Module Design/Outline

One of the most important aspects of a Clinical Research Associate's (CRA) work is to ensure the integrity of clinical research by reviewing data that have been collected at clinical research sites. Clinical research is conducted in large hospitals, university academic centers, or smaller clinics and doctor's offices. Research is conducted according to research protocol, and data are recorded on Case Report Forms (CRFs) (Woodin & Schneider, 2003). However, there is an intermediate step between conduct of study procedures and the recording of data on CRFs with pre-designed data fields, and that crucial step involves use of source documents (2003).

Source documents are paper and electronic sources of information that are completed, collected, or otherwise used during the course of a clinical research study. Examples include patient charts, patient diaries or surveys, physician's progress notes, lab reports, ECG or EEG data, and all other sources where data are first recorded or collected (FDA, 1996). A primary part of a CRA's work is to review all source documentation for study participants to make sure that: a) the study has been conducted according to protocol, b) source documentation is complete, c) data that have been recorded on CRFs match information that have been recorded or collected as source documentation, d) issues and inaccuracies within source documentation and within CRF pages are communicated with site staff and addressed by them, and e) all discrepancies between source and CRF are communicated with site staff and corrected by them. This module is designed to train new CRAs on this process of source document verification and data review and to ensure they will be able to conduct this work.

Lesson Title

This training module is titled “Data Review” and is presented in a manner that is authentic and as close to the real world as possible. The module is self-paced. Morrison, Ross, and Kemp (2007) point out that learners participating in self-paced learning programs work harder, learn more, and retain more of what is learned. Panel Discussion, presented via video to each learner will be utilized to provide the essential points of data review. Case Study will then be utilized to provide real-world scenarios that are studied and worked on by CRA trainees. The case study will utilize a sample protocol along with 3 sets of sample source documents and CRFs. Each set presents “real world” data for a research participant in the mock research protocol.

Learning Outcomes

Four individual, yet related outcomes exist within this module. First, trainees will demonstrate that they are capable of reviewing and understanding a research protocol. In particular study procedures, inclusion/exclusion criteria, adverse event and serious adverse event reporting, and primary and secondary objectives and variables must be properly understood in order for trainees to successfully work on the case study. Second, trainees will develop source documentation review skills. In order to review data, all source documentation must first be reviewed in detail. Since all CRAs taking this training course have had some experience in the past it is not necessary to teach source document review skills from scratch. However, that skill is a learning outcome so as to assure all CRAs in the training program are capable of performing this task.

Thirdly, trainees will develop CRF review skills. In order to know whether there are discrepancies between source and CRF or between CRF pages, a CRA must carefully

review CRF and be able to spot discrepancies. For example, Concomitant Medication CRF lists medications that a research participant may have used other than the main investigational agent under study; Advil for instance. At the same time, Adverse Event CRF lists adverse events that have occurred while a participant is active in a research study; headache for instance. It is necessary that data points between concomitant medication and adverse event CRFs complement one another (Woodin & Schneider, 2003). For instance, two Advil tablets taken on July 4th 2008 should have a matching data point of headache that has begun around the same time.

Lastly, trainees will practice using information contained in source documents to ascertain whether data are correctly recorded on CRFs. In all instances, if mistakes or inconsistencies are noted, trainees must learn how to effectively ask site staff to address them. Data recorded on CRF are data that are ultimately sent to the study sponsor and subsequently analyzed to understand whether a particular investigational agent is safe and/or efficacious. It is important that these data are as accurate as possible and data queries are an important way of making certain that is the case (Woodin & Schneider, 2003). This module will allow CRAs to practice data review and issuing data queries, as they would in the real world. Trainees will learn to review data and to write neutral queries for correction or confirmation of data points.

Course Resources

The first aspect of this module uses video recordings of panel discussion. The panel if formed by one person from data management department, one from clinical operations department, and an instructor. The panel discussion provides an introduction to each department's function within CRO X, reviews the real-world tasks of a CRA

within the confines of the current module. The video will be downloadable to the workstation of each CRA registered for this training module and each trainee may view it when they are ready to begin the module, and repeat viewing as needed. The panel discussion lasts approximately 75 minutes and is designed to provide advice and tips in addition to formal instruction on completing the case study.

The second part of this module involves a case study that is designed to be as close to a real-world scenario as possible. The case study package will be a digital download and includes: a) written instruction for completing the module, in addition to instruction provided in video format, b) the sample research protocol, c) sets of source documentation for three study participants, d) sets of case report forms for the same three study participants. Source and CRF will include data, correct and incorrect, as related to the sample research protocol and procedures and information within it. Source and CRF will contain errors and data inaccuracies or mistakes that trainees will be instructed to find as part of the learning process. Due to time constraints, and to prevent trainees from becoming bored or frustrated, the study protocol will be a simplified study. And source and CRF will be primarily geared towards safety issues and primary outcome variables like medical history, inclusion/exclusion criteria, concomitant medications, adverse events, etc. Such safety profiles, and primary outcomes, are the most important issues in clinical studies and may therefore be a focus in this module.

Individual Activities

Each trainee will complete the module from his or her home office or anywhere else they may have time to work on the module. Activities of the module are self-paced and may be completed within 14 days of the module's start. Just as a CRA may have

resources like lead CRAs, that may answer questions in the real world, an instructor will be available to answer clarifying questions as needed. All content will be delivered digitally to each trainee's laptop. However, with the exception of the video, each trainee can print the content of the module if desire, to make notes, flag important pages, highlight, or otherwise interact with the protocol, source documents, and CRF pages for learning. Printing also allows each trainee to further emulate the real-world experience of monitoring as a majority of clinical studies still use paper for some data capture (Woodin & Schneider, 2003). As electronic data capture gains in popularity, future versions of this module may have purely electronic components, including use of an electronic data capture system. The end result of going through the exercise is a list of mistakes and data discrepancies that each trainee will write in the form of data queries and submit to the instructor. This list is both the results of the exercise, as well as the primary means of assessing each trainee's work as the basis upon which feedback may be provided.

Assessment

Morrison et al. (2007) explain that an important advantage of constructed-response tests, versus objective-type tests, is that high-level cognitive objectives can be more appropriately evaluated with the former test method. They further explain that problem-solving questions, similar to essays, are well suited to evaluating higher-level cognitive outcomes such as application, analysis, and synthesis. Since it is important for assessment to reflect real world conditions which in turn increases validity (2007) the learning materials used in this module are the basis of assessment.

A CRA working in the field is expected to provide data queries to the site that is conducting clinical research and collecting data. The difference between the protocol,

source documents, and CRF that are provided in this module, and what a CRA may encounter in the real world is that in this module mistakes are determined in advance and designed into the module material. This allows for adequate reliability of the assessment in that it is known in advance what the mistakes are before each learner is evaluated on how well they have realized those mistakes. Feedback will be provided not in terms of grades but rather in form of a narrative to let the trainees know how they did on the learning exercise, which items they failed to identify as data mistakes, and which areas are weaknesses for the learner and required further attention. This feedback may also be used by each learner, as discussion points with their manager, following conclusion of the module.

Discussion/Interaction

This module is designed to provide all of the material that is needed for a trainee to get a firm grasp of the requirements for proper data review. After reviewing this material each trainee uses the material as the basis of the learning exercise. However, each trainee is able to discuss uncertainties that they may encounter in the module material and is able to obtain clarification as needed. Since clinical research uses human participants as its primary providers of data, and since humans are not always accurate in what they report, it is possible for confusing or contradictory data to exist (Woodin & Schneider, 2003). As each learner encounters such voids in data or contradictory data, each trainee may speak with the instructor via email or telephone in order to better understand how to handle such matters, which may ultimately be inconclusive.

Upon completion of the module and after the list of data queries have been submitted to the instructor and feedback has been provided to the learner, there may be

additional discussions between the instructor and learner and via teleconference between learners. This more informal discussion may be used to further understand the concepts of data review and allow trainees to share their own real-world experiences on aspects of a research protocol and conducting data review. And also to share instances when a CRA simply can't make further progress in facilitating better data. Knowing when to ask questions and make written queries and when to simply note missing data can make the difference between a happy CRA and a cooperative clinical study site, and a burned-out CRA and a site that views him or her as unrealistic and overly demanding. This discussion can form the basis for future modules that address attitudes and may use role-playing and videotaped scenarios to teach CRAs how to best interact with site staff.

References

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