GE Healthcare
Life Sciences

An environmental life cycle assessment comparison of single-use and conventional bioprocessing technology

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Biopharmaceutical development and manufacturing demand scalable processes that can be smoothly transferred to production. These processes need to be quickly developed and easy to implement. Ready-to-use technologies such as the ReadyToProcess™ platform from GE Healthcare Life Sciences play a crucial role in providing the flexibility to support multiproduct facilities and deliver process time savings, allowing for faster changeover between products. The ReadyToProcess platform is a complete suite of preconditioned systems and accessories for biopharmaceutical production, prepared for immediate use. The platform includes both single-use and reusable products.

GE Healthcare is committed to helping our customers evaluate and make decisions based on performance and environmental criteria for your products. Life Cycle Assessment (LCA) is an internationally recognized methodology (1, 2) that can be used to examine products from an environmental perspective. The methodology can be used across the full life cycle of the product, from raw material extraction and refining through manufacturing, use, and end-of-life disposal or recycling (Figure 1). By including the impacts throughout the product life cycle, LCA provides a comprehensive view of the potential environmental impacts of the product and a more accurate picture of the environmental trade-offs and improvement opportunity.

Fig 1. Product life cycle.

Single-use technologies offer an attractive option for biopharmaceutical manufacturing, but their environmental impact needs be considered. This paper documents the findings of an extensive LCA study comparing single-use and conventional bioprocessing technology for the production of monoclonal antibodies (MAbs) (3, 4). The study examines the life cycle environmental impacts associated with MAb production at three process scales: 100 L, 500 L, and 2000 L. The results presented here focus on the 2000 L production scale, but the overall comparative conclusions for all three process scales were similar. This assessment was conducted according to the ISO 14040-14044 standards for comparative LCA (1, 2) and was independently reviewed by a third-party critical review panel. The results demonstrate that the single-use bioprocess train has lower environmental impacts compared to the conventional process train in each environmental impact category studied. This paper explains why.

Assessing bioprocess technology in detail

The LCA study compares the life cycle environmental impacts associated with the production of MAbs using either single-use or conventional bioprocessing technologies. Calculations were based on a 10-batch campaign assuming 6 g/L titres. The scope of the study includes both upstream and downstream processes involved in the production of MAbs. Figure 2 shows a process schematic of the full process train categorized into 14 unit operations. An additional category included the clean-in-place/steam-in-place (CIP/SIP) infrastructure and common support activities, such as process water and HVAC requirements (collectively labeled 'Support CIP/SIP System').

The bioprocess data used in this study were developed in collaboration with BioPharm Services Inc. and can be considered industry average based on a combination of primary and secondary sources. Data on production of single-use components were obtained primarily from GE Healthcare. Data on transportation, packaging, and end-of-life were gathered through a combination of supplier data (GE Healthcare) and expert interviews. Additional secondary data were obtained from the ecoinvent 2.2 life cycle inventory database (5).

The study looks at the entire life cycle of the process trains for both types of bioprocessing technologies, including:

- Supply chain: materials and manufacturing of all process equipment and consumables required to support a 10-batch MAb campaign, including pre-sterilization of single-use components.
- Use: all activities that occur during MAb production, including cleaning and sterilization of conventional equipment between batches. Electricity was assumed to be US average. Fuel mix for generation of water-for-injection (WFI) was 45% fuel oil, 45% natural gas and 10% electricity.
- End-of-Life: transport to end-of-life treatment, disposal of consumables, and the disposal, re-use, or recycling of durable components. For single-use components such as cellbags, filters, and connectors, disposal was assumed to occur by hazardous waste incineration without waste heat recovery. Non-hazardous waste was sent to landfill or wastewater treatment.

Assumptions

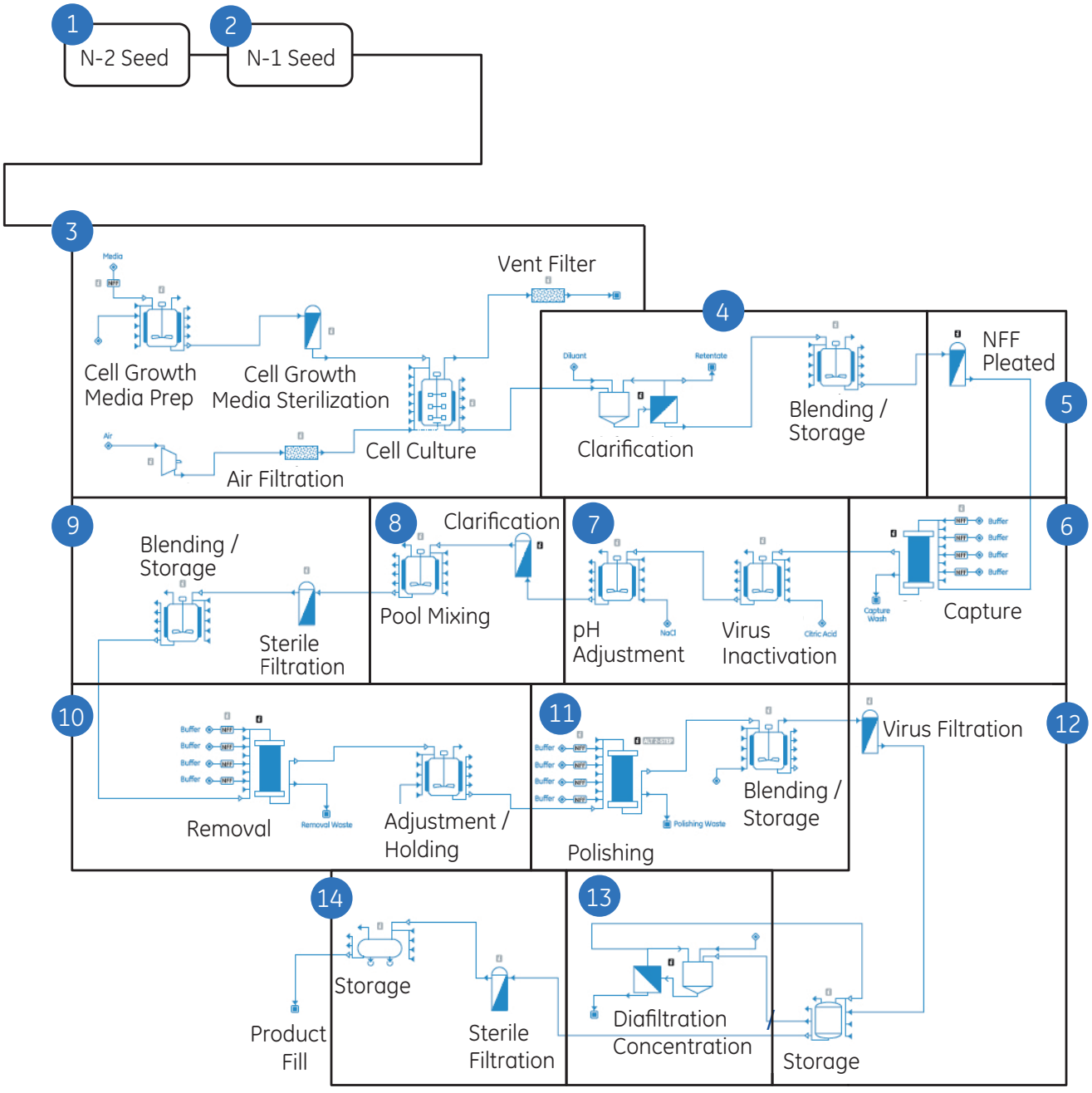
- The study did not account for any potential differences in product yield resulting from choice of process technology. Any such issues are product- or process-specific and beyond the scope of this study.
- The potential for a smaller production facility enabled by the choice of single-use technology was not specifically included in the scope of this study.
- The study did not address any potential differences in labor requirements.

Impact assessment categories

Impact assessment methods are used to convert the life cycle inventory data (material, energy, and emissions inputs and/or outputs throughout the products' life cycles) into a set of environmental impacts. Global warming potential (GWP) was calculated using the IPCC 2007 100a method and included all greenhouse gases specified in the Kyoto Protocol (6). Cumulative Energy Demand (CED) expresses both embodied and process energy that is consumed across the life cycle (7). Water usage (withdrawal) was calculated using a custom impact assessment method that evaluates the withdrawal of freshwater across the life cycle. A comprehensive suite of midpoint and endpoint environmental impact categories from the internationally accepted method ReCiPe8 was also evaluated. A summary of environmental impact categories used in this study is shown in Table 1.

Sensitivity and uncertainty analyses

The sensitivity of the LCA results to variations in key assumptions was extensively analyzed using a Plackett-Burman statistical experimental design. Lifetime of durable equipment was varied from 5 to 25 years. Chromatography column lifetimes were varied from 10 to 100 cycles. Transportation distances varied from 5 to 25 miles (local), 1000 to 5000 miles (domestic), and 1500 to 7500 miles (international). Different ratios of WFI fuel mixes were examined. Durable equipment re-use was varied from 0 to 25%. Equipment recycling was varied from 50 to 100%. Co-60 irradiation facility parameters were also varied. None of the variations in key assumptions had a significant effect on the study conclusions.



Key

1. N-2 Seed
2. N-1 Seed
3. Bioreactor
4. Depth Filtration Clarification
5. Bioburden Reduction I
6. Protein A
7. Virus Inactivation
8. Bioburden Reduction II
9. No Tank Bioburden Reduction
10. Capture IEX
11. Flow Through IEX
12. Viral Filtration
13. UF/DF
14. Sterile Filtration II Support CIP/SIP System

Support CIP/SIP System (not shown)

Fig 2. MAb Process flow diagram (courtesy BioPharm Services Inc.).

Table 1. Environmental impact categories considered

Impact category	Unit	Source method	Reference
Global warming potential	kg CO2 eq	IPCC 100a	IPCC (2007) (6)
Cumulative energy demand	MJ	Cumulative energy demand v 1.08	Jungbluth and Frischknecht (2010) (7)
Climate change	kg CO2 eq	ReCiPe Midpoint (H) v 1.07	Goedkoop et al. (2009) (8)
Ozone depletion	kg CFC-11 eq		
Human toxicity	kg 1,4-DB eq		
Photochemical oxidant formation	kg NMVOC		
Particulate matter formation	kg PM10 eq		
Ionizing radiation	kg U235 eq		
Terrestrial acidification	kg SO2 eq		
Freshwater eutrophication	kg P eq		
Marine eutrophication	kg N eq		
Terrestrial ecotoxicity	kg 1,4-DB eq		
Freshwater ecotoxicity	kg 1,4-DB eq		
Marine ecotoxicity	kg 1,4-DB eq		
Agricultural land occupation	m2a		
Urban land occupation	m2a		
Natural land transformation	m2		
Water depletion	m3		
Metal depletion	kg Fe eq		
Fossil depletion	kg oil eq		

Results

The comparative analysis indicates that, based on the data used and the assumptions made in this study, single-use bioprocessing technology exhibits lower environmental impacts compared to conventional bioprocessing technology in all impact categories studied.

Cumulative energy demand (CED) and global warming potential (GWP) for all three life cycle stages (supply chain, use, end-of-life) are shown in Figure 3.

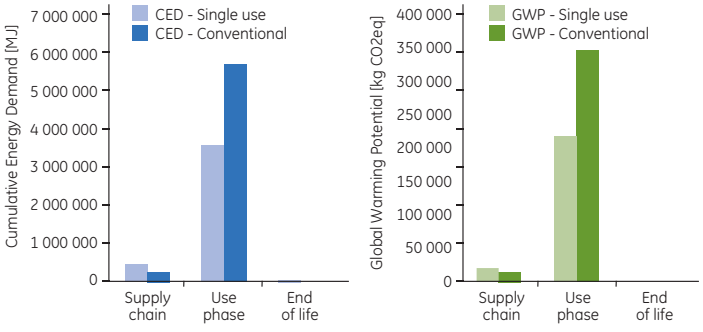


Fig 3. Cumulative Energy Demand (CED) and Global Warming Potential (GWP) results per life cycle stage

- A substantial majority of the impacts occur during the use stage.
- The single-use process train exhibits 38% lower GWP during use and 34% lower GWP across all life cycle stages.
- The corresponding reduction in CED is 38% during use and 32% across all life cycle stages.
- Supply chain GWP and CED impacts are slightly higher for single-use compared to conventional process technology due to the increased manufacturing required to provide the single-use consumable components. However, supply chain impacts represent < 5% of the life cycle GWP impact and < 11% of the life cycle CED impact.
- Environmental impacts from the end-of-life stage are higher for single-use but represent < 1% of overall life cycle impacts.

Single-use bioprocessing technology exhibits lower environmental impacts compared to conventional bioprocessing technology in all impact categories studied.

CED and GWP impacts categorized by unit operation are shown in Figure 4.

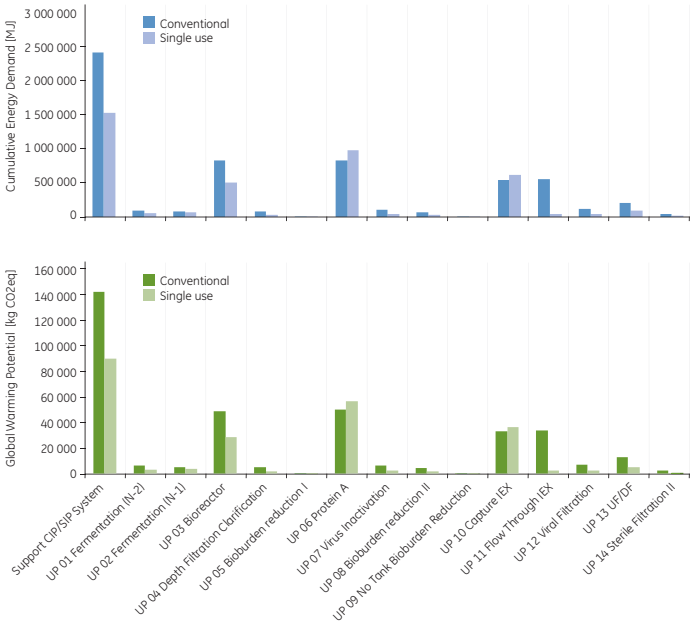


Fig 4. Cumulative Energy Demand (CED) and Global Warming Potential (GWP) results per unit operation

- The most substantial impacts (38 to 40% of both GWP and CED) are related to the Support CIP/SIP System, which includes the CIP/SIP infrastructure and common support activities such as process water and HVAC requirements (the main difference between process approaches in this category is the amount of energy required to generate WFI and steam).
- The use of single-use process technology exhibits lower CED and GWP impacts compared to conventional technology in all unit operations except Protein A and Ion Exchange chromatography, which are higher for the single-use process train since several columns must be used in parallel to reach this scale.

Water usage categorized by life cycle stage is shown in Figure 5. Substantial water savings are realized during the use stage for single-use process technology due to the reduction or elimination of cleaning and sterilization between batches.

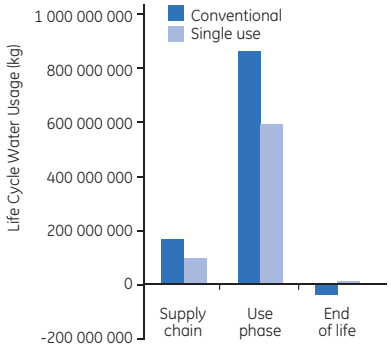


Fig 5. Water usage per life cycle stage

Life cycle water usage categorized by unit operation is shown in Figure 6. As expected, water usage is dominated by activities related to the Support CIP/SIP System. Single-use process technology exhibits lower water usage in all unit operations except Protein A and Ion Exchange chromatography, again due to the need for parallel chromatography columns at this scale. The negative water usage during the End of Life stage reflects credit related to the re-use and recycling of durable components.

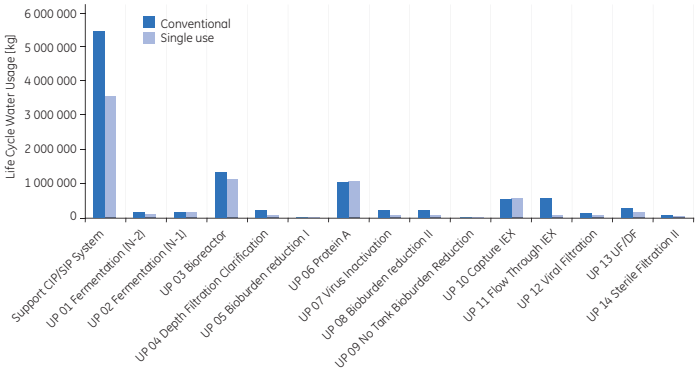


Fig 6. Life cycle water usage per unit operation

A comparison of environmental impacts in all other impact categories is shown in Figure 7. The single-use bioprocessing technology exhibits lower impacts in all impact categories studied. Single-use impacts range from 48 to 85% of conventional impacts.

Although the results in Figures 3 to 7 focus on the 2000 L working volume scale, similar results were obtained at 100 L and 500 L scales. Additional study results and more detailed discussions can be found in two recently published articles (3, 4).

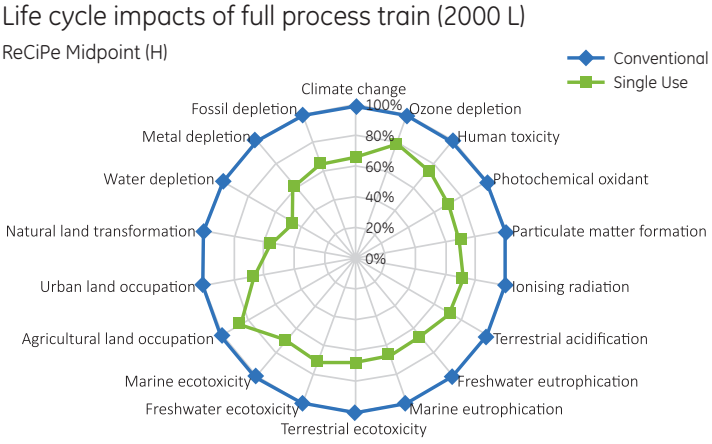


Fig 7. Comparison of other environmental impact categories considered. Results represent life cycle impacts of all unit operations in 2000 L scale process train. Single-use impacts are shown relative to conventional impacts, which are normalized to 100%.

Summary

This LCA study shows that a shift from conventional to single-use bioprocessing technology can result in substantial reductions in global warming potential, cumulative energy demand, water usage, and other environmental impacts for the production of monoclonal antibodies. Although single-use bioprocessing technology introduces a need for the production, distribution, and disposal of single-use components, this approach also reduces or eliminates the need for large quantities of steam, process water and WFI.

Note that a comparative LCA should not be the sole basis used to determine environmental superiority or equivalence, as additional information may be necessary to overcome some of the inherent limitations in the life cycle impact assessment. Even if a study has been critically reviewed, the impact assessment results are relative expressions and do not predict impacts on category endpoints, threshold exceedance, or risks. It is further recognized that there are other tools available for environmental assessment such as risk assessment, environmental impact assessment, and others. LCA was chosen as the best environmental tool to cover the goal and scope of this product comparison. The ability of LCA to consider the entire life cycle of a product makes it an attractive tool for the comparative assessment of potential environmental impacts.

GE Healthcare's commitment to sustainability

At GE Healthcare, we recognize that being a sustainability leader is more than creating products that provide environmental and operating benefits to our customers. GE Healthcare provides transformational medical technologies and services that are shaping a new age of patient care. There are currently over 30 products in the GE Healthcare ecomagination portfolio, providing a range of environmental benefits that include reducing energy use, greenhouse gases, chemical use, water use and waste management, while at the same time providing operating benefits to customers such as improving total cost of ownership or clinical efficiency.

Our broad expertise in medical imaging and information technologies, medical diagnostics, patient monitoring systems, drug discovery, biopharmaceutical manufacturing technologies, performance improvement and performance solutions services help our customers to deliver better care to more people around the world at a lower cost. In addition, we partner with healthcare leaders, striving to leverage the global policy change necessary to implement a successful shift to sustainable healthcare systems.

GE Healthymagination

GE Healthymagination, our $6 billion commitment to global health, invites the world to join us as we continuously develop innovations focused on reducing costs, increasing access and improving quality around the world. Three years into our six-year commitment, we have 53 validated products and services supporting our mission and have touched more than 500 000 000 lives.

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ecomagination

The world's environmental challenges present an opportunity for GE to do what it does best: imagine and build innovative solutions that benefit our customers and society. Ecomagination represents GE's commitment to deliver new natural resource-efficient products and technologies to market for our customers and society. It is a business initiative to create value by enabling our customers to cut costs, improve quality and reduce environmental impacts while reducing our own environmental footprint at the same time. Ecomagination is also about our commitment to using our limited resources efficiently across the entire life cycle. Whether it's the efficient facilities where we design and build our products, or our capabilities for refurbishing or recycling used equipment in an environmentally responsible way, ecomagination benefits the communities that we and our customers collectively serve today and for generations to come.

WAVE Bioreactor™

GE Healthcare is committed to producing sustainable products that result in significant improvements in operating and environmental performance. One of these products is the WAVE Bioreactor. Using disposable bags rather than large stainless steel tanks to produce vaccines and other biotherapeutics, the WAVE Bioreactor system enables cell culturing without requiring cleaning or steam sterilization, thereby reducing water and energy consumption.

Environmental and operating benefits

The WAVE Bioreactor eliminates the need for ultra-purified water used to sterilize traditional stainless steel bioreactors. A production facility that replaces a stainless steel bioreactor with a GE Healthcare 500 L WAVE Bioreactor system with equivalent output can reduce water consumption by over 66 000 liters per year—that's roughly three tanker trucks of ultra-purified water—for savings of more than USD 7300 annually at a water cost of USD 0.11 per liter.

In addition, the WAVE Bioreactor also eliminates the need for steam to heat and sanitize a stainless steel bioreactor, as well as for an impeller to mix the contents of the bioreactor's chamber. This reduces annual energy footprint at the same time. The WAVE Bioreactor, part of the ReadyToProcess product line, is included in GE's ecomagination (10) portfolio.

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