

## "Clinical Research Coordinator Handbook, 4<sup>th</sup> Edition"

Deborrah Norris, 2009, 157 pages, Plexus Publishing, \$39.95

Review by Norman M. Goldfarb

"Clinical Research Coordinator Handbook, 4<sup>th</sup> Edition" is an excellent, hands-on introduction to clinical research for study coordinators, investigators and clinical research associates. This affordable and very clearly written book includes three types of material:

- Brief explanations and comprehensive checklists cover a broad range of clinical research activities. This material provides a framework of key areas where expertise is required, without much elaboration.
- Detailed sections cover selected topics, such as common CRF errors, clinical laboratory licenses, and FDA inspections. Some of this material is not included in books far more lengthy and costly than this one.
- One of the six appendices includes 21 forms that can be adapted for use by a research site.

This book has been selected for  
[The First Clinical Research Bookshelf](#)  
Essential reading for clinical research professionals

An extremely useful section details case report form errors that are likely to generate data queries, and how to find and fix them before submission. There are four common types of data problems:

- Incomplete data
- Too much data (in the wrong place)
- Ambiguous data
- Misspelled words

Here is the section on notes to file:

A common document many clinical sites are asked to create is a Note to File (NTF). Generally, a NTF is a memo and, when used appropriately, can be a positive practice.

A useful NTF includes the following:

- Identification of a problem that occurred during the conduct of the clinical trial
- Procedural change identified to correct the problem to prevent recurrence
- Initiation of a procedural change

In the event of an inspection by the FDA or other regulatory agency, the inspector may still leave a citation for the initial problem, but the change in procedure mitigates the citation and provides the site with a strong response to the finding.

Many in the clinical trial community consider an NTF as a panacea for all things that have not been done appropriately during the conduct of a clinical trial. Make a mistake? What are CRCs told, often by the CRA? Write an NTF, and put it in the Regulatory Binder and/or the subjects' source documents. This practice has become so ubiquitous that new CRAs and CRCs sometimes think NTFs are regulatory requirements, necessary to document and correct the problem to prevent it from

recurring. This is a misconception. There is nothing in the FDA regulations or guidance documents requiring Sponsors and research sites to use an NTF.

Many research professionals think an NTF is a corrective action. Many NTFs are quickly written without regard to correcting the problem. Sometimes, the NTF is generated well after the deviation/problem has occurred, and all is considered right with the pharmaceutical world, when this is not the case. In fact, the FDA recently reprimanded a Sponsor for "after-the-fact-memos."

In an FDA Warning Letter dated October 23, 2007 ([www.fda.gov/foi/warning\\_letters/s6551c.htm](http://www.fda.gov/foi/warning_letters/s6551c.htm)), the FDA wrote: "Our investigation found the Sponsor failed to take any action except to generate numerous memos to file after all the subjects completed the study." The Warning Letter then noted at least 89 memos that were generated after a monitoring visit. Instead of writing an NTF, the Sponsor's time is better spent qualifying the site and training the study staff.

Documenting a mistake means absolutely nothing during an FDA inspection. Corrective action, and whether the corrective action was appropriate, should be what is documented. If a site does not have an effective quality system in place prior to the start of a clinical trial, especially subject enrollment, then the Sponsor, CRAs, PIs, and study staff should have an understanding of how the Protocol will be monitored and how discrepancies will be communicated and corrected. Sponsors cannot depend on post-monitoring visit letters to demonstrate compliance in serious situations.

In my own auditing experience, I have noted that NTFs are frequently contentious issues between CRAs and the study staff. I have seen trivial NTFs placed in Regulatory Binders at the request of inexperienced CRAs. In addition, since they are asked to generate so many, some CRCs have developed a habit of writing NTFs instead of developing good recordkeeping practices, or, in some cases, in place of having SOPs. All an NTF accomplishes is documenting poor performance, and ineffective work rarely impresses the FDA.

Conducting clinical trials according to all the regulations and guidelines is hard work and requires professional cooperation to quickly address queries and genuine findings that need correcting. Once an NTF is written and becomes a study document, it cannot be retracted. The result is a lose-lose situation for everyone involved in the study. These NTFs are a road map for any inspector, showing all the mistakes made during the conduct of the Protocol. Perhaps a better solution is to develop a quality system of SOPs from the beginning. These SOPs should include training on the Protocol, documenting the informed consent process, delegation-of-authority tasks, storage of the investigational product, how data corrections are made, and how problems are identified and corrected. These SOPs should be provided to all study staff so there is consistency during the clinical trial. Sites should document the corrective action and keep NTFs few and far between.

The book consists of 16 chapters:

- Introduction
- Federal Regulations Governing the Obligations of Clinical Investigators
- The Clinical Research Organization
- Investigator Responsibilities
- Duties of the Clinical Research Coordinator
- The Creation of Study Source Documents

- Obtaining Informed Consent and Assent Approval
- Pertinent Forms and Study Records
- The Prestudy Site Visit
- Recruiting and Enrolling Subjects
- Conducting the Study and Keeping Records
- Preparing for an FDA Audit
- Clinical Research: Potential Liability
- Writing the Study Summary
- Achieving Credibility and Recognition as a Clinical Research Coordinator
- Electronic Data Capture

The book is available in bookstores.

### **Reviewer**

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