

Good Clinical Practice Q&A: Focus on Clinical Monitoring

Must all e-mail (i.e., printouts) and fax (including cover sheets) communications from sponsors to sites and from sites to sponsors be retained and stored at the clinical site or by the clinical trial sponsor? What is FDA's inspectional policy regarding these communications, and does the agency currently review this correspondence to ensure that it matches in the investigator and sponsor files?

Although such communications are not addressed specifically in FDA regulations, the ICH GCP guideline seems to suggest, at least indirectly, that such communications should be retained and stored by sites and sponsors. In Section 8 – Essential Documents for the Conduct of a Clinical Trial, the guideline states that, "Essential Documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of GCP and with all applicable regulatory requirements... Filing essential documents at the investigator/institution and sponsor sites in a timely manner can greatly assist in the successful management of a trial by the investigator, sponsor and monitor. These documents are also the ones that are usually audited by the sponsor's independent audit function and inspected by the regulatory authority(ies) as part of the process to confirm the validity of the trial conduct and the integrity of data collected"

Under 8.3.11 – Relevant communications other than site visits, the ICH GCP guideline identifies letters, meeting notes, and notes of telephone calls as communications that should be retained "to document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, [and] adverse event (AE) reporting." It is important to note, however, that some communications are not worth retaining, including e-mails sent to schedule and coordinate visits and flyers with menu choices for meetings. Many sponsors purge these unnecessary communications before storing documents at the end of a trial.

Although it is conceivable that an FDA inspector would visit both a site's and a sponsor/CRO's central files to compare the site's communication records with the same records stored in the sponsor/CRO's investigator files, it is extremely unlikely that the inspector would visit the sponsor's central files. The agency will inspect a sponsor's central files if it suspects that the sponsor/CRO has made changes to data provided by the clinical investigator. An FDA for-cause inspection of central files would, in all likelihood, be conducted by a different agency inspector (i.e., than the one inspecting the site), in part because field inspectors do not generally inspect outside of their assigned districts.

Monitors and auditors should compare records in the central files and site files well before the FDA begins the site inspection process and throughout the study as part of routine monitoring/auditing practices. Inconsistencies and other problems should be addressed as well. Given the large volume of correspondence, paper work, and record keeping involved in a study, a small number of discrepancies in stored documents, even I572s, is not unusual.¹

Do GCP regulations require that a site establish and maintain a monitor visit log? If so, what happens if a monitor forgets to sign it during a visit? And should a clinical auditor sign the monitor visit log?

Neither the FDA GCP regulations nor the ICH GCP guideline identify the need for a “monitor signature log.” It is worth noting, however, that the FDA does instruct its field inspectors, during clinical Site inspections, to determine whether a log of on-site monitoring visits is included in study records. This determination is part of the inspector’s assessment of the sponsor’s monitoring practices (e.g., method, frequency) for the study.

Since site monitoring reports are not maintained at sites, a visit log may provide the only site-maintained evidence, with the exception of correspondence, to “prove” that a CRA made routine monitoring visits. In some cases, the study coordinators also sign the monitoring log to further attest to the visit. The log provides a chronological review of the frequency of visits such that an auditor or inspector can quickly comprehend the intensity of monitoring activity.

In addition, a monitor visit log is an excellent means of establishing that monitoring frequency was appropriate given enrollment rates for specific periods of time. The monitoring log can be compared with the enrollment log to evaluate the adequacy of monitoring visit frequency.

If a monitor forgets to sign the log, he or she should sign it at a later date, noting the actual date of the visit and the date of the late entry. The fact that this is a late entry should be made readily apparent.

Clinical auditors do not sign the monitor log unless there is an institutional or sponsor standard operating procedure that requires them to do so. The only evidence that an auditor made a visit might be an auditing certificate placed in the study binder as well as related correspondence.

Originals of the monitor log should remain at the site. Copies should be forwarded to the sponsor central files. Sponsor staff should be alert to discrepancies between dates on the monitor log and dates of visits listed on monitoring reports. Discrepancies should be brought to the monitor’s attention and resolved. It is acceptable to annotate explanations of unusual events (earthquakes, hurricanes) on the log to help explain why a visit was cut short. Also, it is acceptable to explain that one of the visitors was co-monitoring or in training or present more as an observer rather than as an “official” monitor.²

References

1. “Good Clinical Practice: A Question & Answer Reference Guide”, Barnett International, 2005, pg. 66
2. *ibid*, pg. 66-67

Source

“Good Clinical Practice: A Question & Answer Reference Guide 2005,” is available for \$39.95 at <http://www.barnettinternational.com/>