WHITE PAPER

The shift toward US pharmaceutical manufacturing

Considerations in attaining the right global mix

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The COVID-19 pandemic has brought the global interdependency of pharmaceutical supply chains into sharp focus, exposing weak links and re-igniting discussions around the value of reshoring production. The U.S. Food and Drug Administration (FDA) reports 72 percent of facilities manufacturing APIs for American drugs are overseas, with 13 percent in China.[1] Here, we discuss effective strategies to secure and de-risk pharmaceutical supply chains and reveal how Curia assures the continual production of urgently needed drugs.

SARS-CoV-2 has highlighted global dependency on China for drug production

At the tail end of 2019, a small cluster of pneumonia cases of unknown etiology was reported in Wuhan City, Hubei Province, China. These were subsequently attributed to a novel coronavirus, SARS-CoV-2, the causative agent of COVID-19, resulting in a worldwide pandemic that has claimed more than 6 million lives.[2]

China's immediate response to the outbreak was to enforce a lockdown lasting from mid-January through early April, an approach that is widely believed to have slowed the spread of infection. However, such drastic measures have forced the global pharmaceutical industry to acknowledge global drug development and manufacturing dependency on China.

With pharmaceutical programs worldwide relying on China as a key source of raw materials, intermediates, and active pharmaceutical ingredients (APIs), the Chinese lockdown immediately raised significant concerns. These were founded not only on China's essential role in producing the drugs desperately needed to tackle SARS-CoV-2, but also on the fact that China has become a major player in producing drugs used to treat many other health conditions.

The global interdependency of pharmaceutical supply chains is widely recognized

Prior to the 2008 economic downturn, U.S. and European pharmaceutical companies depended largely on domestic contract development and manufacturing organizations (CDMOs) to support drug production. These were complemented by a smaller number of similar organizations overseas, but it was only when the financial crisis hit that a strong pendulum shift toward offshore pharmaceutical development and manufacturing became manifest.

Motivated largely by a need to control costs, many pharmaceutical companies found themselves turning to countries such as China and India to source drug production. This was especially the case within the highly competitive generics space, where offshoring was driven by market pressure to decrease prices, leaving the production of high-value novel therapeutics, high potency APIs, and more complex dosage forms to be produced largely within the Western Hemisphere.

Although offshoring has been a successful approach to drug production, it has exposed a major weakness within the pharmaceutical supply chain. Namely, relying too heavily on a single geographical location opens up considerable risk when it comes to assuring uninterrupted drug supply. The SARS-CoV-2 outbreak has brought these concerns to the forefront, as the Chinese government mandated temporary factory closures at the beginning of the pandemic[3] and India restricted exports of some pharmaceutical ingredients amid fears of global shortages.[4] This led to industry discussions around the need to redistribute drug development and manufacturing sources to create a more balanced global footprint and ensure security of supply.

One dominant school of thought is that reshoring drug production would remove the uncertainties of geography-specific restrictions exemplified by the COVID-19 pandemic. Indeed, domestic production is currently being heavily incentivized by U.S. government programs such as Operation Warp Speed (OWS), which forms part of a strategy aimed at accelerating the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics within America; and the COVID-19 Joint Acquisition Task Force (JATF). The latter serves to provide assisted acquisition of product lines, including pharmaceuticals, to the Department of Health and Human Services (HHS) and the Federal Emergency Management Agency (FEMA) in response to the ongoing COVID-19 situation.

Relying too heavily on a single geographical location for outsourcing opens up considerable risk when it comes to assuring uninterrupted drug supply.

These programs enable U.S. pharmaceutical manufacturers and their domestic contract suppliers to consider reshoring parts of their supply chains that have been offshored primarily due to cost. However, there will inevitably be a limit to how far such incentivization can go and taking reshoring to the extreme raises its own concerns. Ultimately, the value of a diversified supply chain should never be underestimated because serving patient needs remains the primary focus of any drug development and manufacturing program.

Supply chains must have the capacity to handle disruption

Although cost is a consideration in drug manufacturing, supply chain concerns extend far beyond pricing. Other factors of importance include production volume, dosage form, and the geography in which the product will launch; with regulatory and shipping requirements varying considerably from one country to another, a solid understanding of how these might impact drug production is vital to assure uninterrupted supply.

Of paramount importance is the need to build robust supply chains with the capacity to handle disruption. Although the SARS-CoV-2 outbreak has forced this issue into the spotlight, it is not only a global pandemic that can close sites – fires, extreme weather conditions, political unrest, and hazardous material spills can also be responsible. Ultimately, in geographies where a key component cannot be sourced, drug manufacturing comes to a halt, throwing supply chains into chaos. Planning for disruption means supply chain management cannot be influenced by cost alone.

Dual sourcing is an established approach to mitigate risk

With supply chain continuity underpinning the timely delivery of urgently needed drugs to patients, dual sourcing has become an established mode of operation. Yet for dual sourcing to be effective, whenever possible, it is important that both sources are located in different geographies and that each has its own distinct supply chain in place.

During source selection, onshore and offshore options are not only a cost-play but also a commercial launch strategy; for example, if a source is approved in both the U.S. and Europe, launching becomes far easier from a regulatory perspective.

It can also be prudent to identify and qualify a third source as a back-up as this can prevent the occurrence of a single source scenario in the event of any unforeseen circumstance.

Another important consideration is whether to have both sources through the same CDMO. In instances where a CDMO has multiple sites worldwide, this can be an advantage as manufacturing can rapidly be instigated at a geography and scale suitable to meet demand. Having both sources within the same CDMO can also boost efficiencies by avoiding the many pitfalls of timely organization-to-organization tech transfers, translating to faster time to market.

Supplier qualification takes time

Supplier qualification is an essential component of validation and is explicit in FDA requirements aimed at assuring patient safety. Typically taking a minimum of six months, it entails site visits and comprehensive inspections to ascertain supplier fit within the overall supply chain, followed by regular audits to ensure ongoing compliance.

With travel currently restricted due to COVID-19, reshoring offers a clear benefit. Moreover, as suppliers implement new ways of working to meet rapidly changing development and manufacturing needs, moving production onshore can expedite the mandatory requalification process that must take place every time a change is introduced.

Irrespective of where a supplier is located, it is critical to understand the open capacity, raw material sourcing approaches, and safety stock that is in place and to evaluate suppliers' available resources. For instance, if a supplier routinely runs production at near full capacity, ordering in raw materials only as required, there is little room to maneuver should there be a sudden spike in demand. Likewise, if multiple suppliers are dependent on the same

source or on a single geography for a particular raw material, intermediate, or API, the risk of supply chain disruption is greatly increased.

Track record and quantitative delivery metrics are essential to supplier qualification. As well as having proven cGMP compliance, a trusted supplier should be able to demonstrate centralized quality systems, robust measures for ensuring data integrity, clear channels of communication, and comprehensive back-up plans to cover any eventuality.

Advance planning is vital

For drug development programs to progress smoothly to manufacturing, it is critical to start preparing for drug production during the development phase. Factors such as cGMP, size of equipment, geography-dependent regulations, and additional safety considerations all contribute to longer timelines and greater costs within manufacturing compared to development, making advance planning vital to avoid being late to market and delaying patient access to essential care.

Supply chain qualification is a key part of the planning process. When this is performed retrospectively, it can take 1-2 years for filings to be updated, putting drug manufacturers at great risk. One way of streamlining supply chain qualification is to identify local vendors for starting materials, intermediates, and APIs, whilst recognizing the value of a diversified supply chain to assure continuity. It is also important to budget appropriately, partnering with a trusted CDMO to make decisions based on future forecasts.

Being prepared for drug production has never been more important than now, in the midst of a global pandemic. According to Global Data, clinical investigations of both novel and existing drugs continue to grow, and the number of clinical trials in the U.S. now surpasses the number of trials in China, meaning it can only be a matter of time before an effective therapeutic is developed.[5] Planning ahead to meet demand for such a potential blockbuster is vital as the world unites in its efforts to tackle COVID-19.

More than a CDMO

With nearly 30 years of experience in R&D and manufacturing, Curia has a significant and tenured track record in bringing products to market. This success is due largely to our unparalleled focus on service, whereby we custom-fit each product to the right scale, right site, and right expertise, every time.

Our reputation as a leading partner for drug development and manufacturing globally is underpinned by a far-reaching worldwide presence. Benefiting from a global footprint that spans more than 20 production sites across three continents, and that includes one of the largest U.S. manufacturing footprints of any CDMO, we provide exceptional reliability in assuring supply.

At Curia, we know careful and thoughtful sourcing is critical, especially during a worldwide pandemic. Our efforts to maintain and improve supply chain viability are unrelenting and we take every opportunity possible to ensure duplication in sourcing of starting materials, intermediates, and APIs.

In combination, these factors can guarantee that our customers experience the security of supply so needed during this time of sourcing uncertainty.

An unrivalled capacity to handle supply chain disruption

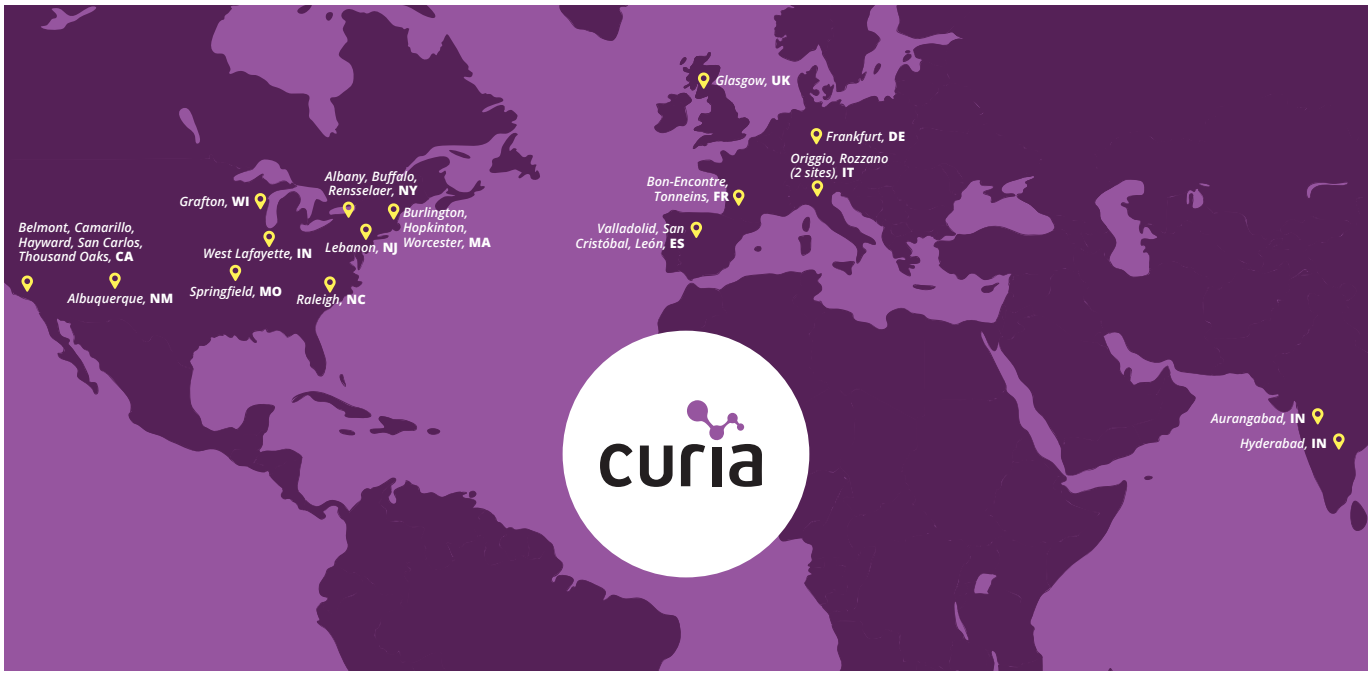
When the COVID-19 pandemic was declared, Curia was ready to react. Processes were implemented rapidly to ensure that customers' projects continued to run on-time, and our robust supply chain once again proved its value in assuring an uninterrupted

supply of urgently needed drugs. In fact, not only were we able to progress current projects, but we also initiated several new projects as well as provided vital support to companies suddenly lacking capacity due to their own COVID-19 impacts.

With multiple production sites balanced across three continents, and the second-largest U.S. manufacturing footprint of any CDMO, Curia was able to respond dynamically as the scale of the pandemic was revealed.

Our resilience to a crisis situation such as that presented by COVID-19 is reinforced by our expansive global presence. With multiple production sites balanced across three continents, and the second-largest U.S. manufacturing footprint of any CDMO, we were able to respond dynamically as the scale of the pandemic was revealed. As just one example, we have consistently been a major supplier of dexamethasone sodium phosphate and following the breakthrough that the commonly used steroid, dexamethasone, has shown promising results as a treatment for patients impacted most severely by the virus, reducing fatalities by about a third,[6] we were easily able to ramp up production to meet increased demand. Additionally, our U.S. research and production sites are driving much of our client COVID-19 support.

As the pandemic situation continues to unfold, thoughtful sourcing to secure supply coupled with demonstrated global manufacturing capabilities are key considerations in navigating the current landscape of choosing the right balance for pharmaceutical production. Maintaining transparency with partners to construct supply chain solutions that make sense; leveraging the benefits offered by new, fast-track regulatory processes; and continuing to nurture a diversified global presence will all be fundamental in moving forward.



During this unprecedented time, learn how Curia will provide expert solutions and assurance of supply to your product across the entire drug continuum – everything from drug discovery, development and commercial production of APIs and sterile fill/finish drug product. **Visit https://www.curiaglobal.com**

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