Advanced Clinical

WHITE PAPER

How a Collaborative and Skillful Approach to Early Trial Planning Mitigates Risk and Achieves On-Time Trial Milestones

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Introduction

In recent years, the path to site activation and First Patient In (FPI) have taken on added complexity and significance, which has the potential to slow the clinical development journey. Now more than ever, successfully achieving site activation and FPI goals requires coordination across multiple stakeholders—driven by Sponsors, Sites and CROs—to bring clarity of these goals to the forefront of every clinical trial planning discussion.

Amongst the list of vitally important goals for the Sponsor, such as patient safety and conducting the trial with high quality and compliance, is having the clinical trial executed on time. Obstacles to site activation and in FPI can present significant challenges, delaying the entire trial, and may result in an over-budget trial if not completed on time. The protocol demand on sites and their competing priorities can negatively impact site performance, which affects everyone from Sponsors to patients. Additionally, complex clinical trials can increase the time for budget and contract review and negotiation due to the varying levels of requirements and approvals at each site.

In the clinical research industry, there is growing interest in complex, targeted therapies to treat smaller patient populations or patients with rare diseases. These factors are likely to increase the number of Sponsors vying for the most qualified sites in an already ultra-competitive market while trying to remain regulatory compliant. These obstacles that Sponsors face directly impact trial planning, site selection, patient recruitment and protocol execution, which is why it is crucial to take a comprehensive approach to early trial planning.

Setting expectations, collective planning and active listening to achieve milestones

At the start of every trial, team members are focused on achieving rapid site activations and FPI. Meeting these milestones depends on the collaboration of multiple stakeholders and can be arduous to achieve due to factors including completing regulatory documents, site budgets and contracts, site activation, study drug supply, and identifying the first qualifying subject to participate in the trial.

The importance of the team truly understanding the Sponsor's compound, study milestones, the Sponsor's corporate goals, the allocated budget, and overall timelines cannot be understated.

All members of the team (Sponsor, CRO, vendors, sites) should meet early and often to establish a solid foundation to learn about the trial, including the goals and key factors that will make the trial a success. Furthermore, it is crucial to listen to the sites and Principal Investigators early in the process, as they are critical stakeholders in support of the patient population and site facilities. Engaging the sites early to better understand their needs and/or limitations will only optimize planning. These tactics will help ensure all parties are aligned and advance the trial in the right direction.

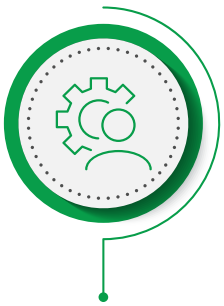
Important requirements emerge in these initial conversations that might be overlooked in early trial planning. For example, if the Sponsor has a protocol that requires an extended walking test, the sites need a long, unobstructed space to perform these tests. If this detail is not included specifically in a general feasibility questionnaire, sites may be selected that lack the space to meet this requirement. This seems rudimentary, but these unique requirements can determine a site's ability to successfully participate in a trial.
Exploring the details upfront ensures that site selection is an efficient process that involves only engaging with sites that would be the best fit for a protocol.

In order for all stakeholders to feel invested in site selection through FPI, teams must think proactively and creatively about critical components including but not limited to:

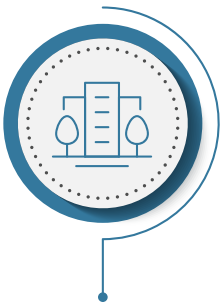
Figure 1: Critical Components for Trial Planning

- Useful feasibility questionnaires detailed with the specific requirements of the trial
  - Is special testing, training and/or personnel needed?
  - The protocol must be thoroughly reviewed, keeping in mind the feasibility questionnaire

- Should DCT components be considered?
  - Home visits, along with eConsent, other modules or platforms, PROs, etc.



- Sites' department structure and capacity to execute the clinical trial
  - Understanding any site-specific challenges to mitigate early on
  - Build relationships with key start-up personnel at the sites



- Sites' facilities

- Availability of subjects
  - Do the sites have the subjects at their clinic? Alternatively:
    - Will they require advertising? Will patients be referred from other sites?
  - Will there be travel expenses?

- Clinical site grant/ budgets and contracts

- IRB/EC approval

Being aware of the competing landscape and the influences impacting sites will allow teams to be prepared during the start-up process. Also, it is important to have an awareness of epidemiology and standard of care for accurate country selection, while potentially leveraging advocacy groups to help identify barriers through the patient journey.

Having the final trial documents from the Sponsor as well as developing trial guidance documents for the sites (logs and forms, inclusion/exclusion criteria chart, visit schedules, etc.) contributes to a seamless path toward the FPI and ongoing trial performance.

Forward-thinking: Leveraging team expertise for proactive planning

Each of the teams involved in a trial has a unique vantage point when it comes to working with different sites and investigators, and those perspectives should be leveraged to make better decisions throughout the trial. Subject matter experts (SMEs) should be consulted to proactively help identify sites that have the most potential to meet trial requirements pertaining to the optimal subjects, facilities and technology. Through early conversations, the team may identify potential risks such as travel burden for participants, the risk or impact of competing trials, and whether sites have access to eConsent platforms and/or other technology tools that will enhance trial start-up and reduce travel demands for patients.

The combined experience lends value to the early planning process. For example:

- The clinical monitoring team works with investigators and staff at many key sites. From previous studies, they can help determine who will be a good fit for a trial and what would enhance their interest in this research. That kind of insight will not emerge from a generic site survey, and it can ensure you select sites and investigators who will be genuinely interested and committed to a trial.
  - This familiarity with a site should also help ensure diversity, equity and inclusion with respect to patient enrollment is a key factor in trial planning, which may not otherwise be included with the feasibility questionnaires.
- The contract team understands the variable site timelines related to contract negotiation required for individual sites, academic centers and institutions, where previous experience with a site should bring an understanding of the preferred language. This helps determine which sites will be ready to rapidly prepare and sign contracts so that start-up dates are accurately forecasted.
- The global start-up team has deep knowledge of the regulatory environment in different countries, such as timelines for submissions, specific requirements and approvals needed. The global study start-up team can also identify what information will accelerate ethics committee approval. Having a team trained and expertly working on the clinical trials information system (CTIS) submissions has become even more critical due to recent regulation updates.

The clinical operations team acts as the first point of contact with sites. They build relationships, establish open lines of communication, review consent processes, and empower the sites by facilitating assistance in any area needed to enhance site activation and subject recruitment. They also participate in Kick Off Meetings to develop a clear understanding of the trial requirements and the technology platforms that will be used for trial execution (EDC, RTSM, PRO's, among others). These early and ongoing interactions establish collaborative relationships—which is the most critical piece—and set the stage for achieving goals and a successful trial.

The insight and feedback from each of these teams can be critical when sites are overwhelmed with requests, which ultimately helps to streamline the start-up process. Additionally, the entire study team must be aligned on goals and expectations, which requires an invested and experienced project leader and team. Streamlining communication helps with achieving success through teamwork (feasibility, clinical monitoring and all functions working together across the Sponsor and vendor partners) throughout the entire study.

Collaboration for a successful trial

Collaboration continues throughout the life of the trial, not just in the early planning stages. Once confirmed, every site should have a dedicated point of contact whom they can call if issues arise prior to receiving their trial documents. The point of contact makes sure all selected sites have the necessary training, technology and documentation to prepare for site initiation visits and site activation well before FPI.

All team leaders, including clinical research associates, should continue to work with site teams throughout the trial, building relationships with key staff and communicating on a regular cadence with Sponsors to share progress and problem-solve so that the trial stays on track, meet goals, and have a successful study close out.

Conclusion: Work with a clinical research partner who understands the value of FPI and early planning

Sponsors who want to accelerate time for site activations and to FPI need a clinical research partner who has experience creating detailed plans for startup and who can leverage the talent and experience of everyone on their team to streamline that process. A good partner will share their plans and experiences for the site selection to complement the Sponsor's knowledge.

Choosing a trusted clinical research partner who cares about achieving your trial goals with a strong plan for attaining these benchmarks will help set the pace for the trial and give senior leaders the confidence that their trial will move forward according to plans and expectations.

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Contact Us

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Mónica is a biologist living in Madrid, Spain who started working in the world of clinical trials in 1996 in a pharma company. After almost 10 years working there, Mónica wanted to explore CRO business work so she moved to a Global Full Service CRO where she could develop various positions as CRA, with some responsibilities as Lead CRA, Clinical Trial Manager while her main duties were to be Country Manager for Spain, Portugal, France and Italy. Since 2015, her main functions were focused on managing the Clinical Monitoring Department in Spain. Finally after 15 years, Mónica decided to switch to Advanced Clinical-FSS Department to have a greater international exposure and to be able to contribute to creating a team, acting as Sr. Clinical Monitoring Manager in Europe.

Tracy Donahue

Senior Global Feasibility & Site Engagement Manager

Tracy Donahue, LPN, has a lifelong career in the medical field, discovering clinical research along the way. With over 20 years in the clinical research industry, Tracy has held many roles across clinical operations, project management, clinical monitoring, site engagement and strategic feasibility at Site Management Organizations and CROs. Her current role as Senior Global Feasibility and Site Engagement Manager at Advanced Clinical allows her to use skills obtained from cross-functional execution to partner with Sponsors to develop and optimize clinical trial strategy and execution.

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