

So, You Want to Run a Decentralised Clinical Trial...

Interactive response technology is proving essential to the clinical trial industry, helping businesses keep up with eClinical trends in a variety of traditional and modern trial designs

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With the pandemic having catapulted decentralised clinical trials (DCTs) from a pipedream to a reality, it's time to think carefully about what's actually involved – particularly as it relates to the interactive response technology (IRT) system supporting virtual and hybrid trials. When contemplating a trial to be conducted virtually, either in its entirety or in part, sponsors should be aware of all the implications for the IRT and how it will randomise patients, raise drug shipments, and track drug assignments, dispensing, and returns. A new set of processes, communication pathways, and safeguards must be in place to ensure patient safety, data integrity, and regulatory compliance, not to mention smooth and efficient operations.

The IRT functions required to support DCT elements should be fully discussed and carefully considered as the protocol is being developed. While much is possible with a sophisticated and flexible IRT system, not everything that's possible is advisable in a given situation. It's important to be able to distinguish functionality that's essential from what is only nice to have or even what may add unnecessary complexity.

The Key to Success in One Word: Flexibility

Notwithstanding all of the many benefits of a DCT model, it is likely that most DCT trials of the future will not be conducted 100% virtually, but rather will incorporate various DCT aspects, to one degree or another. Such a hybrid approach is often necessary due to:

- **Patient preference:** Patients may prefer to see the investigator in person, face-to-face for at least some of their visits
- **Protocol necessity:** Patients may need to be seen on-site in certain instances for drug administration, assessments, or procedures that cannot be performed remotely
- **Regulatory requirements:** Varying regulations among participating countries may prohibit the use of certain DCT aspects
- **Medical necessity:** The need to see a patient at the site may change based on the patient's medical progress/deterioration
- **The type of investigational product:** Not all types of investigational products are good candidates for direct-to-patient (DtP) shipment. Shipping drugs to patients may not be possible

with controlled substances and with drugs requiring preparation or strict temperature adherence, among other criteria

Given these variables, the IRT system must, above all else, be flexible. Because DCTs often need to operate differently by geography (region, country, state), by site, and even by patient, the IRT must have the capability to adapt to different DCT components/systems involved, as well as to account for varying methodologies around drug assignments, shipments, and returns.

What Flexibility in an IRT Really Means

Ideally, the IRT functionality needed to support DCTs – to whatever degree – will be available as configurable options in an IRT system to support both initial study design assumptions, as well as any mid-study changes. This will not only factor into the system cost, but should mean that gathering the requirements and the system-building steps for an IRT to support a DCT will take no longer than for a traditional site-based trial.

The best and most flexible IRT systems will be able to accommodate:

- **Patient Safety:** The system must, without exception, be able to assign the right drug to the patient, regardless of whether the drug will be dispensed and administered at the site or at the patient's home
- **Sponsor Control:** The IRT must be able to accommodate a variety of hybrid trial designs to maximise the benefits. To prevent so much variability from becoming unmanageable, the sponsor should have control over the amount of leeway given to sites and patients – potentially per visit. Ideally, sponsors are given the ability to 'flip the switch' to enable various aspects of DCTs to apply at the study, country, and/or individual site level. Freedom for sites to set or change their preferences can also be enabled/disabled
- **DtP Shipment Options:** For patients completing virtual visits requiring drug assignment, various DtP shipment options may be employed. Unlike with site visits in which the drug assignment is made from inventory stored at the site and directly dispensed to the patient, DtP shipments introduce additional workflow options. In the case of site-to-patient shipments, the IRT will still make the drug assignment from the site-specific inventory or create a patient shipment record for the assignment. Other options could involve depot-to-patient or pharmacy-to-patient shipments where the IRT will assign patient medication from a central stock and generate the patient shipment request
- **Shipment Coordination:** The ordering process – starting with the investigator's order and ending with the delivery of the drug to the patient – must take into account the time involved in physically transporting the drug, the need to coordinate the patient's receipt, and, if applicable, having a healthcare professional at the patient's home to administer the therapy. As the IRT generates the shipment request, multiple parties or systems may require notification of each shipment to the patient
- **Personally Identifiable Information:** DtP shipments introduce the need for patient-specific shipping information which historically has not been collected or stored within the IRT; traditionally IRTs have been used to hold only the data needed for screening and dosage administration. The eClinical solutions involved must ensure data protection, remain in compliance with the appropriate regulations, and ensure proper safeguards are in place. This information is likely already stored elsewhere, and there is no need to duplicate it the IRT. With the growth and shift to DCT, an IRT partner needs to be flexible and able to integrate/work with other systems
- **Temperature Management:** When temperature-sensitive drugs are shipped to sites, site staff can upload the package's temperature data directly into the IRT system and get an answer in real time as to the drug's viability. This prevents the assignment of supplies that are unsuitable for use based on these temperature checks. When preassigned drugs have been delivered to patients' doorsteps, there must be safeguards in place to prevent dispensation/use of non-temperature compliant material. The process and technology should be both easy for the patient and healthcare professional (or courier) to use and able to send out the proper notifications or initiate the appropriate response to mitigate risk
- **Product Replacement:** The IRT must accommodate unscheduled occurrences at the patient's home, such as the need for product replacement in the event of product loss, damage, or being unsuitable for use due to temperature excursion. The system must have the flexibility at the site or patient level to change between in-site or at-home shipment designations for requests to replace and ship a patient's assigned drug
- **Chain-of-Custody Tracking:** Clinical trial drugs must be tracked from the point of manufacture to the point of destruction, with records kept of all supply activities in between (such as shipment, assignment, and dispensation). The IRT is key to allowing real-time visibility to, and reporting of, these study drug activities. With the introduction of decentralised workflows involving DtP shipments, patient activities must be captured in order to efficiently and accurately track the full chain of custody
- **Reverse Logistics Management:** Aside from the logistics involved in retrieving kits from a patient's home, the IRT system can be leveraged for the initiation and tracking process to record the return, reconciliation, and destruction of all kits (whether used, unused, or damaged)
- **Complex Innovative Designs:** A DCT model can be an advantage in recruiting for master protocol, umbrella, basket, and platform trials. In umbrella designs, DCTs can reduce the patient burden in what may be an already small patient population, and the IRT system should be able to handle the added layer of complexity that's introduced from having multiple different drugs under study
- **Integration With Patient-Facing Applications:** Perhaps the most important capability within the IRT is the ability to integrate easily with other systems being used across the study's eClinical ecosystem. Decentralised trials are expanding the number of systems in which the IRT will interact to include DCT platforms and patient engagement applications with features such as eConsent, electronic clinical outcomes assessment (eCOA) electronic patient reported outcomes (ePRO), single sign ons, remote screening, and telehealth. All are critical to the success of virtual and hybrid trials. Today, IRT integrations are commonplace and have proven

to be an effective way to improve data quality and streamline study execution by reducing redundancy. However, with the introduction of more direct patient involvement, it will be more important than ever to ensure that the technology ecosystem is fully integrated and efficient, as well as that there are support and oversight processes in place to resolve issues quickly and effectively

No IRT Is an Island

Designing a DCT or hybrid trial – and building the IRT system to support it – must be a collaborative effort between the sponsor, the various DCT service providers, and the IRT partner. Discussions about the options and the pros and cons of each should begin as early as possible in the study design. Decisions about which DCT aspects to adopt and how technology can enable virtualisation should be made with the goal of improving the patient journey and easing the burden on trial sites. This will ensure that the trial will deliver the best experience possible for all participants and technology users.

Those involved in designing, conducting, and supporting trials that are either completely or partially decentralised will need to maintain an open mind throughout the study design and IRT system build. Pre-conceived notions of how a trial should run may need to be adjusted based on the realities of site and patient preferences, and the way work and information flows may be different. For instance, many of the communication pathways built into the IRT and the automated checks that have been designed with sites at the centre of the trial have to be rethought, with the goal of achieving simplicity and reducing the number of steps involved. For instance, something as simple as automating patient creation in the eCOA system when a patient record is created in the IRT reduces a step for the site as well as increases data quality.

In terms of the trial technology, sponsors should aim for the user experience to be seamless and

intuitive for all involved. Sites, for example, should have a single log on as they work with the various eClinical platforms, and the workflow should be smooth, logical, and guided between the platforms. Patients, too, must have a single interface for their role in the trial, whether that be e-consent, ePRO, telehealth, or recording drug dispensing activities.

Given the need to accommodate site and patient preferences and to keep processes simple, not all that can technically be incorporated into an IRT necessarily should be. Just because a function is possible doesn't mean that it's preferable. In deciding what DCT elements and system enhancements will best serve all stakeholders, it's best to work with an IRT partner who understands what is imperative vs what may be unnecessary. The consulting IRT partner should be willing to say, "Of course, we *can* do that, but the question is, *should* we?"

This argues for selecting an IRT provider who is an expert in clinical trials and operating in a GCP environment, rather than 'merely' a technology provider. The IRT vendor should have a support model in place capable of responding to questions or issues around the clock. The best protocol design and supporting technology configuration will come from an IRT partner who has established relationships with the other vendors in the DCT ecosystem (DCT platform providers, distributors) and who can work collaboratively with them.

DCTs, designed and conducted properly, offer the possibility of improving patient centricity by lessening the burden of trial participation, which, in turn, speeds patient recruitment and strengthens retention. The IRT systems that support DCTs must be properly configured to ensure that patients are treated per the protocol requirements and that all trial processes are efficient and compliant. Proper configuration will require system flexibility (the ability to adjust workflows to accommodate all variations of hybrid trials), a high degree of experience

on the vendor's part, and the ability to easily integrate with the other technologies that make up the eClinical ecosystem.



As the Head of Strategic Partnerships and Alliances at **Almac Clinical Technologies**, **Mike Hutton** oversees several key clients along with developing new and exciting business, partnership, and alliance opportunities in the EU and the rest of the world with Almac's IRT solutions.



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