

Pre-study: Preparing for a Study

GCP includes three main stages with associated activities and essential documents. These stages include 1) pre-study, before the clinical phase of the trial starts, 2) trial conduct, during the clinical conduct of the trial and 3) study completion or termination, after the clinical trial conduct has been stopped. The investigator or delegate, commonly the study coordinator (CRC), must maintain quality documentation to support the investigational site activities related to each stage of GCP. Per ICH E6 GCP, *“Essential Documents are those documents, which 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 Good Clinical Practice and with all applicable regulatory requirements.”* Filing essential documents in a timely manner can greatly assist in the successful management of a clinical trial.

Essential documents are also those that are routinely reviewed by the sponsor monitors, usually audited by the study 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.

ICH E6 Section 8 includes a list of essential documents for investigators and sponsors to maintain during the three stages of GCP. A description of the purpose for each document is included. It is acceptable to combine some of the documents, provided the individual elements are readily identifiable. It is also important to remember that the quality of each individual document meets the ALCOA standard discussed in Chapter 2, and collectively the documents map to other essential documents related to their purpose. For example, individually, an investigator’s curriculum vitae (CV) must be attributable to the investigator, accurately support the investigator’s qualifications to perform and oversee the study, but also link collectively to many other documents to support the investigators qualifications, such as training records. A study coordinator should have the ability to review the documents for quality.

Essential documents are filed at sponsors and sites within their trial master file (TMF). TMFs should be established at the beginning of the trial, both

at the investigator/institution site and at the sponsor's office. The term TMF was derived from ICH E6 GCP and is commonly called a variety of names by sponsors or investigators.

In this chapter, we discuss a number of activities that take place before a site is selected, as well as activities that must be completed before a study site can start to enroll subjects. Topics include: sponsor site qualification, assessing protocol feasibility, budgeting, site preparation for a study, sponsor site initiation, investigator meetings and financial disclosure. Study coordinators are usually involved in all of these activities and need to have a thorough understanding of each of them.

Sponsor Site Qualification

The sponsor site qualification is a critical step for both the sponsor and the site. For the investigator, these visits determine whether the site will be selected to participate and will also give the site time to determine if the study is right for them. For the sponsor, site qualification activities are the primary method of determining the best sites to conduct their studies and, if chosen, to identify the areas of greatest risk for a site.

When a sponsor or CRO is looking for investigative sites to conduct a study, the first contact usually is by telephone or fax. If it appears there is a high level of interest in the protocol on the part of the potential investigator, and if the sponsor feels there is good potential for placing a study at the site, the sponsor will arrange a time to visit the site in person. This will enable the sponsor to better evaluate the investigator's capability to do the project. Many companies require a signed confidentiality disclosure agreement (CDA) before sharing a protocol summary; in this case, they will email or fax an agreement to the site and have it completed and returned before sending the materials. Note that some sponsors and CROs send a preliminary questionnaire to sites to assess their suitability for a particular clinical trial. It is a point in the site's favor to return the signed confidentiality agreement and any questionnaires to the sponsor/CRO quickly. If a sponsor or CRO has worked with an investigator within a certain period of time and the investigator performed well with enrollment and is compliant with the protocol, the qualification visit might be able to be waived or abbreviated if the sponsor/CRO policy supports this. In this case, the sponsor/CRO would verify that conditions at the site have not changed to support the quality conduct of the trial.

When a sponsor representative, often the sponsor site monitor, completes a qualification visit to a potential investigation site, they evaluate the investigator's experience, and interest in the trial, as well as that of the applicable staff and facility. The potential to enroll the sponsor's desired amount of subjects is also assessed. The sponsor's monitoring visit report and study-specific requirements guide the CRA in making the site qualification assessment. There is an example of such a checklist in Appendix D.

FAQ

What are the most important factors in a sponsor's determination of which sites to choose for a study?

Past experience and current capability are probably the most important, but all of the factors mentioned in this section will be taken into account. And many sponsors won't even consider using an investigator who does not have a CRC.

The sponsor should request a copy of the investigator's CV in order to make a general assessment of the investigator's experience and expertise. The sponsor will want to know if the investigator has conducted trials similar to the one being proposed or has worked with similar compounds. The investigator and the study coordinator should read any materials (protocol synopsis) before the evaluation activities so they are prepared for any discussion or completion of a questionnaire.

The sponsor will also evaluate whether the site has sufficient staff and an appropriate facility to conduct the study. Many sponsors will not place a study at an investigative site that does not have a study coordinator. During the evaluation activities, the sponsor will want to meet and spend some time interviewing the study coordinator. Not only must there be appropriate people available for a study, but those people must have sufficient qualifications and time to participate.

During an on-site qualification visit, the sponsor will tour the facilities. The sponsor will want to see that there are appropriate investigational product and study supply storage areas, the equipment necessary for performing the study and a place for the sponsor monitor to work during monitoring visits.

The sponsor will assess the enrollment potential of the site, including whether subjects will come from the investigator's current patient population or if they will be recruited from elsewhere. For investigators that enroll their own patients, access to potential study subjects is easier. But independent research centers usually have good recruiting departments that are efficient in planning and recruitment strategy. In either case, the more thorough the records are concerning access to the study population, the better the enrollment estimates will be.

There are several other items a sponsor monitor will want to discuss during a qualification visit. One is whether or not the site is conducting, or is planning to conduct within the same time period, any competing studies. A competing study is usually one in which similar subjects are to be enrolled. In order to meet the enrollment targets, it's important that a study does not have to compete for subjects with another sponsor's study. Competition for subjects can have a great impact on the ability to meet enrollment targets.

Another factor is the timing for the study related to the investigator and delegate's availability. If the investigator has too many active studies at the same time, a study may not get the attention it needs to be done well.