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Constructive Site Audits

By Gail Grant

The purposes of a site audit are to determine whether the rights and safety of the study participants have been adequately protected and to verify the accuracy of the clinical data. Audits also ensure compliance with regulations, guidances, the protocol, and the sponsor's standard operating procedures (SOPs). Audits are also invaluable opportunities for sites to obtain expert (and free!) advice. These objectives are best accomplished with the site's cooperation.

The site should view audits as valuable learning experiences, not time-wasting inquisitions. It is therefore very important for the auditor to establish and maintain a constructive working relationship with the site. If the site perceives the auditor as an arbitrary, judgmental, nit-picky, fault-finder, the relationship will be tense. If, instead, the site perceives the auditor as fair-minded, expert advisor with a positive attitude, who is willing to discuss issues to find the best solutions, the relationship will be harmonious. The site might even ask the auditor for advice on issues that the auditor would not otherwise detect. Following an audit, the site should be eager take action to correct any problems and prevent future occurrences of similar problems.

The primary work of auditors is to review study documents to identity any deficiencies in study conduct, especially systemic, "big picture" problems. There is wide agreement on the basic requirements for clinical trial documentation, but differences of opinion on the specifics. What a site monitor deems acceptable, another monitor or an auditor may not. Study sites may find themselves reworking study documents more than once as new monitors and auditors arrive with different expectations. In general, auditors have the final word, but what should a site do if that word changes or appears incorrect?

Questionable Audit Findings

Some auditors seem to have strange ideas about how to achieve the objectives of an audit. Their perceived power over sites may lead them to set forth requirements that serve no worthwhile purpose and, to the contrary, diminish the site's ability to focus on useful activities. We question whether some of the findings by auditors at our site add value to the clinical trial process, for example the following:

- The study coordinator did not record the batch number and expiry date of pregnancy kits (supplied by the central study laboratory) in the source documents.

  Recording this information is a reasonable idea (although the sponsor may already have the information from the lab), but not if the sponsor did not request it and there was no place in the case report forms to record it. Neither did the protocol or study handbook require saving the kits for documentation purposes.

- The study coordinator did not record in the source documents the time the investigator entered the clinic room to perform the physical examination or the time the independent joint assessor (IJA) entered the room to perform the joint assessment.

  Collecting this information may or may not be worthwhile, but, here again, it was not required by the protocol, the sponsor did not request it, and there was no place in the case report forms to record it.

- The principal investigator's (PI's) CV did not adequately document his clinical research experience.

  The PI had worked on other studies with the study sponsor. His CV stated that he had 16 years of clinical trial experience, had been a PI for over 150 clinical trials, and had authored over 200 publications. The CV met FDA requirements and had always been acceptable to the sponsor (and other sponsors). Nevertheless, the auditor required a list of all 150 studies, ignoring our concerns about confidentiality.

- The study-specific staff training log was inadequate because it did not include a description and source of the training materials.

  Our log was satisfactory to the sponsors of over 100 previous studies. The materials came from the sponsor, since they were study-specific.

- The site's SOP did not adequately document the IJA's role.

  The auditor demanded changes to the SOP that would have made it specific to the particular study and no longer suitable for general use.

- Screening log was inadequate because it required only a "Yes" or "No" answer.

  The auditor demanded independent documentation (e.g., medical records) proving that a subject had *not* taken a medication. She was not satisfied with the PI's medical history summary, including a list of all previous medications the participant had taken. It is, of course, impossible to prove a negative.

Discussion

We had the opportunity to present our objections to the above findings at post-audit meetings, but with no apparent effect. We did not receive a copy of the auditors' reports to the sponsors, so we do not know their contents. Neither the auditors nor the sponsors invited us to present our case to the sponsors, but we did so in some cases and obtained some concessions. The sponsors' letters directing us to comply with the corrective actions demanded by the auditors did not reflect our objections. The sponsors' letters did not suggest any openness to further discussion. We complied with the instructions.

In our experience, most auditors are fair, knowledgeable and provide constructive recommendations for improvement. However, when the site believes this is not the case, the sponsor should be receptive to discussing the site's concerns. In addition to correcting ill-advised directives, such communications would strengthen the relationship between sponsors and sites. It would also make for a healthier relationship if sponsors instructed their auditors to identify findings that clearly require corrective action. Auditors could leave less-significant findings out of their reports, or identify them as "no action required" suggestions for consideration by the site.

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