CHAPTER TEN

Case Report Forms (CRFs) and Electronic Data Capture (EDC)

Whether using paper forms or electronic forms, recording the data collected during a clinical study is one of the major tasks of the study coordinator. With advances to technology, it is likely that those CRFs a CRC works with will be electronic (eCRF). Technology has influenced an increase in other forms of electronic data capture (EDC) as well that link to data collection, such as randomization and investigational product assignment platforms, such as interactive voice or electronic registration systems (IVRS/EVRS), and electronic patient-reported outcomes (ePRO) for study patient diaries and even electronic informed consent (eIC). A study coordinator is likely to have multiple electronic systems to work with, some not merged with another. The ability to coordinate multiple computerized systems used for a clinical trial is one important skill set that is needed more and more by CRCs.

CRFs

CRFs are used during a clinical trial to record the protocol-required data for each study subject. CRFs standardize the collection of study data and help to ensure that the medical, statistical, regulatory and data management needs of the study are met. It is the "deliverable" data of the study and forms the basis for all analysis of the drug/device. Working with CRFs is a significant part of the workload of many CRCs and is a major factor in the performance of a clinical trial. Some research sites divide the responsibilities of the coordinator into two or three types: 1) patient, 2) regulatory and/or 3) data coordinating. Some CRCs might work more with CRFs than others depending on the study operations structure.

Paper CRFs are being used less and less for studies, but are unlikely to be phased out completely. Some small studies sponsored by startups in early phases and/or some investigator-initiated studies are among types of studies that are likely to continue to use paper due to cost and operation complexity. This chapter discusses the collection of data on paper CRFs first, and then

electronic data entry. In both situations, it is critical to properly record the data from the trial. Remember that decisions regarding the investigational product are based on the observations from study sites, so it is essential that the data recorded are valid and accurate. Additionally, many of the topics discussed for paper CRFs also hold true for electronic forms.

Case Report Form Completion

After or during a study subject visit, the required data need to be recorded for the sponsor.

When completing the CRFs for a subject, the CRC must keep a number of things in mind. The study coordinator must be sure that the data entered on the forms are accurate, complete and legible. The data must be derived from original source data that is linkable to the subject and the author. Thus meeting ALCOA, as covered in Chapter 2.

The CRC should ensure that each item has been completed and each blank filled in. Check that the answers are within range, the form is signed, if appropriate, and by the correct person, and the header is complete and correct. (The header is the top part of each paper form that lists the subject and study identifiers.)

Next, check all the pages for a single visit. Also, check for completeness, correct dates and that the visit was within the allowed window. Check to be sure that the timing of procedures was appropriate. If, for example, there was to be a blood draw followed by another activity, then the blood draw should have been done first, and the times should reflect this. Any time there is a specific order to be followed for activities, that order must be followed. If the source data reveals that the protocol was not followed, then the data should be entered into the CRF as is in the source and the CRC should complete a protocol deviation report or documentation as required by the study sponsor. It is critical that any deviations are documented within the subject's source document with any actions performed in relation to the issue. For example, if it was discovered that a test was not performed at a visit and the subject was called and asked to come in for an unscheduled study visit, this should be documented. The interventions needed due to the deviation might also require additional CRF forms to be completed (e.g., the unscheduled visit CRF page). The CRC will find they are working between the source documents and CRF quite a bit.

The CRC should ensure that there is consistency across forms. If the subject is getting better according to various ratings, then the overall rating should reflect an improvement. If a form says there was a concomitant medication administered for an adverse event, then the medication should be listed on the concomitant medication form and the adverse event entered on the adverse event CRF. In addition, the CRC should think about what appears on the forms, and whether it makes sense given the subject's condition and the study activities. Sometimes it's easy to see individual data but miss the view of the overall data trend.

The CRC should also check the current visit against previous visits. Are the

FAQ

One sponsor insists that we have a source document for every entry on the case report form. Is this in the regulations?

No. However, the sponsor may not agree to let you conduct the study if you cannot meet its internal requirement.

data consistent from visit to visit? Was the timing of procedures appropriate? Do the data match where necessary? Are the visit windows correct over time? Usually each visit window is calculated by going back to the starting or baseline date, not from the previous visit. The reason is that if a subject is always two days late, and if the window is always calculated from the last visit, there is always going to be the addition of two days and two more days and two more days and so forth. After a while, there is not enough study drug for the subject to finish all the visits specified by the protocol. Visit windows should be clearly defined in the protocol, but this is not always the case. The CRC should ask for clarifications if they are not clear. Within a protocol, there is commonly a Table of Events where the study windows are commonly found.

Lastly, the CRC should be sure to have correctly identified the same subject at each visit, with the same initials, numbers and/or other study identifiers. It is always better to straighten out any problems the CRC may find when completing the CRFs before the study monitor comes to review them. Remember that CRAs are on the same team with the same objective—clean, accurate data.

Subject Source Document Review

Source document review (SDR) is when the sponsor monitor reviews the quality of data. This includes the compliance to the protocol, the support for ALCOA and the accuracy and completeness of the data recorded. Sometimes a part of SDR is source data verification (looking for transcription errors, or finding that what is in the source does not meet the CRF). Source data verification (SDV) by itself would not support quality data. For certain critical data points, a high accuracy rate is necessary in the data entered in the CRF (e.g., information about endpoint data procedures and also AEs), but the quality of the source that the data came from is critical. So the focus of monitoring is SDR with some SDV. Study coordinators also perform SDR when completing the CRF and working with the monitor.

A source document is any document on which the data are first recorded. Remember that the investigator is required to maintain adequate and accurate case histories (source and CRFs, 21 CFR 312.62 and 21 CFR 812.140). All observations pertinent to the study should be documented; however, not all of them will be requested in the CRF. The source will have more information than the CRF. The source allows reviewers to be sure the study subject