DRUG DISCOVERY & DEVELOPMENT©

Risk Mitigation Pivotal to Starting Clinical Trials

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By Craig Morgan

While risk management efforts in drug development have focused mostly on post-marketing drug safety, the clinical trials process has its own mix of potential risks just waiting to derail a company's high-dollar development programs. These risks include patient enrollment issues, site staffing shortages, logistical problems with drug supplies, and regulatory delays. Moreover, risk-based challenges are escalating as clinical trials become more global and complex, and as market pressures keep rising for new therapies at an ever-increasing pace.

The goal of risk management is to allow stakeholders to identify clinical trial strengths and weaknesses, and mitigate threats. As defined by the Project Management Institute, risk mitigation is the process of developing options and actions to enhance opportunities and reduce threats to project objectives. It includes tracking identified risks, identifying new risks, and evaluating risk process effectiveness throughout the project. There is also risk assessment, which, according to Linda Sullivan, President of Metrics Champion Consortium (MCC), focuses on quantifying the risk that a potential issue will occur and become a serious problem. She asks, "How frequently has the issue occurred in other studies? When the issue occurred, was it a serious problem? Stakeholders may choose to mitigate risk when it is determined that an event is likely to occur and have a significant impact on the study."

The growing emphasis on risk management, beginning with study startup (SSU), is fueled by competition as well as regulatory forces. The Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have released documents on greater acceptance of risk-based methodologies, which they state should begin from the start of a clinical trial. The FDA guidance mentions that sponsors should be prospective about identifying critical data and processes, and then perform a risk assessment to determine which factors could affect those data or the performance of critical processes. In addition, both regulatory documents comment that in a clinical trial, the degree of risk is predictable, and should be anticipated.

To conform to these regulatory guidance's for identifying and mitigating risk, forward thinking industry leaders have been trading in their Excel spreadsheets in favor of custom-built SSU applications. This approach improves SSU—a continual bottleneck—by facilitating the selection, feasibility and activation of performing sites, budget and contract negotiations, and the tracking of protocol amendments and regulatory documents. These are factors long associated with trial delays and cost overruns.

A major shortcoming of using Excel, the traditional pre-cloud tool for managing clinical trials, is its lack of project- and risk management functionality. For example, it is beyond Excel to define and track SSU milestones in real time, assign risk triggers with milestone re-projections, record the completion of activities, and automatically trigger workflows to begin as others are completed.

Purpose Built Applications

What are some of the ways that purpose-built applications can perform SSU functions and reduce risks at the same time? A few are profiled, to the right.

Value of Purpose-Built Applications

- Intelligent site-profiling
- Real-time metrics & visualizations
- Ensure regulatory/SOP complaince
- Role assignment
- Real-time alerts
- Document dependencies
- Managing expiring documents
- Milestone tracking and re-projection

List 1

Intelligent site profiling

Poorly performing sites has long been a tough challenge for the industry. Half of investigative sites under-enroll, 11 percent of sites fail to enroll a single patient, and a mere 13 percent exceed their enrollment target. In addition, Phase 3-4 study timelines often have to be extended to almost twice their original length to achieve enrollment goals. These statistics have barely budged over the years, as earlier research found that almost 50 percent of clinical trials are behind schedule, with slow patient enrollment named the key reason.

Given this reality, sponsors and contract research organizations (CROs) are embracing a data-driven approach for weighing selection and performance variables when selecting study sites and target populations. Traditionally, site selection has been a manual process, lacking in verification, and resulting in the selection of too many non-enrolling and under-enrolling sites. Even as technology entered the picture, the pain points associated with disparate data sets from multiple systems, such as electronic data capture (EDC) and the clinical trial management system (CTMS), and a lack of institutional memory has further hindered successful site selection.

Purpose-built SSU site selection and feasibility tools can improve site selection capability by combining internal and external data sources so a complete target site profile can be created. 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 which sites have performed best in similar studies. As part of this effort, the technology provides information on start-up time, patient retention and quality. It can also facilitate communications and a desire to build a collaborative long lasting partnership, fostering a foundation of trust and commitment.

Real-time metrics and visualizations

Where are the bottlenecks? Where are studies most at risk of missing timelines? These are obvious questions, but unfortunately, the conventional tools used to conduct clinical trials lack the ability to answer them. Manually prepared data are often too old to reliably convey SSU status, causing executives to demand faster and greater visibility into data generated by SSU activities.

A purpose-built SSU solution helps sponsors and CROs visualize the data, empowers oversight and casts light on bottlenecks by allowing them to quickly analyze and share information. Specifically, this data-driven approach enables stakeholders to be proactive in identifying and resolving bottlenecks in real-time by instantly viewing status, and quantifying the clinical research team's performance. This capability serves to mitigate risk and is a significant improvement over wasting time assembling data manually from multiple systems, such as EDC and CTMS, and more. As Sullivan of MCC explains, "Decisions for risk mitigation are best made using data-driven evidence that is accessible and can be visualized. If data are scattered among multiple systems and loaded into spreadsheets, it can be very difficult to access that information and make timely decisions on risk based on that methodology."

As shown in Figure 1, analytics from a purpose-built solution can improve site selection. This report indicates that the contracted dates at one site are 71 days versus an overall average of 41 days—clearly a red flag that something is amiss at that one site.

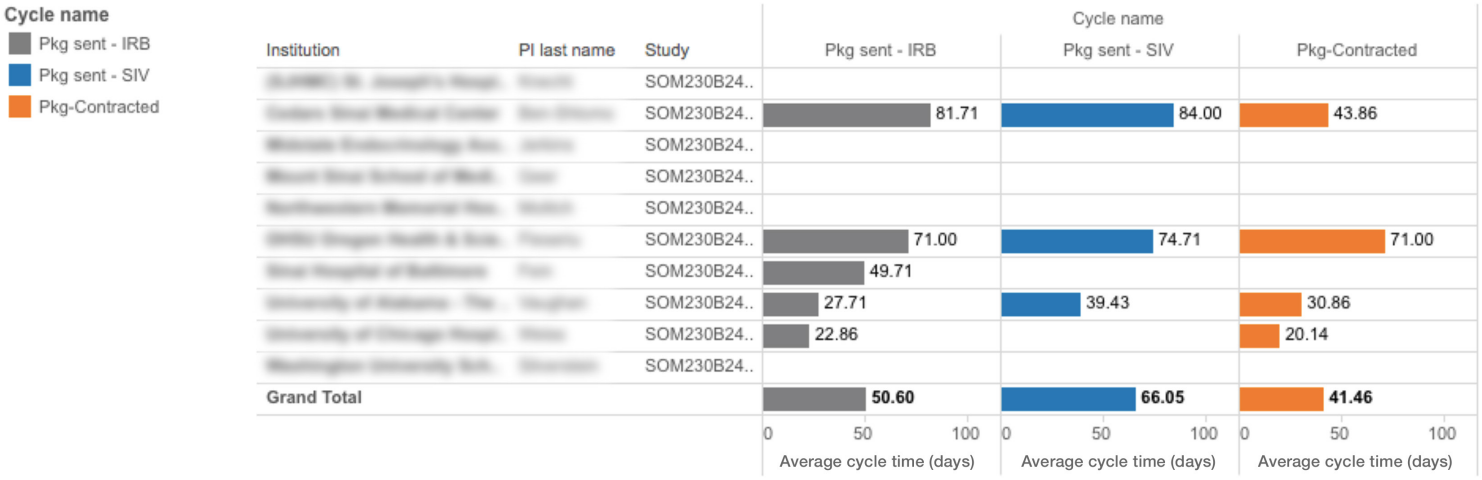

Figure 1

Source: goBalto 2015

There are numerous steps involved in SSU, and without risk management planning, each has potential for causing delays, and ultimately, jeopardizing the study. To mitigate this situation, a purpose-built SSU solution providing risk management capabilities is 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.**

Craig Morgan *is a technology and life sciences management professional with more than 15 years experience in the application of informatics and bioinformatics to drug discovery. He currently heads up the marketing and brand development functions at goBalto, working with sponsors, CROs and sites to reduce cycle times and improve collaboration and oversight in clinical trials.*

Craig Morgan
Head of Marketing | goBalto