Clinical trials and tribulations

Even though they're often a vital conduit between the drug and patient, ancillary supplies are sometimes seen as an afterthought for sponsors, who have been known to request items at the last minute. Medical equipment shortages during the pandemic made it much harder to secure the right tools for the right trial and, in the process, thrust the important role they play into the spotlight. Elly Earls speaks to **Sanjay Vyas**, executive vice-president of Parexel India and head of clinical trial supplies and logistics, and AbbVie's clinical supply project manager, **Aaron Steinbrecher**, to find out how Covid-19 has led to more complexity in the sourcing of ancillary supplies and what strategies they've employed to keep trials running.

When the pandemic started, the healthcare industry's focus shifted to Covid-19. Hospital wards were filled with coronavirus patients, while pharmaceutical companies raced against the clock to develop vaccines. Many patients who were being treated for other conditions, even serious, life-threatening ones – including those participating in clinical trials – were wary of attending their appointments at hospitals or other investigative sites. Others, who had to cross borders to do so, were simply unable to.

Keeping these trials running with patients confined to their homes meant study protocols had to change. Not only did investigational medicinal products (IMPs) need to be shipped directly to patients' homes, but so did ancillary supplies, such as the delivery devices nurses at investigative sites would usually use to administer drugs.

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One oncology patient who lived in Malaysia and usually travelled weekly to Singapore to take part in a clinical trial was no longer able to cross the border. In this case, clinical research organisation (CRO) Parexel worked with the Ministry of Health in Singapore and Malaysia to make a protocol deviation that allowed the nurse to visit the patient's home in Malaysia, as well as shipping the drugs and ancillary materials from the Singapore depot straight to the patient's home.

"This was one of several such examples. In some cases, patients were 200–250km away from investigative sites and, as we were blind to where the patient was, we had to work closely with the site to make sure materials were shipped from the hospitals to the right addresses," explains Sanjay Vyas, executive vice-president of Parexel India and head of clinical trial supplies and logistics. "If the IMP had arrived at the patients' homes and the materials were not there to support the injection of the drugs, it would have been impossible."

Ancillary supplies range from simple things like tubes, bottle caps, syringes, needles and pregnancy kits to custom on-body devices, pumps and centrifuges. Parexel alone has seven clinical distribution depots around the world stocking more than 3,000 different ancillary line items at any one time, and a single trial can require up to 35 of them. Perhaps due to the simplicity of many of these items, sponsors often give little thought to the potential complexity involved in sourcing them.

"People often forget that these are actually the carriers of the IMP to the patient's body, and sometimes you'll end up with a requirement for an ancillary supply landing on your desk at the last moment. The sponsor will say, 'We also need this for the study, we forgot to add it'," Vyas explains.

Regulatory hurdles

Parexel complies with the same standard operating procedures (SOPs) for ancillary supplies as they do for IMPs, following good manufacturing practice (GMP), good distribution practice (GDP) and good tissue practice (GTP) processes. "Having the same standards as IMPs is critical. You can't just put them on a rack somewhere," Vyas stresses. "We cannot forget that the patient is at the end of the line."

Yet, regulations are harder to follow for ancillaries than they are for IMPs. "The sourcing of IMPs is easier and more structured because there are very clear regulations for it. Regulators are very clear about what an IMP is and where it can be sourced from. There's always a clear chain of custody that has been defined. But that doesn't happen with ancillaries. Sometimes you need to have scanned suppliers at several levels – sometimes at country level, sometimes at regional level and sometimes at a global level."

Keeping trials running throughout the pandemic meant that IMPs and ancillary supplies needed to be shipped to patients' homes.

For this reason, it's important for sponsors to have a cross-border compliance strategy. Say, for example, a sponsor has selected 28 sites and plans to recruit 3,000 patients over the next three years in Latin America, Eastern Europe, Russia or Asia. "They need to think about how they are going to get their materials to these sites," Vyas says. "There are some complex countries in these regions, where cross-border compliances are terrible. Sometimes, some materials are allowed, some materials are not allowed. You have to think about proactively planning a global trade compliance strategy."

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In addition, trials themselves are becoming more complicated, as biologics such as cell and gene therapies become more prevalent. "When you start looking at some of these new therapies, some of the new vaccination approaches that have come in, plus the complex requirements of moving these IMPs at a particular temperature, you also require ancillary materials that can support these trials," says Vyas.

Quadruple complications

Add a global pandemic to an already challenging set of circumstances and, according to Vyas, the complexity of ancillary sourcing has "quadrupled" over the past two years. "Borders started shutting down. Planes were on the ground. Many governments started putting restrictions on the materials that

Ancillary supplies can mean anything from test tubes that store biological material to the lab equipment used to conduct tests on it.

were being shipped out of the country because they wanted to hold them for their populations," he recalls. In addition, many non-qualified suppliers started popping up. "We ended up with many fake suppliers in the market; everybody was getting into panic mode."

Even with governments doing their best to regulate prices, costs went through the roof and sponsors were put in situations where they only had hours to decide whether to buy a certain item or not. If you called back a minute too late, Vyas remembers, the material would be gone. "It was a nightmare," he says.

"The processes to source, receive, release, and clinically label these ancillaries has been more complex and has sometimes required the development of new operating procedures."

Aaron Steinbrecher

At biopharmaceutical company AbbVie, the expansion into more and more therapeutic areas over the years has meant their processes have had to adjust to accommodate new and unique ancillaries, including materials used in on-body delivery devices such as pumps, tubing and vial adapters. "The processes to source, receive, release, and clinically label these ancillaries has been more complex and has sometimes required the development of new operating procedures," says clinical supply project manager Aaron Steinbrecher.

The main negative impact of supply chain issues and higher demand for products was longer lead times on some of the standard ancillaries they use, such as syringes and IV bags. In addition, many clinical site personnel couldn't physically get to clinical sites. "Lead times were anywhere between a few weeks to a few months," Steinbrecher says. "But this did not affect clinical trials, as we properly forecasted and had buffers in-house for these supplies."

Lessons learned from the pandemic

If there was one benefit to come out of the pandemic for CROs and clinical supply managers, it was the strengthening of sourcing procedures. Parexel already had a robust set of qualified suppliers and a sizeable amount of stock sitting in their depots. But proactive stocking and keeping a minimum level of often-used items became even more important. "We always conduct studies in certain therapy areas, and we know that these are the standard materials that are always required," says Vyas. "We've also started taking a more holistic view, looking at how we can utilise these ancillary supplies across different studies. With IMPs, you can't do that because it's always specific for a therapy, but with ancillaries, it's possible to cross-pollinate."

More importantly, he and his team learned just how crucial it is to have a seat at the table right at the planning stages of any clinical trial. "The sponsors could have done everything right. They could have set up remote monitoring and direct-to-patient procedures, but what if the material didn't turn up? It would all be useless. [It's ideal to] be part of a protocol design even to the extent where we have influence when they are selecting the sites, but that doesn't happen all the time," he says.

Steinbrecher agrees that, depending on the type of ancillary, the lead time to source, deliver and quality release can vary widely, so understanding these timelines upfront is crucial to be able to start the study on time. As a trial goes on – and evolves – however, he says it's important to be flexible. "One of the biggest lessons we've learned is to set up our clinical trials with as much flexibility as the study design will allow when it comes to sourcing ancillaries," he explains.

AbbVie uses planning and forecasting tools that are integrated with their packaging and inventory systems, so they know exactly what they will need to source – not just now, but for the future and in anticipation of new trials down the line. "These tools are integrated with packaging and inventory and have the capability to forecast for the entire length of a study," says Steinbrecher. "We use them in the beginning stages of study planning, and they have the ability to be updated as study needs change."

The pandemic is far from over and new travel restrictions continue to be implemented at increasingly short notice. Ancillary sourcing certainly isn't going to become any less complex in the near future. But the lessons learnt from Covid-19 so far may be able to help sponsors and CROs build a stronger foundation on which to operate. ●

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Parexel

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