Solving the Numbers Game — THE THREE PILLARS OF LATE-PHASE CLINICAL TRIALS

Each phase of a drug trial presents challenges, but peri-approval and post-approval studies present challenges beyond those experienced by researchers conducting earlier-stage trials. Trial sizes are larger and global in scale, the amount of data is greater, and the studies often run much longer, resulting in greater costs. Given the size and scope of most late-phase studies, greater efficiency in logistics, recruitment, site operations, and information processing is absolutely essential to control costs and handle the huge volume of data.

As manufacturers compete to be the first to bring a new, safer drug to market, they must become more efficient. Sponsors need to be faster and smarter throughout each phase, and to do so, they must consider new, innovative processes and partnerships available to them. Far too many sponsors still rely on traditional methods simply because those are the methods they know and have always used. It is critical in today's industry that sponsors work with partners like CROs to leverage their expertise to ensure its clinical trials are safe and efficient. For a sponsor to improve its peri-approval and post-approval methodology, it must consider three key issues: risk-based monitoring, patient recruitment and technology platforms.

New Methods, New Benefits

Until recently, the FDA's recommended methodology for trial monitoring was to maintain personal contact with investigators throughout the life of the trial. Such regular visits to trial sites take time and carry a considerable cost. However, in August 2011, the FDA issued its draft guidance on risk-based approaches to monitoring clinical investigations. A risk-based approach combines on-site monitoring with centralized monitoring using available technology platforms such as electronic data capture (EDC) and electronic health records (EHR). On-site monitoring should be used for staff training, study documentation and compliance purposes. Centralized monitoring provides investigators with an efficient data analysis platform to identify outliers most at risk of non-compliance. The FDA now recommends an increase in centralized monitoring with a corresponding decrease in on-site monitoring, and that on-site monitoring should still be conducted at least once during a trial.

While a new approach to monitoring means training for staff, new equipment, and other expenses, sponsors must realize the benefits a risk-based approach presents and embrace this methodology. To fully understand the need for risk-based monitoring, first consider one of the biggest challenges in managing peri-approval and post-approval clinical trials – its size and scope. A typical late-phase study could involve more than 5,000 patients from hundreds of sites around the world. The efficiencies offered by risk-based monitoring are essential to managing costs.

Long-term cost savings may be evident, but some sponsors remain reluctant to adopt a risk-based approach. There are many aspects to a trial that a sponsor must take into consideration when designing a monitoring plan, including: complexity of the study, complexity of the population, geography, quantity of data, and patient safety. Safety protocols should be put in place to document critical data and study findings. Risk-based monitoring enables sponsors to put in place specific measures that ensure patient safety and compliance.

For sponsors looking to implement risk-based monitoring, they should consider a partner that is experienced with this trial model. While the FDA's draft guidance is less than a year old, some CROs have been utilizing risk-based monitoring for more than a decade. By leveraging the experience and intellectual capital of a strategic partner, a sponsor will be in the best position to not only ensure compliance and patient safety with the data, but more importantly, ensure data quality. Data measures can also be utilized to ensure quality measures that need to be met are met. In any trial, the most critical component is the trial data, and a risk-based approach leveraging the experience of a CRO is the best way to ensure the integrity of that data.

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Finding the Right Patients

As previously noted, late-phase studies require a much larger patient population than previous phases, with more sites and often on a global scale. Studies continue to grow in number, size, and complexity, forcing sponsors to rethink their patient recruitment strategies. The data the patients provide will be integral to the success of the study, but before any data can be collected, patients must first be identified. If a study calls for 5,000 patients, the task of recruiting can be daunting and resource-in-

tensive. The challenge is not only recruiting enough patients, but the right patients. The challenge of finding enough qualified patients impacts the majority of clinical trials. Having the right patients in the study will yield the most accurate data and enable sponsors to go to market sooner.

The patient recruitment process must be optimized to cost-effectively identify the right patients. For peri-approval and post-approval studies, sponsors increasingly rely on CROs to identify more efficient and scalable ways to recruit patients while controlling the costs. Sponsors and CROs must take advantage of innovative technologies around data-driven patient recruitment to help streamline certain aspects of clinical research.

Before a sponsor implements a new patient recruitment tactic, it should first design a recruitment plan that meets the specific requirements of the trial, including the culture, protocol design and therapeutic area. Recruitment plans should be based on experience and primary and secondary research. Methods can range from patient interviews, chart review, electronic health data, TV, and online outreach, as well as collaborations with patient advocacy groups.

Most traditional patient recruitment methods are inadequate and are not scalable enough to reach a wider patient population, prompt patients to act, and convert action into trial enrollment and retention. As the marketplace has become extremely competitive for clinical trial participants, a different mindset and holistic approach is required, one that also meets the informational needs of patients. Patient recruitment and retention methods can no longer be viewed as an afterthought. Instead, recruitment and retention strategies need to be developed earlier in the development process. More emphasis needs to be placed on the relationship with the patient, especially in lengthy and involved post-approval studies where overall engagement and compliance is challenging.

EHRs and the amount of health data available online is shaping the way biopharmaceutical companies use data to drive more efficient patient recruitment activities. EHRs are an effective and efficient tool for protocol assessment and design optimization, isolation of patient cohorts, site identification and for recruitment of patients. Electronic health data helps identify existing suitable patient registries or facilitate the building of data marts and registries, and can be helpful in verifying value and safety post launch, since monitoring patients allows the discovery of real-world use and the ability to proactively identify safety concerns. Social media is also emerging as an efficient recruitment tool, though many sponsors are still exploring its effectiveness.

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Some traditional methods of patient recruitment still play a key role in the process. Chart reviews still serve as the backbone of every protocol patient identification process. Above all other tactics used, the most critical to a successful recruitment strategy is patient education. Increased education and awareness among patients is essential to increase the numbers of people participating in clinical trials, as well as increasing formal training of physicians. It is imperative that sponsors and CROs work together to educate and engage the patient through a number of channels such as traditional media, digital media, and patient advocacy groups to connect with the targeted patient populations as appropriate for the trial, culture, and therapeutic area. Better education and engagement will not only yield more efficient patient recruitment, but also higher patient retention throughout the course of the trial.

The Technology Advantage

Whether implementing risk-based monitoring or streamlining the patient recruitment process, the keys to success always point back to new technologies. For example, clinical trials can be made easier through centralized monitoring, rather than just on-site monitoring, and electronic health data can streamline the process of recruiting thousands of patients from around the world. And there are multiple social media platforms that enable a sponsor to easily engage a broad audience, or on a one-to-one level. The old methods of clinical trials are simply not enough to safely and effectively administer clinical trials in today's market. New technologies present new challenges, as well as new opportunities.

For manufacturers reluctant to adopt new methodologies and new technology, it is imperative to understand that technology is an enabler. Technology is what allows trial sites to become more nimble, more cost-effective, and compliant. With the FDA sanctioning risk-based monitoring, sponsors must now realize the importance of technology in clinical trials.

Implementing new clinical trial technology is critical, but selecting the right technology can be as daunting as the trial itself. The goals should be simple — to achieve greater efficiency by gathering more data at a significantly lower cost per patient, and to improve product and patient safety. When evaluating new technology platforms, sponsors should seek a solution that meets expanding regulatory and commercialization needs, brings greater cost effectiveness to large-scale studies, and facilitates efficient safety and health outcomes data.

By partnering with a CRO, the sponsor can be assured that it is not only choosing technologies that best meet its clinical needs, but also that the technologies will be properly implemented and utilized, thus yielding the greatest cost efficiencies possible. Large late-phase studies can then be monitored more efficiently, patients can educated more effectively and recruited more accurately, and ultimately, studies can be completed faster and safer, thus allowing the sponsor to bring the drug to market sooner. PV