WHITE PAPER

Sustainable Systems

Evaluating the environmental impact of single-use biomanufacturing technology

PUBLISHED BY:

FIERCE Biotech

PRESENTED BY:

Thermo Fisher SCIENTIFIC

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Executive summary

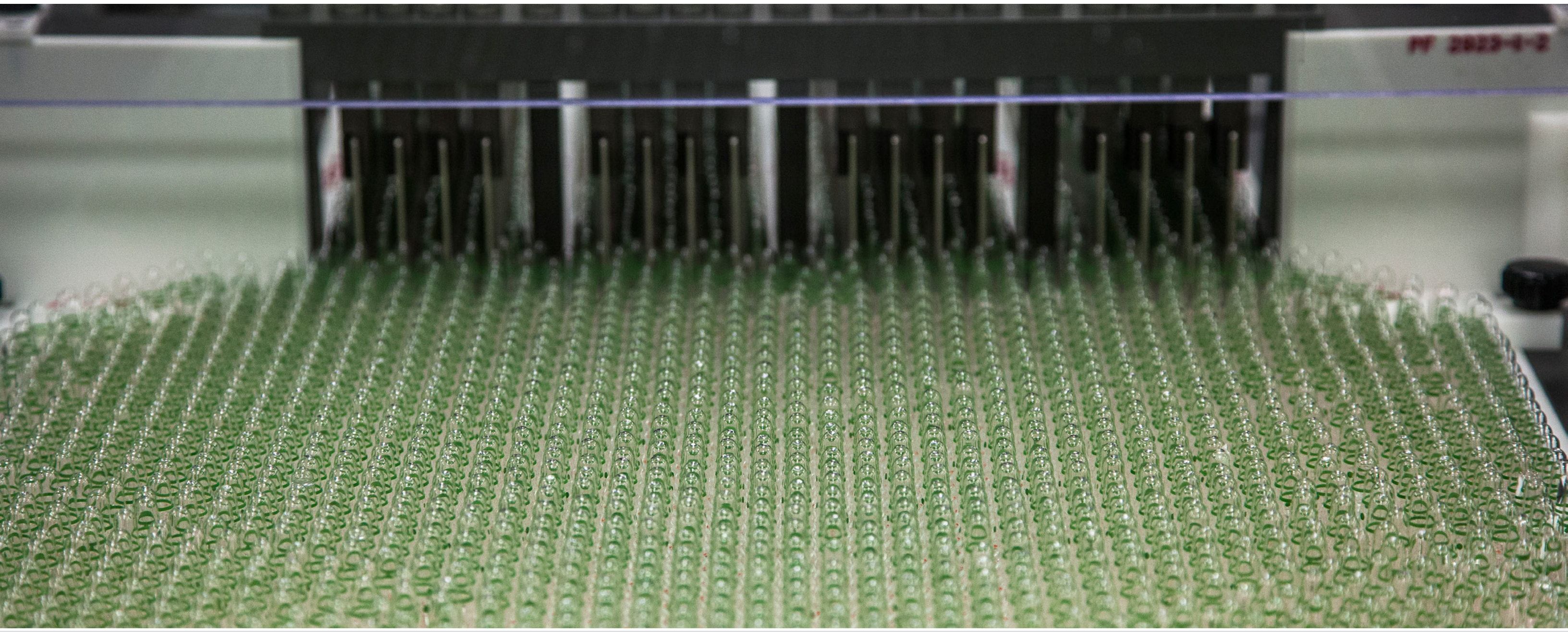
Environmental sustainability is a common concern for biologics developers evaluating single-use and stainless-steel manufacturing technology. Single-use technology (SUT) brings flexibility and efficiency, while stainless steel equipment suits large-volume manufacturing. Both consume significant resources. Given the current trend toward conserving those resources, there's good reason to prioritize sustainability in manufacturing decisions.

Both single-use and stainless-steel technologies generate waste. Stainless steel equipment uses more water and facility energy than SUT, while SUT generates plastic waste with variable outcomes for recycling and reuse.[1]

While necessary to meet sustainability metrics, evaluating sustainability in biomanufacturing adds complexity to an already nuanced decision. Given pressure from government agencies and the public at large however, as well as increased global warming[2], sustainability is no longer a side benefit. It's imperative.

Select contract biomanufacturers have helped advance sustainability initiatives, taking steps to integrate more sustainable technologies and processes. When biologics development and manufacturing work together to make the industry more sustainable, they not only satisfy environmental- and governance (ESG) commitments, but they also benefit from more efficient, cost-effective processes.

This white paper explores the advantages of sustainability with respect to single-use bioreactors, buffer and media hold containers, centrifuges and other biomanufacturing equipment.



The need for sustainable manufacturing

Biologics developers choose single-use biomanufacturing systems over stainless steel for several reasons, including:

- Lower cross-contamination risk
- High process flexibility
- Shorter turnaround times
- Lower capital cost
- Faster start-up

In recent years, executives have also started to run manufacturing equipment decisions through a sustainability lens. Equipment not only has to meet technical and scientific needs, but it must also align with corporate sustainability initiatives.

Sustainable manufacturing practices are both ethical and practical. Industry has limited access to fossil fuels. They don't renew, and the call to phase them out in favor of more climate-friendly, renewable sources is louder than ever.[3] As industry migrates from steel to plastic, they must also responsibly manage the large volumes of waste generated per run.

The pharmaceutical industry has responded to these challenges by taking concrete steps forward. A growing number of companies are transitioning to renewable energy, pledging carbon neutrality and otherwise making ESG commitments.[4] A report from the International Society for Pharmaceutical Engineering (ISPE) states that new job postings for ESG strategists and managers have climbed by 89% since 2020—a sign of forward sustainability momentum.[4]

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However, the pharmaceutical industry faces a difficult path maintaining product integrity while moving from today's state to net zero. To reach that benchmark requires cutting three types of emissions. Scope 3, the hardest to cut, includes raw material production, distribution, product use and end-of-life disposal.[5]

While many large pharma companies have set aggressive targets, others have none.[5] A report from Net Zero Tracker shows about 56% of healthcare, biotech and pharma companies have set emissions targets. For comparison, about 71% of the manufacturing companies analyzed have set targets.[6]

The decision to choose either SUT or stainless steel is an important but small component of a larger sustainable manufacturing strategy. In addition to equipment decisions, manufacturers must also consider:

- The impact of chemicals
- Transportation of goods, services and people
- Water and electricity use
- Incinerated waste
- Sparge gas

All these variables impact the environment to varying degrees. Electricity use during manufacturing accounts for 89% of the climate change impact caused by single-use biologics processes, most of which relates to cleanroom infrastructure. Single-use equipment accounts for 7.5% of environmental impact.[7]

Biologics manufacturing also requires a lot of water due to rigid cleaning requirements between each run. One advantage of single-use technology is the minimized use of water compared to steel. Disposables don't need integrated Clean-In-Place (CIP) and Sterilize-In-Place (SIP) treatment, both of which use large amounts of electricity and water. Disposal of liquid waste from CIP processes adds to the environmental cost,[8] which is negated via the use of SUT.

To safely produce therapies on time and on budget, while also respecting environmental sustainability targets, CDMOs and biologics developers must consider several environmental factors. Those factors, in addition to cost, quality, turnaround time and risk, determine whether SUT is the optimal choice.

Single-use bioreactors

Because of their smaller yearly demand, biologics require manufacturing processes that can be changed over and scaled quickly. Single-use bioreactors meet this demand because of their portable, flexible nature. But are they more sustainable?

The production bioreactor stage of biologics manufacturing is one of the largest contributors to environmental impact because of the cleanroom energy consumed.[7] Although single-use bioreactors (SUBs) generate plastic waste, they use less water and facility energy than stainless steel bioreactors (SSBs).[8]

Other advantages of SUBs over stainless steel include:

- Less cleaning chemicals required
- Less personnel time required
- Less risk of contamination
- Lower capital and operating costs
- Acceptance from regulators due to improvements in leachable and extractable data

For these and other reasons, adoption of single-use bioreactors grew by about 59% between 2007 and 2020, with adoption continuing to rise post pandemic.[9] However, the disposal of single-use components raises concerns around waste generation and potential environmental impact. Life cycle assessments (LCAs) comparing SUBs and SSBs have shown that the environmental impact of both systems is highly dependent on manufacturing conditions and disposal practices.[10]

Single-use centrifuges

With an increase in recombinant proteins, monoclonal antibodies (mAbs) and bioengineered vaccines, manufacturers have seen an increase in the volumes to be harvested via depth filtration. Single-use centrifugation has emerged as a viable solution to reduce the numbers of depth filters required for single-use harvest operations.[11]

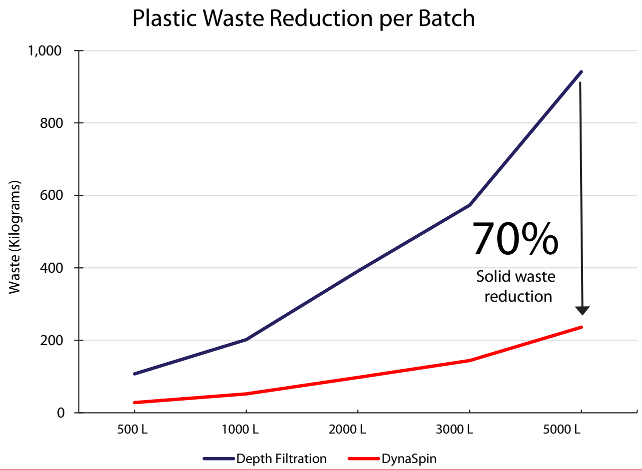
Single-use harvesting solutions have been shown to result in lower cycle times and reduced filtration surface area and buffer requirements as compared to traditional single-use depth filtration steps.[12] Today's centrifuges deliver high performance as well as energy savings, some by more than 70% compared to traditional models.[13]

One reason for their sustainable performance stems from its workflow. DynaSpin™ SUT replaces the first depth filtration stage with a centrifugation step and helps reduce the number of filters needed for the second depth filtration stage.[14]

Because they reduce the quantity of depth filters required, single-use centrifuges produce less waste. Compared to depth filtration, DynaSpin™ SUT generates 74% less liquid waste than depth filtration. It also uses 70% fewer filters on average and requires substantially less harvest suite and warehouse space.

Reduced filter usage leads to less plastic waste associated with each batch. Solid waste generated per batch can be reduced by up to 70% for a 5,000-liter production.[14]

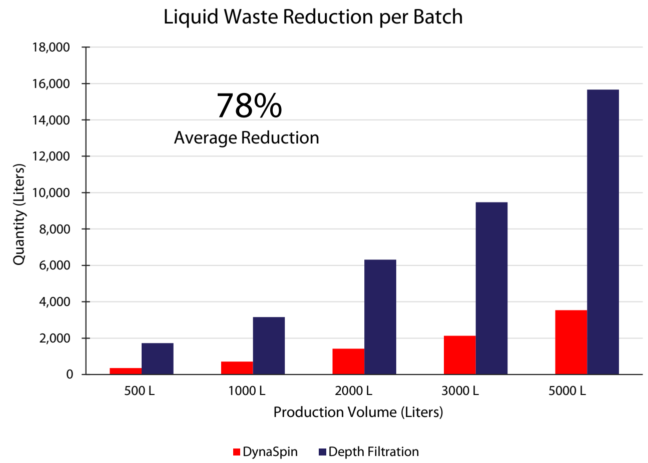
ACHIEVING A SUSTAINABLE HARVEST



Plastic Waste Reduction

Reduced filter usage helps companies reduce the plastic waste associated with each batch

- HVAC burden



Treated Liquid Waste Reduction

Fewer filters means less WFI, buffer, and NaOH is required for each batch

- Waste disposal

Greater yields and time savings

By reducing the number of depth filters used, manufacturers can also reduce labor costs due to less time spent setting up and breaking down the filters. Also realized are the higher yields and lower flush buffer volumes when trying to recover the holdup volume normally found in larger depth filtrations trains that are not encountered when using centrifugation.

Chromatography

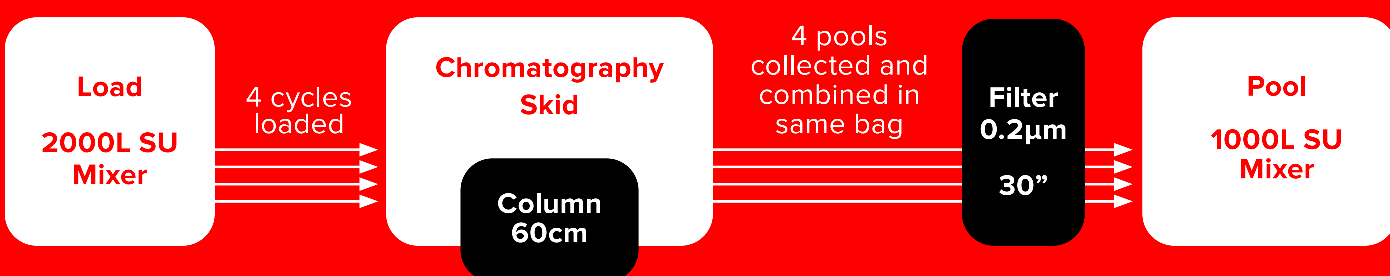
Chromatography cycles collected separately using one filter and into one pool bag per cycle takes more time to set up and uses more plastic than cycles combined into one pool bag. The downside of the latter approach is that if the integrity of the pool bag is compromised, the entire batch is at risk.

CHROMATOGRAPHY CYCLES COLLECTED VIA ONE FILTER AND COMBINED INTO ONE POOL BAG

This is the preferred approach for executing in MFG to save raw material, labour and time costs.

Advantages:

- **Less plastic used compared to separate collections (1 X 1000L SU mixer and 1 X 30" filter capsule)**
- **Less operator manipulation / enables automation**
- **Lower raw material costs for client**
- **Less set-up time**



Disadvantages:

- **Analytical data on separate pools not possible**
- **If integrity of combined pool bag is compromised entire batch is at risk**

The way forward

Equipment choice and process decisions both affect biomanufacturing's environmental impact. Waste disposal is another consideration. Solutions are in the works that could improve upon traditional landfill and incineration.

Ideally, all single-use equipment would be recycled. However, standard recycling programs cannot accept biohazardous or medical waste unless it's sterilized. Standard programs may also not be equipped to handle the types of plastics used in manufacturing. To manage the load responsibly, some pharma companies are partnering with hazardous waste disposal companies to develop more sustainable alternatives.

At Thermo Fisher, reducing environmental impact is factored into many of its processes from the start. For example, when designing a manufacturing process, the company considers the minimum number of steps, filters, and other consumables it can use without impacting quality or speed. In practice, this means process engineers will evaluate using a single larger bioprocessing container (BPC) for collecting multiple product pools in a multi-cycle chromatography unit operation (rather than collecting separate pools using several smaller BPCs).

Thermo Fisher also considers energy and water consumption. Additional efforts to reduce the number of consumables also reduces waste and lowers the cost of goods for the end-user.

Conclusion

Reducing environmental impact has become a high priority for nearly all industries, including pharma/biopharma. More sustainable practices that conserve material, energy and water use go a long way toward meeting ESG goals while also conserving costs. SUT offers clear environmental and financial advantages over reusable stainless steel. It's also ideally suited for smaller-batched biologics that require quick turnaround times and flexible processes.

With every project, biologics developers and manufacturers can work together to develop more sustainable manufacturing processes. By doing so, the biopharma industry can continue to focus on producing life-changing therapies while respecting the environment.

References

1. Ottinger, M, et al. (2022). Single- Use Technology in the Biopharmaceutical Industry and Sustainability: A Contradiction?. Chemie Ingenieur Technik. 94. 10.1002/cite.202200105.
2. Lindsey, R, Dahlman, L. Climate Change: Global Temperature. Climate.gov https://www.climate.gov/news-features/understanding-climate/climate-change-global-temperature
3. Jimenez, D. Cutting the carbon footprint of pharma's supply chain. Pharmaceutical Technology, February 9, 2002. https://www.pharmaceutical-technology.com/features/cutting-carbon-footprint-pharma-supply-chain
4. Bhutani, S, Sarangapurkar, S. Unveiling the Green Prescription: Navigating Sustainability in the Pharmaceutical Industry. Pharmaceutical Engineering, February 23, 2024. https://ispe.org/pharmaceutical-engineering/ispeak/unveiling-green-prescription-navigating-sustainability
5. Philpott, J. Pharma's path to Net Zero: Targeting Scope 3 emissions. Pharmaceutical Technology, November 29, 2023. https://www.pharmaceutical-technology.com/features/pharmas-path-to-net-zero-targeting-scope-3-emissions
6. Net Zero Stocktake 2023. June 11, 2023. https://zerotracker.net/analysis/net-zero-stocktake-2023
7. Budzinski K, Constable D, D'Aquila D, et al. Streamlined life cycle assessment of single use technologies in biopharmaceutical manufacture. N Biotechnol. 2022;68:28-36. doi:10.1016/j.nbt.2022.01.002
8. Single-use vs. stainless steel: the biopharmaceutical manufacturing debate. ThermoFisher Scientific white paper, 2023. https://assets.thermofisher.com/TFS-Assets/BPD/Reference-Materials/single-use-vs-stainless-steel-white-paper.pdf
9. Morrow Jr, K John; Langer, E. Rise of Single-Use Bioprocessing Technologies: Dominating Most R&D and Clinical Manufacture. American Pharmaceutical Review, February 27, 2020. https://www.americanpharmaceuticalreview.com/Featured-Articles/561308-Rise-of-Single-Use-Bioprocessing-Technologies-Dominating-Most-R-D-and-Clinical-Manufacture
10. Sauve, G., Van Acker, K. Integrating life cycle assessment (LCA) and quantitative risk assessment (QRA) to address model uncertainties: defining a landfill reference case under varying environmental and engineering conditions. Int J Life Cycle Assess 26, 591–603 (2021). https://doi.org/10.1007/s11367-020-01848-z
11. Walker J, Lam Y, Loman A, Smelko JP, Rohr M. Evaluation of a single-use disk stack centrifuge for improved efficiency and sustainability at 1000L GMP manufacturing scale. Biotechnol Bioeng. 2023;120(11):3347-3356. doi:10.1002/bit.28519
12. Tripathi NK, Shrivastava A. Recent Developments in Bioprocessing of Recombinant Proteins: Expression Hosts and Process Development. Front Bioeng Biotechnol. 2019;7:420. Published 2019 Dec 20. doi:10.3389/fbioe.2019.00420
13. Graham, L et al. Sustainable Centrifuges: Greener, Cost-Effective, and Performance-Enhanced. Lab Manager, October 7, 2021. https://www.labmanager.com/sustainable-centrifuges-greener-cost-effective-and-performance-enhanced-26826
14. ThermoFisher Scientific internal documents.

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