LIFE SCIENCE CONNECT

Using Improved Communication to Overcome Data Management Challenges from R&D to Commercial Manufacturing

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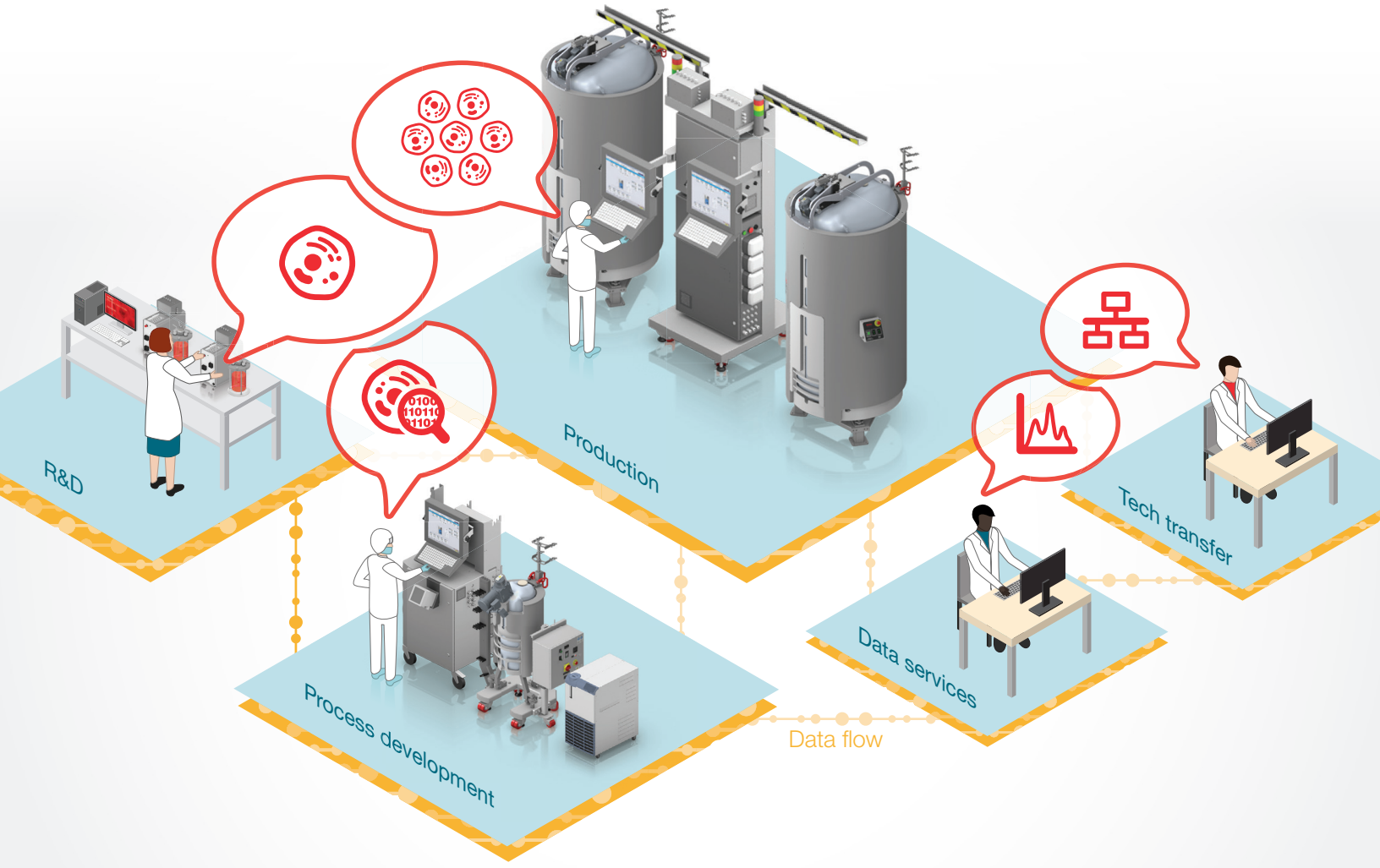
The process of bringing a new drug to market requires a multidisciplinary approach. It involves a wide range of expertise in science, engineering, manufacturing, analytics, quality, and supply chain logistics across the entire product life cycle. All stakeholders work together to ensure that a potential new drug is effective and can be produced in an efficient manner, delivering a high-quality and consistent product that meets clinical quality and commercial demands.

Decisions made early in development, and even in discovery, can send the molecules down very different paths, which will cause challenges in multiple ways. Planning early for manufacturability reduces surprises, such as challenges with reproducibility and scale-up, as the molecule goes through the chemistry, manufacturing, and control (CMC) journey and, upon approval, to the patient. Drug development is rewarding, but the number of approvals each year is minimal compared to how many molecules are in development pipelines.

Many critical decisions are made in process development that can minimize obstacles as a drug is transferred and produced in manufacturing. Scaling challenges, timelines, and regulation pitfalls can be diminished when these teams are aligned with each other's capabilities. Resources, such as capital equipment, can also be conserved. There will always be challenges, but through communication, data, new technologies, and problem-solving, next-generation medications can be delivered safely and in an efficient manner.



The value of process data and communication

Our drug development and manufacturing colleagues are familiar with the fallout when things happen unexpectedly, and while not all of it is within their control, it is nonetheless frustrating. Those responsible for designing and executing effective experiments and then analyzing them know they are an important piece of the journey.

Without the ability to produce material for testing in the quantity necessary to meet patient needs, though, they cannot produce a life-saving (or life-improving) treatment.

Pharmacological and biological development is an iterative process and, often the scientists do not realize there is a challenge until an issue occurs later in the process.

Therefore, even in the most thought-out processes, unforeseen challenges occur, with the root cause generally being a lack of communication between groups. Below is an example where communication between groups and system-wide considerations would have prevented timeline delays and process rework.

Scenario

The upstream bioreactor group increased monoclonal antibody (mAb) titer by 300 percent. However, the downstream purification group reported the following challenges in purification:

- Extended processing time
- Elevated host cell protein levels
- Issues in filtering material due to the higher than expected cell density
- Ultrafiltration issues due to antifoam

Result

The purification team spent significant resources to solve the challenges with the new high-concentration process, and the required changes needed were extensive and costly.

Upstream modified the process and accepted a lower concentration of mAb in upstream in order to increase the overall yield later in downstream.

How could this have been prevented?

The upstream and downstream teams should have discussed the development together to understand how the increased titer might impact purification. With advance notice of the process and also a thorough joint data review, including online digital profiles, both teams could have mitigated the impact.

Knowledge and data acquisition begin in the discovery phase and end once the product life cycle is completed. Data gathering, and how that data is translated across the workflow, plays a critical role, as a tremendous amount of information (quantitative and qualitative) is collected during drug development, and there are many factors to explore and consider as scale changes. It is important to minimize and control issues during those changes while facilitating communication as much as possible.

Using the CMC pathway as a guide is a useful tool in seeing how multifaceted the process is for bringing a drug to market and how connected the teams are that deliver each portion of the journey. Process characterization is a great example of when scales, timing, and data from multiple teams are coordinated to further de-risk a process for Phase 3 and commercial manufacturing. While risk assessments should be conducted throughout development, they are critical—as well as a regulatory requirement—and a prerequisite to process characterization.

Technology transfer is another challenging step in the development and commercialization process. Close collaboration and common documentation between R&D, manufacturing science, and operations during tech transfer will greatly increase the likelihood of success.

Refer to the example on the next page where technology transfer took place, but issues occurred when the bioreactor profiles were different.

Scenario
R&D transferred a mAb process to a contract manufacturing organization (CMO) using a CO_2 overlay. However, the CMO does not typically use a CO_2 overlay, nor do they have the capability to do so.

Result
Manufacturing executed the batch using the information sent by the tech transfer team.

There were no issues with equipment during batch execution, but the growth profiles were slightly different, leading to questions about whether this was due to typical variability and/or differences in scale.

Upon further investigation, it was identified that the gassing profiles were slightly skewed.

How could this have been prevented?
Several factors could have helped prevent this issue:

- Data and profiles should have been shared between R&D and manufacturing (having a common reporting platform would have expedited this).
- Walk though of the process with R&D and manufacturing
- Risk assessment
- Implementation of platform standard operating procedures

Data management for improved communication across the product life cycle

Software applications, such as data historians, capture vital data and store it in disparate locations. Without transparency across processes, decisions are made based on only a portion of a process rather than a holistic analysis of it. This has led to increased interest and a tightened embrace by the pharmaceutical industry around improving communication between R&D, manufacturing science, and operations.

In addition, innovation in today's biologics combined with a complex supply chain has intensified regulatory oversight to ensure continuous drug delivery that is safe and effective, even as the pharmaceutical landscape grows and changes—all while doing so at the fastest speed possible. Having a unified data management strategy and platform that can collect and connect data as a biopharmaceutical manufacturing process transfers from lab scale to large-scale production would streamline communication across the entire process development workflow, enabling responsive decision-making and preventative action that would save valuable time (as demonstrated by the above examples). This focus on communication requires a fundamental shift toward real-time data feedback that supports data integrity and allows for the use of analytics and risk analysis.

These key elements provide an opportunity to demonstrate the effectiveness of utilizing a common automation platform and data historian from the beginning of the product life cycle to the end. Providing a digital fingerprint as the development of a drug's production process is thought out helps align goals between process development and manufacturing.

So, how can you implement data-driven decisions in your lab that help you be effective at any scale without creating new challenges during the life cycle of the product? Begin by partnering with companies that base their solution on a robust, proven, and widely trusted platform that can be used from the beginning of the product life cycle in R&D through to manufacturing. Compliance requirements, such as 21 CFR Part 11, and standards, such as ISA-88 should be considered during R&D and Process Development. This will help streamline the scale-up and tech transfer processes. You can also utilize automation platforms that exchange data between scales and campaigns using a digital fingerprint that eliminates the risks associated with manual data transfer.

The data historian system should provide easy access to data and flexibility to adapt across the life cycle of the product. It should also allow for open architecture that helps enable the integration of third-party products, so that additional equipment or monitoring solutions can be added as needed.

The solution you choose—and the partner that offers it—must provide innovative and state-of-the-art technology, in order to support your growing needs throughout development and manufacturing. Your partner must also demonstrate proven expertise to provide you with the tools necessary to prevent the challenges that will inevitably surface along the way. And with the global footprint of the industry growing bigger every day, it is important that, no matter where you are, they have the resources to support you during discovery, process development, and commercial manufacturing.

A common automation platform from R&D to commercial manufacturing facilitates ease of communication between different teams and allows for an informed decision-making process. The benefits help mitigate errors in manual data transfer, minimize deviations and losses, and uphold communication, which ultimately provides a consistent high-quality product and increases the likelihood of success and a faster time to market.

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