The Central Role of Interactive Response Technology in Today's Clinical Trials

Introduction

The clinical trial process has been undergoing substantial change in recent years – even more particularly in the past 12 months. The first signs of the evolution began in the 2000s when protocol complexity significantly increased. In the ten-year period from 2005-2015, the number of protocol endpoints increased by 86% and the number of planned subject visits increased by 25% (Ref: Tufts). A second key change is the move towards a patient-centric approach to trial management. In a recent ICON survey, 30% of subjects indicated a preference for hybrid or decentralised trials, with a further 33% indicating no preference to remain with the traditional site-based model. Thirdly, drug development costs have increased by 145% in the past ten years, with the average cost of bringing a single drug to market now standing at $2.6 billion. Thus, sponsors and their partners have been under increasing pressure to accelerate timelines in the clinical trial process and subsequently reduce costs. The demand for timeline reduction has been further driven (and thankfully realised in many trials), with the onset of the global COVID-19 pandemic.

The use of technology is a key enabler in this clinical trial evolution. Here we examine the critical delivery elements required from **Interactive Response Technology (IRT)** providers to support this evolution, with particular focus on the needs of COVID trials.

What is the Role of IRT?

In a clinical trial, the selected IRT must provide an effective and efficient technology solution for managing subject enrolment and randomisation, as well as enabling the effective management of the trial drug supply and dosing regimen. The platform must deliver some standard elements including a user-friendly and stable interface. Regardless of trial complexity, the IRT must offer solutions to support all dosing algorithms and it must be supported by a robust information technology infrastructure to enable secure and rapid access for all system users. The IRT is always the first to know. It is the first step for the investigator in triggering the subject enrolment; the data created is required to feed many other critical sources in a real-time fashion.

What Key Elements must an IRT Provider Deliver?

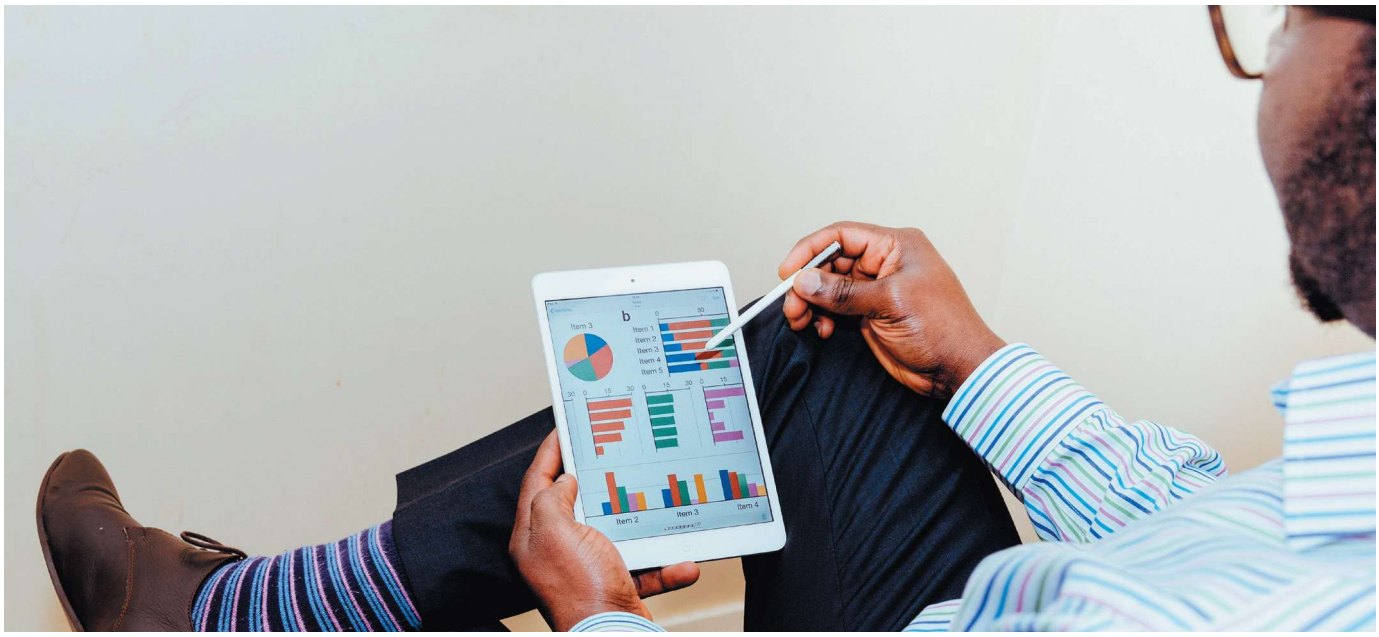
According to a recent publication from Industry Standard Research (ISR) published in August 2020, the top five criteria for sponsors when selecting an IRT provider are: (1) ability to integrate with EDC, ePRO, CTMS and other data systems, (2) startup timelines and speed of build, (3) flexibility in study design, (4) low cost, and (5) integration with sponsor drug supply. This ISR report indeed hits many of the important delivery elements required from an IRT solution. In recent COVID trials, these five elements were certainly of huge importance.

(1) **On integration:** IRT solutions must have strong integration capabilities with the ability to feed study data in a real-time fashion to other systems. This generates efficiencies and enables rapid decision-making. The IRT platform is vital for many stakeholders including site users, data managers, clinical supplies managers, and statisticians as well as the sponsor and broader study team. In recent COVID trials, data integration allowed for real-time data transfer from the IRT to the EDC, sending screening and randomisation information to the EDC as these transactions occurred in the IRT. The automation of this data entry provided an efficient way for the sponsor and clinical team to view data in the EDC in real time and relieved the sites of the burden of entering the same data across multiple platforms.

(2) **On timelines:** With COVID-19 studies in particular, the need to expedite timelines is critical. In a typical IRT situation involving design, development and validation, timelines for a study build of average complexity range from 10 to 12 weeks. With COVID trials, IRTs are often needed in four to five weeks. In order to meet such timelines, IRT teams must be able to operate in an agile fashion. This means that study requirements are often still evolving when development work has commenced. This presents a challenge to the team with a high demand for rework when requirements change. Development and validation must be completed to an extremely high standard with zero quality findings. When the system is provided for user acceptance testing, minimal findings should be identified. With the growing demand to expedite timelines, not just for COVID trials, IRT providers must move towards decreased build times for all studies.

(3) Flexibility is critical and the ability to adapt the IRT mid-study is vital as subject and protocol changes need to be accommodated whilst the trial is ongoing. Many protocols are now designed with multiple cohorts, in which doses are still to be determined. Thus, the IRT must be able to accommodate such changes with no interruption, whilst maintaining complete fluidity of the original study design. Additionally, throughout the duration of the trial, the IRT must enable the project teams to open and close screening, randomisation and resupply in a real-time fashion on the project, country, and/or site level. End users must have the ability to adjust initial, trigger, and resupply quantities in real time to ensure sites have adequate IP stock on hand throughout the duration of the trial.

(4) Costs must be managed carefully and sponsors must be informed promptly of the cost impact of any protocol or scope changes. This should be a standard feature of all IRT providers and again, must be done at high speed, particularly during fast-paced COVID trials.



(5) Integration with the sponsor or third-party drug supply is vital to ensure that drug supply is where it is needed, when it is needed, in the correct quantities, thus enabling maximum enrolment on to the trial. IRT providers must play a collaborative role with IP manufacturers and distributors, as well as have the ability to rapidly pivot to varying enrolment needs. More broadly, relating to decentralised trials, flexibility is key. During the pandemic, IRT providers have been required to collaborate strongly with all drug supply chain stakeholders to fulfil needs where necessary, to provide IP direct to patients' homes.

Additional Critical Elements Based on COVID-19 Experience

Based on recent COVID-19 trials, additional factors should be considered when selecting IRT providers. Most important amongst those are:

(1) **IT Infrastructure**

In COVID trials in particular, an IRT platform and the supporting infrastructure must be able to withstand significant demands. Trials typically involving many months to enrol hundreds of subjects are now not the norm. IRT solutions must hold up to the stern test of enrolling as many as 30,000 subjects in a four- to six-week period. This must be achieved in an extremely secure system, with zero waiting time. Frequent and diligent monitoring of server loads and application performance in a timely manner is vital and in recent experience provided important recommendations for optimising the system on various levels of the technology stack to assist with transaction and report load times. This ensures thousands of randomisations can be supported in as little as an hour.

(2) **Team Experience and Expertise**

With trials moving at a fast pace, critical thinkers and decision-makers must be on hand to support the needs of the broader study team and to provide solutions for oft complex challenges including design solutions. This is not a time for rounds of discussions and drawn-out decision-making processes. Key team members must have the expertise to make informed and educated decisions at great speed and with confidence. Therapeutic expertise is important and the ability of an IRT team to work hand in hand with their clinical project management counterparts can have a significant and positive impact. Teams with years of IRT experience are important in this regard, with access to a well-structured management system who can step in to support at short notice.

(3) **24/7 Cover and Ability to Rapidly Manage Site and Subject Needs**

A 24/7 call centre is a standard offering with most IRT providers. This, in COVID trials, is of course also critical, but it must be supplemented with appropriate levels of support to ensure questions can be answered rapidly and data changes can be made around the clock and around the globe. Emergency un-blinding is often required in a matter of minutes. Thus, it is critical to supplement 24/7 support with experienced team members including application support and other subject matter experts. This can significantly maximise prospects of enrolling subjects into a trial.

Conclusion

Careful selection of an IRT provider that can partner with sponsors to provide a robust and flexible IRT platform, with a team of experts to support it, is vital in today's clinical trials, none more-so than COVID-19 trials. IRT professionals are extremely dedicated to their cause, and choosing an IRT partner with the appropriate technology, expertise and infrastructure can make or break a trial's success.

Michelle Lynskey

Michelle Lynskey is Global Head of Interactive Response Technology and Clinical Supplies Management at ICON plc, leading the delivery of ICON's proprietary IRT solutions and CSM services. Michelle's prior experience includes operational and client oversight roles in ICON's Central Laboratory, as well as several years' experience in Strategic Project delivery, including technology innovations. Michelle holds a B.Sc. in Biotechnology, B.Sc. Technology Management, M.Sc. Science Communication and she is PMP and Lean Six Sigma Black Belt Certified.