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The illusion of safety

By Craig Morgan

Risk is our constant companion, and as clinical trials grow in complexity, so do risk-based challenges to bring new therapies to market at an ever-increasing pace. The continued reliance on Excel, which lacks project- and risk-management functionality, has created an illusion of safety often fueling the rescue study industry.

To date, risk management efforts in drug development have focused mostly on post-marketing drug safety, but regulatory changes and competition are now emphasizing a risk-based management approach beginning with study startup (SSU). The FDA and the EMA have released documents on greater acceptance of risk-based methodologies, which they state should begin from the start of a clinical trial.

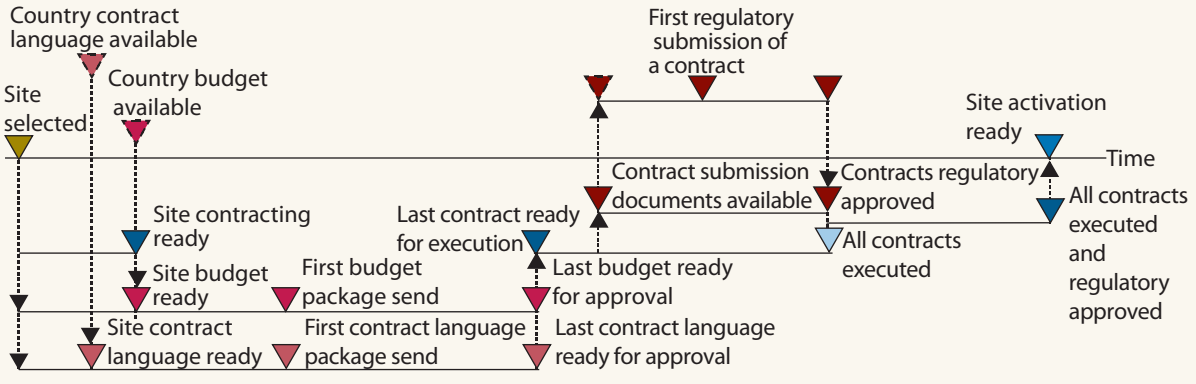
In keeping with the regulatory trend toward identifying and mitigating risk, forward-thinking industry leaders have been trading in their Excel spreadsheets in favor of custom-built SSU applications that can automatically trigger workflows as a trial unfolds, ensuring country-specific regulatory and SOP compliance, as well as generating critical operational metrics.

Focused 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 CROs 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 assesses which 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 the status of packages for the institutional review board (IRB), patient enrollment success and receipt of the 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 real-time views of global study status. In support of risk mitigation activities, real-time alerts help project managers intervene immediately or before a major setback occurs. This is crucial, since in conventional SSU, intervention typically takes place after an issue has occurred, when it is too late to proactively avoid the problem.

The operational metrics associated with contracts (Figure 1 shows site level contracts, tasks and milestones)—a notorious bottleneck in starting trials—illustrate this point. The All Contracts executed milestone normally available in an eTMF as a summary of artifacts does not provide the operational metrics that precede it (e.g., Site Budget ready to First Budget package send, Site Contract language ready to Last Contract language ready for approval, etc.). If the trial timeline is delayed, what caused the delay? The budget? The contract? Or maybe, the template? The reality is you would have no idea an issue even exists until after your planned date for All Contracts

Figure 1: Operational metrics associated with site level contracts tasks and milestones



executed has elapsed, let alone what caused the delay and where to focus your process improvement efforts.

According to KMR Group, overall contract cycle times have doubled from an industry median of 1.5 months from 2009 to 2011 to over three months from 2014 to 2015. Contracts conducted in North America, traditionally a top performer, have increased from 1.3 in 2010 to 2011 to 2.4 in 2014 to 2015. Emerging markets continue to have longer cycle times. Additionally, oncology trials typically have the longest site contracts cycle time compared to other therapy areas. The study evaluated 20,000 recently-executed contracts for phase II/III trials from leading biopharmaceutical companies.

SSU represents a complex array of processes and without tools designed for risk management planning, each has the potential to cause delays and, ultimately, jeopardize the study. To mitigate this situation, purpose-built SSU tools spanning site identification, feasibility assessment and activation that provide risk management capabilities are a critical improvement over traditional manual processes. Stakeholders can view elements in real time related to site performance, such as high patient availability, enrollment and retention and critical cycle-time metrics, and take corrective action. This level of process improvement can help keep studies on track and within budget and, ultimately, speed new therapies to market.

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