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Improvements to Study Startup Underway

Advanced Technology Solutions Key to Efforts

By Karyn Korieth

Sponsors and CROs have widely adopted technologies to manage ongoing clinical trials as part of efforts to improve efficiency and performance in the conduct of clinical trials, yet purpose-built tools for improving study startup have been largely overlooked.

Organizations have primarily managed study startup activities with spreadsheets, internally developed solutions, modified clinical trial management systems (CTMS) or various standalone technologies. For site identification, a critical step in study startup, studies have found that sponsors have traditionally relied on low-tech approaches that are non-evidence based.

"There is no one place in a technology product where you can check on the status of all of the pending items that enable the SIV (site initiation visit) and the green light for screening," said Jeff Pohlig, chief operating officer, Global Site Network, Bioclinica Research. "We had to grab the bull by the horns and take responsibility for managing with all three parties – the site, sponsor and CRO. From a site perspective, it's been a real manual process that requires active management and great communication."

Aside from sponsors and CROs, many principal investigators (PIs) also are dissatisfied with startup technologies, reporting that the new tools can be cumbersome, increase investigative site workload and contribute to study conduct inefficiencies. Sites are already required to manage an average of 10 clinical trial software applications – that don't interact with each other – simultaneously, according to a 2016 CenterWatch study of 250 investigative sites.

Adding to the problems, adopting a new startup system requires a significant amount of effort – the creation of new SOPs, unique logon instructions and staff training, and sometimes duplicative work for site staff. Online document exchange portals, for example, can give investigators a central place to access all documents and adds some transparency and accountability for document submissions. Yet sites need to register with each portal and often need to manually re-enter information into the new system from their CTMS or other eClinical software.

"We have a confluence of different technologies that don't interface well and the industry seems reluctant to standardize on any sort of technologies," said Nicolas Cindric, chief executive officer of PharmaSeek, an investigative site network comprised of more than 240 sites and some 1,000 principal investigators. "That challenge won't be solved anytime soon."

A breakdown in communication between study sponsors or CROs and sites about the use of startup technologies also can lead to confusion. At PharmaSeek, Jill K. Shilbauer, director of Network Operations, said she didn't learn about a CRO implementing a new purpose-built startup technology for a clinical trial until she began receiving email notifications about tasks she was required to complete.

"We are going to see more of a transition to these systems, but it remains to be seen whether they are going to be a helpful tool or whether it's going to add on additional work," said Shilbauer. "The key is the upfront communication and training to the sites and others who are in that process."

Data Challenges in Site Identification and Selection

Traditionally, organizations don't use a single source of data to identify trial sites, but rather employ a combination of non-evidence-based approaches that rely on proprietary databases, personal networks and recommendations from internal team members or CRO partners for site selection.

But these approaches to site selection don't address challenges associated with high investigator turnover rates across the industry. Plus, almost a third of investigative sites in a typical multicenter study are new to the sponsor or CRO, which means they wouldn't appear in existing spreadsheets or databases.

In recent years, sponsors and CROs have sought to incorporate tools that use data-driven metrics and site scoring algorithms to assess site-level performance and used commercially available or shared industry databases to aid investigative site identification. But many databases include self-reported feasibility data from the sites and metrics from CTMS or eTMF systems without independently validating the information.

Databases, whether proprietary or shared, also typically lack quality and performance metrics that could improve site selection processes or provide insights into how they could be expected to perform in the future.

"Some of the things organizations are tracking do not have to do with quality.

They can get an idea of the protocols that a PI has been on, the certifications of the PI or if they have any actions by the FDA," said Gina Robles, owner and director of the California-based Long Beach Clinical Trials research facility and co-founder of SiteScore, a software application that allows study monitors to evaluate quality and quantity metrics at an investigative site and generate an overall score. "There is no way to know how many protocol deviations there were at a site or how long it took to do data entry or enroll the first patient. Those things are vital to study startup."

Investigators also have expressed concerns that databases contain inaccurate data, even when they rely on information that comes directly from a CTMS or eTMF system, and companies lack clear procedures for sites to refute the information and correct errors. Jeff Kingsley, D.O., founder and CEO of IACT Health, which operates 10 sites in Georgia, said database errors could include inaccuracies on the quality of the data from a site, timelines and enrollment due to glitches in the CRO or sponsor system. In a recent example, an organization's database noted that a nurse practitioner had failed to complete trainings and used that information in startup decisions even though IACT Health had repeatedly sent the company notices stating that the staff member no longer worked at the site.

"The downside of these technologies is that they have bad data in them and people are making decisions based on bad data because of the lack of transparency," said Kingsley.

Adoption gaining momentum

In recent years, many organizations have established dedicated startup teams and dedicated budgets to focus on improving startup activities. Many of these dedicated functions have either introduced study startup technology in their organizations or have initiatives to bring in advanced study startup tools. In addition, vendors have seen the number of requests for proposals for purpose-built study startup technologies increase during the past five years.

A handful of purpose-built study software applications and platform technologies that automate workflows, integrate with eClinical systems and enable better decision-making also have become more visible and accepted in the industry.

It's an exciting time to be involved in this space because the rapid change in the data, technology and analytics landscape provides new ways to approach the challenges we collectively face. By embracing innovations available and maintaining a change mentality, we will continue to find better, data-driven solutions.

—Gaurav Bhatnagar, vice president, Strategic Feasibility, Site and Patient Access, PPD

"We are seeing an inflection point now where there could be some dramatic shifts," said Jae Chung, president and founder, goBalto, the first and most established company to market purpose-built study startup software. ''When we look at the adoption lifecycle, we are in the early majority. Five years ago, we had early innovators take a serious interest in buying a packaged software application to address study startup. Today we have clients who have adopted our technology because they are not the guinea pig. It's a proven technology."

CROs, in particular, are leading the adoption of technology solutions and data-driven approaches to site selection and activation, investing 10% more in all areas of study startup technology compared to sponsor companies. Leading CROs, which have developed proprietary systems and work with best-in-class third-party vendors, consider the ability to leverage IT solutions for study startup as a way to differentiate their business and add value for clients. CROs have been collaborating or merging with data intelligence companies as they look to integrate more data sources and advanced technology to direct sponsors to the right sites and improve clinical research performance. Notable transactions include the merger of Quintiles and IMS Health, which has rebranded as IQVIA, and the company's subsequent acquisition of DrugDev. In another deal, PPD acquired Evidera, a provider of evidence-based solutions to demonstrate real-world effectiveness of biopharmaceutical products.

Sheetal Telang, senior director, Therapeutic Strategy Head of Global Site Identification, Therapeutic Science & Strategy Unit, IQVIA, said new data-driven predictive models take the "guesswork" out of site identification and startup by identifying the candidate investigators most likely to be both interested and qualified.

"We use data-driven analytics solutions to drive the optimal country mix per protocol based on treatment patterns and patient availability, pinpoint the location of target patient populations for a specific protocol to identify target sites and speed enrollment," said Telang. "Using our data-driven insights we can increase predictability and reduce risk by selecting investigators with proven performance and

quality to streamline startup by focusing efforts only on sites that can deliver."

Another CRO, Icon, uses a mix of internally developed tools and external systems for site selection and startup. The CRO has developed a searchable site selection workflow tool that integrates multiple internal and external sources of site and investigator information, along with other key capabilities, such as surveying, to help select the right sites. These data sources have a diverse set of information types ranging from experience to start-up and enrollment performance, which are all factored into enrollment projections for a given study. A site activation solution is then used in in regulatory document submission and contract and budget negotiations to share and exchange documents with members of the study team.

"With the explosion of data and better ways to analyze them, including emerging technologies that incorporate machine learning and artificial intelligence, sponsors are demanding more data-driven approaches and transparency into how this is done," said Otis Johnson, vice president, Feasibility & Clinical Informatics, Icon. "Improving the use of data analytics and technology would allow for an increased ability to reuse site information on multiple studies and reduce the time between selection and initiation. Another great opportunity is the promise of AI and machine learning. With these technologies, we would be able to ask open ended questions and develop greater insights from sites and patients on what it will take to successfully deliver a study. These insights can then be incorporated into the operational strategy."

Gaurav Bhatnagar, vice president, Strategic Feasibility, Site and Patient Access, PPD, said technology and data-driven approaches will be key to "bending the cost and time curve" of drug development. In one example, PPD used its proprietary solution for data-driven patient enrollment and site startup in a client's phase III cardiovascular program and was able to outperform all industry benchmarks for median cycle times related to startup, enrollment, activation and randomization by more than 50%. Last year, the CRO also saw its number of non-enrolling sites drop by 15% by targeting only sites with exceptional performance records, eligible patients and engaged investigators.

"It's an exciting time to be involved in this space because the rapid change in the data, technology and analytics landscape provides new ways to approach the challenges we collectively face," said Bhatnagar. "By embracing innovations available and maintaining a change mentality, we will continue to find better, data-driven solutions."

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