Monitoring of Clinical Trial

Topic covered

- ❑ Purpose of Monitoring
- ❑ Frequency of Monitoring
- ❑ Selection of Monitor
- ❑ Monitors responsibility
- ❑ Different types of monitoring visits

Purpose of Monitoring:

- The rights & well being of the human subjects are protected .
- The reported trial data are accurate ,complete and verifiable from source documents.
- The conduct of the trial is in compliance with the currently approved protocol or amendments, with GCP & with applicable regulatory requirements.

Frequency

- Frequency of monitoring visits is not defined by ICH or FDA regulations
- ICH states that “the sponsor should ensure trials are adequately monitored before, during and after the study”.
- The frequency of monitoring depends on the complexity of the study, rate of enrollment, GCP compliance issues

Selection & Qualification of monitors

- Should be appointed by the sponsor.
- Should be appropriately trained & should have scientific/clinical knowledge.
- Qualification should be documented.
- Should be thoroughly familiar with the IP, protocol, ICF, & any other written information to be provided to subjects, the SOPs, GCP & applicable regulatory requirements.

Monitors responsibility

- Acting as the main line of communication between the sponsor and the investigator.
- Verifying that the investigator has adequate qualifications and resources throughout the study.
- Verifying that the investigational product is stored, dispensed and returned properly and that only eligible subjects receive it at the protocol specified dose.
- Verifying that the investigator follows the approved protocol/amendments.

Types of Monitoring Visit

The most common types of site visits for industry-sponsored studies:

- ❑ Site Evaluation/Qualification Visit
- ❑ Site Initiation Visit
- ❑ Site Monitoring Visit
- ❑ Site Close-Out Visit

Site Evaluation Visit

- ICH Guidelines nor FDA regulations specifically require a Site Evaluation Visit.
- ICH does require a pre-trial monitoring report as part of the “Essential Documents” and states that there is a need for on-site monitoring “before, during and after” a trial.
- FDA “Guidelines for the Monitoring of Clinical Investigations” does recommend that a monitor visit the site of the clinical investigation prior to the initiation of the trial.

Site Evaluation visit (cont…)

Investigator's Qualifications:
Up-to-date CV
Specialty
Previous experience in conducting trial.

Adequate Resources:
Retrospective data
Sufficient time
Adequate number of qualified staff
Adequate facilities:
Exam rooms
Pharmacy/Study drug storage area
Laboratory or specimen processing area
Special testing areas (x-rays, CT scans, endoscopy, etc.)
Record keeping facilities

Site Monitoring Visit

Verifying that the investigational product is stored, dispensed and returned properly and that only eligible subjects receive it at the protocol specified dose.
Verifying that the investigator follows the approved protocol/amendments.
Verifying that written informed consent was obtained before each subject's participation in the trial.
Ensuring that the investigator receives the current Investigator's Brochure and safety updates.
Ensuring that the investigator and the investigator's staff are adequately informed about the trial.
Verifying that the investigator is enrolling only eligible subjects.
Verifying that the investigator and the investigator's trial staff are performing the specified trial functions, in accordance with the protocol, and have not delegated these functions to unauthorized staff.
Reporting the subject recruitment rate.
Verifying that source documents and other trial records are accurate, complete and up-to-date.

Site monitoring visit (cont…)

Informing the investigator of any CRF entry error, omission or illegibility. The monitor should ensure that appropriate corrections, additions or deletions are made, dated, explained (if necessary) and initialed by the investigator or a trial staff member that has been authorized to make CRF changes for the investigator. This authorization should be documented.

Determining whether the investigator is maintaining the essential documents.

Monitoring Report

Monitor submits to the sponsor after each trial site visit:

Written report.
Should include date, site, name of the monitor, investigator or other individuals contacted.
Summary of what the monitor reviewed & the monitor's statements concerning significant findings/facts, deviations & deficiencies, conclusions, actions taken or to be taken &/actions recommended to secure compliance.
Review & follow-up of the report with the sponsor should be documented by sponsor's designated representative.

Site Close out Visit

There are no clear ICH or FDA regulations regarding the closeout visit.
ICH GCP requires a close-out monitoring report as an Essential Document.
In general, three activities are required to “officially” close-out a site.

- The sponsor conducts a close-out visit and signs the monitoring log.
- The investigator submits a final report to the IRB stating that the site is closed.
- The sponsor sends the investigator a letter stating that the site is closed.

Close out visit activities

Close-Out Visit Activities

- Final data review/collection of all outstanding data
- Return or destruction of all study drug
- Final review of Regulatory Binder
- Verification that all biological samples have been submitted.
- Return or destruction of all unused study forms/CRFs
- Review and collection of Delegation of Authority forms
- Collection of IRB closure report/letter

References:

- https://ichgcp.net/