Technical paper

Prioritize scalability for an efficient biopharmaceutical product development lifecycle

By standardizing on the right instrumentation, biopharmaceutical manufacturers can ensure seamless scale up from research in the lab all the way to full-scale production.

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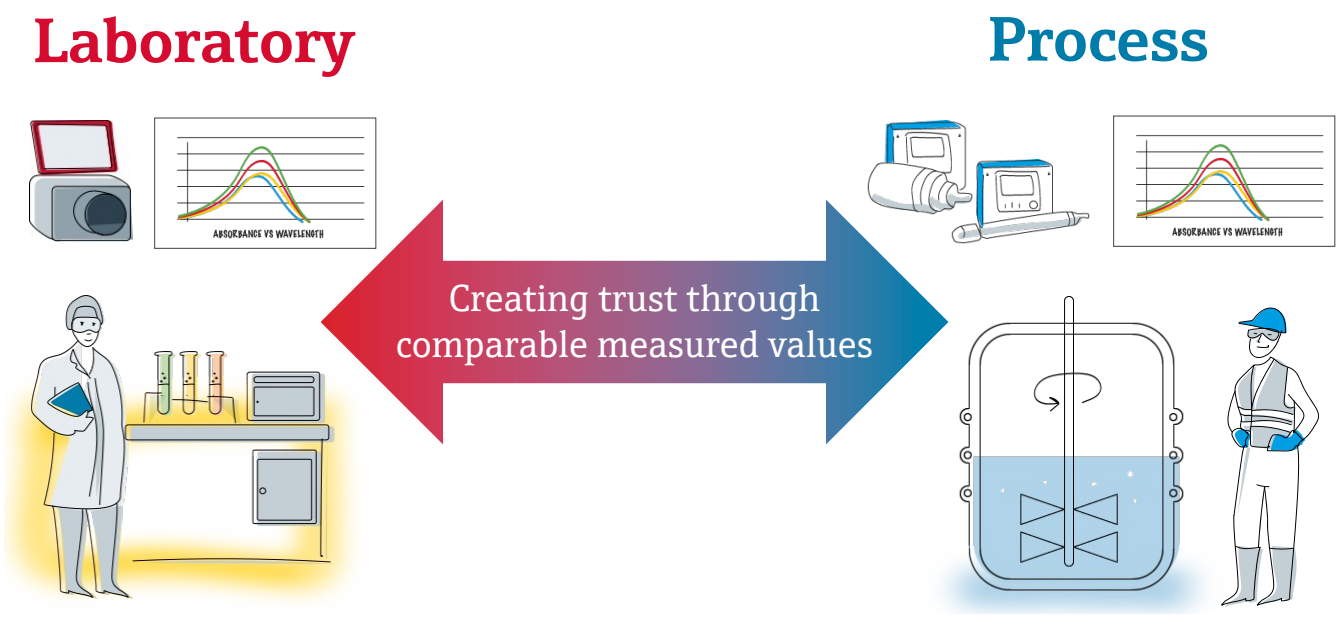

In the fast-paced world of biopharmaceutical development, speed, efficiency, quality, and cost-effectiveness are paramount. Scalability, the ability to seamlessly transition a bioprocess from small-scale laboratory experiments to large-scale commercial manufacturing, is a critical factor driving success in this competitive landscape.

However, scalability is not just about increasing the size of equipment; it is a holistic balancing strategy for operational workflows, processing equipment and instrumentation, software, data handling, and supply chain partnerships. For biopharmaceutical manufacturers, specifying scalable solutions from small-scale experiments to full-scale production can significantly bolster success by accelerating time-to-market, minimizing risks, easing qualification, ensuring process safety, and maximizing yield.

Scaling from the lab to production

The drug development lifecycle begins on the micro-scale with discovery research, including identification, screening, and sample measurements. As promising findings emerge, researchers advance to lab-scale product development, which includes activities such as defining primary process targets and classifying analytical and safety methods.

When a new drug shows efficacy during development in the lab, the next step is process development at a pilot-scale, where manufacturers begin establishing automated production procedures. Analytical measurement technology helps ensure success during this transitional phase, comprised of requirements and design limit definition, process validation, and analytic method qualification.

Once these production baselines are established, manufacturers then pivot their operations and sponsor the required projects and initiatives to increase production to profitable levels for filling order demands. At this stage, inline monitoring becomes vital to achieve high production volume, maintain required product quality levels, and ensure process safety.

Holistic approach to scalability

Scalable bioprocesses hinge on several key elements. The first of these factors is a deep understanding of the process itself, which requires identifying the critical variables that influence performance, and understanding how to optimize them during each stage of product development.

Once this foundation is laid, biopharmaceutical manufacturers can focus on equipment scalability. As production increases, equipment of all types—from bioreactors to utility purification systems—must be considered to ensure smooth accommodation for larger batches and higher volumes, without compromising performance or creating bottlenecks.

And finally, reliable measurement can make or break a scale-up effort. Consistent and accurate data are essential for making informed decisions regarding operational efficiency, production throughput, and quality throughout the project.

Challenges and risks

The journey from lab to production poses several challenges. To begin with, biopharmaceutical manufacturing operates under stringent regulatory compliance, demanding rigorous quality assurance and product safety protocols. With so many variables, measurement discrepancies often arise during scale up, potentially undermining quality assurance and decreasing yield as a result of time-consuming manual sampling and testing.

Adding to the complexity, different stages of product development often occur at separate locations, potentially using equipment from multiple manufacturers that are not set up to share data natively, further amplifying risk. Even similar instruments from different suppliers can exhibit measurement or performance inconsistencies due to variations in design, materials, or compensation algorithms.

Furthermore, transferring calibration protocols, methods, and models across separate facilities and stages of scale up can introduce issues, requiring substantial rework and expertise if not mindfully designed for scalability from the outset. When these threats materialize, they necessitate costly and time-consuming equipment qualification procedures at each stage of scale up for mitigation.

Success at scale

To reduce the risk of encountering these undesirable conditions, biopharmaceutical manufacturers can implement strategies for promoting efficient and consistent processes. Seamless technology transfer between process development in the lab and production at scale is critical to minimize batch variability and enable efficient, continuous, and methodical workflows. When sufficiently planned, scale-up progresses more quickly and robustly, and quality is increased as a result at every stage, contributing to long-term manufacturing viability.

To achieve this success at scale, standardizing on process equipment and instrumentation with native support for scaling is essential. This can drastically reduce the risk of incompatible measurement or data sharing technology, while significantly spurring workflows for calibration, configuration, and validation—primarily because staff must learn and retain fewer technical procedures.

Endress+Hauser's scalable bioprocessing portfolio provides manufacturers with substantial advantages by applying the same measurement technologies in both lab sampling and inline production instruments. Particularly, manufacturers are achieving success by combining real-time Raman spectroscopy and Memosens digital sensor technology for monitoring in their facilities, each of which minimize configuration complexity, reduce the risk of measurement inconsistencies, and improve overall process efficiency.

Inline sensing advantages

Inline analysis reduces the risk of process issues and increases production capacity by continuously measuring product characteristics, and by reporting scaled process values to a host control system in real time. This eliminates the need for personnel to take manual samples, which in addition to being inefficient, presents the risk of detecting issues retroactive to production.

Instrumentation for inline analysis typically consists of a sensor or probe directly inserted in the process, which sends information to a transmitter or analyzer for processing. The instrument then makes process values available for a host control system for near-real-time monitoring, operational decision-making, and process optimization. For example, manufacturers can gain comprehensive insights into almost any biopharmaceutical process by combining inline Raman spectroscopy with liquid analysis technologies, such as potentiometric, conductive, fluorescence quenching, UV, and visible light measurement.

Endress+Hauser instrumentation shares common technology and materials of construction, simplifying protocol transition from research and development to manufacturing. By adopting scalable Raman technology and digital sensors, biopharmaceutical manufacturers can minimize equipment complexity and the risk of measurement inconsistency. Endress+Hauser bioprocessing offerings—including spectrometers, sensors, optics, and calibration tools—cover a wide range of upstream and downstream applications for measuring composition, pH, dissolved oxygen, conductivity, concentration, and other characteristics.

Endress+Hauser Raman portfolio for bioprocessing

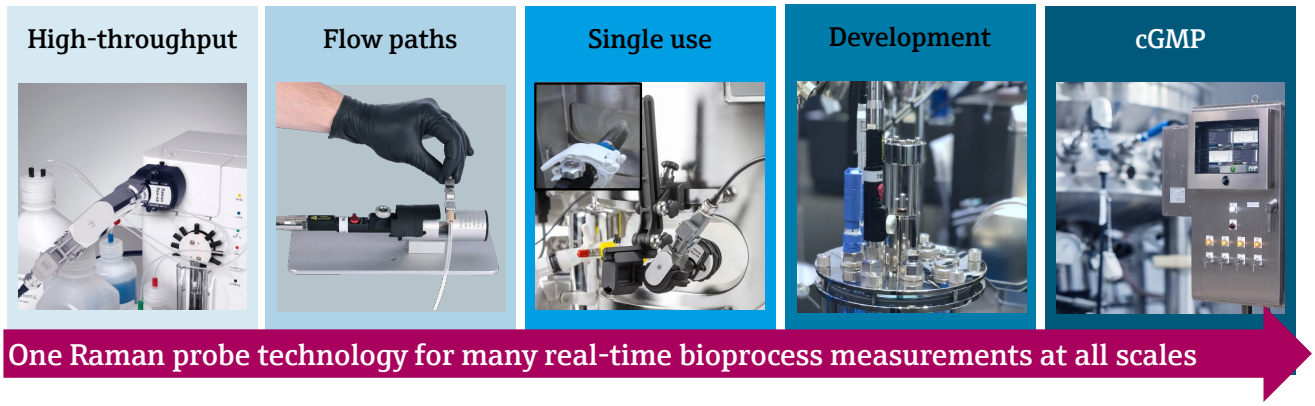

Figure 1: Optimized for both fine-tuned measurement in a lab environment and real-time results in high-volume production, Endress+Hauser Raman systems help biopharmaceutical manufacturers accelerate the transition from lab to process.

The right instrumentation products enable biomanufacturers to use many of the same devices in the lab and in the process to ensure a smooth transition during scale up. For example, Endress+Hauser's Raman systems—measuring chemical composition and concentration via optical methods—provide continuous monitoring of critical process parameters, such as glucose concentration and viable cell density, along with real-time insights for process optimization. The same Raman instruments used for small-scale experiments can be seamlessly integrated into larger-scale bioreactors, providing consistent and reliable data throughout the entire production process (Figure 1).

Similarly, Memosens digital sensors provide unparalleled measurement accuracy and minimal maintenance requirements with their reliable non-contact signal transmission technology. These plug-and-play, pre-calibrated sensors help minimize downtime and ensure consistent performance from the lab to production. Digital data transmission eliminates signal interference and enables predictive maintenance, further enhancing process reliability (Figure 2).

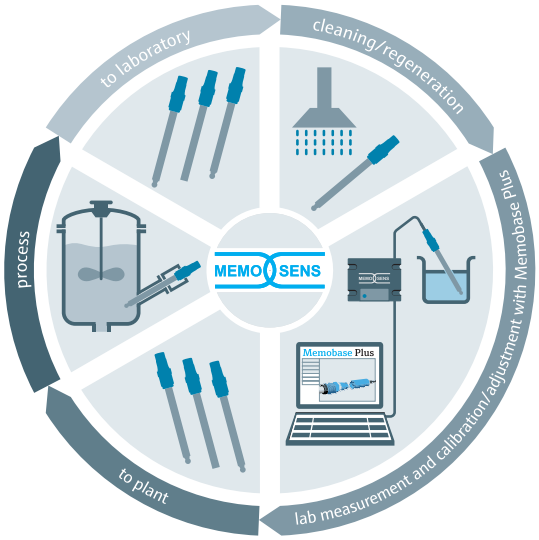

Figure 2: The cycle of Memosens sensor operation, cleaning, and calibration.

Benefits

Endress+Hauser provides:

- **Single-source solution:** An extensive portfolio of industry-conforming products and services lengthen lifecycles.
- **Simplified equipment:** The same devices can be utilized in the lab, pilot plant, and production line, streamlining qualification procedures and minimizing the need for personnel retraining.
- **Faster time-to-market:** Smoothly transition from small-scale experiments to full-scale production.
- **Reduced risk:** Minimize quality risks and simplify compliance efforts.
- **Decreased costs:** Achieve cost savings with less waste and maximized yield.

Agility wins the day

As the biopharmaceutical industry shifts towards new modalities, single-use technologies, and increasing reliance on continuous manufacturing, the importance of scalability is growing quickly and is evidenced widely. Manufacturers must be nimble to continue meeting the demands of this dynamic sector.

By leveraging instrumentation technologies designed with scalability front and center, manufacturers are progressing drugs through the product development lifecycle quickly and safely, delivering life-changing therapies to patients faster and more efficiently.

Endress+Hauser is committed to providing innovative solutions that empower biopharmaceutical companies to navigate this evolving landscape and achieve sustainable success.

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