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Delivering Market Success for Pharma Partners from Concept to Patient

Shari Krusniak
Director, Services marketing strategy

Patrick McLoughlin
Sr. Director, Strategic Programs, CM and Devices

Having registered several years of consistently strong growth, it is widely accepted that the momentum behind both biologics and biosimilars shows no signs of slowing.

One forecast suggests that biologics – already a US$425.5bn sector today – is set to grow at a Compound Annual Growth Rate (CAGR) of 7.6% to 2030, reaching a value of US$710.53bn[1]. The biosimilars market, while considerably smaller, is set to accelerate at a much faster rate, with a stellar projected CAGR of 17.8% pushing it to be worth a predicted US$66.9bn by 2028[2].

With this growth comes changing market dynamics. Since 2015, when the U.S. Food and Drug Administration (FDA) approved the first biosimilar in the U.S. – Sandoz's Zarxio – there have been 44 biosimilar approvals[3], with the latest, Wezlana, indicated for multiple inflammatory diseases, coming in October 2023. As competition increases, so pharmaceutical companies will face an increasing challenge to protect their intellectual property and their market share through product differentiation.

Beyond projected growth, there is another shared truth in relation to biologics and biosimilars: they are both complex and expensive to produce. The estimated development cost of a biosimilar can be up to US$250m[4], which places a significant burden on pharma partners and the wider supply chain to get every aspect of the manufacturing eco-system right first time.

And, as the treatment of cancers and chronic conditions continues to be the fulcrum for many biologics and biosimilars, there is another consideration too – the continued transition from in-patient to at-home care. This trend is being embraced by the widest range of stakeholders, from the World Health Organization (WHO) down. Indeed, as part of its strategy, the WHO speaks of its ambition to reorient the delivery of care 'towards health services that put people and communities at their center' with home care playing a key part in achieving the strategic goal of empowering and engaging patients[5]. Such goals can only be realized, however, through the development of drug delivery devices that are innovative, intuitive, patient friendly and patient safe.

In bringing these devices to market, certain areas of concern must be addressed that are particular to both biologic and biosimilar therapies. One is the use of innovative packaging materials to avoid adverse chemical interactions and maintain the integrity of these sensitive, valuable drugs.

Another is the requirement to accommodate higher volumes, with biologics having created an increased need for innovative systems that can deliver larger dosages over longer periods while remaining intuitive and easy to use.

Taken together, all of the challenges and considerations referenced above mean pharmaceutical and biopharmaceutical companies must tread a delicate but purposeful path in order to capitalize on the projected growth in biologics and biosimilars. As such, there is an absolute requirement for close collaboration with drug delivery system partners to ensure the required formulation, containment, delivery and contract manufacturing expertise is embedded within a 'right first time' development process to optimize decision-making, reduce timelines and minimize costs.

Following successful commercialization, now more than ever, contract manufacturing partners must also deliver continuous innovation and flexibility to accommodate the delivery of a wide range of drugs throughout each product's lifecycle. These partners, either by utilizing existing technology platforms or developing a proprietary drug delivery system, need to support pharmaceutical companies with products and processes that facilitate the development of market-ready therapies that are safe, effective and easy to administer.

[1] https://www.marketresearchfuture.com/reports/biologics-market-1339
[2] https://www.marketsandmarkets.com/Market-Reports/biosimilars-40.html?gclid=Cj0KCQjwwvilBhCFARIsADvYi7LiwY0Nxiivm-3MRll-0d1b49LcW6eY8SmH-T_nbMJFE2wCmwFkQzEaArA5EALw_wcB
[3] https://www.fda.gov/drugs/biosimilars/biosimilar-product-information
[4] https://www.sciencedirect.com/science/article/pii/S0049017221002171
[5] https://apps.who.int/iris/handle/10665/155002

Developing complex, innovative delivery systems

Technology is today entirely ubiquitous in consumers' lives as the driving force of an on-demand culture, with high expectations around service and delivery governing everything from food to medical care. The requirements in drug delivery are no different as we see a rise in self-administration systems that can incorporate electronics to deliver doses at specific intervals and connectivity that allows the patient to monitor and track adherence. Far removed from the days of travelling to a doctor's office for an injection via vial and syringe, today's drug delivery platforms are complex technologies that require contract manufacturers to develop innovative systems used by the patients themselves.

These shifts have created an interesting challenge: While the requirements for self-administration technologies grow more complex, at the same time they must also easily integrate into a patient's life. Irrespective of the platform, medtech innovators and their contract manufacturing (CM) partners must ensure some requisite features are present to bring true value to patients:

Discreet

Many patients are conscious about their self-administration regime and do not want to make it obvious, particularly when out in public spaces. Wearable systems, for example, can greatly reduce that concern.

Frictionless

While patients generally welcome the ability to self-manage and self-administer, adherence can be compromised if, for example, the delivery of a dose requires a series of complex preparation steps. Devices must therefore be developed to simplify delivery, with automatic mechanisms helpful in limiting any concerns associated with needles and the act of injecting.

User-friendly

Regardless of how innovative a delivery system is, its design should facilitate safe and intuitive operation by the target user population. Arthritis patients, for example, may have limited dexterity, which may inhibit their ability to use a delivery system. Likewise, certain patients might benefit from audible or visual indicators that signify injection success. Through rounds of patient testing, manufacturers can ensure the technology is optimized for particular needs.

When drug delivery systems are truly intuitive, safe and efficient, they reduce the impact on patients' daily lives and improve the opportunity for greater adherence, which, in turn, delivers an exceptional user experience that benefits the whole eco-system, from pharmaceutical partner to payer and healthcare professional as well as, of course, the patient.

Building in quality from the start

Patient safety is the first consideration in the pharmaceutical industry, with the FDA requiring drug makers to develop and institute quality processes in manufacturing. As a result, expectations for quality are exceptionally high, and contract manufacturers share the responsibility of making sure the drug delivery platforms they produce meet the highest possible quality standards.

In support of this aim, drug delivery technology partners continue to implement and refine Quality by Design (QbD) processes. QbD helps ensure a high-quality, proven product delivers high patient safety and low risk for the pharmaceutical manufacturer. Although QbD principles require an up-front investment, that investment delivers an improved, data-driven output that provides manufacturers with superior product. QbD initiatives also lead to a process that allows stakeholders to better understand minimize risk.

The information generated to determine the Critical Quality Attributes (CQAs) and Critical Process Parameters will help to:

- Develop a meaningful control strategy.
- Ensure product quality throughout the product lifecycle.
- Increase product and process knowledge to support decisions.
- Increase transparency and understanding for regulators and industry.
- Enhance information needed for identifying and evaluating potential changes.
- Monitor and track critical data for continuous improvement.

Only by implementing a QbD methodology in contract manufacturing processes can drug delivery partners better serve their pharmaceutical partners, reducing potential safety risks and facilitating a faster path to market.

Improving scale-up processes

In order to meet the complex needs of biologic therapies, contract manufacturing organizations are refining their scale-up processes to meet the requirements of a diverse range of therapeutic portfolios. This innovative approach to scale-up delivers several benefits to pharma partners:

- **Understanding regulatory requirements:** For a combination product to successfully reach the market, it must achieve a number of regulatory approvals by each geographic region. Many new delivery platforms include electronics, which require meeting additional standards outside of the pharmaceutical industry. And, of course, regulations are consistently being updated or created for combination products, often after development is well under way. It is therefore important for drug delivery manufacturers to have a close and positive working relationship with regulators to keep ahead of any amendments.
- **Product Design and DFM:** Thorough human factors analysis will uncover challenges and identify improvements that may not be immediately obvious during the design verification stage. As discussed, patients with dexterity issues or vision impairment, for example, may have difficulty administering their treatment. It is also increasingly important that partners input as early as possible into the product life cycle on design for manufacturability (DFM) to ensure products are scalable and can be done so in the most efficient and cost-effective manner.
- **Supply-chain management and scale-up:** Companies are increasingly looking for partners who can provide an integrated supply chain strategy, demonstrating robustness, scalability and a strong approach to mitigating risk. Every pharma company will want to understand their delivery system partner's supply chain from top-to-bottom to ensure manufacturing can meet clinical builds through commercial sales projections at each stage of the lifecycle from growth through to maturity.
- **Assessing capacity and capabilities:** On site, a robust assessment of all assets, including verification of quality management systems, is necessary to ensure production demand can be met. Where necessary, improvements or investments can be identified and costs scrutinized. Upon product launch, further audits should be conducted to determine the readiness for lifecycle management changes.

By fine-tuning scale-up capabilities, drug delivery technology providers are in the best possible position to accommodate the wide-ranging needs of the client in the short term and create an enduring partnership for the long term.

Refining production and monitoring methods

It is incumbent on contract manufacturing providers to deliver the highest quality components and delivery systems that meet global regulatory, market and patient requirements. Furthermore, they should demonstrate a true point of market differentiation.

As a result, many contract manufacturers are moving away from inspection systems that only identify gross anomalies in the manufacturing process. These outdated methods offer little insight into the subtle changes that can affect product integrity.

There is a clear market focus on building in monitoring systems that collect meaningful data to guide output methodology and, ultimately, improve the quality of products. Essential to this initiative is the continuous monitoring of machines to measure manufacturing performance, which in turn can guide training, establish new infrastructures, improve project management and identify capital investment requirements.

It is no longer enough for these monitoring systems to just provide production output figures. In an increasingly transparent world, there is growing demand for manufacturer and pharma partner to share access to real-time data that allows assets to be viewed from anywhere in the world at any time. This framework, and the insights it generates, supports the creation of a truly connected supply chain that is geared towards continuous improvement.

Process monitoring systems then play a crucial role in safeguarding the reliability of equipment and, therefore, continuity of supply.

With access to rich asset data, manufacturers can adopt predictive and proactive maintenance, and implement an as-required replacement strategy. This also allows for identification and reduction of variation in the process caused through wear and tear over time.

Selecting and implementing a common system allows the supply chain to integrate the output into one common repository for data collection and viewing, offering insight into a greater variety of process variables at a significantly higher resolution. This supports the capture of information on planned versus unplanned interventions, which is an increasingly important metric to indicate the robustness and quality of the process. Further goals supported by these processes include:

- Identifying defects immediately and segregating automatically in real time.
- Reducing manufacturing waste.
- Reducing product variation.
- Identifying sources of variation.
- Standardizing the approach to process control across multiple plants.
- Improving up time for post injection molding assembly activities.
- Improving outgoing quality and on-time delivery.
- Increasing customer satisfaction.

Driving innovation and ROI

Pharmaceutical companies rely on their partners to continuously improve and innovate to ensure their drug delivery platforms adopt new game-changing technologies, whether that be an entirely new delivery platform or adapting existing platforms to address new developments.

Wearable drug delivery technology is a good example of how drug delivery system providers continue to stay ahead of the curve. When originally introduced, this platform combined the drug with the delivery system to automatically deliver the therapy, dramatically reducing mistakes by ensuring patients received an accurate dosage at the time they needed it.

To that end, contract manufacturing rosters now include scientists, software developers and engineers knowledgeable in design for six sigma and DFM to make sure the platforms are in sync with the latest technological advances. Many drug delivery platforms will be connected to the Internet of Things (IoT), and companies and their packaging partners are leading the way to bring meaningful features to the patients they serve.

It is critical that these innovative efforts result in return on investment (ROI) for pharmaceutical partners, as they must demonstrate to patients, payers and healthcare professionals that their drug is not only effective, but also provides demonstrable value. Increasingly drug companies have less time and resource to take contract manufacturing in-house and are therefore relying on delivery technology partners to help them in their strive for market differentiation.

Partners must have experience and expertise not just in manufacturing but also in devices, design for six sigma and potential manufacturing solutions to optimize the device and its packaging. The need for partners to treat a product as if it were their own has never been greater, and the passion for quality and the patient experience must be paramount as much for the contractor as it is for the pharma company - they must constantly consider and identify opportunities and gaps the customer may not have seen.

Partner relationships

Strong partnerships rely on open and clear lines of communication, including giving customers access to real-time data (production, quality, inventory levels). This is all the more critical where a multi-supplier situation exists and customers need to pivot from one supplier to another when challenges arise. Clearly defined governance structures must be in place to allow for two-way flow of information, and partners must also ensure that confidentiality is paramount in the minds of not just the partner, but the whole supply chain. This places the onus on partners to establish a wide base of trusted and experienced suppliers.

Partners must also be able to provide, and have built into their plans and models, a flexible approach that allows for sudden increases or contractions in the market and demand. Flexibility in labour, equipment or facility plans should be modelled and agreed early on in the lifecycle to ensure any required adaptations can be made quickly and with minimal disruption.

As well as supporting greater flexibility, close partner working can also unlock improved agility, which can be seen in the adoption of vendor-managed inventory (VMI). This approach acknowledges that the CM is often better placed to identify early warning signals around stock levels, risks to supply and opportunities to increase capacity than the customer and, as such, needs to be an integrated part of the overall supply chain as opposed to just a supplier of devices or parts.

West Pharmaceutical Services, Inc.
530 Herman O. West Drive, Exton, PA 19341 USA
610.594.2900 • www.westpharma.com

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