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Part 1: Introduction



Many individuals and groups are involved in conducting a clinical study. The central roles are those of the Sponsor and Principal Investigator, as defined by Good Clinical Practice (GCP) guidelines.

There are additional roles and responsibilities defined for other individuals and groups whose work is essential to the proper conduct of a clinical study. How these roles are referenced, may vary from one research network to another.

This module will:

- Discuss the roles and responsibilities of the Sponsor, and Principal Investigator as outlined in the GCP guidelines.
- Briefly describe how these roles and responsibilities are fulfilled in clinical studies.
- Discuss the roles and responsibilities of other individuals and groups involved in studies.

Part 2: Responsibilities by Role

The following is a summary of responsibilities, as outlined in the GCP guidelines according to role.

Central Roles:

- Sponsor
- Principal Investigator
- Other Roles
- Research Site Staff

Sponsor:

MONITORING

Data and Safety Monitoring

All NIH–supported multicenter Phase III clinical trials must have an independent Data and Safety Monitoring Board (DSMB). This requirement applies to both studies of drug therapies and to behavioral studies.

Members of each DSMB include experts in the disease area, treatment, clinical trial design, biostatistics, and research ethics. The DSMBs are appointed by and report to the sponsor. Their role is to:

- Protect participant safety by being familiar with the study, proposing appropriate analyses, and reviewing outcome and safety data as they become available.
- Ensure study integrity by reviewing data on issues such as participant enrollment, site visits, study procedures, completion of forms, data quality, losses to follow-up, and other measures of adherence to the study protocol.
- Monitor adverse events and recommend changes in the protocol or operation of the study if necessary. This monitoring function is over and above the oversight traditionally provided by the IRB and is particularly important for multicenter research studies.

Click [here](#) to see the NIH policy document on data and safety monitoring.

QA & QC

Quality Assurance and Quality Control (ICH GCP 5.1)

The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems to ensure that studies are conducted and documented in compliance with the protocol, GCP, and regulatory requirements.

EXPERTISE

Medical Expertise (ICH GCP 5.3)

The Sponsor is responsible for designating appropriately qualified medical personnel to advise on trial-related medical questions or problems.

STUDY DESIGN & MANAGEMENT

Study Design and Management (ICH GCP 5.4, 5.5)

The Sponsor is responsible for designating qualified individuals to carry out all stages of the study process, including:

- Designing the protocol.
- Supervising the overall conduct of the study.
- Managing and verifying the study data.
- Ensuring the safety and rights of human participants.
- Monitoring study performance.
- Planning and conducting the statistical analyses.
- Preparing study reports.

TRANSFER OF OBLIGATIONS

Transfer of Trial-Related Obligations

The Sponsor may transfer any or all of the Sponsor's trial-related duties and functions to a Contract Research Organization (CRO). However, the ultimate responsibility for the quality and integrity of the trial data always resides with the Sponsor. Any trial-related duties and functions that are transferred to and assumed by a CRO are specified in writing.

Principal Investigator:

OVERVIEW

Overview

While studies have a Lead Investigator with primary responsibility over the entire trial, this individual is often the Principal Investigator (PI) at the lead research site and has responsibility over the conduct of a clinical study at that site. For multicenter trials, there are a number of research sites, each with its own Principal Investigator with oversight responsibility and staff involved in the conduct of a study.

The PI retains ultimate oversight responsibility even when specific tasks are delegated to other site research staff. Additionally, PI responsibilities include:

- Documenting the delegation of study responsibilities to qualified and adequately trained research staff.
- Supervising study performance and overseeing the performance of study staff at the research sites.
- Ensuring that:
 - Participants' well-being and safety are protected.
 - All study procedures are conducted at the research sites in accordance with the protocol and GCP.
- Preparing a communication plan for all staff involved in the study.
- Overseeing Investigational product accountability.

Of note, the PI must sign the protocol signature page in that capacity. If the study is being conducted under an [Investigational New Drug](#) (IND) application, the PI must also sign [Form FDA 1572](#).

QUALIFICATIONS & EXPERIENCE

Qualifications and Experience (ICH GCP 4.1)

The PI must:

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the study.
- If the study involves the use of an investigational product, be thoroughly familiar with the appropriate use of that product as described in the study protocol.
- Be aware of and remain in compliance with GCP and applicable regulatory requirements.
- Maintain a list of qualified persons to whom he or she delegates significant study-related duties.

CARE FOR PARTICIPANTS

Medical Care of Study Participants (ICH GCP 4.3)

All study participants should receive appropriate medical care both for study-related adverse events and for all medical conditions unrelated to study participation.

- A qualified physician affiliated with the study should be responsible for all study-related medical decisions.
- The participant's primary care physician should be informed about the participant's involvement in the study, provided that the participant:
 - Has a primary care physician.
 - Agrees that the primary care physician may be informed.

COMMUNICATION

Communication with Institutional Review Board (ICH GCP 4.4)

The PI is identified to the designated IRB. Before and during a study, the PI must comply with all requirements of the designated Institutional Review Boards (IRBs). A study may not begin prior to obtaining IRB approval. (See material regarding the [Investigators' responsibilities to the IRB](#) from the [Institutional Review Boards module](#).)

COMPLIANCE

Compliance with the Protocol (ICH GCP 4.5)

The PI is responsible for ensuring that the study is conducted in compliance with the [research protocol](#). He or she should ensure that all protocol violations are identified, documented, and reported in accordance with sponsor and IRB requirements. Repeated protocol violations may indicate that protocol amendments, procedural changes, or additional training are needed.

USE OF PRODUCTS

Use of Investigational Products (ICH GCP 4.6)

If the study involves the use of an investigational product, the PI is responsible for ensuring that the investigational product is used only in accordance with the study protocol and federal regulations; and that accountability of the investigational product is maintained. (See related material from the [Investigational New Drugs module](#).)

For clinical investigations that use controlled study drug, the PI may be required to have a medical license. When the PI is not required to have a medical license, responsibility for receiving or administering certain

drugs, reviewing safety events, and making independent medical decisions is delegated to qualified medical personnel, such as a physician, physician's assistant, nurse practitioner, or other qualified/licensed medical professional. These delegated responsibilities are documented in the site's delegation of responsibilities log, and the staff assigned may serve as a sub-investigator. Consult local regulations and oversight authorities on medical license requirements for conducting research using controlled drug.

RANDOMIZATION & BLINDING

Randomization and Blinding (ICH GCP 4.7)

The PI is responsible for ensuring that the study's procedures, if any, for [randomization and blinding](#) are followed.

INFORMED CONSENT

Informed Consent (ICH GCP 4.8)

The PI is responsible for ensuring that procedures for obtaining and documenting informed consent comply with GCP and with the ethical principles originating in the Declaration of Helsinki.

RECORDS & REPORTS

Records and Reports (ICH GCP 4.9)

The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of all study data that are reported to the Sponsor.

The PI should provide written reports on the status of the study to the Sponsor and IRB when and as often as required to do so at each institution where the study is conducted.

All serious adverse events must be reported immediately to the Sponsor. The PI must also comply with regulatory requirements to report serious adverse events to the IRB and regulatory authorities.

Final Study Reports (ICH GCP 4.13)

On completion of the study, the PI is responsible for providing:

All required reports to the Sponsor and regulatory authorities.

A summary of the study outcome to the Institutional Review Board.

Records and reports are discussed in greater detail in the Documentation and Record Keeping module. Serious adverse events are discussed in the Participant Safety and Adverse Events module.

SUSPENSION & TERMINATION

Premature Suspension or Termination of Study (ICH GCP 4.12)

If the study is suspended or stopped early for any reason, the PI is responsible for:

- Promptly informing all study participants.
- Ensuring that all participants receive appropriate therapy and follow-up.
- Complying with all requirements to inform regulatory authorities.

Other Roles:

OVERVIEW

Overview

The investigator convenes a Protocol Team to assist with all aspects of the operation of the study. In addition to the responsibilities listed under Principal Investigator, other responsibilities represented on the Protocol Team usually include, but are not limited to, Quality Assurance, Training, and Regulatory Affairs.

QA

Quality Assurance

Quality Assurance (QA) staff is responsible for:

- Reviewing the protocol to check for inconsistencies and problematic wording that will increase the likelihood of protocol violations.
- Reviewing monitoring reports of site visits to ensure that all identified issues are addressed in an appropriate and timely fashion and are communicated to the investigative team.
- Conducting site visits on the behalf of the Sponsor as needed.

REGULATORY AFFAIRS

Regulatory Affairs

Regulatory Affairs staff is responsible for:

- Writing the study informed consent documents.
- Submitting the protocol, consent documents, and Institutional Review Board (IRB) documents to the lead node's IRB and making any changes in those documents required by the IRB.
- Distributing the IRB-approved protocol, consent documents, and Institutional Review Board (IRB) documents to participating research sites to assist them in preparing their IRB submissions.
- Preparing and distributing a checklist of items that participating sites must have, and
- Providing regulatory guidance to the study sites as necessary.

This responsibility continues throughout the duration of the trial e.g. submission of a Protocol Amendment.

Research Site Staff:

RESEARCH COORDINATOR/ASSISTANT

Research Coordinator/Assistant

Under the supervision of the PI at the site, examples of responsibilities for the Research Coordinator/Assistant may include:

- Ensuring that study data is accurately collected and reported.
- Reporting any study or participant problems.
- Maintaining regulatory files at the study site.

- Working with the Node Quality Assurance Monitor and data management staff to identify and resolve data and reporting issues.

The Research Assistant's role frequently also includes interacting with study participants by performing assessments (e.g., the Addiction Severity Index) and protocol procedures.

OTHER STAFF

Nurses, Pharmacists, Counselors, Supervisors and Other Staff

Nurses, pharmacists, and other staff are responsible for carrying out study procedures as described in the protocol (e.g., receiving and dispensing medications, conducting physical examinations, delivering behavioral interventions) and for assessing and reporting adverse events to appropriate staff.

Part 2: Responsibilities by Role

Interactive: Study Roles

Users are instructed to read the scenario, and choose the best answer from the multiple choices provided. Then, consider the feedback.

Scenario: The clinical study team at Midtown Medical Research Park is facing a difficult situation. A participant has died during the trial, and the team has decided to end the study prematurely. While many forms and protocols must be followed in this case, who on the team is responsible for ensuring that the site's study participants receive appropriate follow-up as outlined in the study protocol?

- A. Principal Investigator
- B. Sub-Investigator
- C. Medical Clinician or Physician
- D. Interventionist
- E. Quality Assurance Monitor

Feedback: Which did you choose: A, B, C, D, or E? There is study role primarily responsible for the conduct of a clinical study at a research site, and the individual retains ultimate responsibility even if specific tasks are delegated to others. If a study is suspended or stopped early for any reason, the PI is responsible for: promptly informing all study participants; ensuring that all participants receive appropriate therapy and follow-up; and complying with all requirements to inform regulatory authorities. Therefore, the correct response is A, the Principal Investigator or PI.

Part 2: Responsibilities by Role

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CTN



More on Roles and Responsibilities for Clinical Trials in the CTN

The NIDA Clinical Trials Network has established processes to apply GCP, to maximize its node and multicenter platform, and that adhere to policies for NIH-sponsored research. The following defines the infrastructure variations and processes established in the CTN that may differ from other research.

Medical Expertise (ICH GCP 5.3)

For CTN studies, the Lead Investigator must designate a study medical monitor, who is responsible for ensuring the care and safety of study participants. In addition, NIDA appoints a study medical officer, who has an oversight role and serves as a resource to both the Lead Investigator and the study medical monitor.

Study Design and Management (ICH GCP 5.4, 5.5)

For CTN studies, the Lead Investigator must designate a protocol team that designs the protocol, assists in protocol implementation and prepares any necessary reports. NIDA fulfills its responsibilities by designating independent oversight boards to review all protocols and monitor the conduct of the studies. As noted earlier, NIDA also contracts monitors who perform quality assurance site visits at all research sites where CTN studies are conducted and requires each Node to perform regular site visits at all research sites participating in studies within that Node. Findings from these site visits must be reported to NIDA.

Other Roles and Responsibilities in CTN Studies

Everyone working on a study is responsible for:

- Protecting the rights and safety of study participants,
- Complying with the study protocol, and
- Reporting study data accurately and completely.

The following descriptions are intended to clarify roles and responsibilities that must be fulfilled in all CTN studies, not to define specific positions held by individuals. The position titles used here may differ from those used at each of the organizations involved in CTN research.

NIDA is typically considered to be the Sponsor for studies conducted within the CTN. This consideration may vary in special cases. For example, as far as FDA is concerned, the sponsor is the IND Holder in the case that the study is under IND; and, an agreement for transferring responsibilities is documented with the IND Holder and the partner organization. While the Sponsor maintains primary responsibility for any clinical investigations it conducts, the CTN transfers responsibilities wholly or partially to a partner organization.

Roles and Responsibilities at Participating Nodes

Under the terms and conditions of the grant award for each study, NIDA transfers other responsibilities as Sponsor to the study's Lead Investigator and the Node Principal Investigator, such as Quality Assurance

and Control, oversight, and training.

For CTN studies, NIDA fulfills the Quality Assurance and Control responsibility by:

- Contracting with monitors who perform quality assurance site visits at all research sites where CTN studies are conducted.
- Requiring each Node to perform regular quality assurance site visits at all research sites participating in studies within that Node. Findings from these site visits must be reported to NIDA.

In the CTN, the network infrastructure includes CTN Nodes that have oversight and training responsibilities for regionally assigned research sites. Each CTN Node functions independently and creates its own organizational structure, depending on its needs and resources. As a result, job titles and job descriptions for research staff are not standardized across Nodes. At one Node, multiple staff members may perform one role, whereas at another Node, one staff member may perform multiple roles. The CTN Nodes are also assigned research sites regionally. The following information summarizes the roles of staff at the Node.

Node Principal Investigator

The Node PI (or grantee) is responsible to NIDA for study performance at his or her Node. He or she works with Node staff, the study's Lead Investigator, and the Principal Investigator at the research sites to implement the study.

The Node PI is responsible for ensuring that the study runs smoothly at his or her Node and for taking appropriate action when necessary to assist the Lead Investigator and research site PIs and other research staff. Other responsibilities of the Node PI include:

- Appointing staff to direct study operations.
- Managing the Node budget and staff.
- Appointing a monitor to conduct quality assurance site visits to research sites.
- Ensuring that study staff receives appropriate training to conduct the study.
- Ensuring that the study receives all necessary IRB approvals and follows all applicable regulations, and
- Ensuring compliance of his or her institutional policies at the Node with these policies.

Node Coordinator

The Node Coordinator:

- Coordinates all study activities at the Node.
- Ensures that day-to-day activities are conducted in accordance with GCP.
- Acts as liaison between the Node and the Lead Investigator and the CTN on study matters, and
- Serves as the main contact for study information at the Node.

Node Quality Assurance Monitor

The Node QA Monitor is responsible for monitoring the study within the Node and reporting findings to NIDA, the Node PI, and the Lead Investigator. This individual must be intimately familiar not only with the study protocol but also with GCP.

Node Regulatory Affairs Staff

The Node Regulatory Affairs Staff are responsible for:

- Submitting the study protocol, informed consent form, and any other relevant documents to the Institutional Review Boards (IRBs) at the Node's participating sites.
- Ensuring that Research sites use the most recently approved informed consent documents.
- Assisting with the creation and maintenance of regulatory files for the study.
- Submitting data on adverse events, serious adverse events, and protocol violations to the relevant IRBs, according to their requirements.
- Coordinating continuing IRB review of the study protocol and materials to ensure ongoing IRB approval of the study.



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Part 3: Summary of Key Points

- Good Clinical Practice (GCP) guidelines specifically define the responsibilities of the Sponsor and Principal Investigator of a clinical study.
- The ultimate responsibility for the quality and integrity of the trial data always resides with the Sponsor although some obligations of the sponsor maybe delegated to a partner organization or contract research organization (CRO).
- The Principal Investigator (PI) is responsible for the conduct of a clinical study at a research site and retains ultimate responsibility even if specific tasks are delegated to other site research staff.

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CTN



- The NIDA Clinical Trials Network (CTN) has defined roles and responsibilities for other individuals and groups whose work is essential to the proper conduct of a clinical study.
- NIDA is the Sponsor for studies conducted within the CTN. However, under the terms and conditions of the grant award for each study, NIDA transfers some responsibilities as Sponsor to the study's Lead Investigator and to Contract Research Organizations.
- Based on the study and parties involved under the CTN structure:
 - The Lead Investigator has overall responsibility for the entire study.
 - The Node PI (or grantee) is responsible to NIDA for study performance at his or her Node.
 - For each study in which the Node is participating, the Node PI designates a PI for each research site, who maintains oversight of site performance and has responsibility for study integrity, human participant protection, and staff performance of delegated responsibilities at the assigned research site(s).
 - Each CTN Node functions independently and creates its own organizational structure, depending on its needs and resources. As a result, job titles and job descriptions vary across Nodes.



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