental performance by reducing net emissions through electricity and heat recovery credits.

Complementing these findings, various authors have explored alternative EoL strategies to reduce the environmental burden of SUTs. Jobin and Krishnan (2012), evaluated multiple disposal methods for a 500 L Mobius buffer-media filtration (BMF) system composed mainly of two plastic films, storage and mixing SU bags. Their study compared conventional disposal approaches, such as incineration, waste-to-energy (WtE), and landfill, with alternative strategies, such as "Recycle + WtE", "Recycle + Landfill", "Energy recovery at Cement Kilns", and "Recycle + Energy recovery at cement kilns". The authors proposed these alternatives to take advantage of the high energy content of plastic materials, especially in single-use systems (~37,681 kJ/kg). Notably, CO_2 emissions were reduced by 13% and 14% in the scenarios involving energy recovery at cement kilns and recycling with energy recovery at cement kilns, respectively, compared to conventional incineration. The results highlight the potential of these alternatives to maximise the energy content of plastic components while reducing solid waste.

The growing focus to EoL management is further justified by the significant volume of waste generated during biopharmaceutical manufacturing. For instance, a monoclonal antibody production process utilizing a SU manufacturing train with a 2000 L bioreactor scale can generate between 1.5 and 2.0 metric tons of plastic waste during a 14-day batch campaign (Barbaroux et al., 2021). While the plastics used in the biopharmaceutical sector represent only 0.01% of global plastic waste (Barbaroux et al., 2020), the disposal and treatment of these materials remain a critical consideration for the implementation of single-use technologies (Frank, 2018).

Although recycling is often regarded as the optimal EoL scenario for single-use components, practical challenges remain. The complex multi-material composition matrix, as well as contamination risks from direct product contact, make recycling logistically and technically difficult (Samaras et al., 2022). Furthermore, recycling requires additional steps such as decontamination, disassembly, and sorting (Jobin and Krishnan, 2012), (Sinclair et al., 2008) raising concerns about the feasibility of a recycling supply chain. As a matter of fact, it raises the question of whether any EoL option beyond combustion is truly viable for SUTs (Ottinger et al., 2022).

Nonetheless, circularity-based alternatives have been proposed, including the reuse of buffer bags for liquid waste collection (Barbaroux et al., 2021) and the *downcycling* of plastic materials for their exploitation in other industries (MacDonald, 2019), (Whitford et al., 2021). Additionally, SU component packaging has been an interesting starting point to rethink product design based on recycled materials, since

packaging has no direct contact with the product and can be collected without biocontamination, making it convenient to recycle (Barbaroux et al., 2021). Finally, process intensification through the integration of upstream and downstream operations is another interesting opportunity for SUTs to investigate further. Diminishing single-unit operations and creating a continuous system could substantially reduce the quantity of single-use equipment required. Such strategies not only minimise material consumption but also reduce the overall environmental footprint of biomanufacturing processes (Barbaroux et al., 2021).

4. Conclusions

This study provides a comprehensive assessment of the environmental trade-offs between single-use and conventional stainless-steel technologies for laboratory scale protein production. By establishing a quantifiable life cycle inventory, this case study offers robust evidence for strategic decision-making regarding technology adoption based on measurable environmental performance.

The findings demonstrate that single-use technologies (SUTs) exhibit superior environmental performance compared to conventional stainless-steel systems across all the 16 evaluated impact categories. The SUB achieved a total climate change impact of 8.7 kg CO_2 eq., representing a 42% reduction compared to the 14.9 kg CO_2 eq. produced by the SSB per gram of protein. The detailed assessment revealed that for the SSB, the primary environmental burdens are rooted in high electricity and steam consumption required for recurring Cleaning-in-Place (CIP) and Sterilisation-in-Place (SIP) operations. In contrast, the SUB impact is characterized by the production and disposal of plastic components, alongside operational electricity.

In the current global context, where sustainability is a fundamental pillar of industrial development, the disposal methods for single-use components cannot be overlooked. The analysis confirmed that the End-of-Life (EoL) pathway significantly influences the SUB's environmental profile, with Incineration with Energy Recovery effectively mitigating carbon and resource scarcity burdens. To further enhance SUT sustainability, the industry should focus on enhancing existing recycling strategies, exploring innovative ways to utilise plastic from single-use components, and designing components with a circularity approach are essential steps toward making SUTs more sustainable within the biopharmaceutical industry.

From a broader perspective, the transition towards single-use technologies should aim to establish a circular value chain that incorporates principles of waste reduction and energy efficiency. Thereby, creating a sustainable value chain that minimises environmental burdens while fostering economic and technological growth.

CRediT authorship contribution statement

Michelle Andrea Gonzalez Monroy: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing – original draft. **Flavio Lippi:** Conceptualization, Supervision. **Filomena Ferrara:** Conceptualization. **Adalgisa Sinicropi:** Conceptualization, Methodology, Validation, Writing – original draft. **Maria Laura Parisi:** Conceptualization, Data curation, Methodology, Project administration, Supervision, Validation, Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclepro.2026.148858.

Data availability

Data will be made available on request.

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