How to achieve greater efficiency in biopharmaceutical process development

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GE Healthcare
Life Sciences

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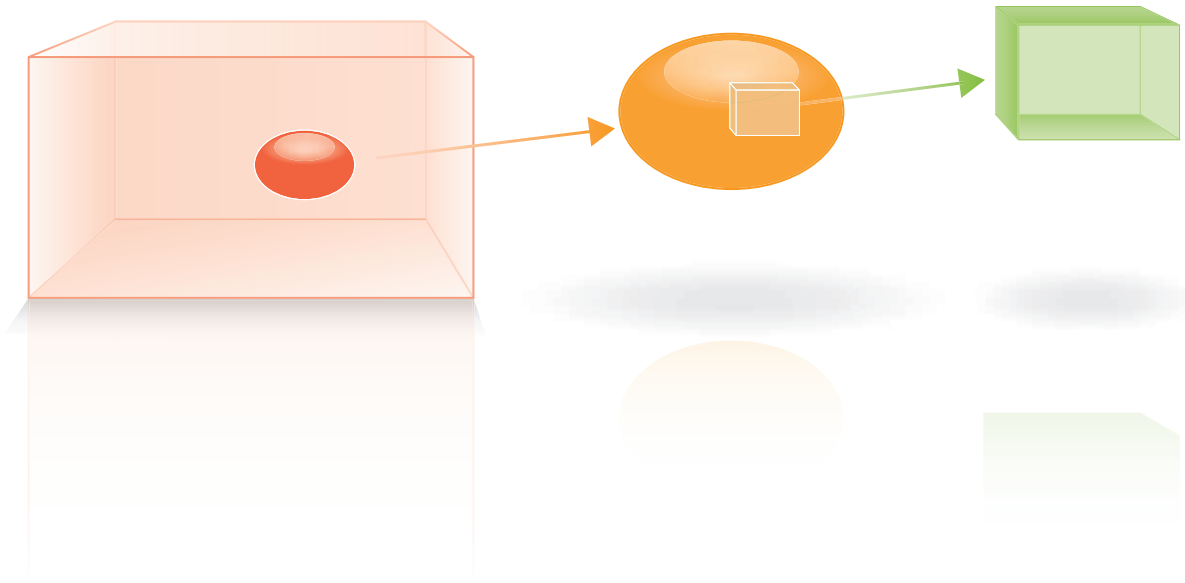
Be fast to first-in-human



Fast to first-in-human

Effective process development is crucial for the overall efficiency of biopharmaceutical development. GE Healthcare Life Sciences supports all stages of the biomanufacturing process development, from early discovery to the development of clinical material, with numerous products and services developed to improve:

- Process understanding
- Scalability in process development
- User independent operations

Enhanced throughput with parallel assessments

Increasing demands from the regulatory authorities for better process understanding, one of the cornerstones of the Quality by Design (QbD) initiative, contribute to the need for more efficient process development tools. A solution for enhancing efficiency in process development is the use of high throughput miniaturized parallel experimental technologies.

The high throughput process development (HTPD) approach facilitates simultaneous evaluation of a large number of experimental conditions, providing greater information about a particular unit operation, while consuming less material in the early stages of the development. The collected information forms the basis for earlier and more informed decision-making. Better process understanding results in less time spent on less promising process concepts. Applications and successful use of the HTPD concept in areas related to biomanufacturing process development include, for example, clone selection, optimization of upstream operations, and development of downstream purification processes.

Miniaturized formats for parallel experiments, such as PreDictor™ 96-well filter plates and PreDictor RoboColumn™ units, allow for parallel screening of a variety of chromatography conditions such as buffer conditions for binding and elution. Data generated using the PreDictor product platform show good correlation with data obtained running packed chromatography columns, making them excellent tools for initial screenings of process conditions. To facilitate HTPD using PreDictor plates, Assist software has been developed. The software supports experimental setup and data evaluation.

Automated solution for efficient screening

Screening experiments can be performed either manually or in automated workflows with robotic systems. The implementation of automation leads to a dramatic acceleration of process development by increasing the throughput of experiments and by improving the quality of the data obtained. Automated procedures minimize user interactions, thus leading to more efficient use of personnel and reduced risk for errors.

The Tecan Freedom EVO™ platforms are flexible workstations for automation. They are suited for HTPD and small-scale protein purification, as well as for further downstream applications. PreDictor plates and PreDictor RoboColumn units can be easily integrated in the Freedom EVO platform. Together with the Freedom EVOware™ wizard-guided software for process preparations and setup, a fully automated screening solution for the PreDictor platform is enabled.

Improved process understanding

Design-of-experiments (DoE) is used to identify or screen input parameters that could affect the process output. DoE techniques enable us to learn about process behavior by running a series of experiments, where a maximum amount of information is obtained in a minimum number of runs. In addition, systematic and unsystematic variability is difficult to estimate and assess without a DoE designed series of experiments (Fig 1). PreDictor plates and PreDictor RoboColumn units allow for a DoE approach that is aligned with the regulatory QbD initiative.

UNICORN™ software, with built-in planning knowhow, is used in all ÄKTA™ chromatography systems for all stages of bioprocessing—from lab bench to full scale production. Predefined methods enable convenient and easy generation of reliable results and the ability to design your own methods increases the flexibility.

Reliable process development upstream

Cell line development is the starting point for bioprocessing, whether intended for small-scale research or large-scale manufacturing purposes. To ensure reproducible outcome and valid results, stringent operating practices and careful selection of raw materials should be followed.

The single-use technology of Xcellerex™ XDR and WAVE Bioreactor™ systems minimizes the risk for cross-contamination and the need for cleaning and validation. For reproducible results, automated control systems provide reliable maintenance of your culture conditions.

WAVE Bioreactor systems offer a cost-efficient and effective solution for small-scale cell cultures. Intuitive software simplifies start-up, while the single-use technology, integrated with a functional and ergonomic system design, allows for a quick changeover between runs.

The linear scalability of Xcellerex XDR bioreactor systems can help ensure that the robustness and purity of the scaled-up process are comparable to those of the small scale process, thus eliminating the need for costly and time-consuming process redesign.

With the cell-type specific ActiCHO™ Media System, designed for Chinese hamster ovary cells (CHO-DG44), the time it normally takes to find a suitable cell culture media formulation for a production process can be significantly reduced.

Scalable process development downstream

In a high-pressure and competitive environment, mistakes can occur. In process development, the ability to efficiently gather reliable data is key to achieving a deeper understanding of the process and can help to facilitate the transfer of the process into the production hall. Direct, reliable scalability, using the same chromatography media (resins) and convenient column formats, means cost-effective process development using smaller unit operations.

The PreDictor product platform can help explore a larger *Experimental space* (Fig 1) to identify regions where critical quality attributes are successfully met.

To establish a *Design space* for a downstream protein purification process, the scalability of column formats makes ÄKTA avant 25, designed for media screening and method optimization, and ÄKTA avant 150, for scale-up to larger columns, suitable choices.

When a *Design space* has been established, defining a *Control space* is the next step. For process scale-up, ÄKTA avant 150 and ÄKTApilot™ chromatography systems are suitable choices and can operate both laboratory-scale and production-scale column formats.

ÄKTA ready is a suitable system for clinical-scale production. The system has a disposable flow path and can operate prepacked ReadyToProcess™ single-use columns as well as user-packed, reusable columns.

UNICORN software combines the flexibility needed for method and process development with the strict requirements for commercial manufacture of biopharmaceuticals.

Versatile filtration solution

For process development, ÄKTAcrossflow™ together with UNICORN control software puts you in control of your cross flow filtration process, allowing for a consistent simulation of large-scale conditions and for obtaining data for comprehensive analysis of results. The system is suitable for use in both ultrafiltration and microfiltration.

Analytical tools supporting protein characterization

In today's QbD regulatory environment, more analytical data will be required to define the process design space and to determine and verify the process robustness as drug candidates advance through each development step. GE Healthcare offers a wide range of technologies that can provide the process developer with a clear understanding of the process and how it is affecting the quality of the biotherapeutic candidate.

Analytical chromatography systems

ÄKTAmicro™ system is recommended for analytical work because of its wide flow rate range, pressure specifications, and minimized dead volumes. Together with GE Healthcare's robust chromatography media, a high resolution of different molecular variants can be obtained. Superose™ and Superdex™ gel filtration columns as well as analytical ion exchange media, such as MonoBeads™ media, prepacked in Tricorn™, HR, and PC column formats, are useful for analysis and characterization of proteins and other biomolecules.

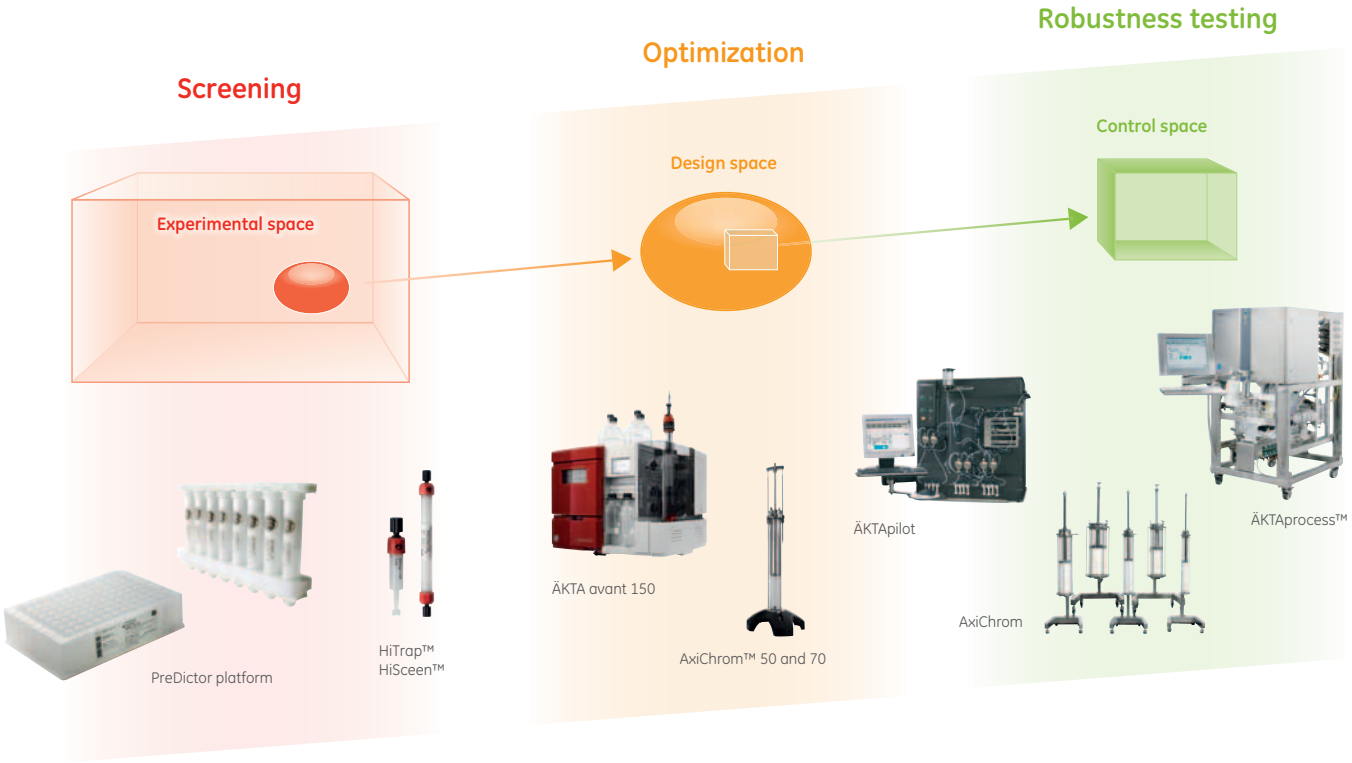


Fig 1. DoE approach aligned with QbD for deeper process understanding and realiable scalability.

Label free interaction analysis

Label-free analysis using Biacore™ and MicroCal™ systems provide confident binding assays and biomolecular stability analyses.

Biacore systems are based on surface plasmon resonance and characterize molecules in terms of their specificity, selectivity, affinity and kinetics in molecular binding interactions.

MicroCal systems for isothermal titration calorimetry (ITC) and differential scanning calorimetry (DSC) provide fundamental information on the thermodynamics of biomolecules, which can be utilized to elucidate the structure and function of biomolecules including proteins, nucleic acids, lipids, and drug candidates.

Electrophoresis

GE Healthcare offers a broad range of high-quality products for complete process development workflows, covering 1D and 2D electrophoresis, Western blotting, and 2D difference gel electrophoresis (2D DIGE). Useful in all of these workflows is our image capture portfolio containing a range of versatile and upgradeable imagers providing detection modes—from densitometry, through phosphorimaging to fluorescence and chemiluminescence—allowing you to select the best analysis solution for your applications.

Along the way

Our aim is to help bioprocessing teams to map the optimal plan to transform an idea into results, with greater flexibility and confidence, reducing time and costs along the way. Our global team of bioprocessing experts will support you in the optimization and troubleshooting of existing unit operations or in the design of efficient and cost-effective processes that meet current regulatory demands and can help reduce time–to-market. From efficient process development to production, we provide products for each step of the process. We can bring knowledge and experience to your organization through Fast Trak training and consulting services as well as through specific, individual collaborations. No matter what your needs are, we support you along the way.

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