# Guidance for Industry

## GUIDELINE FOR THE MONITORING OF CLINICAL INVESTIGATIONS

U.S. Department of Health and Human Services
Food and Drug Administration
Office of Regulatory Affairs
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Comments on the contents of this guideline are invited and should be addressed to the following office and identified with the docket number:

Dockets Management Branch (HFA-305)
Food and Drug Administration
Docket Number 82D-0322
5630 Fishers Lane, rm. 1061
Rockville, MD 20857

For copies of, or further information regarding the guideline please contact:

Bioresearch Monitoring Program Coordinator (HFC-230)
Food and Drug Administration
5600 Fishers Lane
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## Purpose

The purpose of this guideline is to present acceptable approaches to monitoring clinical investigations. Existing requirements for sponsors of clinical investigations involving new drugs for human and animal use (including biological products for human use) and medical devices under 21 CFR Parts 312 and 511, and 812 and 813, respectively, require that a sponsor monitor the progress of a clinical investigation. The monitoring functions may be delegated to a contract research organization as defined under 21 CFR 312.3. Proper monitoring is necessary to assure adequate protection of the rights of human subjects and the safety of all subjects involved in clinical investigations and the quality and integrity of the resulting data submitted to the Food and Drug Administration (FDA).

## Introduction

This guideline, issued under 21 CFR 10.90, reflects principles recognized by the scientific community as desirable approaches to monitoring clinical research involving human and animal subjects. These principles are not legal requirements but represent a standard of practice that is acceptable to FDA. A sponsor may rely upon this guideline or may develop different procedures. A sponsor who selects different procedures for monitoring a clinical investigation may, but is not required to, submit those procedures to FDA for review and comment to avoid the possibility of employing monitoring procedures that FDA might later determine to be inadequate. Sponsors wishing to obtain such a review should contact FDA's Bioresearch Program Coordinator (HFC-230), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FDA may amend this guideline from time to time on the basis of comments submitted by interested persons or information obtained from agency inspections of sponsors, monitors, and investigators.

### A. Selection of a Monitor

A sponsor may designate one or more appropriately trained and qualified individuals to monitor the progress of a clinical investigation. Physicians, veterinarians, clinical research associates, paramedical personnel, nurses, and engineers may be acceptable monitors depending on the type of product involved in the study. A monitor need not be a person qualified to diagnose and treat the disease or other condition for which the test article is under investigation, but somewhere in the direct line of review of the study data there should be a person so qualified.

For any given study, the factors that should be considered in determining the number of monitors and the education, training, or expertise necessary should include:

- The number of investigators conducting the study.
- The number and location of the facilities in which the study is being conducted.

- The type of product involved in the study (i.e., drug for human use, drug for animal use, medical device).
- The complexity of the study.
- The nature of the disease or other condition under study.

B. Written Monitoring Procedures

A sponsor should establish written procedures for monitoring clinical investigations to assure the quality of the study and to assure that each person involved in the monitoring process carries out his or her duties. A single written monitoring procedure need not be developed for each clinical investigation. Rather, a standardized, written procedure, sufficiently detailed to cover the general aspects of clinical investigations, may be used as a basic monitoring plan and supplemented by more specific or additional monitoring procedures tailored to the individual clinical investigation.

C. Preinvestigation Visits

A sponsor is responsible for assuring, through personal contact between the monitor and each investigator, that the investigator clearly understands and accepts the obligations incurred in undertaking a clinical investigation.

Prior to the initiation of a clinical investigation, the monitor should visit the site of the clinical investigation to assure that the investigator:

- Understands the investigational status of the test article and the requirements for this accountability.
- Understands the nature of the protocol or investigational plan.
- Understands the requirements for an adequate and well-controlled study.
- Understands and accepts his or her obligations to obtain informed consent in accordance with 21 CFR Part 50. The monitor should review a specimen of each consent document to be used by the investigator to assure that reasonably foreseeable risks are adequately explained.
- Understands and accepts his or her obligation to obtain IRB review and approval of a clinical investigation before the investigation may be initiated and to ensure continuing review of the study by the IRB in accordance with 21 CFR Part 56, and to keep the sponsor informed of such IRB approval and subsequent IRB actions concerning the study.
- Has access to an adequate number of suitable subjects to conduct the investigation.
- Has adequate facilities for conducting the clinical investigation.
- Has sufficient time from other obligations to carry out the responsibilities to which the investigator is committed by applicable regulations.

D. Periodic Visits

A sponsor is responsible for assuring throughout the clinical investigation that the investigator's obligations, as forth in applicable regulations, are being fulfilled and that the facilities used in the clinical investigation continue to be acceptable. The most effective way to achieve this assurance is to maintain personal contact between the monitor and the investigator throughout the clinical investigation. The monitor should visit the investigator at the site of the investigation frequently enough to assure that:

- The facilities used by the investigator continue to be acceptable for purposes of the study.
- The study protocol or investigational plan is being followed.
- Changes to the protocol have been approved by the IRB and/or reported to the sponsor and the IRB.
- Accurate, complete, and current and current records are being maintained.
- Accurate, complete, and timely reported are being made to the sponsor and IRB.
- The investigator is carrying out the agreed-upon activities and has not delegated them to other previously unspecified staff.

E. Review of Subject Records

A sponsor is responsible for assuring that the data submitted to FDA in support of the safety and effectiveness of a test article are accurate and complete. The most effective way to assure the accuracy of the data submitted to FDA is to review individual subject records and other supporting documents and compare those records with the reports prepared by the investigator for submission to the sponsor. Therefore, during a periodic visit, the monitor should compare a representative number of subject records and other supporting documents with the investigator's reports to determine that:

- The information recorded in the investigator's report is complete, accurate, and legible.
- There are no omissions in the reports of specific data elements such as the administration to any subject of concomitant test articles or the development of an intercurrent illness.
- Missing visits or examinations are noted in the reports.
- Subjects failing to complete the study and the reason for each failure are noted in the reports.
- Informed consent has been documented in accordance with 21 CFR Parts 50 and 56.

F. Record of On-Site Visits

The monitor or the sponsor should maintain a record of the findings, conclusions, and action taken to correct deficiencies for each on-site visit to an investigator. Such a record may enable FDA to determine that a sponsor's obligations in monitoring the progress of a clinical investigation are being fulfilled. The record may include such elements as:

- The date of the visit.
- The name of the individual who conducted the visit.
- The name and address of the investigator visited.
- A statement of the findings, conclusions and any actions taken to correct any deficiencies noted during the visit.