Tanner Pharma GROUP

How Technology is Transforming Clinical Trials

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Introduction

The drug development process is a lengthy one. From initial research to market approval, it is not uncommon for operations to span ten to 15 years or longer. Any disruptions to this process can prove catastrophic, especially during the clinical trials phase where interruptions are not only impacting sponsor budgets and resources, but ultimately a patient's access to vital treatments.

The global outbreak of Covid-19 and its variants severely affected this process, forcing operators to rethink current approaches and adapt. To adjust to the new protocols and restrictions, clinical trial operators have turned to technology to continue with their programs and mitigate interruptions. And while the traditional clinical trial model is hardly going to disappear, the role of technology is only expected to increase.

In this white paper, we will detail the extent of the disruption caused by Covid-19 and explain how technology is starting to change clinical trials by enabling decentralization, via means such as telemedicine and remote monitoring. We will also look at the importance of the pharmaceutical supply chain and the deployment of new logistics-focused technologies and real-time data to meet changing demands.

Evolving challenges with clinical trials

The established approach of recruiting clinical trial participants to test promising treatments has saved millions of lives and reduced the suffering of many more. These range from the development of new types of drugs to treat different forms of cancer, to the successful approval of vaccines to protect against life-threatening diseases.

However, while the technologies and processes that underpin the development of potential new drugs have evolved at a rapid pace to significantly reduce the overall timescale from discovery to approval, the clinical trial model has been largely confined by physical and geographical constraints. Traditionally, participation in a clinical trial has been heavily restricted by participants' proximity to the site where it is being carried out. As a result, the initial pool of participants is limited to those close enough to initially apply. And the longer-term requirement to regularly return for treatments has led to many withdrawing before completion.

According to research by GlobalData, this has resulted in up to 80% of clinical trials in some countries failing to recruit the necessary number of trial participants within their recruitment timeframe.

“It has become increasingly difficult to recruit clinical trial patients as a result of saturation rates in hospital sites, but also entire countries becoming quite saturated. Constant effort is required, particularly for contract research organizations supporting patient recruitment, to access new markets in emerging regions, often with unknown or incomplete regulations,” explains Georg Schulz, Executive Vice President of Clinical Trial Services at Tanner Pharma Group. “And then there’s the effort required to constantly stay on top and ensure compliance with a dynamic regulatory environment.

“Depending on whether a clinical trial sponsor is a big multinational company with large resources on the ground, or whether it is a biotech company perhaps just doing the first phase two or phase three global clinical trial, the challenges can be enormous just to get the product started and keep it on track as it progresses, seven years off investigation.”

Furthermore, this traditional approach has in some cases resulted in poor levels of ethnic diversity among participants. Studies have found that clinical trials are made of 62.2% Caucasian patients globally. While in the US, this increases to 84.2% from a Caucasian background, with 7.3% of African-American descent, 3.4% being Asian 3.4%, and Latinos making up 2.8%. [1]

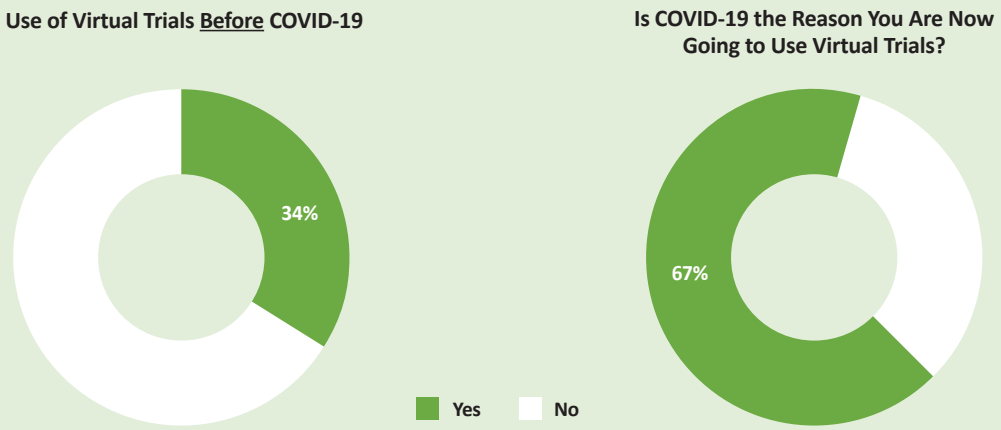
In addition, costs of the traditional clinical trial model have only risen, with hospital and investigator fees cited as some of the main reasons.

Offering a further challenge, studies have shown that almost a third (30%) of participants who sign up to take part in clinical trials later withdraw before the end, according to GlobalData figures. [2] The frequency of visits, lack of patient support and little to no reimbursement of expenses have all been cited as key factors for withdrawing.

Combined, these issues and the delays they create for the trials can result in an inefficient process that is also expensive. Anything between $600,000 and $8m can be lost each day that a trial runs beyond its enrolment deadline, according to GlobalData.

But now, technologies are starting to make a difference and result in decentralized, or virtual, clinical trials. And disruption caused by Covid-19 has accelerated the adoption of technologies to enable this.

Covid-19 Accelerated Use of Virtual Trials



Q: Was your company previously using decentralized/virtual clinical trials before COVID-19? (n=150)
Q: Is COVID-19 the reason you are looking toward this now? (n=150)
Source: GlobalData, Coronavirus Disease 2019 (COVID-19) Sector impact: The COVID-19 Pandemic Impact on Clinical Trials

How Covid has accelerated the use of technology in clinical trials

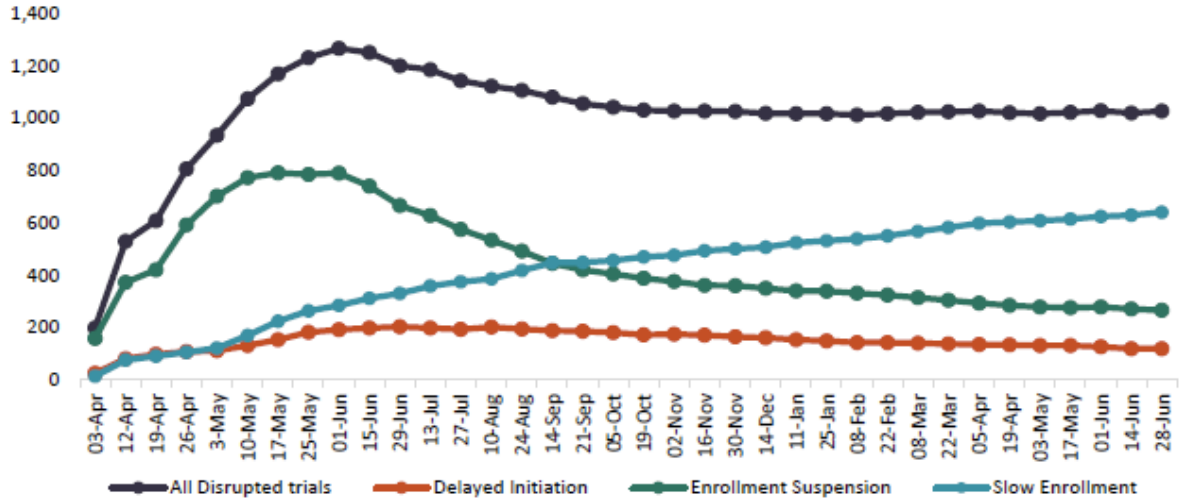
The benefits of the decentralized trial and its ability to overcome unique challenges have become more apparent since 2020 due to the global pandemic. Decentralized clinical trials have strong potential to significantly reduce costs and enhance participant satisfaction. By taking patients out of a traditional clinical setting and bringing the trial to them, there is opportunity to increase participation levels and help ensure retention due to the greater convenience. [3]

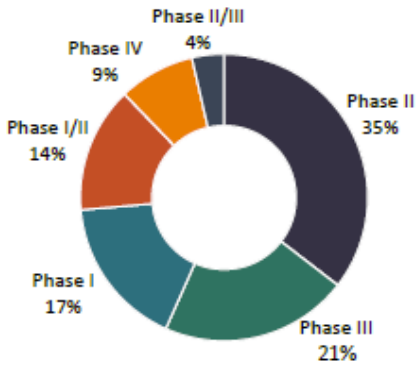
“There must be an argument for driving activities away from these centers, if they can be conducted elsewhere by non-hospital staff,” adds Schulz. “It’s becoming harder to find patients and to retain patients. So, we need to make it more attractive and more convenient.”

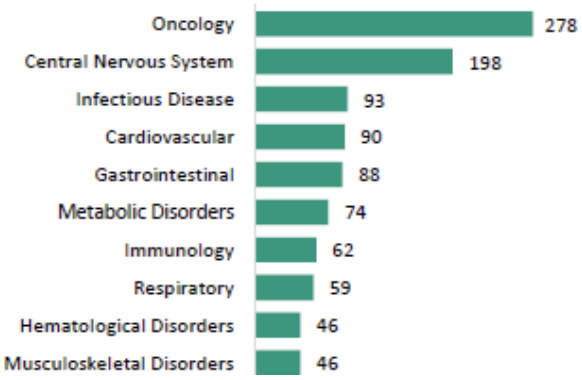
Virtual trials started becoming more common around five years ago, but they weren’t as widely used until Covid-19 caused large numbers of ongoing clinical trials to transition to decentralized models in order to adjust to the restrictions of movement put in place and help reduce the spread of the virus.

To support this newer process, specialist providers of clinical trial support services and logistics worked closely with trial sponsors to enable the trials to safely proceed without impacting their scientific integrity. Many trials continued to completion through a combination of telemedicine and remote monitoring technologies, and by extending the supply chains from the medical facilities where they had started to the trial participants’ homes.

According to research by GlobalData, disruptions to trials reached a peak in June 2020 when 1,265 different trials had been disrupted by either delayed initiation, complete withdrawal of planned trials or suspended enrolment. The research also found that oncology clinical trials suffered the highest amount of disruption.







Approvals that rely on real-world data from expanded access (EA) programmes

Generic Name	Indication	FDA	EMA	Studies
Amphotericin B	Fungal Infections	1997	N	10CT (n=2038), 1 EA (n=133)
Anagrelide	Essential thrombocythemia	1997	2004	2 SACT (n=35 + 254), 1 EA (n=245)
Cholic Acid	Inborn errors of bile acid metabolism	2015	2015	2 EA (n=63 + 22)
Clarithromycin	Mycobavterium avium complex	1993	N	1 RCT (n=154), 1 SACT (n=25), 1 EA (n=469)
Dinutuximab β	Neuroblastoma	N	2017	1 RCT (n=370), 1 SACT (n=44), 1 EA (n=54)
Fish Oil Triglycerides	Parenteral nutrition-associated cholestasis	2018	N	1 SACT (n=144), 1 EA (n=37)
Glucarpidase	Elevated metrotrexate levels	2012	W	1 SACT (n=147), 1 EA (n=22)
Lutetium Oxodotreotide	Neuroendocrine tumours	2018	2017	1 RCT (n=229), 1 EA (n=558)
Nitisinone	Tyrosinemia	2002	2005	1 EA (n=207)
Sodium Phenylaccetate/benzoate	Acute hyperammonaemia in urea cycle disorders	2005	N	1 EA (n=316)
Uridine Triacetate	Fluorouracil or Capecitabine overdose	2015	N	2 EA (n=75+60)
Velmanase α	Alpha-mannosidosis	N	2018	1 RCT (n=25), 1 EA (n=35)
Vestronidase α	Mucopolysaccharidosis vII	2017	2018	2 SACT (n=3+12), 1 EA (n=2)

Source: GlobalData, Pharmaceutical Intelligence Center (Accessed June 28, 2021)

While significant disruption remained throughout the worst of the pandemic, the use of remote patient monitoring and virtual trials were found to have minimized disruptions. The highest proportion of respondents to a 2020 survey of GlobalData pharma clients stated that they were using technologies to mitigate the impact of the pandemic.

As a sign of greater acceptance of the decentralized model, one-third of survey participants were already using decentralized trials beforehand, with more than two-thirds (70%) of those who hadn't previously were now planning to start using them.

This can be seen as a symptom of the fact that the pharmaceutical industry is typically risk-averse in adopting innovations and operations models. But faced with no other options, it was forced to adopt the decentralized trial model.

"There's an interesting dimension here when using technology. The emergence of the virtual trial design responded to a need of two groups. On one side, there is the need for patients to not have to go to a hospital because it's being deemed a high-risk environment for clinical trials that involve healthy subjects. But on the other side, there is the hospital site and the needs of their staff. It's the question of how we protect the health care workers from exposure to patients who have an infection that could pass on to them, with workers obviously vital to the whole infrastructure," adds Schulz.

"So, digitalization and the decentralized trials have created a safe pathway where requirements of both groups could be met, and conditions improved. And I wouldn't be surprised if that technology matures over time to not only be used in clinical trials but become a regular part of the healthcare system in areas such as telemedicine for certain consultations."

While much of the disruption of the pandemic has passed, what remains is the potential to increase the use of decentralized trials to further the appeal of participating alongside minimizing the disruption to patients. Therefore, it seems highly likely that decentralized trials will only continue to rise. Yet if there are to be an increase in international clinical trials, a lack of regulatory harmonization will need to be resolved.

Telemedicine and remote monitoring devices driving decentralization

In recent years, the outdated and inflexible model of conducting clinical trials has started to evolve and take advantage of new technologies that are enabling a new approach.

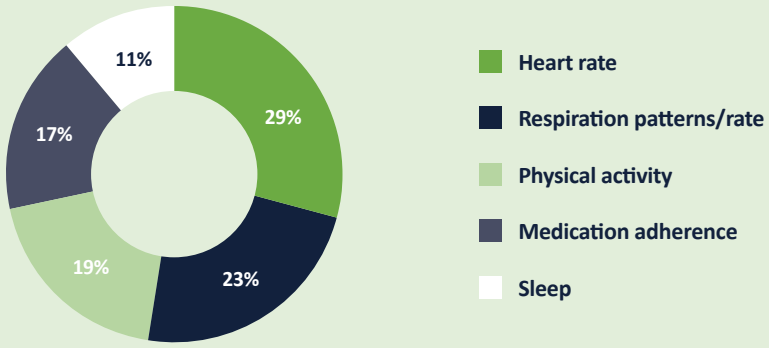
Decentralized, or virtual, clinical trials deploy a range of technologies to enable an increasing amount of activity to be carried out remotely. Previously, this would have been performed within a formal clinical setting between a medical practitioner and the participant. The shift towards decentralized clinical trials has been made possible by technological advances in a range of areas that have reshaped the potential model, removing traditional barriers.

One of the main areas where this has been most prominent is the rise of telemedicine applications and technologies. These have enabled trial organizers and participants to communicate and carry out appointments virtually, rather than in person.

Technologies such as specialist teleconferencing solutions have drastically reduced the need for patients or practitioners to travel, which has widened the scope for potential participant recruitment. And in tandem with telemedicine, the development of an extensive range of remote monitoring medical devices capable of tracking and reporting a participant's condition has enabled the trial sponsors to access real-time data across the pool of subjects.

Monitoring devices can be specially developed units or wearable monitors that interact with a smartphone app. Heart rate and respiratory patterns are the areas where digital measures are showing the most potential for clinical trials, according to a GlobalData survey.

Digital Measures with the Most Potential for Immediate Use in Clinical Trials



Q: Which markers measured by digital health technologies have the most potential for immediate use in clinical trials?
Source: GlobalData; 280 respondents who visited the Clinical Trials Arena site during February 8-May 18, 2021

As a result of these new technological capabilities, the decentralized clinical trial model has become increasingly in demand over recent years and has been shown to remove the barriers that previously meant trial operators struggled to recruit participants, even pre-pandemic.

According to a study by the Tufts Center for the Study of Drug Development (CSDD) from 2020, the recruitment rates for studies increased from 47% in 2012 to 77% in 2019, which was largely attributed to the increased use of mobile data collection, virtual trials and other factors that increased the focus on patient requirements.

This shift to adopt a more patient-centric approach for clinical trials has also been shown to positively increase participants' engagement and ultimately their full participation for the duration.

According to a 2020 study carried out by the Economist Intelligence Unit, which compared 4,000 patient-centric trials to 20,000 traditional trials, positive results were recorded in 90% of the former, compared with just 70% in the latter. Furthermore, the study found that patient-centric trials took half the time to complete recruitment.

These findings, and the increased use of virtual trials in recent years, highlight that the decentralized model will become increasingly widespread, putting trial participants' needs at the forefront while avoiding delays and additional costs for trial organizers.

Success will be underpinned by the supply chain

For the potential of the decentralized model to be realized, it is not only reliant on the technologies that connect the medical practitioners with the patients, but also on the supply chain that underpins the delivery of the drugs and vital equipment. Yet the needs for clinical trials go further than the treatments, with considerations such as taking samples of urine, blood, and tissue from trial participants to measure how they are responding to treatment for example. All samples need to be collected and shipped to a lab quickly while meeting the necessary temperature and storage requirements to keep them intact. The other factor is that the treatments or equipment sent out may be faulty and need replacing. And the pandemic has shown just how vulnerable the supply chain is to disruption, with numerous delays and shortages at the height of Covid-19.

“One of the main learnings I see from the entire pandemic is the need for a greater emphasis on risk management and assessment in the planning of a clinical trial. Perhaps there’s not been enough consideration given to risk management in the past,” suggests Schulz.

“For example, not only the sudden surge in transportation demand for certain control temperatures, but also the general shortage of medical supplies and the availability of comparative drugs.

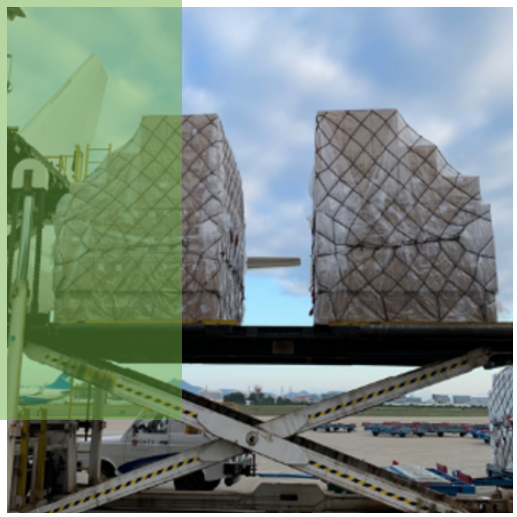
“If a clinical trial is not supported by an adequate and risk-free supply chain, we have all seen how quickly it can cause disruptions in providing patients and sites with the materials that they need to support the trial. And I think the industry has become more aware of that.”

Under the traditional clinical trial model, the supply of drugs and medical equipment would typically be a relatively linear process of transporting it from suppliers to the clinical setting. In comparison, decentralized clinical trials have reshaped both the complexity and the criticality of the logistics partner. There may also be issues with regulations that need to be resolved if the intention is to conduct a decentralized trial across different countries.

For decentralized trials to succeed, the management and delivery of medical supplies across a larger number of sites must be carried out so that medication across participants spread throughout a wider geographical area can be delivered and taken at precisely the right time. This means that even a minor shortage of supplies could impact a trial.

The new demand has given rise to a new type of specialized logistics provider within the clinical trial sector that takes on responsibility for all aspects of the supply chain and works closely with the trial sponsor to ensure the successful completion of the trial process. Under this new operations model, specialist providers must not only ensure the safe collection of the medication from the supplier and the end delivery of it to the patients' home, but they must also manage the process so that all deliveries fit within the timeframe set out within the trial.

This means that they must manage the timeframe in which the delivery is carried out, while ensuring that the integrity of each delivery is maintained throughout the process. To enable this, both the quality assurance and the traceability of each item must be tracked at each stage and any delays or potential issues should be identified quickly enough for them to be resolved.



Furthermore, the logistics providers are also charged with ensuring that there is a secure chain of custody throughout its transportation and that all relevant local and international regulatory requirements are complied with.

Some medications are also controlled substances or of high value. In hospitals, there is greater awareness surrounding security. Yet supply chain security and prevention of organized interference may be overlooked for home deliveries, which will increase the risk to the industry.

And another critical aspect of home delivery worth noting is the use of packaging systems that are both cost-effective and environmentally friendly. Sustainability is a key topic in many industries including pharma and should be taken into consideration as clinical trial processes adapt and evolve.

Real time-data and temperature tracking in the supply chain

One area where this new level of criticality of logistics to the overall success of clinical trials is most evident is the increasing need for decentralized trials to deliver temperature-controlled supplies both to patients in the form of drugs, and to trial sponsors in the form of patient samples.

In this case, the need to ensure that the supplies are stored, handled, and transported in a manner that makes certain they maintain the required temperature, increases the complexity of each stage of the process.

Under the traditional model, while cooled products would be shipped with a device to monitor the temperature throughout its transport, the reading of the device would only be taken once it had reached its end destination. As a result, this meant that any shipments that had risen above or fallen below their required temperature would only be identified at the end of the process, which ultimately caused costly delays.

Products that are transported through extremely high and low temperatures, humidity and other weather patterns must be protected to ensure integrity. It is essential for transportation partners to continuously risk-assess and select the right solution at the right time for the specific product.

Given recent advances in technology, specialist logistics providers can now ensure that both the temperature of the supplies and their location are constantly monitored in real-time with the data being relayed back to them. Consequently, this means that if at any point the product changes in temperature or there is a risk of that occurring, an immediate alert will be sent so that preventative measures can be taken to avoid any delays or problems.

This drastically reduces the likelihood of products arriving at their end destination having fallen out of their temperature range while at the same time easing the regulatory burden, with real-time data acting as evidence of compliance.

The use of real-time data and analytics has reshaped the way clinical trial deliveries are tracked and managed. These technologies have enabled logistics providers to not only ensure that temperatures are maintained, but also make any adjustments that might be required during transportation, such as with a change to the trial protocol.

Furthermore, it also provides a real-time overview of the location of supplies, which enables a quick response in the event of any shortfall in supplies or delays to shipments. As a result, this new data-led and technology-focused approach to managing the clinical trial supply chain has shown that the potential benefits of decentralized trials can be realized.

“There’s no point in having a supply chain that isn’t robust and doesn’t meet the needs of the sponsor or customer,” adds Jonathan Bracey, EVP of Corporate Development at Tanner Pharma Group. “Ultimately, we work to protect the product and protect the patient because that’s what it’s all about. That’s what the sponsor needs, and the patient deserves.”

How Tanner Pharma Group can help

Tanner Pharma Group has a dedicated Clinical Trial Solutions (CTS) division, which is at the forefront of this specialist field. The division partners with pharma companies and clinical research organizations (CROs) to help develop and manage clinical trials through product sourcing, supply and logistics.

Tanner offers GDP-compliant distribution of pharmaceutical products to and from countries around the world, and a depot network of GDP-compliant facilities, with 2°-8°C and frozen capabilities. With over 100 employees on three continents, the team has extensive experience delivering medical products within short timeframes and managing all logistics and storage demands, with a global network of validated and trusted partners, couriers, and freight agents. The company provides services to customers in the CRO, pharmaceutical, and biotechnology spaces among others

Tanner has leveraged its strengths in the clinical supply chain throughout the years to enable drug trials to go ahead, while also embracing new technologies. The Tanner team is continuously evaluating ways to optimize efficiencies and offer innovative solutions for partners throughout the clinical trial timeline.

Other aims of Tanner's dedicated CTS division are to:

- Forge partnerships with CROs to offer services that better integrate clinic information with that of logistics and supply chain
- Procure IT hardware and wearables for trials, providing technical support and maintenance when defective
- Offer an end-to-end supply chain for timely delivery to decentralized sites for patients
- Remain ahead of the curve with cold chain technology
- Offer home nurse support for product receipt, administration, data capture, and monitoring through collaborating with partners

Whether it's procuring comparator drugs, packaging, labelling and kitting, or distributing drug products and supplies to hundreds of clinical trial sites, you need a smart, agile partner with the ability to manage complex supply chains and global logistics.

By choosing Tanner Pharma, you gain:

- Access to a dedicated, experienced team
- Teams based in multiple time zones, accessible 24 hours a day, 7 days a week
- A technology platform that tracks product, timelines, and other logistical details
- A cost-effective solution with a high-touch service
- Unwavering commitment to quality and compliance

For additional information please contact ctsinfo@tannerpharma.com

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