WuXi Biologics
Global Solution Provider

Responding to a Changing Drug Product Global Supply Chain

Rapid response by Leverkusen, Germany drug product fill facility helped ensure critical supply of vaccines during the pandemic.

Of the many lessons learned during the pandemic, one overriding realization was that utilization of the primary, single-location manufacturing site, although the simplest and potentially most cost-effective strategy, can have significant consequences to the availability of critical life-saving biologics and vaccines. This scenario not only applies to drug product but also to drug substance and the wide range of raw materials used throughout the manufacturing supply chain. The speed at which the pandemic spread also did not allow drug manufacturers to quickly bring secondary suppliers up to speed or to provide the secondary manufacturing sites to obtain the critical raw materials as those too required time for secondary suppliers and distribution networks to be established. It also does not take a global pandemic for the consequences of a primary / single-source manufacturing strategy to show its vulnerability.

Thus, the need for ongoing production from multiple drug substance (DS) and drug product (DP) manufacturing sites around the globe as a risk mitigation approach, to ensure that the supply of biologics and vaccines is provided in a reproducible, reliable, timely and cost-effective manner, is becoming a necessary operational strategy. Regional manufacturing can be efficient and cost-effective when factoring in tariffs, currency fluctuations, taxes, shipping and logistics costs and even more critically opportunity costs for supply delays. In addition, regional production may result in shorter delivery times and reduced logistical issues and can act as a means to simplify regulatory compliance issues from a Chemistry, Manufacturing and Controls (CMC) perspective. Coupling DS supply with DP manufacturing on a regional basis helps reduce risks even further for all the reasons previously described.

Benefits of Regional Manufacturing

Factor	Impact
Reduced Local Logistics/Shipping costs	++
Reduced Risk to Global Supply	+++
Fewer Regional Regulatory Compliance Issues	+
Ability to Attain Raw Materials	++
Reduced Regional Taxes/Tariffs	+
Reduced Regional Delivery Times	++
Reduced Regional Currency Exchange Rate Fluctuations	++
Reduced Market Opportunity Cost due to Supply Chain Issues	+++

The concern for drug manufacturers are the increased costs of vetting and establishing multiple manufacturing sites and contract manufacturing entities and meeting the differing regional regulatory agency guidelines and compliance standards. In addition, certain regions may have higher cost structures. However, WuXi Biologics, a leading Contract Research, Development and Manufacturing Organization (CRDMO) understands these concerns and from its inception has worked diligently to provide its manufacturing partners with a “Global Dual Sourcing” strategy for its manufacturing clients. The company has already established multiple

manufacturing sites in China and the company often co-locates drug substance and drug product manufacturing for optimal supply chain efficiency. The company then addressed industry biologics manufacturing supply challenges one step further. In the spring of 2018, WuXi Biologics began establishing multiple DS and DP sites throughout Europe, Singapore and the United States often co-locating DS and DP supply in each of those region as well.

In December 2018, WuXi Biologics initiated the build of a commercial-scale biologics drug substance manufacturing plant in Ireland and then to meet the need for the subsequent EU-based drug product supply, the company completed its acquisition of a commercial-scale formulation and fill site from Bayer in Leverkusen, Germany in April 2020 just as the pandemic was spreading throughout the world. This 13,000 m^2 state-of-the-art drug product filling line provides sterile filling for liquid and lyophilized drug dosage forms at a capacity of up to 10 million vials per year. The high-throughput, fully-automated filling line utilizes a flexible isolator-based filling system.

The system includes automated loading/unloading, isolator decontamination, vial washing, depyrogenation, sterile filling, stoppering, capping, lyophilization, automatic visual inspection and tray loading for validated vial container closure systems (CCS) from 2R to 50R. Able to take advantage of single-use components and with 2 x 23 m^2 lyophilization

systems, the facility is designed to meet global modern biologics and vaccines (BSL-1-only) GMP fill requirements. The facility, with the ability to expand even further to provide dedicated or other multi-use commercial-scale fill lines, is designed to handle the growing regional production needs of the European continent. And, the availability of a site of this caliber could not have come at a better time for one of WuXi Biologics' vaccine development clients.

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As pharmaceutical and biotech companies raced to bring COVID-19 vaccines to countries around the globe it became readily apparent regional supply chains would be required as the pandemic caused entire countries to close their borders, and workplaces began shutting down on an inconsistent basis to control the spread of the virus. When WuXi Biologics was approached to see if the Leverkusen, Germany facility would be available to help supply final vialed material for a vaccine, the company did not hesitate to say "yes." But to get the facility ready for GMP production and regulatory scrutiny would take a monumental effort under normal circumstances. The pandemic had also spread throughout Germany adding another layer of complexity. In addition, the site was originally purpose-built to handle biologics (e.g., monoclonal antibodies) and making the necessary adjustments to fill a viral-based BSL-1 vaccine would be necessary.

The site would need to be commissioned and certified as no operations had started at the time of acquisition, and hundreds of employees, across all operational, manufacturing and quality functions would need to be hired and trained. Yet, in just under a year, while working every day including all holidays, the Leverkusen facility, completed equipment and critical systems installation qualification (IQ)/operational qualification (OQ)/performance qualification (PQ) and validation. WuXi Biologics then successfully completed the requisite media fills and passed its first regulatory inspection to manufacture over 10 million doses of the vaccine for the fight against the pandemic.

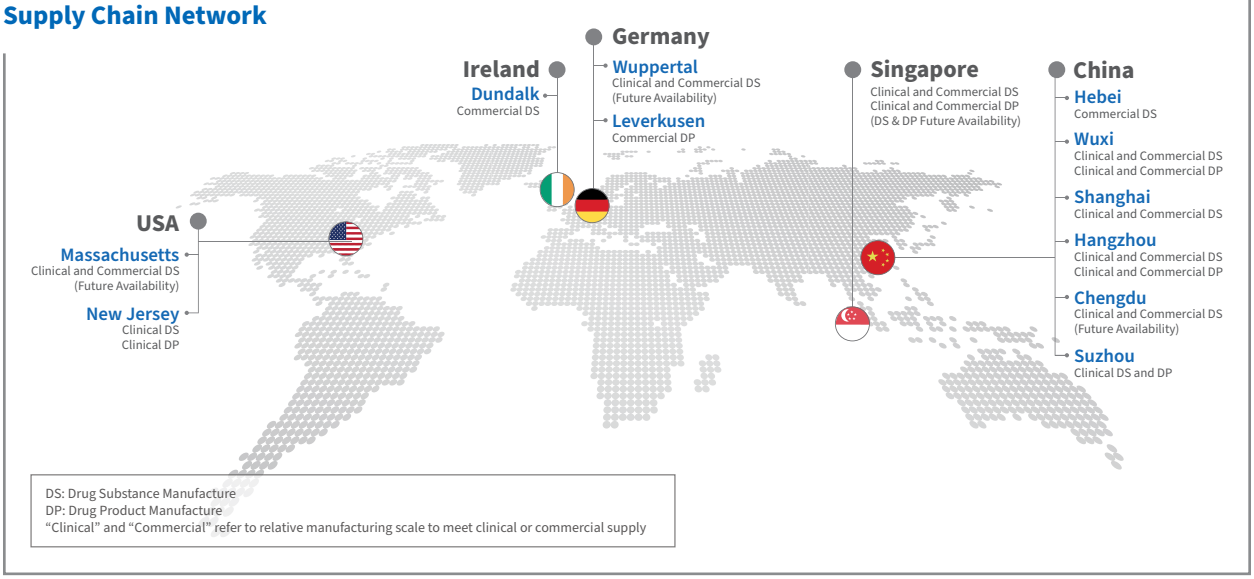
Additionally, WuXi Biologics continued to expand its European manufacturing footprint. Just one year after the Leverkusen site acquisition, WuXi Biologics completed another acquisition from Bayer by purchasing a biologics drug substance site located in Wuppertal, Germany just 45 minutes' drive from Leverkusen. The 12,000 L bioreactor capacity site in Wuppertal, along with the 54,000 L bioreactor capacity drug substance site in Dundalk, Ireland gives WuXi Biologics' clients a critical joint,

one-stop DS and DP manufacturing option for the European continent that all falls under the harmonized European Medicines Agency (EMA) regulatory umbrella. Combined with the existing China-based production options and the future commercial-scale DS and DP manufacturing options being built in Singapore and the United States, WuXi Biologics can provide global manufacturing sites and provide significant efficiencies and cost-savings via this offering.

becomes the other major benefit as WuXi Biologics can quickly leverage its vast network of DS and DP facilities.

With the help of the dedicated, skilled, and hardworking WuXi Biologics staff at the drug product facility in Leverkusen, a critical regional response for vaccine supply to the pandemic was achieved. In addition, WuXi Biologics has responded to the challenges posed by the global pandemic by establishing

WuXi Biologics "Global Dual Sourcing" Supply Chain Network



The benefit of this single-organization supply chain approach comes in the way of utilizing a single unified quality system that has been vetted by over 10 different regulatory authorities. Not only is the quality system harmonized but manufacturing equipment, procedures and best practices are standardized and utilized by the various global WuXi Biologics' manufacturing entities to provide efficiencies in technical transfer and GMP manufacturing and QC process consistency. Since audits, contracts, service and quality agreements and materials supply will only need to be coordinated with one organization, additional efficiencies and lower transaction costs can be obtained. Flexibility then

multiple drug substance and drug product manufacturing sites on a regional basis, providing a risk mitigation strategy for biologics and vaccines supply. This "Global Dual Sourcing" strategy can be efficient and cost-effective and a much-needed risk-mitigation strategy for future biologics and vaccines supply. The company has been able to establish a global manufacturing network, including drug substance and drug product facilities in Germany, with a unified quality system and where applicable harmonized equipment, providing additional efficiencies and lower transaction costs, thereby providing a flexible, robust, global manufacturing footprint to enable the supply of critical medicines.

About WuXi Biologics

WuXi Biologics is a leading contract research, development and manufacturing organization (CRDMO) that provides end-to-end capabilities to healthcare organizations worldwide. With operations in China, the United States, Ireland, Germany, and Singapore, we enable our partners to effectively and efficiently bring biologics and vaccines to patients worldwide through our comprehensive and high-quality drug development model.