Effective Use of IRT in Decentralized and Hybrid Clinical Trials

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The increasingly complex protocols, disparate patient populations, and evolving needs of modern clinical trials have necessitated solutions geared toward simplifying, digitizing, and democratizing studies. Patient-centric trials, such as decentralized clinical trials (DCTs) and hybrid trials, have all emerged as potential answers to this complexity, owing to their flexibility when compared to traditional on-site studies. Yet despite the advantages of increasingly remote, technology-supported clinical trial models, there remain a number of hurdles to their widespread adoption. One of the central challenges to enabling these trial designs lies with the technologies developed to support trial logistics, drug distribution, and patient randomization.

Interactive Response Technology (IRT) is likely to play an increasingly significant role in addressing the complex challenges of drug management and distribution for decentralized and hybrid clinical trials. IRTs are designed to help trial sponsors manage the distribution of medications, forecast trial supply, and integrate workflows with other technology platforms. As the primary system for managing a trial's patient randomization and clinical supplies, having an effective IRT can serve to simplify trial oversight and management. Establishing an IRT that allows for right-sized logistical management and secure patient oversight requires an understanding of the sponsor's clinical protocol and defined business processes to develop the proper data integration and workflow optimizations necessary for trial success.

Understanding the Importance of IRTs (and Getting Them Right)

Typically, the utility of IRT is two-fold, functioning as both a trial supply management technology and as a tool to support patient randomization. The IRT generates information based on patient data to inform trial logistics, whether related to the volume of drug substance that must be shipped to a repository or clinical site, or to determine which patients are set to receive a treatment and when. This contrasts with traditional trial supply management, which has historically been performed by individual personnel assigned a set number of trial participants to oversee manually. As trials continue to grow in number and scope, the value of an IRT for a given sponsor may compound, minimizing the number of personnel devoted to managing logistics and reducing the potential for error in the process.

Within the larger framework of a trial's management, IRTs are very niche. Yet their importance in the overall administration of a trial cannot be overlooked – an IRT, poorly calibrated for a trial design or logistical paradigm, can serve to invalidate a trial. These technologies are nearly always the only systems that house unblinded data, creating the potential for patient privacy issues if adequate safeguards are not put in place to prevent unblinded data from interacting with other platforms. This reality has likely served to stall complete adoption by the industry (especially in early phase clinical trials) which has understandably taken a conservative approach to innovation related to trial management. But adopting an IRT, especially when incorporated before subsequent supporting technologies, can help improve the overall interoperability of these systems and reduce the potential for data breaches.

There are, of course, limitations to an IRT's reach. When considering DCT and hybrid trials, many drug manufacturers are unwilling to fulfill direct-to-patient shipments of clinical supplies or will only do so at a significantly higher cost, necessitating the typical workflow wherein therapies are shipped first to a clinical site before going out to a patient. An IRT cannot circumvent this necessity. Likewise, while IRTs can support patient-centric protocol designs, such as home-based visits, patient preference is paramount: patients may prefer to receive their treatments in a clinical setting, and a useful IRT platform will be flexible enough to accommodate this preference. Technologies such as IRT are not intended to supplant clinical oversight or circumvent provider intervention; retaining patient interaction with a doctor or nurse where it may be necessary or judicious is still a crucial element of trial management. For trials with a large number of patients, less invasive treatment modalities, or otherwise inaccessible participant populations, IRTs can relieve site-related burdens.

Integrating IRT: When (and Whether) to Do It

One of the chief advantages conferred by IRT is cost savings. While many sponsors may elect not to implement IRT in the early phases of a trial to put money toward other considerations, the use of IRT for larger Phase 3 trials in particular can serve to greatly reduce the human intervention necessary to perform trial management. It can also improve its execution simultaneously, preventing drug waste and supply delays. This savings can extend to early-stage trials, should sponsors be willing to invest in IRT early – this, coupled with the advantage of integrating IRT sooner in a trial management paradigm, can help sponsors foster an interconnected system of technologies optimized to support their unique trial needs. All the activities that IRT is able to automate, multiplied over hundreds, thousands, or even tens of thousands of patients, can create significant cost savings for sponsors as a trial progresses.

Trial randomization is another key function of IRTs, one that can offer trial teams simplified, optimized double blinding that is more secure and more calibrated than traditional methodologies. Additionally, trial designs have become more complex, and randomization schemes may be adapted midstream based on interim analysis data. For example, a Phase 3 oncology trial may be randomizing at a 2:1 ratio, with two participants receiving the study drug for every one participant receiving a currently approved Standard of Care (SoC). If the interim analysis data indicates that participants are showing a more positive response to the study drug than the SoC, a sponsor may decide to alter the randomization scheme to a 3:1 ratio – ensuring that more participants have a chance to receive the study drug. Adaptive randomization schemes using manual methods would be laborious, if not impossible. In contrast, a secure, digitized, flexible randomization initiated by IRT can better safeguard patient information, reducing bias and minimizing the potential for human error. It also can handle complex algorithms with ease.

Having an IRT platform that features the capabilities a trial needs is one thing; finding a supplier with the expertise to help troubleshoot IRT for a given trial is just as important. For example, a sponsor may be exploring IRT for a rare disease trial being conducted in as many as two dozen separate countries. While IRT may be in place to sort out the surface logistics of such a paradigm, having a partner able to vet the feasibility of automating drug shipments that align with the regulations of more than 20 countries can help determine whether IRT is even a viable solution for the trial in question. Ultimately, concepts such as direct-to-patient shipments utilizing IRT are unlikely to coalesce soon, hindered by necessary oversight and regulatory considerations.

In the end, a successful IRT is automated to exactly the right degree, with the flexibility needed to adjust for protocol changes, participant loss, and other variables that can impact trial management. Furthermore, ensuring that the right data integration strategies are in place to link IRT to electronic data capture (EDC) and other relevant technologies is critical. In the right setting, IRTs can help trial organizations easily manage shipping, returns, and storage, including automated, predictive, and blinded patient shipments. Additionally, IRT can afford sponsors improved trial randomization, both simple and complex, as well as improved data speed and accuracy, reducing investigator burden and optimizing workflows.