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Study Startup Solutions Improve CRO Oversight Through Collaboration

WHITEPAPER

This white paper defines CRO oversight, describes the importance of relationship building among stakeholders, and takes a look at innovative solutions for streamlining study startup across CROs, a critical step toward managing study status in real-time.

Contents

Executive Summary

The relationship between sponsors and contract research organizations (CROs) is strengthening as outsourcing becomes a clinical trial mainstay. CRO oversight has become part of the mix of relationship building along with centralized monitoring and study-related quality metrics.

One of the areas in great need of CRO oversight is study startup, a perpetual bottleneck that continues to be handled largely by spreadsheets, shared file drives, and unsecured email, making data gathering and the timely sharing of data difficult in today's global market. For sponsors, improving oversight of this function means real-time visibility into study startup progress, affording greater confidence in the reports they receive from the CROs involved in studies across the portfolio.

By transitioning to purpose-built data-driven solutions used by all CROs across the portfolio, oversight improves, and sponsors can build and retain reliable institutional knowledge about CRO performance, ensuring stakeholders realize the full potential of collaborative outsourcing arrangements and better position clinical trials for success.

Facilitate CRO Oversight with Real-Time Access to Study Startup Data

The relationship between sponsors and contract research organizations (CROs) is strengthening as outsourcing becomes a clinical trial mainstay. Making this connection as productive as possible means continuing the transistion away from tactical projects and toward strategic partnerships with both stakeholders have a vested interest in greater operational effciency. This transition is taking many forms, but at the core is a desire to build a collaborative long lasting partnership, which requires open and transparent communications, fostering a foundation of trust and commitment.

CRO oversight has become part of the mix of relationship building along with centralized monitoring and study-related quality metrics. These practices help sponsors fine tune their tracking of clinical trial progress, and together, these operational changes form a solid basis for continuous quality management as studies unfold.

One of the areas in great need of CRO oversight is study startup, a perpetual bottleneck that continues to be handled largely by spreadsheets, shared file drives, and unsecured email, making data gathering and the timely sharing of data difficult in today's global market. As evidence that more study startup oversight is needed, it can take an estimated eight months to move from pre-visit through site initiation.[1] For sponsors oversight of this function means real-time visibility into study startup progress, affording greater confidence in the reports they receive from the CROs involved in studies across the portfolio.[1]

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What is CRO Oversight?

As sponsors turn attention to their core competencies and continue to outsource, it makes sense that they would need a roadmap for building productive strategic relationships. Simply handing off multi-million dollar studies to CROs without carefully crafted plans for communications and reporting operational data as the study unfolds is hardly a wise move, yet what kind of oversight is needed?

This question is worth considering as reliance on CROs is on the rise. A 2015 CRO outsourcing survey of 375 industry professionals, 80%, anticipate growing demand for CRO services, particularly strategic services (60%) rather than tactical (40%).[2] In addition, there is an expected 7.4% compound annual growth rate for the CRO market through 2019,[3] with market penetration reaching a bullish 72% by 2020.[4] This trend is rooted in intense competition to improve productivity, driving sponsors to contain operational and infrastructure costs while completing projects better, faster and more efficiently.

The issue of CRO oversight by sponsors is raised in the 2013 guidance released by the Food and Drug Administration (FDA) on the risk-based monitoring.[5] According to the guidance, if a sponsor delegates monitoring responsibility to a CRO, FDA regulations require the CRO to comply with them. Also, the sponsor retains responsibility for oversight of the work completed by the CRO(s) they select (Chart 1). The guidance spells out oversight as the sponsor's periodic review of monitoring reports and performance or quality metrics, as well as documented communication between the sponsor and CRO regarding monitoring progress. Importantly, both parties are to establish processes to exchange this key information.

Delegating Monitoring Responsibilities to a CRO

Although sponsors can transfer responsibilities for monitoring to a CRO(s), they retain responsibility for oversight of the work completed by the CRO(s).

Sponsor oversight of monitoring performed by a CRO may include the sponsor's periodic review of monitoring reports and vendor performance or quality metrics and documented communication between the sponsor and CRO regarding monitoring progress and findings.

Sponsors and CROs should have processes in place for timely exchange of relevant information (e.g., significant monitoring findings, significant changes in risk for a trial).

Chart 1

Source: FDA Guidance 2013

Moving to Purpose-Built Applications

Oracle Health Sciences offers an end-to-end suite of purpose-build applications providing an array of information critical to an improved study startup process. This includes highlighting the status of protocol amendments, regulatory documents, and budget and contract documents Oracle Health Sciences Activate Cloud Service; data visualization and easy identification of bottlenecks Oracle Health Sciences Analyze Cloud Service; facilitating the selection, feasibility and activation of performing sites Oracle Health Sciences Select Cloud Service; and Oracle Health Sciences Analyze for Insight for Activate Cloud Service transitioning CROs from tactical to strategic partnerships and delivering transparency to sponsors outsourced studies. These solutions are playing an expanding role as research suggests it is the responsibility of CROs and sponsors to implement state-of-the art technologies to better execute study startup tasks, such as communication among stakeholders, distribution of questionnaires to investigators, and generating reports.[6] These tools help deliver real-time updates while increasing transparency, track study startup milestones in real time, assign risk triggers with milestone re-projections, and automatically trigger workflows to begin as others are completed. These functions are essential for minimizing risk.

About Activate

Activate is revolutionizing how stakeholders collect and handle the massive volumes of data generated by study startup activities. It integrates data from other cloud-based solutions, such as electronic data capture (EDC), the clinical trial management system (CTMS), and the electronic trial master file (eTMF), and offers seamless sharing and visibility of study startup documents in real-time across the globe. This integration is possible through the use of an application program interface, which optimizes the flow of data among various integrated components.

Accessed through a dashboard, Activate is workflow-based, allowing study teams 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 be continuously tracked and mitigation strategies can be adapted much earlier in the decision-making cycle due to multiple features (Chart 2).

A few are profiled here:

Key Benefits of Activate

- Manages alerts
- Manages study team members
- Manages milestones
- Views of global study status
- Can access study data anytime, anywhere
- Drives data-based business decisions
- Improves collaboration with sites
- Exchanges documents securely
- Consolidates information in one place
- Predicts study progress more accurately
- Avoids redundant processes

Chart 2

Manages Alerts

Activate features an Activities List, which shows which activities are assigned to which individuals. Stakeholders can filter alerts so team members will only see alerts for their specific activities, advising them of the due date, and only when they are the inidividuals assigned to the site or country associated with those alerts.

Real-time alerts help decision makers 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 occured, when it is too late to proactively avoid the problem.

Manages Study Team Members

Activate allows stakeholders to assign team members to more than one study and to the role each team member is to play within each study. This permits members to view information only for those involved with a particular study, clearly defining what is expected of each member. For example, one individual might be given the role of managing all regulatory documents for an array of studies. That person can receive alerts, notifying them that certain documents need attention. This approach may increase the likelihood of compliance, and lower the risk that specific timelines for regulatory submissions will be missed or that documents will be improperly completed.

Manages Milestones

Stakeholders can configure Activate to track certain country and site milestones, which appear at the top of each country and site details page. This ensures that members of the study team see and track the same milestones. There are three types of dates for each milestone (Figure 1):

- Baseline - The date projected for completion of the milestone. Once entered, this date cannot be changed.
- Planned - A re-projected date for the milestone. The reason for the change appears on the Timeline Change History and Critical Path Tracking reports.
- Actual - Shows when the milestone was actually completed and Activate automatically enters the date on the study timeline During configuration, the study team specifies which activity triggers completion of the milestone.

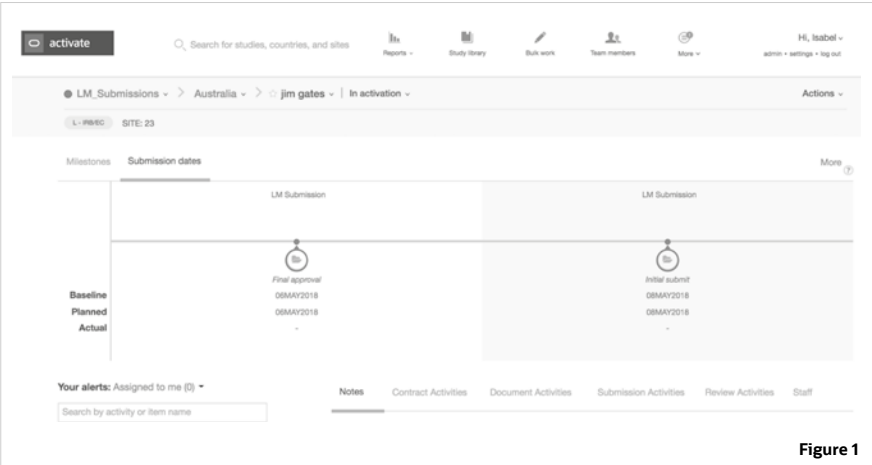

Figure 1

" Real-time alerts help decision makers intervene immediatlely or before a major setback has happened, instead of after the fact."

This level of careful management of milestone serves to reduce the risk that milestones will not be met in a timely manner as there is transparency and communication among stakeholders to plan and set the necessary milestone dates.

Overall, to minimize risk and for purposes of compliance, Activate's smart workflows standardize processes and guide study teams to complete and track the specific documents and tasks required for any site, country, or study based on regulatory requirements and a company's standard operating procedures (SOPs).

This degree of functionality allows the project management team to drive discussions and decision-making on bottlenecks impacting site activation. Significantly, time is not wasted charting data and compiling status updates, a practice that is typical with older methods, such as Excel.

About Analyze

Analyze is a reporting tool that creates reports using data analytics to aid stakeholders in visualizing study status of multiple studies as part of a risk-based study startup strategy. This functionality uses data from Activate and Select and is accessed through a dashboard. Analyze helps identify bottlenecks across protocols by evaluating completion of documents on the critical path, such as site contracts or an informed consent form, tracks cycle times across individual sites (Chart 3), and shows sites activated per study (Figure 2). If a report signals a trend toward longer completion time for contracts, for example, the CRO can act quickly to steer lagging sites back on track, or consider adding new sites. This data-driven approach enables stakeholders to be proactive in identifying and resolving risk in real-time by instantly viewing status, and quantifying the clinical research team's performance. This capability is a significant improvement over the time-consuming method of assembling data manually from multiple systems or spreadsheets, rendering those data too old to reliably convey study startup status.

Standard reports supplemented with ad hoc reports can be shared with team members via a simple click and an e-mail address to authorize those team members to see a dashboard of the reports.

Key Benefits of Analyze

- Helps identify bottlenecks
- Track real-time metrics such as cycle time, and key performance indicators, keeping study startup on track and within budget
- Proactively supports risk identification by creating data visualization across multiple trials and partners
- Easily shares standard and ad hoc reports amoung team members, replacing manual preparation of routine reports
- Provides actionable status information
- Quantifies the clinical research team's performance
- Expedites collaboration with global study teams
- Encourages high transparency partnerships

Chart 3

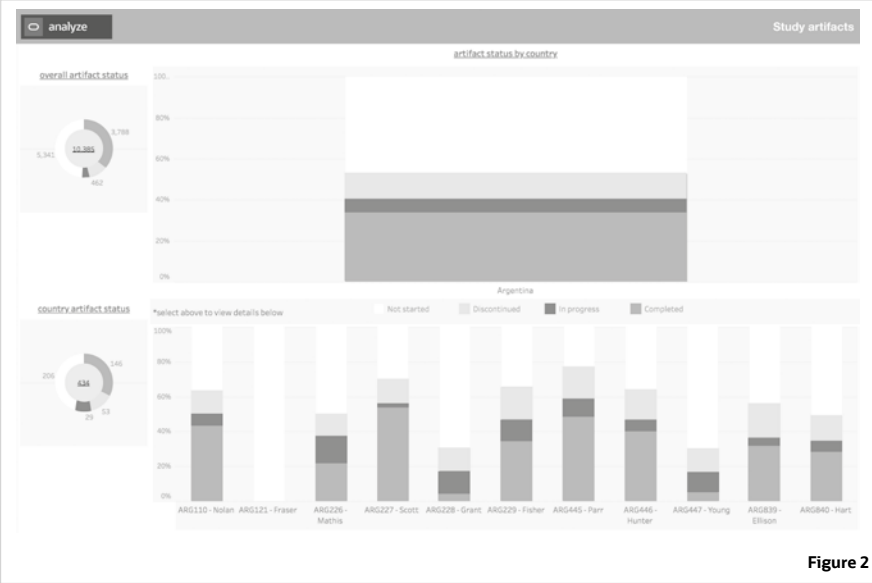

Figure 2

About Select

Poorly performing investigative sites have long been an intractable challenge for the clinical trials industry. Half of sites under-enroll, 11% of sites fail to enroll a single patient, and a mere 13% exceed their enrollment target.[7] Phase II-IV study timelines are often extended to almost twice their original length to achieve enrollment goals. These statistics have remain unchanged over the years, as nearly 50% of clinical trials are behind schedule, with slow patient enrollment generally cited as the top reason.[8]

Much of this scenario reflects the fact that site selection remains a manual process, lacking in verification, and resulting in the selection of too many non-enrolling and under-enrolling sites. The growing impact of cloud-based technology notwithstanding, challenges associated with disparate data sets from multiple systems, such as EDC and the CTMS, and a lack of institutional memory continue to plague successful site selection. Beth Harper, President of Clinical Performance Partners, comments on this continual reliance on manual methods. "Despite the plethora of data and information available to us, evidence-based site selection processes still seem to elude us as an industry. Perhaps it is a matter of information overload or inability to integrate the data from multiple sources, but in my experience, teams continue to rely on archaic tools and subjective criteria for selecting sites, only to find a significant number of sites failing to enroll," she remarks.

Given this reality, sponsors and contract research organizations (CROs) are embracing Select, a workspace that uses a data-driven approach to intelligent site selection (Chart 4).

Key Benefits of Select

- Automates site identification, feasibility and selection processes
- Reduces site selection risks
- Profiles patient populations to design and tune protocols
- Analyzes patient-to-site proximity and selects most appropriate sites
- Provides built-in reports into start-up time, patient retention, and quality
- Expedites collaboration with global study teams
- Drives data-based business decisions and customizes data presentation
- Enables access to site selection data anytime, anywhere

Chart 4

This purpose-built tool facilitates site selection by using an algorithm to weigh data sources so a complete target site profile can be created (Figure 3). The weighted score is tailored to the study protocol and organizational priorities, and is composed of study fit (i.e., site feasibility), site performance (i.e., study startup metrics), and experience (i.e., site, investigator).

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. To aid in this effort, Select has built-in reports that give insight into start-up time, patient retention, and quality.

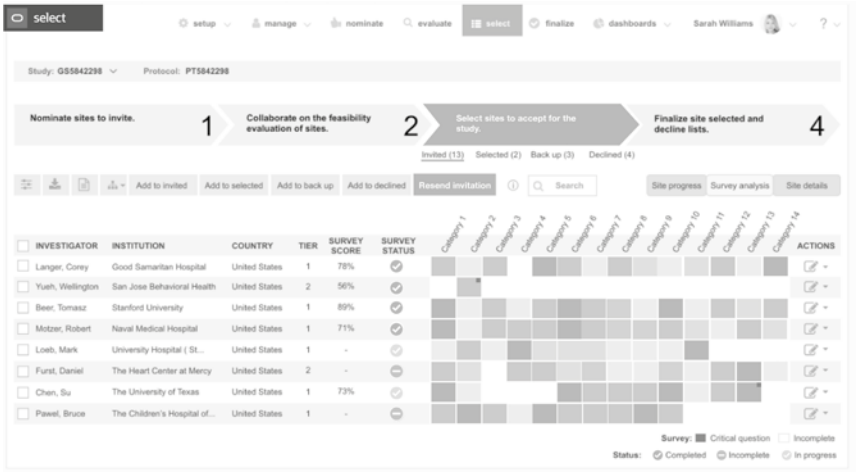

Figure 3

About Analyze Insight

Outsourcing of clinical trials introduces additional complexities. Communication and transparency are required to move the clinical trial forward efficiently, but how can sponsors do this when their working with multiple CROs all using inconsistent reporting conventions?

Reconciling CROs data across the sponsor portfolio with different reporting formats can make timely oversight difficult and obscure performance trends. Readily proving studies are on track can be an ongoing challenge.

Analyze Insight addresses these challenges by providing real-time access to a wealth of data across a sponsor's study portfolio and CRO partners, replacing the need for the manual preparation of routine reports and eliminating time wasted on non-productive activities, such as status meetings (Figure 4).

Key Benefits of Analyze Insight

- Standardizes performance metrics across all studies and CRO partners
- Enables real-time assessment of concurrent studies with multiple CROs by tracking cycle time metrics
- Improves governance of outsourced studies and quantifies performance of CRO partners
- Encourages high transparency strategic partnerships and improves operational efficiency by eliminating time wasted on nonproductive activities
- Builds institutional knowledge on study dimensions to aid in proactive planning of future studies

Chart 5

Analyze Insight improves transparency, communication and collaboration with CROs, leading to enhanced performance and governance of outsourced clinical trials (Chart 5).

Figure 4

Better Risk Management for Study Startup

There are multiple steps tied to study startup, 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 study startup solutions from site feasibility assessment and selection through to activation provides real-time management capabilities and transparency. Contributing to this effort are data-driven analytics, which are a critical improvement over traditional manual processes for making better and faster decisions. Stakeholders can view elements in real time 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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