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On Site: Steps for Sites to Prepare for Risk-Based Monitoring

As the industry moves toward risk-based monitoring models, which reduce the frequency of study monitors' site visits, sites must begin to change how they do business.

Donna Dorozinsky, president of DWD & Associates, a clinical research operations consulting company, said risk-based monitoring means many activities routinely done by study monitors now become the responsibility of site staff. Sites will be expected to have processes in place for reviewing source documents, ensuring all adverse events have been reported and resolving data queries quickly.

"The investigative site now has to pick up some of the gaps," said Dorozinsky, who has worked in the clinical trials industry for more than 15 years and now assists sponsors and sites with the operational challenges of clinical research. "There has to be some type of quality system."

Since the model uses risk assessments and analytics to determine where to focus monitoring activities, key performance indicators at sites become even more critical. Dorozinsky said sponsors and CROs will closely monitor metrics — such as the number of days from patient visit to data entry, the time it takes to close queries, and the numbers of significant protocol deviations and unreported serious adverse events — as they evaluate where to target resources.

"If risk drives visits, then the goal is that a site has evidence of low risk," she said.

Investigators — including private-practice physicians who conduct research part time — should prepare for risk-based monitoring, Dorozinsky said, by implementing quality systems at their sites, including active investigator oversight, a way to track and address non-compliance, and a focus on building quality into overall study conduct. She offered insights into how sites can be prepared for risk-based monitoring:

Ensure investigator oversight. Sponsors want evidence that principal investigators (PIs) are actively involved in their clinical trials and that they don't delegate critical study activities to coordinators or other site staff. This oversight should include PI review of patient screening data and a formal, documented process for the PI to approve patient enrollment. PIs should review and sign diagnostic reports, rather than leave this responsibility to coordinators. In addition, PIs must review adverse events and assignment of causality; if a PI signs for causality, there must be a process in place to show the adverse event was properly documented.

Sites also need a process that demonstrates PIs review all protocol deviations and monitor the so-called notes to file, written to explain protocol deviations or clarify information about study documents. With remote monitoring models, Dorozinsky said sites should be especially careful about writing an excessive number of notes to file about minor issues. "If you are writing lots of notes to file, you have a quality issue," she said.

Track GCP/protocol non-compliance. Importantly, sites need to establish processes to track both protocol deviations and issues of Good Clinical Practice (GCP) non-compliance. Sites also must show how they monitor for non-compliance, particularly since they won't be able to rely on routine visits from study monitors to detect deviations. PIs then need to review protocol deviations or issues of GCP non-compliance to determine their impact on human subject protection, safety and data quality. In addition, Dorozinsky said PIs should evaluate not only deviations found in individual studies, but also their frequency across many studies. "If we begin to see a trend, we know we have site quality issues," she said.

Establish quality processes. Before a study begins, PIs need to review the protocol, make sure they understand the requirements, and ask for clarification when needed. With risk-based monitoring, sites can't rely on regular contact with monitors to answer questions about the study. "If there is any question at all, you need to make sure you get clarity from your sponsor," said Dorozinsky. "Push until you get an answer. Your answers can't be vague."

A quality process also requires developing procedures for core activities, such as complying with GCP requirements, obtaining informed consent, approving patients for participation, and reviewing charts and diagnostic reports.

Processes for training and keeping staff updated about amendments and ongoing protocol issues are other critical elements of a quality system. In addition, sites should have Corrective Action Preventative Action (CAPA) Planning programs that include provisions for identifying the root cause of a problem and ensuring effective corrective and preventative actions.

"When sponsors find a problem with a site and communicate it back to the site," she said, "they want the site to be taking some kind of action to resolve the problem."

Review source records. Dorozinsky said many sites currently lack a process for source document review; traditionally, they have depended on monitors for this task. But with the risk-based monitoring model, sites need to establish processes to review source documents to identify gaps, inconsistencies and under-reporting. Sites need to review patient visit records and laboratory reports; they also need a system to maintain accountability for investigational products each time a drug is dispensed, rather than recording the information at the end of a trial. Overall, the process should ensure that source review is attributable, legible, original and accurate.

Despite the operational challenges, Dorozinsky believes risk-based monitoring presents a great opportunity for sites that adopt quality processes to reduce their number of monitoring visits. "They can take the time they were spending with their monitoring visits," she said, "and get down to the business of conducting clinical research."

— Karyn Korieth

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