



Supporting advances in MAb process development and manufacturing

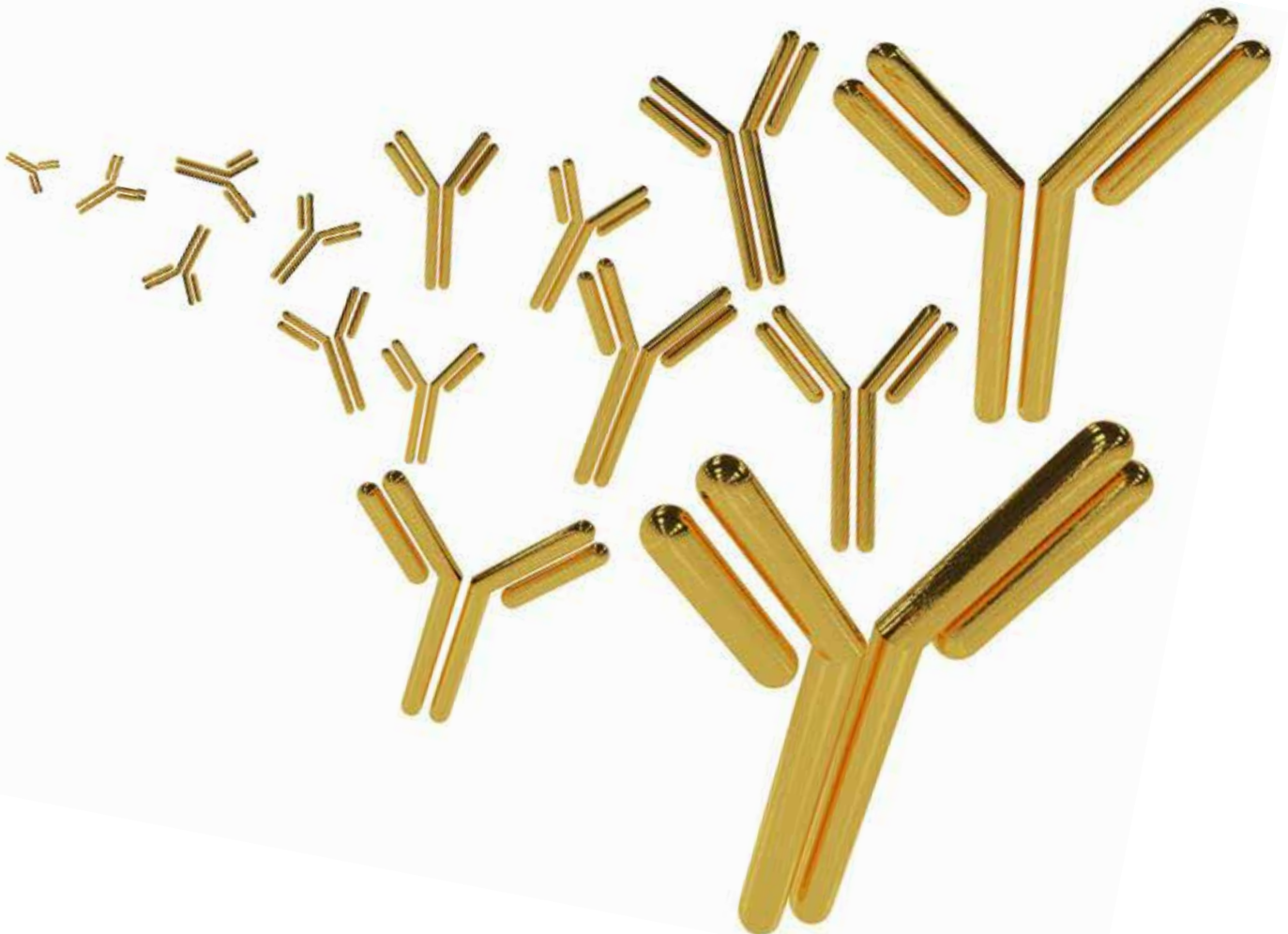
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GE Healthcare is a \$17 billion unit of the General Electric Company (NYSE:GE), employing more than 46 000 people worldwide. The company provides technologies for biomedical research, biotherapeutic development, and biopharmaceutical manufacturing.

With more than 50 years of experience of the biotech industry and being a key solution provider to monoclonal antibody (MAb) process development and manufacturing, GE Healthcare Life Sciences offers a wide range of technologies, products, service, and knowledge. Our tools and experience can help to take your MAb from research, through process development, to full-scale manufacturing.

Challenges that inspire

MAbs have proven highly successful as targeted therapeutics for a variety of diseases, including several forms of cancer, multiple sclerosis and immunological disorders such as rheumatoid arthritis and psoriasis. Today, approximately 50% of the revenue in biopharmaceuticals is generated by MAbs, making them a very important group of molecules.

However, with high demands on productivity and cost-efficiency, the bioprocessing industry is facing many challenges. Efficient process development, adaptability to market demands and the ability to handle multiple projects in production

require flexibility in process scale, manufacturing capacity and facility utilization. With our long experience in laboratory and industrial-scale processes we can provide insight and troubleshooting regarding process design and optimization as well as regulatory standards in different regions and countries for the development and manufacture of your MAb.

Looking ahead, Fabs and other antibody fragments hold great promise for new and more effective therapies. They are becoming therapeutic alternatives to full-length MAbs since fragments can be produced more economically, are smaller, and possess advantageous properties in certain therapeutic applications.

Start-to-finish solutions

GE Healthcare Life Sciences provides MAb bioprocessing solutions designed to your specifications, whether you choose single-use, hybrid or traditional technology. In addition to our processing tools, we provide validation support to lighten the regulatory load, collaboration on critical projects, or even support in the design, construction and start-up of an entire plant. Our most extensive solution is KUBio™, a fully functional bioprocessing facility designed to deliver a rapid response to local manufacturing requirements. KUBio is preengineered and provides an off-the-shelf solution for your MAb manufacturing needs.

Versatile upstream BioProcess™ solutions

Today it has become more common to make smaller batches of several products in one facility instead of making tons of a single blockbuster drug substance in a dedicated plant. Our single-use biomanufacturing technologies bring you flexibility in process scale, manufacturing capacity and facility utilization, without sacrificing reliability. WAVE Bioreactor™ systems offer a convenient, cost-efficient solution for small- to large-scale cell culturing. Intuitive software makes start-up effortless and the single-use technology, integrated with a functional and ergonomic system design, allows for quick changeover between production runs.

The linear scalability of Xcellerex™ XDR™ single-use stirred-tank bioreactor systems makes the process of scaling up for commercial production more predictable. Using the XDR systems can help ensure that the robustness, purity, and potency of the scaled-up process are comparable to that of the small-scale development process, thus eliminating the need for costly and time-consuming process redesign.

GE Healthcare Life Sciences also offers cell-type specific culture media, optimized for high performance and protein yield, which can help you get more out of your culture. For large-scale MAb production, ActiCHO™ media system is designed to support high cell densities and protein yields while facilitating process control.

The products in our upstream portfolio can be used in combination with our solutions for harvest and further downstream processing of your MAb.

Agile downstream BioProcess solutions

Our comprehensive MAb purification toolbox offers a range of the latest generation chromatography media (resins), which fully match the modern platform approach to MAb purification. MabSelect SuRe™ chromatography media family, based on the innovative alkali-stabilized protein A ligand and high-flow agarose base matrix, offers high capacity and allows for high flow rates in downstream processing. The ability of MabSelect SuRe media to withstand repeated cleaning-in-place with sodium hydroxide provide for considerably better process economics. For subsequent purification steps, the MAb purification toolbox includes Capto™ and Capto ImpRes multimodal and ion exchange chromatography media, which are designed for the polishing steps of MAb purification processes.

The MAb purification toolbox can, together with the wide range of AxiChrom™ columns with features like intelligent column packing for fast and reproducible packing of your chromatography media, significantly improve the productivity, cost-efficiency and flexibility in your downstream processing.

With an expanding toolbox, GE Healthcare Life Sciences offers a similar purification platform for antibody fragments as the already well-established for MAbs. With the introduction of Capto L and LambdaFabSelect chromatography media, the industrial platform for the purification of antibody fragments emerges.

Other products of the GE Healthcare Life Sciences portfolio include:

- ReadyCircuit™ bags and tubing assemblies, easily connected with ReadyMate™ disposable connectors, simplify system assembly and reduce the need for cleaning and validation.
- ReadyToProcess™ prepacked columns deliver the same performance level as available in conventional processing columns.
- ULTA™ normal flow filters provide prefiltration and sterilizing grade filtration suitable for MAb purification.
- PreDicator™ plates and PreDicator RoboColumn units support high throughput process development by allowing parallel screening of chromatography media and conditions for binding, wash, and elution, and design-of-experiment that fits well with the regulatory initiatives Quality by Design.
- ÄKTA™ systems with UNICORN™ software enable scale-up of MAb purification from ÄKTA ready, with a disposable flow path, and ÄKTA avant to large-scale manufacturing with ÄKTApurify™.
- Inline Conditioning system enables buffer formulation precisely at the time of use, reducing the size and number of buffer hold tanks and saving valuable time. This functionality can be part of both chromatography and filtration systems.
- FlexFactory™ is a manufacturing platform built almost exclusively with disposable technology. The FlexFactory is organized into several discrete modules, each of which is self-contained in its own controlled environment, thereby eliminating the need for expensive clean room facilities.
- Biacore™ label-free analysis systems provide confident binding assay suitable for MAb characterization.

Innovative solutions for essential improvements of process economy

Günter Jagschies, Strategic Customer Relations Leader, GE Healthcare Life Sciences and winner of 2012 BioProcess International Award "Downstream Thought Leader of the Decade" gives some future-looking remarks.

"The previous island or bucket focus in technology development and improvement implying that, for example, upstream and downstream processing might be largely independent, leaving room for uncoordinated improvements will not be helpful in addressing future challenges. The main trends in this industry — the increasing cost of R&D output, the need for efficiency improvements in process development, and the cost reduction demands in manufacturing — will not be addressed successfully with such simplification of the approaches. For example, increased product titers from cell culture alone do not address the manufacturing cost aspect. Without development of more powerful purification technologies they would mainly lead to facility fit issues for processes.

It may also be somewhat naïve to expect breakthroughs in certain technologies 'just-in-time' when any given project needs them. The breakthroughs do not come from revolutionary new inventions either, but from smart combinations of what we already have in front of our eyes but without seeing the connections. What is predictably successful is to work on the

use of technology in smarter ways and combinations while maintaining a long term improvement and innovative focus on the research. This is what process engineers, who will have a lot more influence in our industry than ever before, do and this is what we do at GE Healthcare Life Sciences.

We would like to believe that ten years from now we will not need to go to conferences about single-use and debate it, as we will have witnessed the final breakthrough for single-use technology and a settlement on where it really adds value. Ten years from now there will be a significant number of cases where various approaches of continuous processing on single-use platforms will be established, and where process steps will be connected in a smart way to delete costly wait and hold installations and time.

We already see that the rise of molecule categories, with potential to succeed the full monoclonal antibodies, are triggering a demand for novel affinity solutions in an approach that maintains the power and robustness of the established affinity-based platform strategies. Further development of chromatography media and other purification tools, providing answers to specific impurity challenges and capacity levels enabling plant fit for high productivity cell culture processes, are under development as we speak, and upstream solutions are being developed at our R&D with a total process mindset of integrating rather than isolating the development."

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LambdaFabSelect incorporates BAC BV's proprietary ligand technology, which has been exclusively licensed to GE Healthcare for use in chromatography separation. Other use of this product may require a separate license from BAC BV, Huizerstraatweg 28, 1411 GP Naarden, The Netherlands.

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