Clinical Monitoring Guidance for Sponsor Investigators

University of Cincinnati
Office of Research Compliance and Regulatory Affairs
Clinical Monitoring Guidance Document for Sponsor-Investigators

Purpose:

The purpose of this Guidance Document is to assure that sponsor-investigators are aware of their responsibility to monitor clinical studies.

Scope:

This Guidance Document applies to all sponsor-investigator clinical studies where the sponsor-investigator is a University of Cincinnati faculty member.

This Guidance Document has been written to apply to sponsor-investigators conducting single site clinical trials.

Responsibilities:

The sponsor-investigator has responsibility for assuring compliance with this guidance document.

Reference:

This Clinical Monitoring Guidance Document is based on Section 5.18 of the ICH Guidance for Industry, E6 Good Clinical Practice: Consolidated Guidance. April 1996.

Monitoring Guidance:

1. Purpose. The purposes of trial monitoring are to verify that:
(a) The rights and well-being of human subjects are protected.
(b) The reported trial data are accurate, complete, and verifiable from source documents.
(c) The conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP, and with applicable regulatory requirement(s).

2. Selection and Qualifications of Monitors.
(a) Monitors should be appointed by the sponsor-investigator.
(b) Monitors should be appropriately trained, and should have the scientific and/or clinical knowledge needed to monitor the trial adequately. A monitor's qualifications should be documented.
(c) Monitors should be thoroughly familiar with the investigational product(s), the protocol, written informed consent form and any other written information to be provided to subjects.
(d) Monitoring responsibilities may be transferred to a Contract Research Organization.

3. Extent and Nature of Monitoring.
The sponsor-investigator should ensure that the trials are adequately monitored. The sponsor-investigator should determine the appropriate extent and nature of monitoring. The determination of the extent and nature of monitoring should be based on considerations such as the objective, purpose, design, complexity, blinding, size, and endpoints of the trial. In general there is a need for on-site monitoring, before, during, and after the trial. Statistically controlled sampling may be an acceptable method for selecting the data to be verified.

4. Monitor's Responsibilities.
The monitor(s), in accordance with the sponsor-investigator's requirements, should ensure that the trial is conducted and documented properly by carrying out the following activities when

relevant and necessary to the trial:

(a) Verifying that the staff and facilities, including laboratories and equipment, are adequate to safely and properly conduct the trial and these remain adequate throughout the trial period.

(b) Verifying, for the investigational product(s): (i) That storage times and conditions are acceptable, and that supplies are sufficient throughout the trial.

(ii) That the investigational product(s) are supplied only to subjects who are eligible to receive it and at the protocol specified dose(s).

(iii) That subjects are provided with necessary instruction on properly using, handling, storing, and returning the investigational product(s).

(iv) That the receipt, use, and return of the investigational product(s) at the trial sites are controlled and documented adequately.

(v) That the disposition of unused investigational product(s) at the trial site complies with applicable regulatory requirement(s). (c) Verify that all modifications to the study plan have been submitted to FDA and IRB prior to implementation.

(d) Verify that all modifications to the study plan have been approved by IRB prior to implementation.

(e) Verifying that the sponsor-investigator follows the approved protocol and all approved amendment(s), if any.

(f) Verifying that written informed consent was obtained before each subject's participation in the trial.

(g) Ensuring that the sponsor-investigator's trial staff is adequately informed about the trial.

(h) Verifying that the sponsor-investigator and the trial staff is performing the specified trial functions, in accordance with the protocol and the sponsor-investigator has not delegated these functions to unauthorized individuals.

(i) Verifying that the sponsor-investigator is enrolling only eligible subjects.

(j) Reporting the subject recruitment rate.

(k) Verifying that source data/documents and other trial records are accurate, complete, kept up-to-date, and maintained.

(l) Verifying that the sponsor-investigator provides all the required reports, notifications, applications, and submissions, and that these documents are accurate, complete, timely, legible, dated, signed, and identify the trial.

(m) Checking the accuracy and completeness of the CRF entries, source data/documents, and other trial-related records against each other. The monitor specifically should verify that: (i) The data required by the protocol are reported accurately on the CRF's and are consistent with the source data/documents.

(ii) Any dose and/or therapy modifications are well documented for each of the trial subjects.

(iii) Adverse events, concomitant medications, and intercurrent illnesses are reported in accordance with the protocol on the CRF's.

(iv) Visits that the subjects fail to make, tests that are not conducted, and examinations that are not performed are clearly reported as such on the CRF's.

(v) All withdrawals and dropouts of enrolled subjects from the trial are reported and explained on the CRF's. (n) Informing the sponsor-investigator of any CRF entry error, omission, or illegibility. The monitor should ensure that appropriate corrections, additions, or deletions are made (this is done by drawing a single line through the error), dated, explained (if necessary), and initialed by the sponsor-investigator or by a member of the sponsor-investigator's trial staff who is authorized to initial CRF changes for the sponsor-investigator. This authorization should be documented.

(o) Determining whether all adverse events (AE's) are appropriately reported within the time periods required by GCP, the protocol, the IRB, and the applicable regulatory requirement(s).

(p) Determining whether the sponsor-investigator is maintaining the essential documents. (Essential documents are those documents that individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced.)

(q) Communicating deviations from the protocol and the applicable regulatory requirements to the sponsor-investigator and taking appropriate action designed to prevent recurrence of the detected deviations including reporting deviations to IRB and FDA.

(r) Verify that the final study report has been written and that: (i) The accuracy of the final study data has been compared and verified against the primary source documents.

(ii) A complete set of source documents is maintained.

(iii) A copy of the final study report has been submitted to FDA and IRB and a copy retained by the sponsor-investigator.

(iv) The sponsor-investigator is the individual with authority for final verification of records.

5. Monitoring Procedures.

The monitor(s) should follow established written monitoring procedures for monitoring a clinical

trial.

6. Monitoring Report.

(a) The monitor should submit a written report to the sponsor-investigator after each clinical monitoring activity.

(b) Reports should include the date, site, name of the monitor, and name of the sponsor-investigator or other individual(s) contacted.

(c) Reports should include a summary of what the monitor reviewed and the monitor's statements concerning the significant findings/facts, deviations and deficiencies, conclusions, actions taken or to be taken, and/or actions recommended to secure compliance.

(d) The review and follow-up of the monitoring report by the sponsor-investigator should be documented.