Accelerating Biologics Manufacturing:
Strategies for Efficient Production Timelines

Optimised development and manufacturing processes that accelerate biologic production timelines while keeping costs down are critical to meeting the market demand. Streamlining drug product (DP) manufacture helps shorten timelines for biologic production, but it requires expertise and experience.

As a result, an estimated 26% of biotech companies outsource activities to contract development and manufacturing organisations (CDMOs),[1] forming a trusted partnership model for the production of biologics.[2] Working with a biologics-focused CDMO partner gives companies access to specialist facilities and expertise, with the capacity to streamline and accelerate production timelines.

In this article, Jinhyeok Jeong and John Thomas, Senior Directors of DP Inspection & Packaging and DP MSAT, respectively, at Samsung Biologics, explore the major areas of DP manufacturing that can accelerate timelines along with the necessary qualities that should be sought after in a specialist service-providing partner.

Overcoming Challenges to Market

Developing a drug product is complex and comes with scientific, technical, and regulatory challenges potentially hindering progress to market. Companies are increasingly outsourcing activities to CDMOs to overcome development and manufacturing barriers. These barriers include scaling up biologic production while maintaining quality and the need for specialised equipment and expertise in drug product fill/finish to ensure clinical studies are supplied with product on time, the PPQ batches effectively challenge critical process parameters, leading to commercialisation and continuous monitoring of commercial batches. Specialised CDMOs offer the proficiency and knowledge to overcome these obstacles, helping to streamline production processes. The capability of CDMOs to streamline workflows reduces production costs while increasing efficiency and capacity to help organisations gain a competitive market advantage.

The CDMO sector's capabilities to handle increased demand in the future are reflected in the projected CDMO outsourcing market development, which predicts a compound annual growth rate of 9.2% and an increase of $287 billion between 2023 and 2030.[3]

A Strategy for Accelerated Timelines

In the highly competitive biopharmaceutical industry, bringing a product to market at speed positions an organisation for commercial success while potentially improving patient outcomes. To reach milestones quickly and demonstrate to investors the potential for return on investment, drug developers in DP manufacturing require a key set of attributes. The main aspects of streamlining manufacturing speed include:

1. Effective Communication and Alignment of Goals

Engaging with a CDMO early in the development process ensures that goals are clearly defined, providing full awareness of the needs of the project and the desired product outcomes. Establishing a timeline that outlines the required capabilities and embeds strict milestones facilitates streamlined production and upholds project momentum.

Communication between the CDMO and the client should be built and baked into the collaboration from the beginning. Working together as a single unit allows production goal alignment and incorporates originator client and CDMO expertise into technical and strategic planning workflows, positioning the project for success.

2. Minimising Production Risk

When outsourcing biologic manufacturing, the early conversations help identify time constraints and process limitations that could lead to delays further down the development pipeline. Earlier gap assessment of components and processes enhances available processes and systems that are then gauged against production goals to identify any areas that require additional attention to detail.

Having a proactive approach and addressing these potential issues at an early stage allows for a mitigation plan to be put in place. Implementing preemptive strategies can prevent manufacturing challenges and outline actions that can be added to the manufacturing process to prevent roadblocks. With this plan in place, the risks of delays to drug production are significantly reduced.

3. Building a Solid Manufacturing Process

DP manufacture is complex, made up of numerous procedures and processes that need to run smoothly for accelerated production timelines. Ensuring that all essential factors have been optimised before manufacture can prevent potential delays. These considerations include:

- **A robust supply chain:** Reliable access to materials (such as raw materials, single-use items, primary packages, etc.) and the equipment required for production can minimise delays caused by long lead times.
- **Prepared documents:** All documentation should be ready early in collaboration with the client. Standardisation of documentation ensures that all GMP tech transfer activities are completed accurately and quickly to meet demanding timelines. At the same time recognising the drug being transferred to the CDMO may need specialised processes should be identified early in the process.
- **Skilled workforce:** A comprehensive training plan ensures that all staff from manufacturing, quality control/assurance to validation have been fully trained for manufacturing,

testing, and documentation filing required. Prior to manufacturing, additional training is often provided by DP MSAT to provide operator's with a review of the drug (the why?) and specific action required per pre-approved protocols.
- **Readiness of equipment:** Pre-testing of all required equipment guarantees it will run as intended with the necessary materials for successful batch production.

The combination of measures to increase manufacturing speed helps to minimise potential bottlenecks, reduce delays and ensure efficient production processes.

4. Efficient and Timely Batch Release

To continue to meet stringent timeframes, once a commercial batch has been manufactured, it should be released within the defined time frame of 30 days. Quality control (QC) testing is completed to prove that a product meets the defined good manufacturing practice (GMP) guidelines before release, fulfills the client's needs and is safe for patients. As part of this process, the quality and manufacturing teams review the master batch release (MBR) documentation, thus ensuring that a batch can be released quickly. Information spanning all processes and procedures, drug formulation and equipment details, including the electronic audit trail of all software systems used, should be included in the MBR documentation. Having all the required elements in place upon final DP completion means no time is wasted and documentation can be filed and a batch released immediately. Each commercial batch is reviewed by DP MSAT and the Continuous Process Verification (CPV) begins for each commercial batch, the Critical Quality Attributes are monitored to ensure the commercial production process remains in control.

5. Meeting Client Needs for Capacity and Flexibility

Having the capacity and capability to manufacture both the drug substance (DS) and DP at a single site can significantly accelerate drug production timelines. When this occurs, the DS can be conditionally released for continued manufacture and funnelled into subsequent processes for DP fill/finish, reducing the overall batch release timeline. As QC testing on the DS must be performed within 45 days of release, a small proportion of the DS batch could be held back for this testing while the remainder is used to complete the fill/finish process. Standard processing times in releasing the DS will work in concert with the progression to DP manufacture and release. The flexibility instilled through conditional release allows DS batch release and DP manufacture to run in parallel, helping to balance the demand for critical treatments with patient safety. The final batch release of both the DS and DP are often run in parallel to demonstrate the competitive advantage for end-to-end batch manufacturing.

6. Regulatory Excellence and Meeting Changing Regulations

Throughout manufacture, all processes and procedures must abide by regulations. To ensure regulations are met, CDMOs are required to integrate a strict quality management system (QMS) so that every raw material, component of drug production, and manufacturing process is well characterised and defined to meet all GMP regulations. Integration of QMS acts as a framework for quality, safety and efficacy, aiming to instil consistent and regulatory-compliant standards.

Part of the QMS is producing a quality policy, which is a statement that defines the organisation's commitment to quality. Guiding decision-making and actions across the business, the quality policy outlines the overall quality objectives, guiding principles and values. A built-in and well established culture of compliance within a company demonstrates employees actions that embrace and strive for high-quality and regulatory-compliant products at all times.

As part of the QMS, regular audits are performed to highlight any areas for improvement, which are constantly under revision to ensure quality standards remain high. Having a QMS in place eases the process of proving regulatory compliance when bringing a product to market as quality is built into the manufacturing process, streamlining approval and timelines to market.

The success of bringing a DP to market and to patients rests on the ability of an organisation to navigate the ever-changing regulatory landscape. As demonstrated by the recent updates to Annex 1 of the GMP, which saw changes to the way sterile products are handled, regulatory guidelines are constantly revised to enforce the highest safety standards. An organisation must maintain regulatory awareness so that any changes to regulations are flagged early, allowing the time to incorporate any modifications into practice. Failure to respond could result in delays through non-compliance or lead to batch rejection. Outsourcing to a CDMO can provide regulatory expertise thanks to its experience in progressing DPs throughout the regulatory lifecycle.

Having regulatory expertise is a prerequisite for a CDMO to deliver client products on time. The regulatory landscape for drug development and manufacturing becomes increasingly complex as regulatory agencies continuously improve stringent requirements that evolve with the advancement of the sector. In-depth knowledge and compliance with guidelines are essential for a CDMO to ensure that necessary approvals and documentation are in place, minimising disruptions during the approval process. On-time delivery is of significant importance to many stakeholders:

- **Clients:** Ensuring market competitiveness and revenue potential by reaching the market on schedule.
- **Patients and their families:** Quick access to life-changing therapies that can improve outcomes and give family and friends reassurance of a patient's prompt treatment.
- **Healthcare professionals:** Facilitating seamless healthcare planning and continuity of care.

The implementation of regulatory expertise and timely product delivery enhances patient well-being and meets healthcare demands effectively.

7. Experience and Expertise in Reaching Commercialisation

Technology transfer is an essential process in preparing a production line for commercialisation, facilitating the transformation of small-scale production into scaled-up operations. As part of this strategy, an assessment of process needs evaluates the requirements for the successful transfer of technology. Early planning helps to identify and mitigate any potential roadblocks that could occur while introducing

changes. The insight provided by a CDMO with expertise in technology transfer can be essential in ensuring the transfer process runs smoothly.

Key assets a CDMO must have to bring DP success to clients include:

- Dedicated Single Use Systems designed to reduce timelines, define and harmonise cleaning validation evaluations, and smoother CTD Regulatory processes
- Fill-volume accuracy achieved through cycle development, engineering batches leading up to the GMP production process
- Process robustness based on MSAT experience leads to standardisation across product platforms.

Having a clear understanding of both the product and the process beforehand is essential as it can preempt any challenges that are identified when a project is in the early stages through the product lifecycle. The impact of successful technology transfer on biologics production cannot be overvalued, as a small change to manufacturing could result in unexpected impact on the product.

Comprehensive standard operating procedures are detailed guidelines that outline specific processes and protocols and can be invaluable for the efficient transfer of technology by providing a structured framework. This helps to ensure consistency, facilitate knowledge transfer and assure compliance with regulations through effective quality control. Comprehensive documentation also aids regulatory compliance and assures process traceability.

A CDMO should have the flexibility to scale up and scale down production based on the diverse needs of the client and the market. Building this flexibility into production lines is key for adapting manufacturing systems without hindering progress which leads to on-time, right-the-first-time production capability, and mindset.

The Future of Biologics Manufacturing Through Collaboration

Forming a supportive and free-flowing communicative partnership with a CDMO can propel the manufacture of biologics. Access to expert knowledge and specialised equipment can be gained through collaboration with a CDMO, which helps streamline production processes. In addition, DP manufacture disruption risks are mitigated by forming a partnership early and proactively incorporating preventative measures.

Partnering with a CDMO can help drive forward biologics manufacture thanks to continuous innovation to accelerate timelines to market and gain a competitive advantage. Technological advancements aid accelerated production outcomes. Automated manufacturing and AI systems are streamlining processes and data analysis, providing real-time insights into procedures to continuously improve current systems and manufacture. Where manufacturing traditionally relied heavily on manual input, biologic production is being streamlined through the incorporation of technology into production systems. As technological advances continue, their impact on the pharmaceutical industry, with a particular focus on biologic manufacture, will keep accelerating.

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