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FDA Warning Letter Teaches Sites Lessons on How to Avoid Doomed Trials

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To avoid being caught out by sponsors that don't follow clinical trial regulatory requirements, sites should make sure before they accept a trial that its monitoring, site activation and site coordination efforts are compliant, a lesson driven home by a recent FDA Warning Letter.

Nobles Medical Technology II, a vascular suture device developer, chose to suspend a recent significant-risk multicenter device trial after the sponsor's October 2023 FDA inspection turned up four major compliance problems:

- Failure to ensure proper monitoring and IRB review/approval
- Failure to select qualified investigators and monitors
- Failure to obtain a signed agreement from each investigator that includes a statement of the investigator's commitment to conduct an investigation in accordance with the agreement, investigational plan, applicable FDA regulations, conditions of IRB approval and conditions of FDA approval
- Failure to obtain a signed agreement from each investigator that includes sufficient and accurate financial disclosure information to allow the sponsor to submit a complete and accurate certification or disclosure statement

Investigators were not given information key to conducting the trial, including signed protocols, investigational brochures and labeling, and the sponsor lacked a written monitoring plan with procedures for monitoring the investigation, managing protocol deviations and handling investigator noncompliance, the warning letter reads. In addition, documentation was missing for investigator financial disclosures, continuing site review and IRB approvals, as well as for showing investigators had the experience and education needed to conduct and monitor the study.

Data integrity concerns were present, too. The FDA found site monitoring reports did not include documents reviewed, associated findings or communications with site staff, including whether source documents were compared with case report forms (CRF). Some CRFs were not signed by investigators on time; four CRFs were signed eight-to-12 months after monitoring visits and 11 CRFs were not signed at all.

All of these issues should be red flags for a site when it signs on with a sponsor. Look for sponsors that design study monitoring plans to be highly detailed and followed in order to ensure the trial is run in line with the protocol, participants are protected and data integrity is present, with the education and experience of those in charge of monitoring documented in the trial master file, Trevor Cole, WCG's director of client delivery, site and strategic operations, tells *CenterWatch Weekly*. Sponsors that don't do this run the serious risk of conducting trials that produce noncredible, inaccurate data and ultimately fail.

"Reports should document the monitoring activities detailed in alignment with the monitoring plan and illustrate what was monitored, when it was monitored, by whom, and observations or action items from the monitoring activities," Cole added. "Sponsors should also have procedures describing monitoring, handling of protocol deviations and investigator noncompliance."

"It is important for investigators to be knowledgeable in expectations for the study in regard to how oversight and involvement is documented and to perform those activities in as close to real time as possible," he continued. "For example, sign off on CRFs should be completed in timelines documented in study plans and contemporaneous to results when possible."

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