THE CLINICAL TRIAL LANDSCAPE is continually evolving and with it, efforts in the improvement of participant safety and data integrity. CROs are beginning to transition from on-site monitoring, with 100% point-to-point source data verification, toward a risk-based monitoring (RBM) approach that utilizes source data review and more centralized monitoring techniques better adapted for mitigating risk.

While RBM has gained considerable attention in recent years, reluctance still remains around the approach – from uncertainty arising from the use of “risk” employed in its name to sponsors being wary of potential implications on data quality and regulatory inspection outcomes.

Despite these concerns, there is a growing consensus that risk-based approaches to monitoring, focused on risks to the most critical data elements and processes necessary to achieve study objectives, are more likely than routine visits to all clinical sites and 100% source data verification to ensure subject protection, data integrity, and overall study quality.

Reducing Risk with RBM

The word risk raises concern among sponsors, but RBM can actually reduce the risk in a clinical trial. A risk-based approach with good judgment and sound reasoning can greatly curtail the need for clinical research associates (CRAs) to be road warriors. In some cases, a risk-based strategy could replace the need for such frequent site visits to quarterly or even once a year instead of the industry standard of every four-to-six weeks. A robust Clinical Monitoring Plan, with defined triggers for adapting on-site monitoring efforts, can establish the pathways needed for effective and appropriate on-site efforts.

Currently, most pharmaceutical companies perform on-site monitoring visits at pre-determined intervals with 100% source data verification of all case report form (CRF) data, under the belief that this is the FDA’s preferred monitoring strategy. In contrast, academic-based coordinating centers often use on-site monitoring less extensively with between-visit reviews performed centrally.

The FDA’s 2011 draft guidance on risk-based monitoring strongly encourages sponsors to tailor monitoring plans to the design and operations of the trial. There is increasing consent among regulatory agencies that risk-based approaches to monitoring, such as scrutinizing only the most critical data elements (e.g., those data supporting the primary and secondary safety and efficacy evaluations), will ensure subject protection, data integrity, and overall study quality. The agencies also contend that a well-designed clinical monitoring plan that includes a risk-based, abbreviated level of SDV; on-site monitoring; and centralized oversight monitoring will frequently enable sponsors to oversee the conduct of clinical investigations more effectively than routine visits to all clinical sites with 100% SDV. It allows for a more real-time and ongoing review of the data.
How CROs can help implement RBM

A good CRO partner can help manage sponsor concerns when it comes to using the RBM approach during a trial. Sponsors should look to their CROs to do the following in order to have a successful RBM trial outcome:

- Develop a monitoring plan appropriate for your trial. Conduct early discussions with your team members to clearly define how to assess risks, outline statistical analysis, and identify what monitors review (i.e., eligibility, particular data) either on-site or remotely.

- Develop a robust risk management plan at the beginning of the study. Potential risks and the strategies to mitigate them should be reviewed regularly with Sponsor/CRO partners throughout the life of the trial to optimize efficiency in decision making and in taking action when risks become reality.

- Establish solid communication pathways for issue discussion and escalation with key team members.

- Pull together different values and perspectives from various team members and start with the end in mind.

- Be actively involved in identifying triggers, trending and modeling, and programming for data as it is ongoing.

- Frequent, ongoing communication with Project Managers, CRAs, Data Managers, and Biostatisticians involved in report generation and central reviews, so CRAs can go back to the site to see what is going on and come up with a solution quickly and efficiently. This will enable on-site time to focus on identified issues and on what cannot be reviewed remotely.

- Get data managers more active on an ongoing basis to raise red flags when necessary.

- Focus less on source verification and more on source data review and analysis. Analysts look at trends and the data site to determine if something looks right or wrong.

- Support clinical sites in developing their own internal quality management plans. Training sites to perform quality control reviews of their own efforts on an ongoing basis does not replace independent monitoring by any means, but can serve to support the overall goal of safety and quality in the trial.

With the right CRO partner and a clearly defined RBM monitoring plan that fits the complexity of the study, sponsors should be less fearful and more willing to embrace risk-based monitoring on their next trial.

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