AmerisourceBergen
World Courier

From just-in-time to risk-based logistics

Pandemic underpinning adoption of new approaches to sourcing and manufacturing

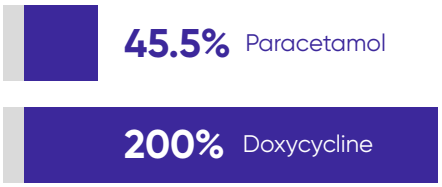
Introduction

The pressures on drug manufacturing directly caused by the COVID-19 pandemic have been dramatic and continue to affect the supply of both active pharmaceutical ingredients and finished pharmaceutical products.[1]

Single-use equipment sourcing, raw material shortages and price increases are the most notable problems resulting from COVID-19 induced economic pressures, political interventions and varying national health governance approaches.

For example:

- In February 2020, the Chinese government imposed strict containment measures, including the extension of the national Lunar New Year holiday, and the lockdown of Hubei province along with large-scale mobility restrictions. This essentially closed circa. 37 Active Pharmaceutical Ingredient (API) manufacturing facilities for an extended period. The Government subsequently nationalized control of the production and distribution of medical supplies in China - directing all production for domestic use.
- In March 2020, the Indian government's Ministry of Commerce and Industry announced a restriction on exports of APIs and formulations containing them (the list would expand to 27). The APIs included such products as paracetamol, aspirin, the antibiotic Amoxicillin, and the blood pressure medication Valsartan. The decision was reversed a month later but highlighted how even short-term disruption could cause international concern.
- In May 2021, the price of raw materials used to manufacture key COVID drugs jumped by up to 200 percent in some instances. This included a 45.5 percent increase for paracetamol and a 60 percent increase for vital antibiotic, Doxycycline.[2]



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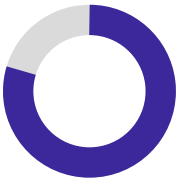
1 https://www.healio.com/news/hematology-oncology/20210827/covid19driven-shortage-of-tocilizumab-may-impact-delivery-of-car-tcell-therapy
2 https://theprint.in/health/pharma-industry-warns-of-covid-drug-shortages-as-raw-materials-prices-surge-200/650792/

Introduction



75-80%
of the APIs imported to the US are from China and India

To further highlight the scale of the problem and the global impact of these decisions, US trade statistics suggest that, as of 2020, nearly 75-80 percent of the APIs imported to the country are from China and India[3]. China's Hubei province is home to producers of agents for 136 drugs including antibiotics, with 90 percent of active ingredients used in generics produced in the country.

As Ken Kent, Senior Vice President, Chemical Development and Manufacturing Operations, Gilead Sciences put it while speaking at the Drug, Chemical & Associated Technologies Association's (DCAT) annual DCAT Week 2021[4]:

"Every component that touches your product… [was] under pressure. For example carbon dioxide was in short supply because it's a byproduct of the fuel industry, and [pharmaceutical manufacturers] use it in processing. So simple things like this could trip you up and it really made us look a lot deeper into our supply chains."

3 https://www.mordorintelligence.com/industry-reports/global-active-pharmaceutical-ingredients-api-market
4 Webinar: 'Manufacturing and Supply - Lessons Learned from the Pandemic', July 13

Challenges of shipping and storing APIs

Lockdowns and limited availability immediately illustrated the extent to which a few countries dominate the world supply of APIs and their chemical raw materials.

This has highlighted the need across the industry to shift away from traditional single supplier strategies. Just-in-Time (JIT) approaches (the concept of receiving and shipping raw materials and products as they are needed) which have become de facto in most industry supply chains have been stress-tested by the pandemic and their frailties exposed. However, JIT isn't 'dead'. At an International Society for Pharmaceutical Engineering (ISPE)-sponsored webinar[5], Gilead Sciences Corporate Operations Senior VP Joydeep Ganguly offered that:

"Supply chains that have been heavily reliant on large inventory levels, which were touted as being super inefficient in the past, are the ones that are now being touted as super resilient."

"The pandemic and its impact on pharma," he said, "has taught us that we really cannot be arrogant about having one model that drives a pervasive view on how we structure our supply chain."

Single-use equipment sourcing pressures

Early in the COVID-19 pandemic, it was recognized by the industry that the speed and flexibility needed to make novel vaccines meant that manufacturing would largely rely on single-use bioprocess systems and materials.

However, during the pandemic, some biomanufacturers were waiting up to a year for single-use equipment, according to ABEC (a leading global provider of stainless steel & single-use integrated solutions and services for biopharmaceutical manufacturing). And while vendors responded by expanding capacity, these projects took months to come online[6].

Essential kit for making vaccines was in short supply—exposing how the chain is reliant on a handful of countries, and even companies when it came to the sterile bags used for cell cultivation in bioreactors[7].

5 Webinar: COVID-19: Pharma Supply Chain Security & Robustness During Global Pandemic: https://ispe.org/webinars/video/covid-19-pharma-supply-chain-security-robustness-during-global-pandemic
6 https://bioprocessintl.com/bioprocess-insider/upstream-downstream-processing/single-use-lead-times-up-to-12-months-as-covid-takes-its-toll/
7 https://www.bmj.com/content/375/bmj.n2375

Challenges of shipping and storing APIs

Logistics – further pressures and solutions

To navigate the sourcing and manufacturing shortages and alleviate them where possible – pharma companies needed to quickly reestablish API and materials supply and intelligently plan with logistics partners to ensure this was maintained.

Lockdowns and border closures however had further ramification on pharma, as reductions in ocean freight and flight capacities challenged logistics and heightened pressure on providers across the globe.

The reduction in direct flights also meant that products were and still are spending more time in transit, requiring longer lead times and more handling points.

The response from logistics companies to keep medicines moving has varied but broadly included:

- Shifting airline utilization from passenger to cargo
- Utilizing more transport routes and methods to ensure delivery
- Commissioning charters to ship vital medicines
- De-prioritization of some products with more complex handling/ choreography requirements, which led to specialist companies like World Courier needing to quickly develop new solutions to address this market need

Case study:
Keeping our customers' shipping running as normal

A long-standing World Courier customer required shipment of anaesthetic products to four overseas island territories. Our standard transport approach wasn't viable, as ferry services and commercial flights were suspended due to the pandemic.

For transport between two of the islands, we were able to charter a small private jet. For another lane, we implemented contingency planning, including shifting temperature control solutions to accommodate new aircraft requirements and coordinating tight connections.

As a result, public hospitals on the islands received the injectable general anaesthetic products they desperately needed, with a shipment performance rate of 99.5 percent in specification.

"Having the answer and being able to deliver these much-needed anaesthetic products speaks to the agility ingrained in our operations and mindset. We can flex in times of extreme flux – meaning we can ensure essential medicines reach their destination in the most trying circumstances, as has been the case with the pandemic."

Christopher Engel, Commercial Supply Chain Service Director, World Courier

Diversification of supply

Supplier diversification is likely to be a long-term solution put forward to address the shortcomings highlighted by the pandemic. Although the 'one-stop shop' model is and will remain popular in parts of the pharma industry, the trend to diversify the supply chain and use more local options has been intensified because of the urgency of the situation. McKinsey estimates that:

38-60 percent of the international pharma trade worth $236 billion to $377 billion in 2018, could potentially be considered for sourcing diversification[8].

Reshoring, localization and increasing the use of regional storage and transport options however will not be as simple for pharma as it will be for other industries. As noted, the industry has a significant reliance on raw materials and APIs supplied in India and China and to shift sourcing these materials will take years.

Government initiatives will likely be needed to energize the domestic production of drugs and Governments are increasing funding for local manufacturing. The EU for example has pledged $10 billion for the pharma industry to promote EU manufacturing capacity for APIs and pharmaceutical starting materials.

8 https://www.mckinsey.com/industries/life-sciences/our-insights/four-ways-pharma-companies-can-make-their-supply-chains-more-resilient

Managing risk is the new currency

For manufacturers in the short-term, finding alternative suppliers is essential for continuity and risk-mitigation. In the long-term, key changes will likely be focused on more local production, reshoring and more local sourcing[9].

'More' is a vital word here - Medicines for Europe has advocated global coordination of drug supply as opposed to 'rampant reshoring'[10].

Logistics' role then in the coming years will be to facilitate and manage risk in supply chains in flux:

- Localizing where desired but maintaining global capabilities where necessary
- Shifting greater bulk where possible while developing capabilities to handle increasingly higher-value and smaller-scale therapies
- On-boarding more suppliers while maintaining relationships
- Pivoting away from JIT where it's deemed too high-risk yet keeping it where appropriate

Flexibility and adaptability across the supply chain were and still are key. The pandemic has shown that it is difficult to effectively plan for every eventuality –logistics companies need to have flexibility ingrained and the ability to anticipate problems and implement contingencies to respond appropriately when challenges arise.

In the pre-COVID logistics environment, efficiency was of the utmost importance and paved the road towards JIT approaches. Peri-, and hopefully, post-COVID, managing risk out of global pharma supply chains will be prioritized. Currently more attention from pharma is being given to the risk profiles of logistics, management, assessment, and details of shipments – Quality Assurance teams are now more directly involved than previously.

Ultimately, finished drug distribution is not possible without a lean and robust manufacturing supply chain which includes strong logistic partners.

World Courier understands the complexity and criticality of sourcing and logistics during manufacture, and that there is no room for failure in a potentially very high-risk environment. Managing risk has become a more important consideration than ever – this is where World Courier has deep expertise and a strong history in handling very fragile and temperature sensitive materials while shipping them between continents in a very timely manner.

"Every shipment decision is essentially a risk management decision. A risk-based approach is a default at World Courier because of the complexity of, and the importance we place on, the products we handle."

Mads Skovvang, KAM & Commercial Supply Chain Manager, World Courier

9 World Courier white paper: Protecting your supply chain: lessons learned from COVID-19
10 https://cen.acs.org/business/outsourcing/Europes-drug-supply-chain-ready/98/i46

Do manufacturers need to adapt to a 'new normal'?

A key consideration for many manufacturers and logistics organizations was whether the need for and competitive race for commercializing COVID-19 vaccines would compound existing sourcing and capacity challenges.

More than

1000

vaccines and therapies in development

36

vaccines and therapies approved

As of September 2021, there were more than 1,000 vaccines and therapies in development for COVID-19, and 36 vaccines and therapies approved (or granted emergency use authorization).

The number of contract manufacturing agreements for COVID-19 vaccines and therapies that have been publicly disclosed to date stood at 230, but the number of undisclosed is estimated to be conservatively 10, but potentially 50 times higher.

Adding multiple billions of doses of a vaccine to the supply chain was always going to have an impact. Six billion doses equate to circa sixty thousand extra metric tons of product.

Putting the numbers in context, however, reveals that the effect on capacity has been minimal. Early data released in September 2020 showed that countries and trading blocks around the world had ordered 5 billion vaccine doses. While a critical effort, in practical terms data shows that vaccine distribution only called for approximately 0.3 percent of 2019 airfreight capacity[11].

While this means the supply chain has been under much less additional stress than expected, it still needs careful planning and monitoring.

This is indicative of a larger trend in biopharmaceutical logistics: volumes of biotech products are increasing but not challenging current capacities. The complexity of their supply chains however is growing.

11 Seabury Capacity Tracking database, Seabury Consulting (Part of Accenture) analysis (September 2020) Preliminary

Do manufacturers need to adapt to a ‘new normal’?

If we look at the logistics requirements alone of the Pfizer-BioNTech COVID-19 Vaccine (COMIRNATY)[12], the choreography of shipping materials and finished product to ensure rapid and safe commercial distribution is incredible.

Choreography of Pfizer’s Covid-19 vaccine

Pfizer’s Chesterfield facility is the only source of plasmids for its COVID-19 vaccine, but finishing the vaccine requires several more steps and shipments to and from several other facilities.

01 Each bottle of DNA is frozen, bagged, sealed and packed with a small monitor that records temperature in transit.

02 Up to 48 bottles are packed in a container with enough dry ice to keep them frozen at −20°C (−4°F). Containers are locked to prevent tampering and shipped to Pfizer research and manufacturing facilities in Andover, Massachusetts and Mainz, Germany which process the DNA into mRNA, the active ingredient of the Pfizer-BioNTech vaccine.

03 Following testing, the bags of mRNA are frozen to −20°C (−4°F) and shipped to a Pfizer facility in Kalamazoo, Michigan from the Andover site and to Puurs Belgium from the German site. Here they are processed into the finished vaccine.

04 Samples are also sent back to Pfizer’s Chesterfield facility, where they are tested again.

05 Storage, vaccine assembly and sterile vial fill finish then takes places. Samples are returned to Chesterfield for continuous testing, before batch release, at which point trays of vials are pulled from freezers and packed into shipping boxes with temperature and location sensors. Each box contains 45 pounds (20.4 kg) of dry ice.

06 The vaccines are then shipped across the world.

12 The NY Times: https://www.nytimes.com/interactive/2021/health/pfizer-coronavirus-vaccine.html

World Courier supporting reliable delivery of COVID-19 vaccines

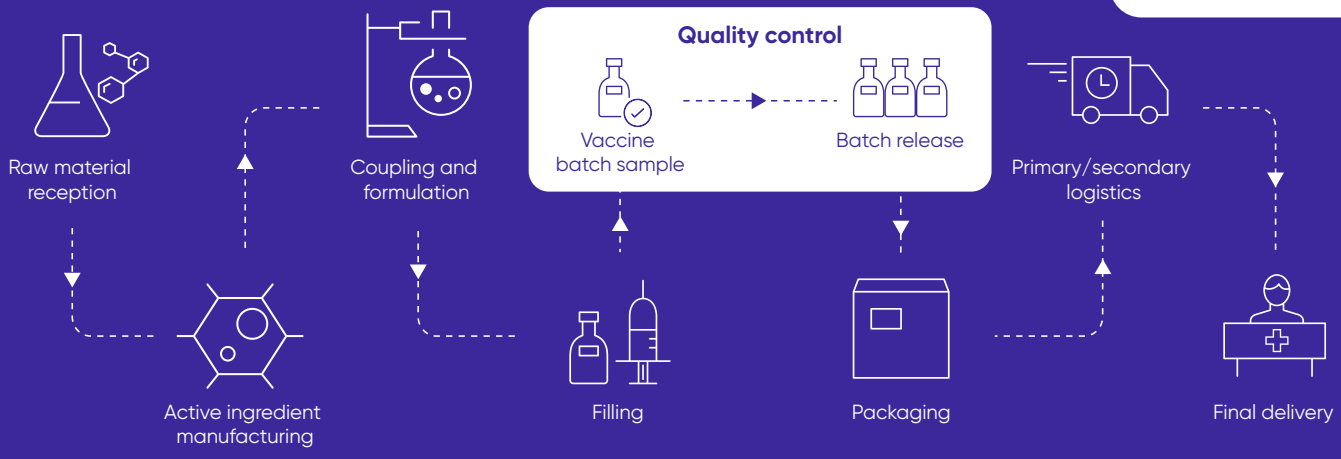
Through its network of global businesses and capabilities, AmerisourceBergen has supported the distribution of more than 100 million COVID-19 vaccine doses across 30-plus countries, providing an array of logistical services and support such as third-party logistics (3PL), importation and temperature-controlled packaging and storage.

Case study: Ensuring good manufacturing practice in the race against COVID-19

When the COVID-19 outbreak was declared in January 2020, the race to develop, approve and manufacture treatments and vaccines began. Pharmaceutical and biotechnology companies joined forces to accelerate development and testing in record time.

Our customer, a large pharmaceutical company, approached us to transport vaccine batch samples, daily, from their manufacturing site in Europe to laboratories across the continent and in the US. These batch samples would form the basis for the later stages of the vaccine manufacturing.

Download the case study



The vaccine manufacturing process

Solution: Increased visibility and peace of mind

A bespoke solution was designed including the selection of adapted dry ice packaging and a monitoring system as well as the introduction of a dedicated centralized team to manage all shipments, 24/7. This enabled our customer to receive constant communication and real-time tracking information about their precious shipments.

Outcome: A part of something bigger

Delivering a performance rate of 100 percent, we support a critical part of a naturally complex supply chain, which is essential during the manufacturing process, at the rate of 15 to 200 samples per day and 10-15 shipments per week.

Thanks to a best-in-class experience, we helped our customer comply with the quality control requirements in a timely manner so they could move forward to the subsequent steps of their manufacturing process with the aim to ultimately produce, package and deliver high quality vaccines to communities around the world.

From JIT to risk-based logistics

The hangover from the pandemic will be a long one, but it will catalyze positive change – pre-pandemic logistics may have been exposed as inadequate for some supply chains, but some methodologies will still have a place in future planning.

JIT for example will be one of many acts that support a more risk-based approach to creating resilience in pharmaceutical supply chains and logistics.

Greater expectations are being placed upon logistics providers to deliver enhanced services in this evolving space – transparency, security and flexibility will be expected almost as standard.

Better-prepared organizations will set themselves apart by offering less transactional, more consultative partnerships – the problems caused by COVID-19 will come again, and every stakeholder will need to be ready.

As more personalized biopharmaceuticals are commercialized around the world, access to a broader range of temperature-controlled packaging solutions to accommodate different needs will be essential. Manufacturers have sometimes been used to ship in bulk and struggled to get smaller quantities of API or finished dosages from one region to another as they used oversized and over-engineered containers. Volumes vary so manufacturers need to be prepared and have flexible and customized solutions in place to satisfy the needs of smaller volumes for both transport and storage.

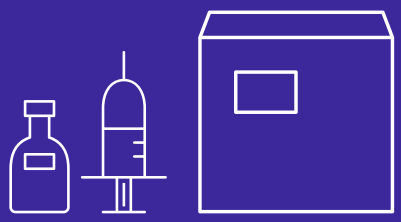
Expert logistics partners that can connect the dots both literally and figuratively within organizations and then across global supply will be better positioned to deliver against post-pandemic logistics needs. Transport and logistics departments have previously worked in silos across the lifecycle of a drug. Now with the realization of the risks that they must route their products through, greater collaboration is needed.

From JIT to risk-based logistics

To transition to this risk-based logistics methodology, World Courier has identified three fundamental practices that manufacturers will need to adopt:

- **Engage and align internal stakeholders early**
  Manufacturers need to be internally aware of the requirements of commercialization. All stakeholders must be involved and aligned before validation and qualification of shipment, making it easier for providers to respond to their requirements.
- **Explore more than one option and develop more contingencies**
  Manufacturers should avoid being over-prescriptive on carrier routes as this limits flexibility. Manufacturers need to think outside of the box and evaluate the best option for every shipment on a case-by-case basis.
- **Adopt a total cost-benefit approach**
  A more holistic approach to understanding cost is needed. Stakeholders across the value chain of a drug need to provide insight into the cost-benefit realities of choosing a logistics solution. The frailties of the supply chain highlighted by the pandemic have led many manufacturers to understand that cost is not the most crucial factor here – reliability, quality and success are.

Case study:
Maintaining Good Practice standards (GxP) for door-to-door shipping and temperature management (-20°C) of semi-finished bulk vaccines



World Courier had an established relationship with the clinical division of a global pharmaceutical company. The company required door-to-door shipping and temperature management (-20°C) of three pallets, twice per week of semi-finished bulk vaccines from the US to sites in Europe.

The client was previously relying on several suppliers: a designated logistics service provider, a box provider and a third party handling the X-ray process.

This solution was resulting in poor visibility, especially through the x-ray process, and inadequate communication as they had to deal with different contacts. The pallets were often held in customs, resulting in a mix of temperature excursions and delay in final production and distribution, ultimately impacting the patient experience and health.

Solution:
After meeting a senior supply chain lead from the company during an event where we presented our Cocoon packaging solution, we carefully analyzed their existing supply chain and where it was falling short of their expectations.

Our experts designed a consolidated customized solution for them, with a single vendor (World Courier) managing transportation and local packaging provision.

Outcome:
From collection, packaging and in-house screening to customs brokerage and last mile delivery, we now handle the whole logistics process, maintaining GxP standards and vastly improving communication and performance throughout.

Summary

World Courier provides specialty logistics services to drive the clinical and commercial success of our partners around the globe.

From the AIDS crisis to the Icelandic volcano, the Ebola outbreak and now the COVID-19 pandemic, we know what it takes to keep shipments moving, even during the most difficult of circumstances

World Courier has established an international network, with local experts across the globe that can transport your consignments wherever they need to be, pivoting when necessary. We reliably transport pharmaceuticals to difficult-to-reach places, keeping within strict temperature ranges – we have an exemplary record for consignments delivery.

World Courier designs tailored logistics solutions to fit your supply chain requirements. Learn more about our API solutions or contact an expert now.

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