

## Lessons Learned from 20 Years as a Site Monitor

By S. Eric Ceh

In over 20 years as a site monitor, I have learned many lessons, but the following are the most important:

### Knowledge

Site monitors cannot do their job without learning the rules, the protocol, the medical condition, the medical specialty, and the site.

Learn the rules:

- 21 CFR Parts 11, 50, 54, 56, 312, 314, 812 and 814, and related FDA guidances
- ICH Guidelines: Good Clinical Practice (E6), Clinical Safety Data Management (E2A), General Considerations for Clinical Trials (E8), Statistical Principles for Clinical Trials (E9)
- Declaration of Helsinki (for principles that go beyond the regulations)
- Local regulations, e.g., the European Good Clinical Practice Directive 2001/20/EC and 2005/28/EC in the European Community

Learn the protocol. First, scan through the document to identify any unfamiliar vocabulary and familiarize yourself with these words. Understand the tests and procedures. Understand how adverse events (AEs) will be handled per the protocol, since monitors spend a good bit of time on the site's identification and documentation of AEs.

Learn the medical condition, including the natural course of the disease, symptoms, diagnostics, procedures, standard treatments, and their side effects. Ask the study sponsor to provide training by a physician in that specialty.

Learn the medical specialty, including personnel, office organization, terminology and approaches to disease management. It makes it a lot easier to converse with site personnel.

Learn the site, including study personnel who will be responsible for what, and how and where study activities will be performed. Are there handoffs that might be problematic? Talk to your sites about any differences between the flow of study visits versus their normal practices; such differences often generate problems. If the study sponsor provides source document worksheets to the sites, advise them to modify the worksheets to follow their clinical flow and avoid unnecessary duplication of documents.

### Conduct

Site monitors should have many attributes, but the most important one is objectivity. The documents a site monitor produces should mostly present *objective* findings. If an issue cannot be documented, preferably with two or three examples, with a protocol or regulatory citation, there probably is not much of an issue.

Opinions and speculation can be difficult to defend. They can be problematic in an FDA inspection. Even misconduct can probably be documented with objective findings without adding a conclusion that misconduct was found. Any attempts by project management to sanitize documents by deleting objective findings should be strongly resisted.

Objectivity facilitates constructive relationships with site personnel. The parties might disagree on a finding, but objectivity keeps the discussion at a practical, problem-solving level. The focus should be on the events documented in the findings, not on the people. Site personnel do not like being judged, but they can't argue with accurate findings. Of course, site monitors make mistakes too, which should be corrected based on site feedback.

If a site monitor perceives an underlying problem with a site, he or she should alert project management of his or her concerns as soon as possible with objective findings and documentation, before the problem grows larger. Keep in mind that project management is likely to perceive a site that is weak on GCP but strong on enrollment as a great site.

## **Tools**

The following tools are very useful. Creating a Site Summary and Subject Summaries will pay off later in efficiency, accuracy and timeliness.

### **Site Summary**

For each site, create a Site Summary that lists IRB activities, site personnel information (CVs, licenses and training), lab certificates, study drug/device receipts, notes to file, correspondence, and other documents typically found in a regulatory binder. (See Site Summary example at [http://www.firstclinical.com/journal/2014/Example\\_Site\\_Summary.docx](http://www.firstclinical.com/journal/2014/Example_Site_Summary.docx).) Use this document during visits to identify and address site regulatory issues. Between visits, update the document based on communications from the site of IRB actions and other pertinent developments.

### **Subject Summary**

Create a Subject Summary (also known as monitoring notes) for each of your sites' study participants. (See Subject Summary example at [http://www.firstclinical.com/journal/2014/Example\\_Subject\\_Summary.docx](http://www.firstclinical.com/journal/2014/Example_Subject_Summary.docx).) This document is mainly used by the monitor to track the extent of monitoring and key data points. It can be shared with site or project management for clarification purposes.

Subject Summary contents vary by study, but usually include the activities listed in the protocol timetable. After arriving at a site, populate this document from source documents before reviewing the case report forms (CRFs). Once you begin reviewing the CRFs, highlight the datapoints you listed on the Subject Summary that were missed or incorrectly entered by the site that need to be queried, along with observed deficiencies that can be included in the visit report and/or post visit letter.

Use the Subject Summary to facilitate the generation of effective queries and informative findings. When writing a query, whenever possible, use your Subject Summary notes to identify the data point and corresponding source document in question so the issue is clearly presented, e.g., "The medical history included excess bleeding per the pre-op note dated 6/17/13. Please confirm to add this condition to the subject history." Refer to the Subject Summary and attached documents when writing the Visit Report, e.g., the extent of the review during a visit and findings like adverse events, deviations, source document issues, and drug/device accountability. This tool enables a quick response to project management inquiries about a subject.

For studies that use electronic database capture (EDC), review the database entries prior to a site visit and populate the Subject Summaries. Upon arriving at a site, first review the source documentation and update the Subject Summaries, and then monitor the data in the EDC system.

## **FDA GCP Q&A Service**

The FDA has a small team of GCP experts who can clarify tricky regulatory questions. This office normally responds within a few days to GCP questions emailed to [gcp.questions@fda.hhs.gov](mailto:gcp.questions@fda.hhs.gov). A free, searchable database of past Q&As is available at <http://firstclinical.com/fda-gcp>. Pertinent FDA guidances, information sheets, past Q&As, and other resources can be found at <http://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm>.

## **Work Product**

Often prepared without due care, the following documents should accurately portray the work performed and protect the monitor if things go awry:

### **Visit Report**

Visit Reports should consist almost entirely of objective findings and cite two or three examples that clearly delineate each issue observed during a visit. If possible, attach copies of source documents or regulatory binder documents to support your findings. When writing a Visit Report, draw details from the Site Summary and Subject Summaries.

### **Post-Visit Letters: Action Items**

The primary purpose of post-visit letters is to help sites correct and improve their performance through specified action items. To facilitate the tracking and completing of site action items, consolidate them in the following three sections:

- Action items completed since the last visit
- Action items still pending
- New action items

## **Conclusion**

"Fear slows you down." Site monitors who have mastered the regulations, guidances and protocols, use tools that facilitate their work, and arrive at a site well prepared are much more likely to complete a study visit accurately, efficiently and without friction with site personnel.

I salute all who have endured and fought the good fight so we can have the best medications and medical devices in the world.

## **Author**

S. Eric Ceh, DPM, CCRA, is President of SEC Clinical Consulting, a provider of monitoring, quality assurance, and project management services. Contact him at 1.207.926.8086 or [sec\\_consulting@sbcglobal.net](mailto:sec_consulting@sbcglobal.net).