Navigating the Challenges of Clinical Trial Design

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Optimized clinical trial design and execution are pivotal factors in successfully bringing a drug to market. Yet, the road to a well-crafted clinical trial is rife with challenges that can often trip up even the most experienced sponsors.

Finding an effective recruitment strategy, designing the trial, and communicating with regulators are some of the many factors that can impact progress. Sponsors need to work through each step carefully and consider the common challenges and obstacles that often arise as they navigate the process.

ENSURING PATIENT DIVERSITY IN CLINICAL TRIALS

Recruitment of a diverse patient population is critical to clinical trial design and **required by federal regulators**. Many sponsors face challenges in anticipating the diversity (or lack thereof) of their patient populations. A sponsor may use one traditional recruitment strategy and assume it will bring in a wide range of participants meeting the inclusion criteria of their study.

That's not always the best solution, Allucent's vice president of regulatory strategy, Sugato De, told Biospace. Sponsors increase their risk of oversampling from one patient profile, a problem that has collectively and historically **plagued clinical trials**. Instead, De suggests tailoring recruitment strategies to target patients who meet different profiles, opting for intentionality and flexibility to maximize patient diversity.

His suggestions echo a growing sentiment amongst patient advocacy groups and health equity initiatives. Sponsors must garner a deep understanding of their targeted patient populations and develop individual recruitment strategies that optimize engagement for each one. De explained, "Implementing a strategic, diversified recruitment strategy in trial design

means sponsors have anticipated a need for more diversity and actively sought to address it."

Sugato De
Vice President of Regulatory Strategy
Allucent

Decentralized trials have emerged as a popular solution for this problem, especially in therapeutic areas like neurology and in rare disease settings overall. These designs aim to lessen patient burden during the clinical trial by minimizing in-person visits to increase patient access and the total number of trial participants. A rise in innovative digital tools and new technologies has naturally coincided with this trend to assess patient outcomes outside the clinic.

Such measures may improve patient recruitment and facilitate the development of a more diverse patient pool. Yet, this may not be the right design for every trial, said De. "The fully decentralized landscape that was envisioned for a period of time even in advance of the pandemic — I think that'll take a little more development to really be put into place." He added that standard centralized or hybrid designs may better serve studies with larger target patient populations or those in highly competitive therapeutic spaces — for now.

WHEN TO ENGAGE REGULATORS IN CLINICAL TRIAL DEVELOPMENT PLANS

Timing the initial engagement with the FDA can also present challenges for sponsors as they create and execute their trial development plans. Reaching out too early could leave regulators with little to consider. Waiting till later holds potential risks for pushback on trial design and outcomes. Ideal timing depends on the type of trial, therapeutic area, how novel the intervention may be, and many other factors.

Generally, De recommends engaging the FDA when non-clinical and chemistry, manufacturing, and control development plans are refined, implementation has started, and the design of the IND-opening study is ready. "Sponsors will want to make sure that regulators agree with the preclinical development plan and with all parameters of the IND-opening study," he said, "including endpoints, sample size, and other major aspects of the program."

Continuing to seek feedback from regulators as appropriate during the conduct of the study can also bode well for sponsors. Regulators can assess real-time risk and can potentially collaborate on mitigation strategies, reducing the likelihood of unwelcome surprises as the trial progresses toward completion. Collaboration with the FDA during trials "seems to exit the equation sometimes while the trial is underway," said De, "And I think that is a mistake."

His sentiments reflect those **shared by the FDA**, which recommends reaching out to start a discussion early and often, especially for more innovative

interventions. **They encourage** sponsors to at least engage during critical milestones, such as before new drug applications, at the end of Phase 1 and Phase 2, and before submitting marketing authorization applications.

MAJOR CONSIDERATIONS IN DEVELOPING AND OPTIMIZING A PATIENT-CENTRIC TRIAL

Ensuring effective and appropriate primary outcomes is a cornerstone of good trial design. It is a conversation that should gather opinions from internal teams and invested parties like patients and key opinion leaders. The idea is to define well-supported primary outcomes and optimize the study protocol to ensure maximum value for each patient visit. In this way, sponsors are designing a trial with the patients in mind that will have a higher likelihood of being well-received by regulators.

The design of primary outcomes can also impact future studies, reinforcing its importance in trial design and requiring careful and informed consideration. "Each individual study should not live entirely in a silo. It should be thought of in the context of the full clinical development program and how it will inform the next study and eventually a marketing authorization," said De.

Increasing globalization has thrown another factor into this picture as many sponsors look to conduct initial trial phases outside the US. The last estimates from the Office of Inspector General of the Department of Health and Human Services indicated that **80% of approved marketing authorization applications** included multinational site data.

"Seeking input from the FDA and regulators in the intended target markets remains central to success in the scenario," said De, and getting feedback on the totality of data collected. Sponsor intentionality, from trial design to timely engagement of regulators and thought partners, is the crux of executing an optimal, fit-for-purpose trial.

FINDING THE RIGHT PARTNER IN A CRO

Having a seasoned thought partner can go a long way in facilitating trial design and execution. For example, while sponsors may struggle with patient diversity and lean on one recruitment strategy, a reputable CRO with targeted experience will likely consider various approaches. This flexibility allows sponsors to select the approach best suited for their target populations and act strategically in their recruitment process.

CROs also assist with the timely and effective engagement of regulators. Thought partnership throughout the trial process is the cornerstone benefit of engaging a CRO — especially for small to mid-sized sponsors. Having only a few pipeline products and a limited budget means missteps are more detrimental to the process and the company. Getting the trial design and execution right by making well-informed decisions will aid in minimizing sponsor risk.

"That is where a CRO can have a significant impact in helping sponsors to be thoughtful and intentional with their trial designs and development plans," said De. An experienced CRO should walk you through every step, from drug discovery to marketing authorization. "I think it's really important in this space to have a partner that can take you every step of the way."

Learn more about Allucent **here**.

*The insights team analyzes and comments on industry trends and creates thought leadership content for BioSpace and clients. The head of insights, Lori Ellis, can be contacted via **lori.ellis@biospace.com**. Follow her on **LinkedIn**.*

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