

Completing the Puzzle: Technology in Decentralised Clinical Trials

The COVID-19 pandemic has pushed decentralised clinical trials (DCTs) to the forefront of clinical research as companies have adopted innovative ways to ensure trial continuity amid site closures and social distancing measures. From telemedicine and wearable sensors to home health visits and direct-to-patient drug shipments, the increased flexibility and new capabilities afforded by home-based DCTs have largely been embraced by patients, sites and sponsors alike.

While opportunities abound, practical implementation of DCTs requires a skilled hand to create and deploy an effective strategy that integrates patient feedback, site preferences, regulatory expertise and the relevant tools and services into a coordinated DCT programme. Clear and thoughtful planning combined with stakeholder input are critical to informing DCTs, as the smallest of details can influence patient perceptions and behaviours. For example, in some cultures there is a degree of secrecy surrounding illness and home nursing is not welcomed, so finding neutral venues – such as nearby hotels or pharmacies – is proving to be a viable alternative.

Equally important is the DCT technology itself, which must be clear, simple and intuitive for patients, sites, depots and CRAs to use for telehealth visits, eConsents, and data transfer and access. When these processes are seamlessly enabled, study compliance is high and data quality is optimised – both essential elements of successful DCT implementation.

In this article, we will discuss new DCT technology platforms and best practices for employing them across the clinical trial continuum, as well as the growing regulatory acceptance of remote and real-world data that are fuelling widespread use of DCTs across the industry.

Technology Connects the Pieces

Running a DCT can be like assembling a jigsaw puzzle, connecting the various

elements such as direct-to-patient drug shipments, sensors, telemedicine, patient apps and home health visits to piece together a complete view of trial components. Companies are increasingly turning to smartphone apps to integrate protocol elements on a single technology platform to simplify the process for patients and sites, which can sometimes prove challenging in remote or rural areas with slow or absent internet access.

To overcome this challenge, new technology platforms enable data to be stored locally on a user device, then subsequently uploaded to the cloud when internet connection becomes available. Such devices and their preprogrammed apps also allow for video calls if the user has intermittent windows of internet access, thereby keeping patients connected to sites from afar. In this respect, DCTs have actually removed barriers to clinical trial participation for many patients who would otherwise be too far from physical sites to participate.

While each DCT technology platform has its own customisable features and functionality, the most effective ones provide the full range of capabilities required to satisfy the varied requirements of all decentralised trials – among them, electronic clinical outcome assessment (eCOA), eConsent, telemedicine, notifications/alerts and patient engagement and education.

Having a flexible approach using a pre-validated and vetted toolbox from which to pull components of different shapes and sizes, and plug them into the DCT equation, ensures there are no gaps when running trials across varied protocols, patient populations, disease states, geographies and study designs.

Selecting the Right Technology Vendor: Best in Class versus Home-grown

Choosing the right vendor partners requires a deep dive into their respective capabilities and proven successes across a range of studies. A vendor that has run hundreds or even thousands of trials has thoroughly tested their software under a

broad range of conditions and has worked through the inevitable kinks along the way, vastly reducing the potential for technology glitches or failures throughout the trial.

Moreover, the very process of ongoing vendor vetting is a valuable exercise. Staying abreast of the latest technology options allows for rapid selection of fit-for-purpose partners to accommodate the varying needs of specific protocols, sponsor preferences, and unique patient populations. Lastly, continuous vetting allows the freedom to test multiple technology solutions simultaneously without investing in a costly product that may prove to be a mismatch for you or your customers' needs. This approach has proven particularly valuable in the face of the pandemic, in which an instantaneous shift to remote monitoring and electronic documents has necessitated quick decisions about moving to cloud-based platforms to securely upload confidential documents and conduct source data reviews.

Behind-the-scenes Clinical Supply Logistics and Automation

One of the most essential and perhaps least recognised components occurs behind the scenes in the majority of clinical trials, whether traditional, hybrid or fully remote. Informally known as RTSM or IRT – randomisation trial supplies management (RTSM) system or interactive response technology (IRT) – this automated system randomises subjects in a trial, documents patient visits, allocates medication to patients, and automates supplies and resupply to depots and sites. In short, RTSM systems are customised for each respective trial to ensure the right medication gets to the right patient at the right time.

Because it uses a forecasting algorithm to manage provision of clinical supplies, including medications, RTSM systems can instantly respond to new input and adjust trial logistics accordingly. It is the infrastructure behind the technology, though, that enables seamless and accurate operations. When enrolment rates are different than expected (faster or slower), or in times of crisis – such as the recent pandemic and natural disasters – a flexible



RTSM system allows study teams to adjust clinical trial supply strategies and therefore maintain patient access to study medication. For example, an RTSM system might be reprogrammed to frontload warehouses and reassign medications shipments directly to patients to mitigate supply chain risks in anticipation of site closures. Successful deployment of this approach has been a critical part of DCT implementation during the pandemic.

DCTs and the Regulatory Process

COVID-19 has magnified the urgent need for new drugs and more accessible and patient-friendly ways of evaluating them. The quest for effective COVID vaccines and treatments has condensed two-year development plans into months with the introduction of innovative technologies, more flexible regulatory guidelines and new emergency programmes to expedite testing and approvals. These rapidly evolving regulatory guidelines require an experienced, global regulatory team to navigate the wide variation of in-country requirements and the expansive geographic reach of DCTs.

Simultaneously, greater reliance on remote subject enrolment, remote data collection and the use of real-world data (RWD) is paving the way for novel trial designs, such as synthetic control arms. This approach utilises previous trial outcomes and real-world data such as electronic medical records, disease registries, claims data and wearable devices to statistically create the control arm, instead of recruiting and assigning actual patients to a control arm.

Regulatory authorities are increasingly accepting these types of innovative trial

models, which is speeding trial timelines and, in turn, drug approvals. This shift was already underway but is now accelerating across the globe as health authorities align their regulatory guidelines to make submissions faster, more efficient and less costly.

Among the many examples, sponsors can now apply in parallel to the FDA and EMA for orphan drug designation using the same data and a single common form, and the Eurasian Economic Union (EAEU)'s new guidelines allow the five member states to operate a national medicines market in a single space. This means they can apply for registration of medicines and their release in all five markets simultaneously under common procedures and reduced administrative costs.

Health authority inspections and regulatory meetings are now being conducted virtually or with careful social distancing techniques. Many health authorities are also accepting soft-copy versions or non-legalised documents in place of physical copies, with the provision that the physical or legalised copy is provided when feasible. Timelines have become more flexible, particularly in countries where an in-person submission appointment is required, to allow for adequate protection of agency staff and visitors.

Additionally, the pandemic has highlighted the need for more robust investment in electronic systems and software programs. Using cloud-based systems allows for multiple users to access and edit documents simultaneously, thereby simplifying document management and control while also allowing for real-time discussion and collaboration between team members.

Technology and the Central Site Model

Technology has the power to unify people, processes and data in a single location. Even before the pandemic struck, the industry began exploring the potential of the central site model, in which a remote team of investigators, study coordinators and nurses enrol patients and oversee their participation. Technology such as telemedicine and patient apps allows the central site to remotely collect, monitor and evaluate study data. The benefits of a central site model include cost-efficiency, real-time data access, reduced variability of data, a larger geographic reach and greater diversity of trial participants.

However, a host of complex and nuanced patient and data privacy issues complicate the tactical execution of central site models. First, widely varying laws and regulations in each region or country dictate access to and transfer of patient information. Select countries, for example, require data to reside in the country where it was obtained, thereby complicating the process for data transfers to a central site located outside the country. Second, sponsors, sites and study teams must carefully delineate in advance how patient and data privacy will be protected within technology systems to ensure the right people have the right access at the right time. Third, the sponsor must clearly define – in accordance with in-country regulations – what comprises personal data (e.g., anonymised data may or may not be considered personal data). Sponsors, CROs, vendors and sites often enlist a privacy officer to navigate these and a multitude of related challenges and ensure best practices that protect patient privacy.

Keeping Patients First

Among technology's greatest assets is its ability to expand access to far greater numbers of eligible patients around the world. No longer is geographic distance a barrier to clinical trial participation. Telehealth visits and home health nurse visits are replacing many in-person site visits, while wearable monitors transmit data directly to the cloud. Patients can even obtain their own blood samples

using a novel home device that allows simple collection and shipment to a site or lab.

Patients are embracing these decentralized approaches because they reduce their burden of travel, financial impact, childcare challenges, and time away from work or school, especially for patients and caregivers who live far from a study site. Early in the pandemic, these

benefits played an essential role in clinical trial continuity for patients whose medical conditions could not wait for the pandemic to end. Today, DCTs are critical to safely evaluating preventive and therapeutic options for COVID-19. Looking toward the future, the adoption of DCTs closely aligns with the industry's collective commitment to designing clinical trials *with* the patient and *for* the patient to accelerate the development of new therapies.



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Rosamund Round

Rosamund is Vice President of Parexel's Patient Innovation Center and spends her time devoted to simplifying the patient journey in clinical trials. Focused on the reduction of geographical, financial and practical barriers to study participation, Rosamund is excited by the industry shift towards a truly patient centric approach.



Nick Darwall-Smith

Technology executive with 28 years in clinical research and development, including R&D Operations, IT and consulting, focused on enhancing the patient experience and optimizing sites and clinical trial teams through the right technology enablers.

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