White paper | Sustainability

Single-use technologies

Advancing sustainability

Single-use technology and environmental responsibility in biopharmaceuticals

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Introduction

Global concerns regarding climate change and greenhouse gas emissions continue to grow, with biopharmaceutical companies increasingly accepting responsibility for their impact on the environment. The biopharma industry is under growing pressure to maximize productivity and accelerate time-to-market, while simultaneously combating rising costs associated with the development and manufacturing of biologics. As the industry strives to meet increasing demand, companies are actively seeking ways to optimize processes that can reduce resource consumption while potentially supporting time and cost savings.

Finding meaningful ways to implement environmental sustainability practices is challenging when evaluating the bioproduction landscape. Productivity goals need to be maintained while working within a designated budget under accelerated timelines. Additional challenges in implementing sustainability goals include maintaining or improving ROI, product quality, and time-to-market, as well as meeting regulatory compliance. Implementing successful initiatives that support more sustainable processes and systems requires awareness and collaboration across different leadership roles and groups.

A typical manufacturing workflow requires upstream and downstream equipment distinctly categorized as single-use technology (SUT) or stainless steel. Regardless of the equipment type, different types of waste and greenhouse gas emissions result from the workflow processes. Thermo Fisher Scientific is committed to considering sustainability when designing products and has been striving to develop SUT workflow solutions that support sustainability efforts. Single-use technology has observed remarkable growth in the bioproduction market due to its flexibility, scalability, speed, and cost advantages, and has been observed to have less environmental impact than traditional manufacturing with stainless-steel. This piece examines the current environmental sustainability landscape, the potential productivity impact of integrating sustainability initiatives into SUT development, and the influence regional manufacturing has on scope 3 emissions.

Keywords

Single-use technology, environmental sustainability, bioprocessing, process intensification, life cycle assessment, DynaDrive bioreactor, DynaSpin centrifuge, stainless steel, bioproduction, biomanufacturing, bioreactor, emissions reduction, harvest, scope 3 emissions

Landscape overview

Three key areas of focus for improving sustainability in bioproduction are emissions reduction, waste reduction, and water conservation.

Emissions

Sustainability challenges in manufacturing include the reduction of greenhouse gas emissions associated with bioproduction and its respective manufacturing processes. When evaluating the source of greenhouse gas emissions, environmental impacts have been categorized into a framework of scope 1, 2, and 3 emission types [1]. Scope 1 emissions emerge from sources owned by a company including on-site burning of fossil fuels and the use of company vehicles. Scope 2 emissions are associated with the purchase and transport of electricity, heat, or steam for use at the facility. The responsibility of scope 1 and 2 emissions falls directly with the facility's owner. Scope 3 emissions, however, refer to the indirect emissions that emerge from the value chain, including transportation and the use and disposal of goods during their life cycle. Bioproduction facility design, size, and workflow efficiency are all important factors that contribute to scope 1 and 2 emissions. To mitigate these impacts, many pharmaceutical and biotech companies have aligned themselves with global climate commitments and set clear targets for reduction in CO_2, SO_2, NO_2, and NH_3 emerging from transportation and bioproduction processes [2]. Biologics production requires a specific environment with strict control parameters maintaining cleanroom standards within designated functionally closed suites within production facilities [2]. While these cleanrooms are a crucial component for ensuring product quality, they consume substantial amounts of energy for particulate control and reduction, and for heating, ventilation, and air conditioning (HVAC), all of which contribute to emissions.

Certain unit operations within the bioproduction workflow use materials such as sparging gases, which additionally contribute to emissions [2]. By evaluating the multiple sources of emissions, a few areas of focus for supporting reduction can include regional manufacturing, optimizing efficiency within specific unit operations and across the workflow, and reducing the physical space associated with facilities, warehouses, and cleanrooms.

Waste

Waste in association with bioproduction emerges from multiple sources, including packaging materials, laboratory waste, and byproducts from the manufacturing process. The amount of plastic waste generated by biopharmaceutical manufacturing represents a small fraction of the world's total plastics waste, approximately 0.01% [3]. Companies are actively working to minimize waste generation by implementing more efficient processes and products, adopting sustainable packaging practices, and exploring ways to repurpose or recycle waste materials.

In the context of reducing the environmental impact of bioproduction, several factors contribute to waste generation and potential mechanisms for waste reduction and disposal options. These factors include the level of contamination of the waste, the feasibility of separating out components that can be recycled, and the proximity of the manufacturing site to recycling facilities. Unlike consumer plastic products, SUT products and equipment in biopharmaceuticals are subject to rigorous collection, decontamination, and treatment procedures at the end of their life cycle. Post-use waste disposal methods may include recycling, incineration with energy recovery, or incineration without energy recovery [2].

Water

The use of water is a primary area of focus for environmental sustainability within bioproduction. Water plays a key role in upstream cell culture and the downstream purification process, specifically in unit operations such as chromatography [2]. The water used in these processes, water for injection (WFI), must meet high-quality standards for use directly in contact with a drug substance. Typically, it is produced using resource methods such as osmosis, electro-deionization, distillation, and membrane ultrafiltration. These WFI purification steps require high energy input, which compounds the impact of water usage by acting as a contributor of higher bioproduction emissions [2].

Life cycle assessment

The key to understanding sustainability in the bioproduction landscape lies within a comprehensive analysis that considers all phases of a product's existence, commonly referred to as a life cycle assessment (LCA). An LCA is an evaluation of the environmental impacts of a product from raw material extraction to manufacturing, usage, and eventual disposal or treatment [2]. The LCA provides an understanding of the aspects associated with a specific process or product and aims to measure these impacts across distinct categories such as greenhouse gas emissions, energy consumption, water usage, and resource depletion.

LCA's impact on sustainability goals:

- **Comprehensive understanding—**Provides an understanding of how a process or product impacts the environment. This knowledge allows stakeholders to identify the environmental effects at each stage of the life cycle. It is essential for making informed decisions and prioritizing areas that need improvement.
- **Identifying environmental hotspots—**Can help pinpoint stages or aspects of a process that have a high environmental impact. By addressing these hotspots, significant reductions in burdens can be achieved.
- **Comparative analysis—**LCAs enable comparisons between products, processes, or technologies. This analysis helps organizations choose options and guides research and development efforts toward creating greener alternatives.

Various industries must adhere to regulations and sustainability standards. LCAs provide a foundation to demonstrate compliance with these requirements and therefore mitigate reputational risks. LCAs shed light on inefficiencies and wastage within processes enabling organizations to improve resource management [1]. This may lead to cost savings and reduce ecological impact. LCAs often unveil opportunities for products that have environmental impacts. By conducting LCAs based on these core principles, valuable insights are gained highlighting the environmental impact of systems and processes that support making informed choices on how to achieve sustainability goals.

By quantifying the impact of these processes, biopharmaceutical companies can:

- **Establish specific metrics—**LCAs provide the data to define specific, measurable, achievable, relevant, and time-bound (SMART) sustainability metrics. For instance, companies can set goals to reduce energy usage, water consumption, and carbon emissions for every unit of product they manufacture.
- **Identify areas for improvement—**LCAs help identify the stages or processes that have the greatest impact. Whether it's energy operations or resource-intensive phases, this information helps guide efforts toward optimizing operations and reducing burdens.
- **Enhance resource efficiency—**By understanding patterns of resource consumption throughout the life cycle, companies can make decisions on how to improve resource efficiency and minimize waste.
- **Assess performance—**Companies have the ability to compare their performance with industry standards and best practices. This allows them to evaluate how effectively they are meeting sustainability targets compared to their peers [4].

LCAs play a role in quantifying and enhancing the sustainability of processes and products. They provide a foundation for establishing sustainability metrics driving progress toward achieving sustainability goals and ensuring that industries are environmentally responsible and aligned with global sustainability initiatives. Implementing goals based on LCA data outputs can lead to meaningful and impactful changes for environmental sustainability.

Initiatives supporting design for sustainability

The transition to single-use technologies has been driven by a need to create more efficient processes that meet biopharma's complex and interconnected productivity demand and sustainability goals. As bioproduction processes evolve, particularly in the realm of intensified cell culture processes, the limitations of legacy systems continue to emerge. Balancing design for sustainability within the context of intensified and specialized processes requires a multifaceted approach. Each segment of the product's life cycle in the bioproduction workflow needs to be assessed. Data from a comprehensive LCA can be applied to the workflow to help derive potential solutions to meet environmental sustainability targets. Here we will highlight a few innovative design solutions that can help to support the transition to a more environmentally sustainable bioproduction workflow.

Production: efficiency improvement

A major goal during the production phase is to support strong cell growth and productivity through optimization of the bioreactor's parameters and settings. The Thermo Scientific™ DynaDrive™ S.U.B. was designed to support protein and monoclonal antibody (mAb) workflows. Building on extensive experience and nearly two decades of end users' feedback, the DynaDrive S.U.B. was carefully engineered to enable high performance and process flexibility. The innovative design of the DynaDrive S.U.B. in terms of closed system processing capabilities and process intensification facilitates emissions savings from multiple sources within the same unit operation.

Upstream bioproduction has seen a substantial movement in the industry toward single-use systems. The shift has been driven primarily by the need to reduce contamination risk and cleaning requirements when compared to stainless steel systems. The shift to single-use technologies allows for faster changeover of equipment between batches and eliminates the need for clean-in-place (CIP) and steam-in-place (SIP) processes, working in tandem to support efficiency and sustainability, and driving water, waste, and emissions reductions. At the same time, bioprocessing manufacturing processes have matured, and intensification of cell culture processes have pushed the limits of more legacy single-use systems. Traditional seed train approaches involve multiple vessels and complex logistical steps, leading to involved processes that require additional materials to complete each run. These approaches can also produce more waste and are therefore less sustainable than processes with workflow efficiency designed into their baseline functionality.

Designing a S.U.B. with an improved turndown ratio improves seed train efficiency and can potentially eliminate the need for vessels at multiple volumetric scales. The higher turndown ratio of at least 10:1 and up to 20:1 in the larger sizes of the DynaDrive S.U.B. increases efficiency and optimizes the duration of each run thus reducing the emissions associated with every production batch. The higher turndown ratio significantly improves operational efficiency by limiting the number of intermediary-sized vessels required to scale up a process. By reducing the number of unit operations, the GMP activities take up a smaller footprint in the cleanroom areas. This reduction in footprint allows for smaller, more efficient processing of the same total kg of protein within a more concentrated footprint. Reducing the cleanroom space can then allow for reduced HVAC support, utilization of the space for other GMP activities, or both. Figure 1 illustrates the ability of the DynaDrive S.U.B. to enable a streamlined seed train for cell expansion. Utilizing the DynaDrive S.U.B. at 5,000 L supports process intensification that reduces seed scale-up steps and the number of depth filters by 80%. This material reduction helps with improving overall waste generation. Throughput is improved based on fewer unit operations needed for the intensified seed train process, which in turn drives a reduction in consumables and associated waste.

In addition to emissions savings using an intensified seed train process, consumables, and therefore physical waste, are reduced in tandem. The compounding of reductions in both emissions and waste sets the DynaDrive S.U.B. apart as a viable solution within the upstream workflow to make a meaningful impact on environmental sustainability goals. Pictured below in Figure 1 are a number of unit operations that can be bypassed by inoculating from a concentrated seed bag directly into the 500 L DynaDrive S.U.B., saving valuable days in GMP production, while reducing the number of SUT items that would be used.

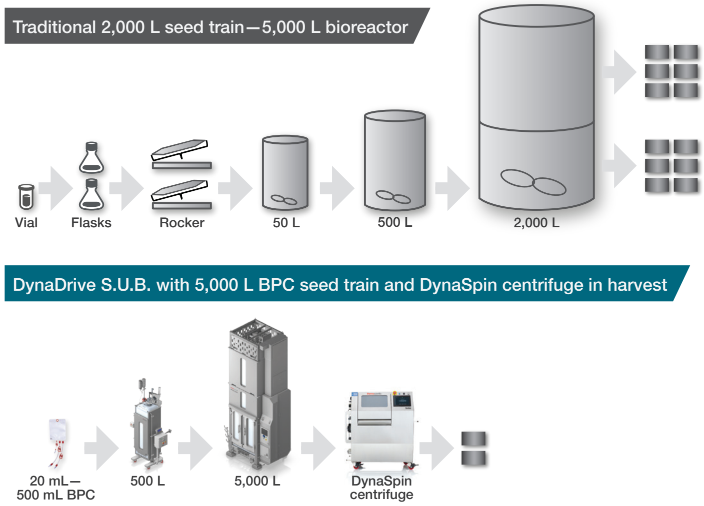


Figure 1. Improving throughput while reducing waste [5].

Harvest offering results in reductions for water, waste, and emissions

To address the need for more sustainable offerings, the Thermo Scientific™ DynaSpin™ Single-Use Centrifuge focuses on the three main environmental impact areas—water usage, waste, and emissions. A pure depth filtration harvest approach generally employs two filtration steps, where the product is passed through a clarifying filter, and then passed through a secondary filter that is sized smaller to achieve proper clarification. As illustrated in Figure 2, centrifugation greatly reduces the total number of filters utilized, requiring only a single type of depth filtration step.

A crucial aspect of sustainability is minimizing solid waste. Traditional methods of depth filtration and stainless steel centrifugation often result in large amounts of waste thus raising concerns about the disposal of plastic materials, with post-use disposal usually ending up in landfills or being eliminated by incineration. It is increasingly possible to treat and recycle this waste either through mechanical or chemical recycling. A two-stage traditional depth filtration process during a 2,000 L harvest can generate on average 700 kg of waste from filters. In contrast, using the DynaSpin centrifuge at the same volume produces on average 200 kg of solid waste, a reduction of 70% [6]. The total count of depth filters used in a traditional depth filtration step compared to single-use centrifugation using the DynaSpin centrifuge is illustrated in Figure 3 [7]. Total filter reduction of 74% at the 1,000 L scale and 75% at the 5,000 L scale has a significant impact on sustainability in terms of solid waste reduction and the associated volumes of flushing and decontamination solutions.

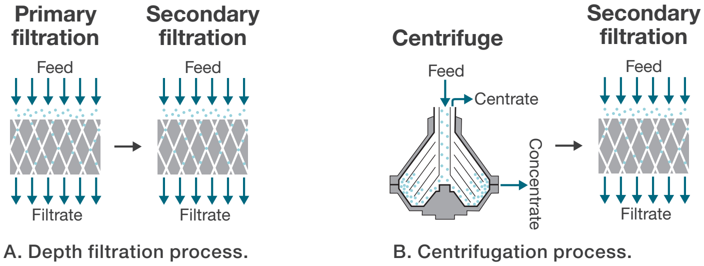


Figure 2. Traditional depth filtration process (A) compared to a centrifugation process (B).

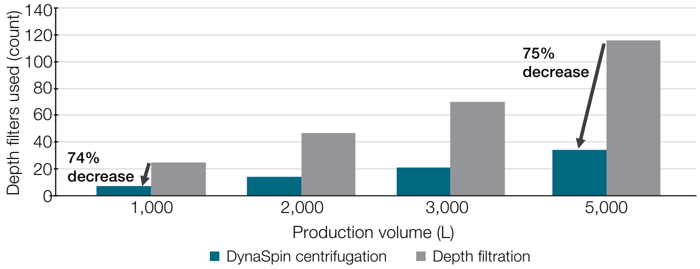


Figure 3. Total filter usage comparison: DynaSpin centrifugation vs. traditional depth filtration.

"Traditional methods of depth filtration and stainless steel centrifugation often result in large amounts of waste thus raising concerns about the disposal of plastic materials, with post-use disposal usually ending up in landfills or being eliminated by incineration."

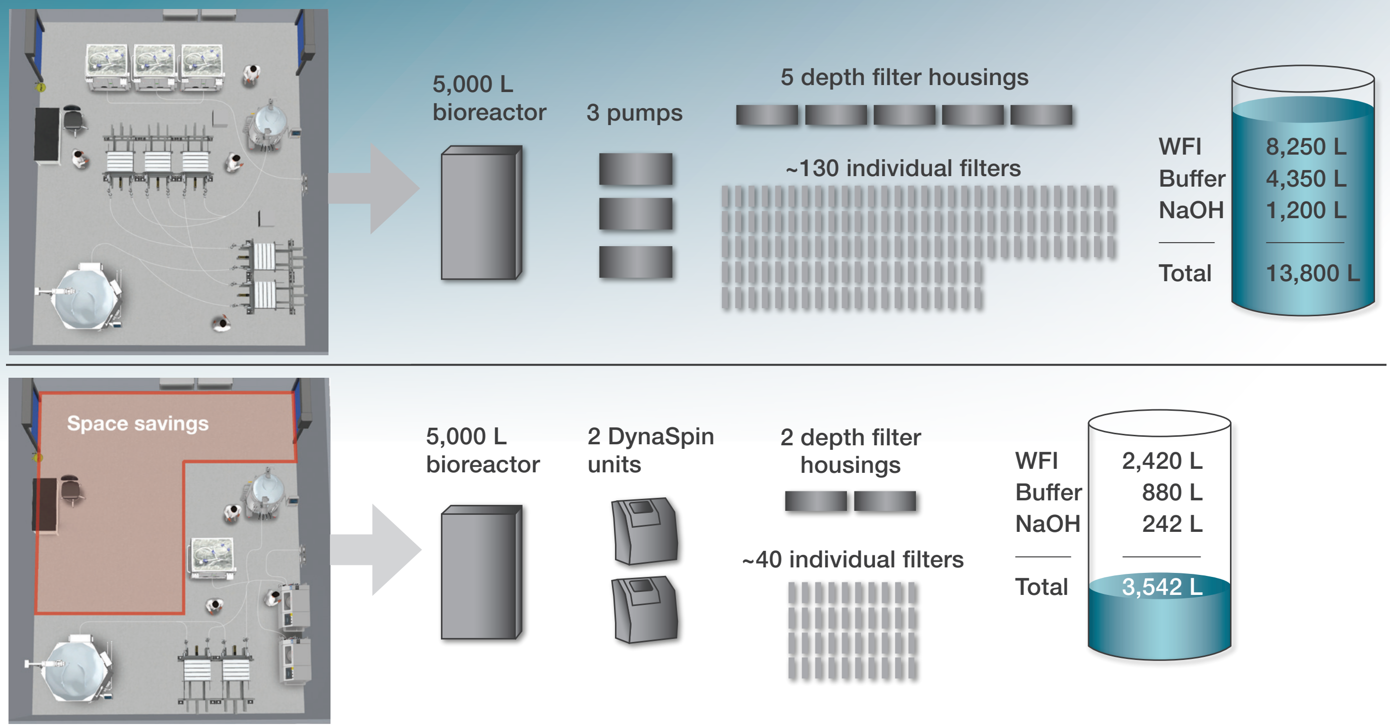


Figure 4. Footprint optimization and consumable and water reductions.

Another concern is the consumption and disposal of resources, such as water. Depth filtration often involves water usage during the flushing and equilibration processes. When using a two-stage depth filtration system for a 2,000 L harvest, approximately 9,000 L of water can be consumed during that harvest operation. By performing harvest processing using the DynaSpin centrifuge, the same 2,000 L harvest volume only requires 2,600 L of water—this results in a reduction of >75% in total liquid waste. It is important to note that liquid waste during the harvest step includes water and buffers used throughout the process. The combined reduction of these liquids contributes to water conservation and liquid waste reduction sustainability goals.

The DynaSpin centrifuge has a unique design that supports the reduction of consumables as well as physical space both in cleanrooms and in facility warehouses, resulting in overall operational footprint reductions. Figure 4 visually demonstrates the differences in footprint between traditional depth filtration methods and the harvest workflow using the DynaSpin centrifuge, for bioreactor capacity of 5,000 L. The DynaSpin centrifuge brings value by decreasing the number of depth filters, in turn reducing inventory and warehouse storage requirements and supporting sustainability by reducing filter and buffer waste.

Waste reduction in packaging

Finding ways to minimize waste associated with manufactured goods is supportive of improving sustainability practices. Addressing the waste associated with packaging of consumables for bioproduction can have a positive impact on overall reduction.

The Thermo Scientific™ Labtainer™ Pro BioProcess Container (BPC) is a next-generation bioprocess container facilitating strong performance, reliability, and quality assurance. BPCs are single-use, flexible container systems commonly used for critical liquid-handling applications in the biopharmaceutical industry. BPC systems are cost-effective alternatives to conventional stainless steel systems. They employ a novel design approach that is valued for its versatility and utility. BPC components are readily integrated into a variety of high-performance systems for all steps in the production of biologics.

As illustrated in Table 1, the Labtainer Pro BPC utilizes sustainable packaging principles to reduce packaging by 24% compared with the previous packaging design, without any impact on product integrity [8]. The corrugated cardboard packaging of the Labtainer Pro BPC uses less material than the original, thereby requiring fewer resources, emitting less greenhouse gas during transit, and generating less packaging waste.

Table 1. Comparison of updated and original corrugated cardboard box weights for Labtainer Pro BPCs.

Container	Weight (g)	Packaging reduction
Labtainer Pro BPC corrugated cardboard box	2,040	24%
Original corrugated cardboard box	2,680	

Maximizing scope 3 emission savings through in-region manufacturing

A top-ranking priority for achieving sustainability within bioproduction is scope 3 emission savings [1]. Scope 3 emission is categorized as an indirect source of emissions. It encompasses emissions associated with a company's activities, but from sources not owned or directly controlled by that company. These sources result from production and transportation associated with the supply chain and end-of-lifecycle treatments including sanitization, disposal, recycling, and others. To reduce scope 3 emissions, adopting a multifaceted and strategic approach is crucial for driving effective change.

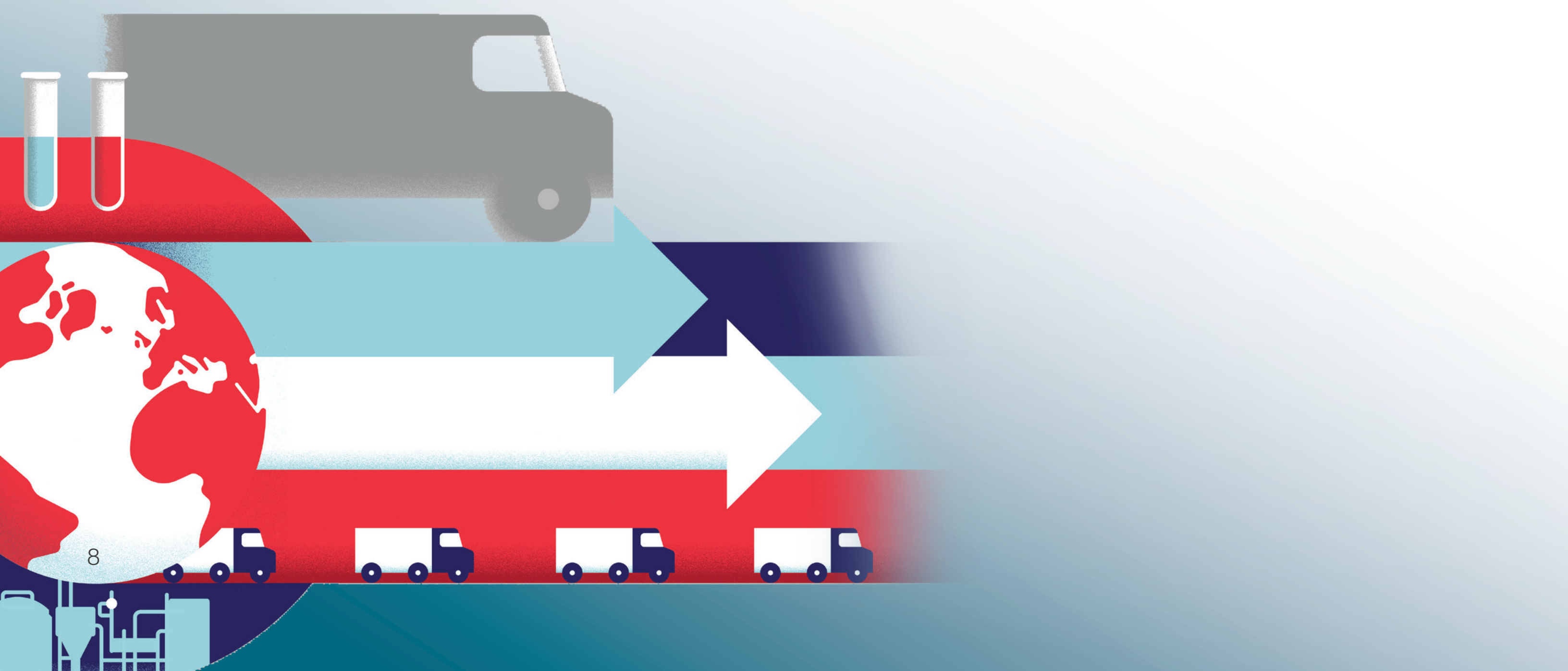
A way to address scope 3 emissions while optimizing the supply chain is through the use of in-region manufacturing. A more localized manufacturing approach can reduce emissions and enhance sustainability through an interconnected network of production facilities. By establishing production facilities localized to the regional areas representing the highest distribution needs, suppliers can significantly decrease shipping distances and cut down on the need for excess transport via air, sea, and road. Thermo Fisher Scientific has invested heavily in a global network with in-region manufacturing over the last few years, with facilities strategically positioned across key regions worldwide. Expanding manufacturing space in North America, Europe, and Asia-Pacific has increased production capabilities allowing for rapid adaptation to shifts in market dynamics within each region.

With multiple facilities operating as a network to build redundancy and enable surge capacity, decentralized production has a positive impact on supply chain resilience and helps to reduce risks associated with global disruptions. In-region manufacturing works to intertwine key business objectives with sustainability goals, highlighting the commitment of Thermo Fisher Scientific to delivering an improved customer experience using innovative solutions.

The significance lies in how this approach helps to directly impact and minimize the carbon footprint associated with product distribution. In a customer case study, optimizing the manufacturer site to in-region and point of use for all single-use flexibles purchased in a year, a ~1,300 metric ton reduction in CO_2 emissions was observed. Using a more regional approach on a global scale allows for greater reach and greater impact. This commitment mitigates risk and accelerates production, streamlines manufacturing, and global distribution to enable shorter lead times, increases inventory management efficiency, and supports sustainability improvements associated with scope 3 emissions.

In-region manufacturing advances extend beyond lowering scope 3 emissions. The ripple effect of localized production and distribution has far-reaching implications for global sustainability.

> "A more localized manufacturing approach can reduce emissions and enhance sustainability through an interconnected network of production facilities."



Conclusion

The biopharmaceutical industry is currently facing two very diverse challenges, increasing productivity and keeping costs down while also addressing impact and climate. This paper focuses on the role of SUT in driving a more sustainable balance in biomanufacturing. By conducting LCAs the industry can gain an understanding of the environmental impact associated with bioproduction workflows, which serves as a foundation for establishing meaningful sustainability metrics.

LCAs provide insights into areas that have an environmental impact allowing stakeholders to pinpoint areas that need improvement. Comparative analyses facilitated by LCAs help guide research and development efforts toward alternatives. These assessments are crucial in establishing measurable and evidence-based sustainability goals. They assist in demonstrating compliance with regulations and standards, managing risks effectively, and optimizing resource management for cost savings and reducing impact.

This review has highlighted sustainability advancements in the bioproduction sector in regard to product design, such as the DynaDrive S.U.B., Labtainer Pro BioProcess Container, and DynaSpin Single-Use Centrifuge. These innovations can play a role in reducing emissions and waste, and promoting sustainability. They support alignment with climate agreements and initiatives aimed at achieving a sustainable future.

The adoption of localized manufacturing approaches has been discussed as a method to address scope 3 emissions and enhance sustainability. By reducing transportation distances and corresponding carbon emissions, this holistic approach emphasizes the industry's commitment to making a global impact in favor of environmental sustainability. By utilizing state-of-the-art SUT efficiently, these new technologies can help the end user drive toward their sustainability goals while intensifying their process and gaining greater productivity.

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