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Managing Increasing Complexity in the Clinical Trial Industry

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Clinical trials for pharmaceutical products continue to grow in complexity and scope. Research conducted by the Tufts Center for the Study of Drug Development (CSDD) during the past 15 years has demonstrated that, compared to 10 years ago, protocols have more endpoints, procedures, eligibility criteria, CRF (case report form) pages, amendments, and investigative sites[1] - complicated further by the convolution of outsourcing and globalization. With outsourcing of trials estimated to exceed 70% by 2020[2], and recent data from clinicaltrials.gov showing 46% of registered trials being conducted entirely outside the US, as compared to 39 percent taking place in the US exclusively, it is not surprising to find 72% of clinical trials running more than one month behind schedule.

In this constantly evolving environment it is not surprising that the task of managing global trials is more demanding than ever and increasingly requires a robust risk management strategy from the start. Interestingly, while most of the industry's risk management efforts have focused on post-marketing drug safety[3], the clinical trial process holds a broad array of other potential risks that could jeopardize a company's multi-million-dollar product development investment—risks such as site staffing shortages, patient recruitment issues, logistical problems with drug supplies, or regulatory delays.

Risk management in clinical operations really starts with effective project management. Project managers are the front line in ensuring that the objectives of the study are met. To do so, they must be equipped with the skills and tools necessary to monitor risks and overall study progress. With a keen focus on risk management, project managers must have the ability to adjust to the unforeseen contingencies that arise in every trial and keep the study team moving forward without unnecessary delays[4].

Despite this inherent logic, many clinical trials fail to deliver because they lack a structured, practical, businesslike approach to trial management[5].

The numbers tell a sobering tale. According to research from Tufts CSDD, 37% of sites selected for clinical trial studies under-enroll, and 11% fail to enroll a single subject. Eventually, 89% of studies meet enrollment goals, but often at the expense of sponsors faced with doubling the original timeline due to poor enrollment. Other research cites slow patient enrollment as the top reason clinical trials are behind schedule. Overall, poor site selection, the inability of sites to predict the rate of enrollment, and the subsequent need for study rescue may increase cost of trials by 20% or more[6]. And perhaps most disturbing is the fact that cycle time has not changed in more than two decades. Ultimately, sponsors stand to lose up to $8 million for each day that the trial delays a product's development and launch[7].

Mitigating Study Risk Requires People, Process, and Technology

Just as clinical trials are unique, so are the organizations in which they're carried out. Organizations have their own styles, cultures, and ways of communicating that influence how project work is performed and influences their ability to achieve project success.

But any study, particularly a large trial, needs robust computerized systems and procedures that monitor every aspect of the day-to-day running of the trial. A reliable system that will monitor recruitment, randomization procedures, stock control, data management, data cleaning, and central data monitoring and that will produce useful reports should be developed. Every essential piece of paper that relates to a trial participant should be logged and tracked through the system. There needs to be a logical and transparent structure, concise documentation (standard operating procedures) and accountability of every process employed in the trial. If the trial is international, these systems should take account of differing clinical practices, working environments and governance regulations[8].

Currently, project managers in clinical operations rely on matrix teams to complete deliverables and work across multiple functions depending on the stage of the trials. To add to the complexity, more than one project manager is assigned to a product portfolio increasing the communication and consistency issues throughout and across the associated studies.

To reduce complexity, project managers need the ability to collaborate across multiple trials, countries, sponsor and CRO stakeholders, as well as, investigator sites. Effective communication skills are the key to a successful project and has been has been reported as the number one soft skill of a successful project leader. Yet the ability to ensure effective communication is hindered by the myriad of systems and multiple functions that a project manager must coordinate.

The Problem with the Traditional Tool Kits

In the past, the most significant risk management focus has been in the area of patient recruitment, however, significant risk is seen in both site selection and site activation phases of a clinical trial. Current eClinical systems, such as clinical trial management system (CTMS), electronic data capture (EDC), enterprise planning tools, and trial master file (eTMF) simply do not provide the data granularity or process focus needed to manage these risks. Hence, a lack of focus on site selection and site activation has left a gaping hole in the project manager tool kit.

How Better Tools Can Drive Risk Management

In keeping with the regulatory trend toward identifying and mitigating risk, forward thinking industry leaders have been trading in their Excel spreadsheets in favor of custom-built SSU applications that can automatically trigger workflows as a clinical trial unfolds and provide data analytics. Focusing on site selection and site activation (current gaps in the project manager tool kit), these new tools bring workflow-based processes to study teams, allowing both sponsors and collaborators to visualize key data in real time and identify bottlenecks early on. Using quantitative data to perform intelligent site selection (i.e., relying on algorithms to weigh data sources) drives better site selection and reduces overall study risk. This technology mitigates risk factors for recruitment and retention by finding the optimum alignment of top-performing sites with substantial patient databases, and quickly assessing with sites have performed best in similar studies.

For site activation, such tools enable project managers to discover meaningful patterns in the data for tasks such as status of packages for the institutional review board (IRB), patient enrollment success, and receipt of study drug. Risk can thus be continuously tracked and mitigation strategies can be adapted much earlier in the decision-making cycle due to features such as: activity alerts, study team member assignments and role management, milestone tracking along the critical path (and milestone re-projection warnings), and real-time views of global study status (including anywhere, anytime access to study data). In support of risk mitigation activities, real-time alerts help project managers intervene immediately or before a major setback has happened, instead of after the fact. This is crucial, since in conventional study startup, intervention typically takes place after an issue has occurred, when it is too late to proactively avoid the problem.

Why is this important? Increased transparency of site selection data and site activation progress will allow the project manager to provide strategic guidance with regard to the big picture within and across studies to the team and help define risks to support risk mitigation activities.

As a result, better risk management becomes possible. Another essential ingredient for these tools which should be mentioned is a reliance on cloud-based technology, which reduces traditional burdens associated with data sharing and tracking risk across organizations.

Conclusion

There are multiple steps tied to starting clinical trials, and without tools designed for risk management planning, each has potential for causing delays, and possibly jeopardizing the study. To mitigate this situation, an end-to-end suite of purpose-built SSU solutions from site feasibility assessment and selection through to activation provides real-time management capabilities and transparency. Project managers can view elements in as they unfold related to site performance, such as site selection, patient enrollment and retention, and critical cycle-time metrics, and take as-needed corrective action. This degree of process improvement is key to keeping studies on track and within budget, and ultimately speeding new therapies to patients.

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