Case study

Streamlining mAb scale-up with high-performance media and feed solutions

A Thermo Fisher Scientific collaboration with the Zurich University of Applied Sciences

The development of protein-based therapeutics, such as monoclonal antibodies (mAbs), is a rapidly growing field within the pharma industry—driven by the rising global demand for newer, more effective treatments. To meet this demand, mAb developers need to maintain consistent productivity and product quality across scales so they can reach clinical and commercial manufacturing efficiently.

It is therefore crucial to find the optimal medium and feed for a particular workflow during process development. Evaluating multiple options can be a time-consuming task, so a platform system—designed for a specific cell line and optimized for performance and scalability—can offer significant advantages. Complete workflow solutions can help further boost efficiency, helping to ensure compatibility and reducing the need to screen additional feed options.

With this in mind, Thermo Fisher Scientific collaborated with the Centre for Cell Cultivation Techniques, Tissue Engineering, and Medical Biology at the Zurich University of Applied Sciences (ZHAW) to demonstrate the performance and scalability of Gibco™ media and feed solutions.

A leading Swiss research institution, ZHAW has longstanding expertise in life science and pharmaceutical innovation, with more than 20 years of bioprocessing experience.

Combining expertise with trusted products

Working with Thermo Fisher, the team at ZHAW developed antibody production processes with CHO-K1 cells in fed-batch and perfusion processes, from small to 50 L pilot scale. This study aimed to demonstrate the performance and scalability of

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two Gibco media and feed solutions—**the Gibco™ Efficient-Pro™ Medium and Feeds System,** designed to optimize fed-batch CHO-based bioproduction, and the **Gibco™ High-Intensity Perfusion (HIP) CHO Medium,** developed to enable exceptional performance in perfusion processes. Another focus of this work was to create a simplified scale-up process so biopharmaceutical developers could utilize these data to scale up individual processes without great effort.

In a conversation with Vivian Ott, Scientific Assistant at ZHAW, she spoke more about their work.

"The center specialists develop, characterize, and cultivate cell lines delivering products such as bio- and cell therapeutics. Using our biological, bioengineering, and process technology knowledge, we help rapidly develop biotechnological production processes. We naturally tackle all challenges that arise and are constantly expanding our expertise. This includes selecting the right production organism, medium, process control and bioreactor. Troubleshooting is a core competence when developing and scaling-up new processes with new bioreactors."

This deep subject matter expertise made ZHAW an ideal collaborator for showcasing the scalability of Gibco media and feed solutions, and demonstrating methodology for simplified scale-up.

Navigating scale-up challenges

Early-stage developers may face several obstacles when scaling up. A key challenge is maintaining the same conditions at both small and large scale. However, this is not always possible. A common misunderstanding when developing a scalable, consistent process is that a large-scale process will mimic a small-scale one. A more effective strategy is to use a top-down approach. Ott explained how the bioengineering parameters of a small and large bioreactor must be compared, and a decision made as to which parameters are critical.

"In perfusion processes in which very high cell densities of >100 million cells per mL are achieved, for example, it is necessary to ensure the oxygen requirement. However, this must not be accompanied by excessive gassing rates or stirrer speeds, as otherwise the cells could be exposed to excessive shear forces and the product yield would be reduced or the product quality impaired. Another factor is high CO_2 concentrations in large bioreactors, which may need to be reduced in order to protect the cells," said Ott.

> During process development, we were in constant contact with the scientists at Thermo Fisher. Together, we were able to discuss our challenges on a scientific basis.

"Before we developed the processes on a laboratory scale, we looked at the bioengineering parameters of our pilot bioreactor and developed the process on a small scale based on these. In the perfusion processes, the focus was on the oxygen supply to the cells. In the fed-batch processes, we focused on the stirrer tip speed as a scaling criterion. Both bioengineering parameters are easy to determine for stirred reactors and can therefore be used by a wide range of users for scaling their processes."

Exploring the key findings

The studies showed promising results for scaling workflows with both media systems.

Fed-batch process

Using a fed-batch process with CHO-K1 cells, the performance of the Gibco™ Efficient-Pro™ Medium and Gibco™ Efficient-Pro™ Feed 1 was evaluated at 250 mL, 3 L, and 50 L. The system was shown to support consistent, high-quality fed-batch mAb production at a range of scales, helping maximize scale-up efficiency. Strong and similar trends in cell growth and viability were maintained at all production volumes and IgG titers ranging between 4.5 g/L and 5.2 g/L were achieved at all scales. Key protein quality attributes, including charge variants, protein aggregation, and N-glycosylation, remained consistent.

Continuous perfusion process

Using a continuous perfusion process with CHO-K1 cells, the performance of the HIP CHO medium was evaluated at 3 L and 50 L. The medium supported sustained high performance for perfusion-based mAb production during scale-up. Cell growth and viability were maintained at both production volumes and average IgG titers ranging from 1.7 to 1.9 g/L/day were achieved during steady-state production with scale-up. The medium also

enabled the use of very low perfusion rates with <10 uL per mm3 viable cells a day. Total process harvest yields ranged from 2,700 to 3,000 g of mAbs, demonstrating the high efficiency of a continuous perfusion process with modest scale-up to 50 L.

The results of this study demonstrated that both the Efficient-Pro system and HIP CHO medium can support consistent, high-quality mAb production at a range of scales, for fed-batch and perfusion-based processes respectively.

Further considerations for successful scale-up

In addition to the performance of the media and feed systems, it is vital to consider other factors that can support or derail a reliable and efficient workflow. Firstly, both the medium and feed should be available in formats designed for large-scale production. A dry granulation media format, for example, can offer numerous benefits. Besides lowering shipping costs and storage requirements, an advanced format can support rapid reconstitution, reducing preparation time.

Furthermore, to maintain process consistency, chemically defined, animal origin–free (AOF), and serum-free or serum-reduced formulations can reduce the risk of variability and supply chain concerns. It is also important to choose a supplier that can dependably deliver consistent quality products. The supplier should have a robust mitigation strategy in place, including a global supply network with built-in redundant and harmonized manufacturing capacity, to minimize supply chain interruptions.

Technical support is also invaluable. With easy access to regulatory documentation and field application scientist insights, developers can confidently scale their processes knowing they have the products, experience, and data they need to help chart the best route forward.

“During process development, we were in constant contact with the scientists at Thermo Fisher. Together, we were able to discuss our challenges on a scientific basis. This included, for example, the development of the feeding strategy for the fed-batch and perfusion processes, as well as the selection of the exact cultivation conditions based on the biochemical engineering parameters. It was an excellent cooperation which resulted in several papers, application notes, and presentations at conferences,” Ott explained.

Guiding mAb developers on their journey to commercialization

Early-stage developers face many challenges when trying to rapidly and efficiently develop optimized, scalable processes and decrease time-to-market. With formulations specifically designed for performance and scalability, platform systems can help accelerate mAb process development. When combined with dedicated technical and regulatory support to streamline scale-up, these solutions are a powerful option for developers looking to gain a competitive edge.

By identifying the optimal solution from a reliable supplier, developers can utilize media and feed systems to confidently develop and scale optimized mAb manufacturing processes, helping them accelerate their journey to commercial production.

Vivian Ott

Vivian works within the Cell Cultivation Techniques group—a part of the Centre for Cell Cultivation Techniques, Tissue Engineering, and Medical Biology at ZHAW. She is involved in R&D projects, including the development of cultivation processes from small to pilot scale, as well projects that focus on the development of new devices and systems to meet the current needs of biopharmaceutical producers.

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