Accelerating the Pace of Study Start-up

Launching a new clinical study is an exciting stage of product development. There is tremendous hope that a new drug will cure illness or bring relief to patients. Inspired, the team jumps in with a sense of urgency – but as documents and tasks pile up, bottlenecks emerge that delay getting actual research started and threaten the team's ability to meet key study milestones for product registration.

Study start-up has many moving parts, with numerous activities happening among multiple parties in parallel. The protocol is written, investigator sites are evaluated and selected, clinical trial applications are prepared, ethics committee submissions are developed, investigators and clinical trial team members are trained, an investigational product is formulated and packaged – and the list goes on. To further complicate matters, different regulatory requirements must be met across the globe, and various disciplines and stakeholders (i.e. researchers, physicians, lawyers, regulators, ethicists, investigators, scientists, and monitors) are involved in the process. As is so often the case today, many team members are added to the mix in support of the study – CROs, labs, technology vendors, and others.

The study "Benchmarking the Study Initiation Process", published in *Therapeutic Innovation & Regulatory Science*, collaborated with 11 pharmaceutical and biotechnology companies to examine 105 global clinical trials and confirms this inefficiency. "Due to the volume of activities required at study start-up," the researchers reported, "many companies have recognised this phase as a bottleneck and are looking specifically at the study initiation process as a key improvement area."[1]

"Any delay in the start-up process will inevitably impact on the time available for the study itself, and the longer the start-up phase, the shorter the patient recruitment period," says Luigi Visani, CEO of Exom Group. "To keep to the planned timelines and costs, and to guarantee clinical investigators a proper patient enrolment period, it is important to be as efficient as possible during the start-up phase. Unfortunately, delays are quite frequent – on average, in a multi-centre clinical trial, 30–40 % of sites get started some months after the first site activation."

Manual Processes Prevent Progress

The life sciences industry continues to rely heavily on paper-based processes and low-tech systems to share and collaborate on critical study start-up materials. Documents or disks are mailed or couriered across the globe, and spreadsheets are used to track and manage progress. When a typical Phase III study requires hundreds or even thousands of patients to confirm efficacy, many international investigator sites are needed, each with local regulatory and institutional site initiation requirements. With this volume and complexity, it's not surprising that clinical research teams struggle to make progress using Excel spreadsheets to manage their work.

In addition to being inherently slow, these manual processes prevent all stakeholders or process participants from overseeing progress or tracking statuses. The problem is compounded with international teams, as regional groups often maintain their own records, which may not correspond with records at headquarters. Almost no one on the study team has real-time visibility, which forces organisations to always be *reactive* – looking back at problems instead of taking preventative action. This situation creates many opportunities for error, exposes companies to risk, and plays a direct role in study setbacks.

Lack of Integration Leads to Inefficient Study Start-up

The biggest flaw in current technology solutions for study start-up is that they provide a detailed picture of either the documents or the operational data, but not both at the same time. While some solutions help because they enable the team to see and access all needed documents in one place, they don't connect the documents with operational information the team needs to efficiently initiate the study. Existing systems often do not help manage the work processes involved, either. Automating simple workflows, such as routing documents for approval or quality control, can have a large impact on time to first patient and time to first visit.

There are a handful of specific study start-up applications on the market today, but spreadsheets and clinical trial management systems (CTMSs) are the most commonly leveraged tools across the industry. Spreadsheets don't provide global team visibility, create version-control issues, and require tremendous manual effort for entry, updating, and checking. The CTMS specifically offers functionality for planning and tracking, but this type of system can be extremely complex and inflexible in managing the local requirements in a global study start-up process. The CTMS provides no or very limited ability to manage or process documents.

Some of the specific study start-up solutions endeavour to combine operational data from different systems and provide a very clear visualisation of the start-up process in one place so everyone can see where progress is lagging and where they need to take corrective action. If the data is updated in real time, this is a big help, but delays in integrating data can cause frustration and inefficiency for study teams. And although the data is visible, these systems don't link the data to the documents the team needs in order to take action immediately.

"Many sponsors and CROs have traditionally used unsophisticated, disparate, and incompatible proprietary and customised approaches and e-clinical solutions to manage study start-up and initiation activities," says Ken Getz, associate professor at CSDD Tufts University School of

Medicine. "This has contributed to the historically high level of inefficiency and inconsistency that we've observed in investigative site engagement and activation."[2]

Bridging the Information Divide

Through the evolution of study start-up applications, it is now possible to bring documents and data together to provide a single source of truth and allow all team members from all geographies to see what they need in one place and take action on it. Sponsors, CROs, and local study team members can update documents and operational data at that central source and manage workflows and work processes, ensuring version control, enabling planning, and speeding the activities of study start-up.

Often, because of the complexity in the clinical study process, team members simply don't have the information they need to properly prioritise their work. They need to know which activities are most vital for keeping study start-up on the critical path, and which occurrences will delay the projected study start date. Integrated solutions improve communication among team members spread across the enterprise, as well as between sponsors and CROs, which increases visibility of all tasks, eliminates redundancies, and enables the team to move forward at a faster pace.

For example, when clinical team members can see all information for an upcoming planned site initiation visit, the team can use the combined data to prioritise in advance which contract needs to be developed and reviewed, collect all necessary documentation for investigational medicinal product (IMP) release, and ensure that the monitor is prepared to conduct the study initiation visit. The work can be done quickly and in the optimal sequence because team members can all access up-to-date operational data together with the latest version of the documents from the same source. When all material is ready in time for the site initiation visit, the visit takes place quickly and on schedule so patient enrolment can begin, which drives the clinical study to the next step as planned.

"In the past few years, new clinical trial management tools have become available that provide a more systematic approach to capturing metrics," says Getz in the benchmark study report. "With the new tools available and more clinical trial professionals focused on study start-up, not only are more metrics on the horizon, but we also hope they will potentially offer more value for companies."[1]

Creating Industry-wide Standards

Awareness of the problems with study start-up is very high, and a number of efforts to solve them are under way. Many organisations have created new positions solely with the objective of overseeing and improving the start-up process. Accelerating the time to first patient is seen as key to driving study efficiencies.

Additionally, many industry groups are also focusing on simplifying and speeding the time it takes to begin research. TransCelerate BioPharma Inc., a coalition of large pharmaceutical companies, has launched a programme focused on speeding study start-up timelines by developing standard criteria for recognition of good clinical practice (GCP) training and site qualification.[3] The TMF Reference Model, maintained by an industry group of almost 200 life sciences companies, provides standard structure and taxonomy for maintaining a GCP-compliant trial master file (TMF), which includes many of the documents collected during study start-up. The Metrics Champions Consortium has outlined a number of activities related to site activation as part of its clinical trial performance metrics set.[4]

These types of industry-wide collaboration are essential and pave the way for meaningful transformation of the study start-up process. Consistent processes and industry-wide standards help sites, CROs, sponsors, and regulatory authorities work together more effectively. The application of new technologies represents the other side of the solution. Linking documents and data for a complete view of the start-up process, and then being able to act on that information, provides a new opportunity to solve the study start-up challenge once and for all.

References

1. "Benchmarking the Study Initiation Process," by Lamberti, Brothers, Manak, and Getz, Therapeutic Innovation & Regulatory Science (2013) 47: 101. For more: http://dij.sagepub.com/content/47/1/101
2. FDA, "Frequently Asked Questions—Statement of Investigator (Form FDA 1572)," (2010). For more: http://www.fda.gov/downloads/regulatoryinformation/guidances/ucm214282.pdf
3. "TransCelerate Initiatives," by TransCelerate BioPharma Inc., (2013). For more: http://transceleratebiopharmainc.com/?4a17eb50
4. "J&J, Lilly, Merck Plan Clinical Trial Site Database," by D. Beasley, Reuters, (2012). For more: http://www.reuters.com/article/2012/11/15/us-pharmaceuticals-trials-idUSBRE8AE0XS20121115
5. "Veeva Systems Unveils Clinical Trials Study StartUp Solution," [press release]. For more:
6. https://www.veeva.com/resources/veeva-systems-unveils-first-fully-integrated-clinical-trials-study-start-up-solution/

Rik van Mol is Vice President, R&D Strategy, Europe, at Veeva Systems, where he is responsible for strategy for Vault R&D Solutions, focusing on the European market. Rik has 15 years of business/IT consulting and regulated content management experience in the global life sciences industry from companies such as IBM and PricewaterhouseCoopers. He has developed strategies and solutions in business areas across the life sciences value chain.
Email: rik.vanmol@veeva.com.