Life Science Leader

Magazine Article | December 1, 2023

# Manufacturing And Supply Chain: Making Space Between A Rock And A Hard Place

Source: Life Science Leader

By Ben Comer, Chief Editor, Life Science Leader




With the enthusiasm surrounding innovative product types and therapeutic approaches — and the corresponding rush to bring these new products to market — company leaders should double down on internal manufacturing and CDMO oversight to prevent unanticipated delays. Supply chain shortages are likely to continue next year, but biopharma leaders suggest that collaboration with government regulators can help grease the skids; in other scenarios, some of which are described below, operations executives have been able to turn other company's shortages into their own opportunities.

A dedicated focus on the environmental impact of manufacturing and supply chain processes is more evident in the executive responses this year compared with last year, a welcome indicator for a warming planet. At the same time, costs have gone up for raw materials and other upstream supply chain materials, and cost-effective sourcing — while maintaining environmental standards — will require fresh thinking and flexibility. Selecting the right partners and service providers across manufacturing and supply chain operations and maintaining strong communication channels will benefit manufacturers next year, as well as patients who rely on a consistent supply of medicine.

***Do you anticipate an increase or a decrease in the number of drug shortages next year, and what are biopharma companies doing to prevent shortages?***



**Omair Ahmed, COO, Nexus Pharmaceuticals:** We are anticipating an increase in drug shortages in the short term. The supply of critical drugs will continue to be strained as demand for these medications increases and manufacturing quality issues persist. The biopharma industry has been attempting to mitigate this by bringing more capacity online through brand new facilities and expansions. The issue, however, is where that capacity is being allocated and whether critical commodity products will be prioritized. Nexus Pharmaceuticals, a U.S.- based pharmaceutical manufacturer, has specifically brought online capacity for the critically needed drugs in question. By creating a state-of-the-art facility with an emphasis on quality, Nexus hopes to make serious progress in the battle against drug shortages. Moreover, the biopharma industry is attempting to work directly with healthcare facilities to provide a long-term supply of products outside of the normal distribution channels to help stabilize market fluctuations, in turn, leading to a reduction in spot shortages on the market.

**Ankit Patel, Head of Operations, Tris Pharma:** I am optimistic that manufacturers and government agencies will continue to work together in the coming year to find solutions that decrease the number of drug shortages taking place. There is a lot we can learn from each other and experiences we can share to help mitigate the shortages taking place that are greatly impacting patients nationally — ultimately, we need to put the patients first. At Tris Pharma, in response to nationwide shortages of ADHD medications, we've managed to not only maintain but increase supply of methylphenidate and amphetamine ADHD medicines without any interruptions. There are three specific, proactive steps that have helped us avoid shortages: strict adherence and maintenance of DEA compliance, robust and



flexible in-house manufacturing capabilities, and deliberate communication across commercial, sales, and manufacturing teams. Through continued collaboration with our government partners, and responsive and proactive solutions by the collective pharmaceutical industry, we can navigate free of the obstacles posed by medication shortages and make possible a healthier future for the patients who count on us.

***What are the biggest manufacturing challenges the biopharma industry is likely to face in 2024, and what steps can biopharma companies take to overcome them?***



**Roger Bakale, Ph.D., SVP, Manufacturing and Supply Chain, Kura Oncology:** A confluence of factors resulting in supply chain consolidation in western markets is producing high demand for existing and limited manufacturing capacity. The cost of upgrading existing facilities and equipment as well as expansion of capabilities for manufacturing both active ingredients and drug products are putting higher pressure on cost of goods considerations at a time when many regulatory authorities worldwide are advocating for more price concessions for patients. Supply chain risks are increasing due to geopolitical contagion, resulting in more complex logistics considerations, additional regional import and export restrictions, and new tariffs and duties on goods and services. The added increase in the cost of raw materials, intermediates, excipients, and labor in addition to other fixed cost inflationary pressures further add to the manufacturing challenges faced by the biopharma industry. Potential shortages of key raw materials due to quality issues and environmental restrictions at manufacturers create additional bottlenecks in importing from Asia Pacific. Careful selection of the CDMO, rigorous technical inspections of facilities and staff, along with quality assurance audits can help mitigate these risks in the supply chain network. Once the supply chain network is established, maintaining the quality systems and integrity of all manufacturing elements and processes associated with the active ingredient through finished product manufacturing including packaging, labeling, and distribution, is essential in order to mitigate the risk of product failures and recalls.



**Andrew Wirths, SVP, Americas Supply, AstraZeneca:** The biopharma industry is increasingly recognizing the critical role we all must play in protecting our planet, which I think will be both a key challenge and a key opportunity in 2024. At AstraZeneca, we believe there is a clear connection between healthy people, healthy society, and a healthy planet, and everyone involved in the research, development, and delivery of healthcare must work together to build a sustainable future. Due to the nature of manufacturing and supply, it is no surprise that operations organizations are typically responsible for a vast majority of a company's total energy usage, along with Scope 1 and Scope 2 greenhouse gas (GHG) emissions. With approximately 5% of global GHG emissions emitted from the healthcare sector, it's important that we work diligently toward delivering net-zero healthcare. In the near term, biopharma companies must continue to identify ways to decarbonize their manufacturing sites — this can be done by introducing new energy-efficient equipment, optimizing existing equipment and processes for efficiency, and sourcing renewable energy. In 2023, we announced a first-of-its-kind collaboration with Vanguard Renewables in the U.S. to enable the delivery of renewable natural gas to all of our research and manufacturing sites by the end of 2026, using agricultural and food waste as the source of clean heat. This innovation is already being used at our manufacturing site in Newark, DE.

***How are novel product types, including increasingly personalized medicines, for example, changing the way biopharma organizations build manufacturing capacity or contract with suppliers?***



**Lars Dreesmann, Ph.D., President & Site Head, Boehringer Ingelheim Fremont:** While biologics have transformed the treatment of many life-limiting diseases, healthcare systems are continuing to face a financial challenge to meet the needs of patients. The utilization of high-quality, lower cost biosimilars can improve the sustainability of healthcare systems, providing the potential for more patients to benefit from biological medicines. As one of the largest producers of biologic medicines in the world, Boehringer Ingelheim hopes to increase the availability of safe, effective, high-quality therapeutic options to patients worldwide. The biosimilar manufacturing process is inherently complex and requires a high degree of technical innovation and regulatory expertise. Our more than 35 years of experience in biologic manufacturing uniquely positioned us to bring our first biosimilar, Cyltezo, to patients. Developing and manufacturing a biosimilar could be considered more challenging than producing a new biological entity because you have to achieve clinical equivalence with criteria established by the reference product. In essence, you have to thread a much, much smaller eye of a needle when creating a biosimilar. Cyltezo is manufactured at our only U.S. manufacturing site in Fremont, CA — a state-of-the-art, highly-automated facility where nearly 500 people were focused exclusively on preparing for its launch. The facility is composed of a diverse group of people coming from all over the world, collaborating across different functions.

**Cliff Carroll, Executive Director, Global Technical Operations for New Modalities, AstraZeneca:** While our R&D colleagues continue to push the boundaries of science and explore new ways to make a meaningful difference to patients' lives, in operations, we are sharpening our focus to deliver on our pipeline of modalities, such as cell therapies, antibody-drug conjugates, mRNA, and oligonucleotides. At AstraZeneca, our portfolio of synthetic molecules and traditional biologics is complemented by these new modalities, which represent over 25% of our coming pipeline with more growth anticipated. While these new medicines hold so much potential for improving patient outcomes, they also will challenge us to rapidly evolve our manufacturing processes and capabilities in ways that are, in some cases, drastically different from how medicines are manufactured today. Further, we must do so in a way that ensures supply for



clinical trials in the nearer term while being scaled up for commercialization in the longer term. In these new and complex areas, such as cell therapy manufacturing, we are taking a strategic, stepwise approach to how we scale up our operations. We will strike a careful balance between investing in and building up internal capabilities, while collaborating with external partners that have strong capabilities in manufacturing specific types of therapies or supplying to patients in specific geographies. Looking further ahead, our industry must explore ways to reduce indirect greenhouse gas emission sources in Scope 3 — to ensure we are truly reducing our carbon footprint across the entire value chain. Our supplier and partner engagement is vital here — we need everyone to pull in the same direction!



**Igor Bilinsky, Ph.D., COO, Iovance Biotherapeutics:** Personalized medicine, such as individualized cell therapies, are revolutionizing how biopharmaceutical organizations approach manufacturing. Pending FDA approval, we are actively preparing for a potential U.S. launch of lifileucel, the first one-time, individualized cell therapy for solid tumors. Initially in development for advanced melanoma, lifileucel is a differentiated tumor infiltrating lymphocyte (TIL) cell therapy that harnesses patient-specific cells to recognize and attack diverse cancer cells. By targeting a variety of neoantigens unique to each patient's tumor, our TIL therapy platform may be applicable for many solid tumor cancers. Academic research centers initially produced TIL therapy with site-specific processes that cannot serve sizable patient populations. Iovance was founded to broaden access to TIL therapy by developing multicenter trials and centralized, scalable manufacturing processes to enable regulatory approvals and commercialization. Iovance's proprietary technology includes manufacturing and logistical efficiencies aimed at optimizing treatment, decreasing production time, and streamlining distribution. Our internal Iovance Cell Therapy Center (iCTC) is one of the largest cell therapy manufacturing facilities and the first dedicated to manufacturing TIL therapies, allowing us to control time, quality, and cost of our therapies. Biopharma organizations with individualized therapies must have the flexibility to expand capacity to meet patient demand, and potentially collaborate with contract manufacturers to ensure a broad supply. Ultimately, collaboration, innovation, flexibility, and a relentless focus on patients must guide the personalized medicine approach today and into 2024.

***What existing or emerging technologies will most improve the biopharma manufacturing function in 2024?***



**Roger Bakale, Ph.D., SVP, Manufacturing and Supply Chain, Kura Oncology:** Application of more green technology and process intensification techniques, such as continuous process capabilities as well as new and expanded flow chemistry options for the manufacture of pharmaceutical ingredients and products, have increased overall efficiency and productivity, while reducing waste. Further optimization of cell-lines, media, and bioreactor designs is improving monoclonal antibody production output while concurrent optimization in immunoassays and immunohistochemistry are more broadly available. These advancements provide significant opportunities for advancing more complex and efficacious biomolecules for patients. Improvements in biocatalysis capabilities through increased application of directed evolution technology to produce more selective biocatalysts with increased throughput and efficiencies improve the reliability and scalability of manufacturing processes, while lowering the overall cost of production. Further advances and broader application of CRISPR technology for mRNA therapies and vaccines along with higher capacities and cell line sources are coming online for manufacturing biologics and gene therapies (oligonucleotides, CAR T-cell therapy, monoclonal antibodies, and antibody drug conjugates). The worldwide increase in High Potent Active Pharmaceutical Ingredients (HPAPI) and drug products manufacturing capacity and capability for new therapeutics with higher potency and pharmacologic activity requiring a higher level of control and safeguards in manufacturing are becoming more readily available. Small molecule precision medicine manufacturing requires an increased focus on rapid development of low-cost manufacturing processes that are efficient and robust to afford transferability across CDMOs as capacity requirements dictate in a fluid marketplace.