COVID-19 and the Clinical Supply Chain:

Mitigating risk and maintaining business continuity

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As the COVID-19 pandemic began to affect global supply channels, clinical supply organizations had to quickly pivot to ensure Investigational Medicinal Product continued to reach its final destination. Initially, to ensure patients already participating in ongoing clinical trials continued to receive their medication and, later, to facilitate the supply of potential COVID-19 therapies.

Many biopharmaceutical companies also took things a step further and shifted to a direct-to-patient model, a type of decentralized clinical trial (DCT) that incorporates a hybrid of traditional/virtual elements in a trial, such as home nursing and/or shipment of clinical trial materials directly to the patient's home. By expanding the reach of the traditional clinical supply chain, DCTs have shown improved patient retention rates and have also helped address potential staff and patient safety concerns, a factor that has been particularly important during the pandemic.

From the clinical supply chain perspective, rapidly incorporating these patient-centric elements and ensuring the continuity of trials was challenging, requiring an abrupt change in strategies along with new approaches.

Four specialists – spanning the biopharmaceutical industry, a specialist courier service, and a clinical supplies packaging, and distribution organization – recently met at the Global Clinical Supplies Group (GCSG) virtual conference, held September 21-25, 2020, and participated in a panel session to share their unique experiences with the clinical supply chain during the COVID-19 pandemic. This paper summarizes highlights of the discussion spanning risk mitigation, business continuity and lessons learned for preparing for future disruptions.

Experiences from the biopharmaceutical panelists

Trial delays due to site closures were noted as the main impacts from panelists Summer Doty, Director of Clinical Supply Chain at Gossamer Bio and Ana-Zeralda Canals Hamann, Senior Clinical Trial Supplies Manager at Debiopharm.

"We had some site closures and many sites with restrictions preventing on-site visits, for patients and support staffs," said Summer. "Lab work was also restricted for analyzing blood samples and patient biopsies, which caused some slight enrollment delays."

She reported that Gossamer Bio quickly implemented direct-to-patient distribution for their active studies.

"We have successfully completed direct-to-patient shipments in the U.S., U.K. and the Ukraine," she explained. "I recently learned that people assume that direct-to-patient is 'depot-to-patient,' but in our case, we are shipping from the clinical site to the patient's home."

The Gossamer Bio team also adjusted their monitoring and accountability practices.

"We are having our CRAs [Clinical Research Associates] perform remote monitoring and accountability which has been possible with some of our products in blister packs. For products where they're unable to perform accountability, such as our 30-count bottles, we moved the accountability over to our packager. This provides a higher degree of accountability down to the tablet level that we would not have done previously, at the packaging site."

Summer stressed that she felt maintaining patient data privacy was an ongoing concern in the direct-to-patient model and shared that the team put controls in place with the IRT [interactive response technology] to ensure that they maintained privacy with every transaction.

Meet the four panelists

Summer Doty, CPIM
Director, Clinical Supply Chain, Gossamer Bio

Summer Doty is responsible for end-to-end clinical supply management and oversight for the IBD and Oncology programs with additional CMC project management responsibilities. Summer joined Gossamer Bio in September 2018 with 19 years of global supply chain management experience in commercial and clinical supplies at Becton Dickinson Biosciences and Fisher Clinical Services. She has a BA in Chemistry from University of San Diego and is Certified in Production and Inventory Management (CPIM) through APICS.

Ana-Zeralda Canals Hamann, PhD
Senior Clinical Trials Supplies Manager, Debiopharm International S.A.

Ana-Zeralda Canals Hamann has been working in the pharmaceutical industry for over 12 years, working on the sponsor side. She has a broad experience concerning clinical operations, CMC, supply chain management, regulatory, IP, project management, and preclinical services. Ana-Zeralda holds an MSc in Clinical Research Administration, as well as a PhD from the University of Oxford in Molecular Medicine. She is currently Senior Clinical Trials Supply Manager at Debiopharm and she has previously worked for Sanifit Therapeutics in different roles where she managed different clinical trials between Phase 1 and 3, as well as all the supply chain management.

Ana-Zeralda reported similar COVID-related delays with her work. When the pandemic was first declared, she had been working with the biopharmaceutical company Sanifit to support the supply chain for dialysis patients. Several sites had closed without notice, even though clinical supplies were already en route.

Despite these challenges, "COVID did not really pose a huge issue at the time as dialysis centers remained open or the patients were diverted to alternate centers," said Ana-Zeralda. "We had to find ways to maintain these patients. But direct-to-patient was not possible because of this patient population."

Several weeks later, Ana-Zeralda took a new position with the Swiss-based biopharmaceutical company Debiopharm and found that the impact of the pandemic was similar with a few site delays and site closures.

Perspectives from a clinical supplies packaging and distribution organization

From the clinical trial supplier's viewpoint, Paul O'Connor, Global Vice President of Quality, Almac Clinical Services shared his organization's process during the pandemic.

"Over the last few years, we had adopted a business continuity plan that was modeled on the U.K. Fire and Police Service," he explained. "We manage critical incidents based on a 'gold, silver, and bronze' command structure. We find that to be very effective for us in establishing small, agile decision-making teams that can react very quickly as things change."

Paul's team found that daily meetings helped them push out information to their sponsor organizations.

"We sent out in-country shipping status reports and found that those reports were really important to settle the nerves of a lot of organizations that were struggling to manage their own personnel issues as well as trying to handle issues with supplies."

Paul O'Connor
Global Vice President of Quality, Almac Clinical Services

Paul O'Connor is responsible for leading the Quality function on all sites encompassing over 220 professional staff in areas of Quality Assurance and Control, Regulatory Support, Quality Systems, and Validation. Prior to that, Paul held other Quality Assurance and laboratory roles in relation to investigational and licensed medicinal products in Almac and Galen Holdings in a pharmaceutical career of over 25 years. He is eligible to act as a European Union Qualified Person (QP) since 2001 and also holds a BSc First in Biochemical Sciences from the Ulster University. Paul has written multiple industry articles and presents regularly at Investigational Medicinal Product conferences on Quality Assurance and Qualified Person matters.

David Spillett
Global Account Director, World Courier

David is a pharmaceutical services professional with over 15 years of experience in the provision of GXP compliant services. He is a Clinical Supplies Specialist and one of the few GMP/GDP professionals whose experience includes the administration of investigational products in a clinical setting, gained whilst working as a Research Physiologist with a Phase 1 Clinical Research Unit. David holds a post-graduate diploma in clinical research and is currently Global Account Director at World Courier where he is often called upon to assist in solving the supply chain challenges associated with novel therapies. He has previously worked as a Clinical Supplies Lead for Penn Pharma where he managed pharmaceutical development and supply chain projects for a variety of pharmaceutical companies.

The Almac Clinical Services team also had to manage its own personnel.

"We also had to quickly determine how to do our work with packaging, distribution and QC activities as we managed the new reality. It was a bit like 'a swan on the lake' where the water looks calm on the surface for our clients, but underneath the water we were working very, very hard."

Even though there was a lot happening beneath the surface, Paul found that it was important to keep everyone abreast of the latest news.

"We were working very closely with sponsors to make sure that the different ways we were working were communicated to them and in the direct-to-patient model, the investigators as well, because the investigators were in danger of feeling a little out of the loop. We needed to make sure they understood their obligations to the patients and stay very close to them."

Perspectives from a medical courier services organization

As the airline industry was severely disrupted, delivering clinical supplies to sites became an enormous undertaking. David Spillett, Global Account Director, World Courier, shared his involvement with adapting to the sudden change.

"In April and May, there was around a 75% reduction in the number of flights as compared to the year before," explained David. "We had to keep product moving and learn how to adapt, but it hasn't been without its challenges."

Before the pandemic, the traditional shipping providers that World Courier used had offered a range of services that include temperature-controlled storage facilities at the origin and destination airports. But as David's organization had to switch to alternate freight providers, they had to adapt their temperature control strategies to ensure products remained stable.

"As routes were no longer open to us, we had to go into other ports of entry. Initially, flights were being cancelled a few hours before the flight was due to depart, even after we'd tendered a consignment," he explained. "And, in some instances, consignments were halfway to their destination and then subsequent connection cancelled, forcing us to reroute."

Ana-Zeralda from Debiopharm cited similar experiences when flights weren't available, opting for ground routes to cross international borders.

"We had a study with radiolabeled products," said Ana-Zeralda. "We found that we had to drive the product through borders when it was impossible to fly. We had to risk mitigate to find the most appropriate way to reduce any possible issues because our radiolabeled products have a very short lifespan of just over 48 hours. It was very stressful when you don't know from one day to the next what is going to happen at each border, especially if you have to cross several borders."

David shared that his team had a similar experience with delivering supplies across borders.

"When Italy was effectively closing down, we were sending drivers to both sides of the border to hand off products," he said.

"Then in India, the region closed down and we couldn't cross the borders. We met internally to determine how to get different permits to enable us to move medicine because fundamentally there had to be a route to get this through."

Paul added, "It was really important to have control of the medicine arriving in good condition and be able to check it on arrival.

We needed to capture the data very quickly, especially in cases when patients needed their medicine in a hurry."

Regulatory and auditing experiences

The panelists also shared their experiences working with regulatory agencies and ensuring compliance as guidance evolved.

"We found that regulators weren't keeping up and initially sticking very rigidly to their ways of working," said Paul. "We saw that the sponsors were pushing the boundaries a little bit, and then seeking forgiveness rather than permission. Some countries were not used to seeing direct-to-patient activities. Sponsors needed to force the issue to make it happen. Then, gradually we saw the regulators appear with supportive measures to allow those changes to happen."

Summer at Gossamer Bio cited several regulatory-related changes to their process as a response to the pandemic.

"The U.S. FDA released new guidance which gave us leniency to supply drugs with other methods due to the pandemic. We updated our protocols and made some submissions. In some 'emergency' cases, we just did a risk assessment to ensure that we weren't going against anything that was in the protocol and that we were maintaining patient safety so that we can implement the changes faster. We also updated our informed consent and received IRB approval."

David added that depot-to-patient is a workable solution but feels that using in country depots licensed to dispense medication is the safest option.

"GCSG had some conversations with the FDA, and the FDA said they didn't feel there was anything to prevent depot-to-patient at a federal level," he said. "Throughout the world, I think depot-to-patient is viable but it does become more challenging when you have international borders in play."

Paul also added that they dealt with a few special cases where they had to seek direct permission from regulatory agencies to ship medication into the country.

"We approached regulators in the patient's home countries to seek permission for a degree of flexibility and compassion," he said. "In each case, the agencies sought to understand the trial and get assurance that the patient was on a trial. Then they issued a letter approving the movement of medication with an appropriate degree of local medication supervision."

Accelerated solutions and technologies due to COVID-19

As direct-to-patient solutions were accelerated to address the impact of the pandemic, other technologies and solutions also came to the forefront.

"At Gossamer Bio, we accelerated our virtual audits," said Summer. "We had some audits scheduled with our drug substance and drug product GMP manufacturers – in Canada, the EU, Korea and Spain – but the sites had restricted visitors. Internally, we performed a risk assessment to determine if a virtual audit was a good option

for each of our vendors. We factored in the phase of our trial, our product, the vendor's regulatory history, and their quality systems. Now we have conducted five virtual audits globally. We worked really closely with some of the vendors and our QP to ensure they would accept it and have successfully received QP declaration and QP releases with our ongoing trials."

Paul reported that his team at Almac Clinical Services has already undertaken approximately 50 virtual audits.

"We made sure that we have the ability to make our premises and our processes very visible to our clients, recognizing that due diligence still needed to occur," said Paul. "We created self-guided virtual tours with the ability to review the documents all online. We also introduced live streaming of certain activities, so companies can get really up close and personal with what we're doing as well. It's been enormously successful."

David shared a similar experience at World Courier.

"We were opening a new depot in Turkey and awaiting a regulatory initiative action. Initially the license was delayed, but then we had virtual audits and were successful."

Ana found that virtual training and onboarding has been accelerated at Debiopharm.

"With employees working from home, training and onboarding has been mostly done remotely," she said. "Our monitors are also doing a lot of remote monitoring and using Zoom in some cases to perform drug accountability when they weren't allowed to visit the pharmacies. We had to innovate with online training."

Decentralized clinical trials as the new normal

The panelists were in agreement that they believe many different hybrid and/or virtual solutions will become commonplace in trials, even after the pandemic.

"I think that direct-to-patient will be the direction we're moving into, especially with patient compliance," said Ana.

"I agree," added Summer. "I think that virtual trials will become more common and we'll start seeing some applications for point of care. The technology and digital platforms are going to be more common and the use of direct-to-patient will increase."

Summer's organization has added an additional appendix to all protocols titled "*Guidance to Address a Pandemic and Other Global Health Emergencies: The Potential to Impact on the Clinical Trial*."

"We have two new studies starting up this quarter, and they include the appendix," she said. "This allows us to perform a direct-to-patient shipment and allows CRAs to perform remote monitoring, among other things. We have completed the submission in the U.S. and our trial is now live. It's a new process that will be standardized going forward."

At Ana's organization, they are looking into direct-to-patient elements for upcoming studies.

"The screening visits would require the patient to be present and we're determining if further study visits can be remote if the patients don't need an MRI. It depends on the budget of the study, but we're trying to make the study as virtual as possible to minimize the number of times the patient has to go to the site or any place where they could potentially be infected by COVID," she said.

Summer added that in one of their new studies with pulmonary arterial hypertension (PAH), they specified in the protocol which visits were allowed to have direct-to-patient with home health care nurses. However, in an oncology study they are working with investigators to assess if patients can receive a shipment at their homes.

Looking ahead to maintain business continuity

Now that the pandemic has been underway for over half of the year, the presenters were asked to reflect on lessons learned.

Summer mentioned that in hindsight it would be valuable to revisit business continuity plans more often and have more specific detail on how to move supply in case of an emergency.

Ana-Zeralda shared that her team increased its mitigation plan and the frequency of meetings to at least twice a week so they can take immediate action on potential issues.

Paul said their team would have bought more IT equipment earlier and learned the lessons earlier from their Singapore and China-based activities as teams there were the first to experience the impact of COVID-19 before the pandemic was official. Paul also stressed the importance of documentation for managing business continuity.

"I think companies should think about the eventual climb out of COVID. In our company, every time we introduced emergency measures, changed our standard operation procedures (SOPs) or adjusted our expected commitments, we recorded those and have kept a long rolling list.

We continue to revisit these items to either improve them, close them, or keep them live. When regulators come back and look at your inspection, they will be asking, 'What was the impact of COVID? What did you do that was abnormal? And what have you done to fix it?' It's important for companies to have those changes recorded."

GCSG is greatly appreciative of the panelists' perspectives and looks forward to continuing this important conversation at the GCSG 2021 US Virtual Conference planned for April 25-30, 2021.

GCSG would like to thank Bay Area Research Logistics for co-sponsoring the development of this important industry article.

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