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Part 1: Introduction



What is quality assurance?

Quality Assurance (QA) in clinical trials consists of planned, systematic activities that are conducted to ensure that a trial is performed—and that trial data are generated, documented, and reported—in compliance with the protocol, [Good Clinical Practice](#) (GCP) guidelines, and all other applicable regulatory requirement(s).

Why is QA important?

Research that is not conducted according to high standards of quality yields invalid data. It is also unethical because it may put research participants at risk. (Protection of the safety, rights, and well-being of research participants is discussed in the [Introduction](#), [Institutional Review Boards](#), [Informed Consent](#), and [Participant Safety and Adverse Events](#) modules.)

Audits conducted by the U.S. Food and Drug Administration (FDA) find that several [problems](#) commonly occur in research studies.

Quality data are critical to ensure that the results of studies are interpreted correctly. Sloppy or incorrect data can lead to misleading conclusions. Careful attention to standards of quality also ensures that studies are completed in a timely fashion. Timely completion of high quality studies bridges the gap between research and practice by bringing effective new treatments to clients more quickly.

Who is responsible for QA?

All members of the protocol team are responsible for QA.

While it is common for QA and monitoring-related duties and functions to be transferred to a CRO, the [sponsor](#) has ultimate responsibility for implementing and maintaining QA systems. (ICH GCP 5.1.1) This responsibility includes oversight of all QA systems as well as any trial-related functions performed or managed by other parties (i.e. the CRO, or a subcontractor to the CRO) on behalf of the Sponsor (ICH GCP 5.2.2)

Investigators and every member of the protocol team are expected to perform his or her duties diligently

and thoroughly, thus ensuring that the trial is conducted according to the highest possible standards of quality.

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CTN



QA Roles and Responsibilities in the NIDA Clinical Trials Network



The CTN Policies and Procedures on QA



The sponsor is responsible for ensuring the trial's integrity and for developing a risk-based monitoring plan. As the sponsor of all studies conducted by the network, NIDA CTN has transferred the regulatory responsibility of all monitoring to the Clinical Coordinating Center (CCC).

The CCC develops systematic, prioritized, and risk-based (ICH GCP E6(R2) 5.18.3) monitoring plans to be utilized for each CTN study. This plan is customized for each trial and describes the strategy, methods, responsibilities, and requirements for monitoring the trial (ICH GCP E6(R2) 1.64). Additionally, the plan provides operational guidelines to ensure the quality and integrity of data collected in accordance with CTN protocols. This document also ensures consistency in the conduct of CTN studies across multiple sites and protocols. This monitoring plan:

- Emphasizes the monitoring of critical data and processes.
- Ensures the quality and integrity of CTN clinical studies.
- Ensures the protection of human participants.
- Advances collaboration between treatment and research staff at CTN sites.

Roles and responsibilities of the Lead Investigator

The Lead Investigator (LI) is a CTN-specific role for the investigator that has overall responsibility for the entire study. The LI convenes a Protocol Team that assists with all aspects of the development and operation of the study. In other studies outside of the CTN, this role may be considered the Principal Investigator.

The Project Director (or Protocol Coordinator) is the LI's "right hand." He or she is responsible for coordinating and carrying out day-to-day study operations. The Project Director is a member of the Protocol Team and is the primary contact for questions about the overall study. Other roles and responsibilities represented on the Protocol Team usually include, but may not be limited to, the following:

- Data Management
- Quality Assurance
- Training
- Regulatory Affairs

Roles and Responsibilities of the Node Principal Investigator

The Node PI (or grantee) is another CTN-specific role that is responsible to NIDA for study performance at his or her Node. He or she works with Node staff, the Site Principal Investigator(s), and the Lead Investigator to implement the study at that Node. 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 Site PI(s) and the Lead Investigator. Other responsibilities of the Node PI include:

- Appointing the Site PI and Study Coordinator.
- Managing the Node budget and staff.
- Appointing a monitor to conduct Quality Assurance visits at research sites within the Node.
- 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.
- Knowing the policies of his or her institution/university and ensuring compliance at the Node with these policies.



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The Monitoring Plan

The monitoring plan sets out monitoring strategies, the monitoring responsibilities of all parties involved, the various monitoring methods to be used, and the rationale for their use. It also describes monitoring procedures, types of visits, what is involved in the conduct of those visits, and the quantity or percentage of each type of document to be monitored. These procedures can be further defined on a protocol basis depending on the purpose, design, size, complexity, and primary outcome measures of the trial (ICH GCP E6(R2) 5.18.3).

According to GCP guidelines, "the Sponsor may choose on-site monitoring, a combination of on-site and centralized (remote) monitoring, or, where justified, centralized monitoring alone... Centralized monitoring processes provide additional monitoring capabilities that can complement or reduce the extent and/or frequency of on-site monitoring and help distinguish between reliable data and potentially unreliable data without the need for total source data verification" (ICH GCP 5.18.3). The rationale for the chosen monitoring strategy is documented in the monitoring plan.

In general, on-site monitoring is required and remote monitoring may occur at any given research site before a trial begins, while it is in progress, and after it concludes or is terminated. In many instances,

study monitors may visit each site after the first one to two participants are enrolled and then schedule subsequent visits based on multivariate criteria, such as the rate of enrollment, volume of data to review, site performance, and other considerations.

Study monitors conduct site visits according to the procedures describes in the monitoring plan and in accordance with [Good Clinical Practice](#) (GCP) guidelines.

Part 2: QA and Monitoring Roles

Monitoring Role for Sponsors

The Good Clinical Practice guidelines state that the sponsor is responsible for selecting monitors and for ensuring that the following criteria are met (see ICH GCP 5.18.2).

- Monitors are appropriately trained and have the scientific or clinical knowledge needed to monitor the trial adequately. Monitors qualifications should be documented.
- Monitors are thoroughly familiar with the investigational product(s), protocol, written informed consent form, and any other written information about the trial to be provided to study participants, the Sponsor's SOPs, GCP, and the applicable regulatory requirement(s).

Quality Assurance (QA)/Study Monitor Role

QA/study monitors perform the following study activities:



- Conduct initiation, interim, and closeout visits.
- Conduct centralized monitoring, as applicable.
- Provide training on protocol-specific issues and Good Clinical Practice, when needed or appropriate.
- Follow-up on issues identified during earlier monitoring visits.
- File reports with the sponsor and other applicable parties, as required.

Monitoring responsibilities are described in detail in ICH GCP 5.18.4. [Click here](#) for a summary.

Part 3: Trial Monitoring Activities

BEFORE

Site Initiation

Initiation visits occur before a research site begins participant recruitment for protocol participation and after the necessary IRB approvals are obtained. During a site initiation visit, study monitors review trial documents to ensure that they are complete and in order. A listing of documents to be retained by sites before, during, and after a trial can be found in ICH GCP Section 8. They will also inspect sites to ensure that the facilities are appropriate, that the work and storage space necessary to conduct the trial are available, and that equipment, medication, and supplies needed to start the trial are available. They ensure that adequate staff is available and properly trained.

Study monitors will document action items that need to be performed by the site prior to site activation. Research sites cannot begin participant recruitment until the Investigator(s) and sponsor have provided their approval.

IN PROGRESS

Interim/Routine Monitoring Visits

The requirements for monitoring while a trial is in progress are documented in the Monitoring Plan. In general, monitors perform the following activities while a trial is in progress:

- Assess the trial's progress.
- Verify that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with GCP guidelines, and with applicable regulatory requirements.
- Verify that participant rights and well-being are protected.
- Verify the reported trial data (including source documents) are attributable, legible, contemporaneous, original, accurate, and complete. All data must be verifiable from source documents.
- Verify that the site has the adequate resources to continue the trial.

[Click here](#) for a list of specific monitoring functions during an interim visit.

[Click here](#) for a list of documents and activities that monitors may review during an interim site visit.

COMPLETED

Closeout

After the trial is completed, study monitors must conduct a closeout site visit to ensure that:

- Drug accountability records have been finalized.
- Unused medication has been destroyed or returned, or alternatively disposed of as per the study sponsor and regulatory requirements (see [21 CFR 312.59](#)).

- All sponsor-provided trial equipment and supplies have been returned to the sponsor and/or supplier.
- All data queries have been resolved.
- All trial documentation are complete and ready for storage, and the sponsor has been notified of their final storage location.
- Notice of trial closure and all required reports are filed with the proper entities (e.g., the sponsor and Institutional Review Boards).

Part 3. Trial Monitoring Activities

QA is the responsibility of every member of the research team. The role of monitoring is to support and assist members of the research team in adhering to high quality standards.

Interactive: Quality Assurance Strategies

Users are instructed as follows:

The following list includes seven strategies, some to assist every team member in assuring quality in clinical trials as well as other strategies that are not helpful. For each strategy listed, choose **Yes** to indicate that the strategy is helpful for assuring quality or **No** if it is not. Then, consider the feedback.

Strategy 1:

Thoroughly reviewing the research protocol, operations manual, standard operating procedures (SOPs), training manuals and materials, and other relevant documents before the trial begins.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is Yes.

Strategy 2:

Choosing to monitor research sites arbitrarily, instead of developing and following a monitoring plan.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is No.

Strategy 3:

Following all instructions specified in the research protocol, operations manual, and SOPs, and doing so in a timely manner.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is Yes.

Strategy 4:

Requesting clarification of any instructions that are confusing or unclear.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is Yes.

Strategy 5:

Communicating openly with other members of the protocol team.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is Yes.

Strategy 6:

Documenting all actions.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is Yes.

Strategy 7:

Avoid following Good Clinical Practice guidelines.

Feedback: Is this strategy helpful for assuring quality in clinical trials: Yes or No? The correct answer is No.

Part 3. Trial Monitoring Activities

Additionally, sponsor organizations can help to assure quality by:

- Providing all research team members with adequate training before the trial begins.
- Monitoring progress early in the trial to assess the quality of screening, recruitment, randomization, and documentation practices (for example, after the first few participants have been randomly assigned to a treatment group). This helps to ensure that any deficiencies are detected early and at the source (i.e., at the site where the research is performed), that inefficiencies and wasteful procedures are eliminated, and that any necessary retraining is performed in a timely fashion. Early monitoring also helps to reduce the likelihood that errors will occur later in the trial, by providing additional information to help troubleshoot for future risk mitigation strategies and risk-based monitoring of the study.
- Increasing the frequency of monitoring when necessary to correct any deficiencies in the conduct of the trial or to provide technical support.

Part 4: Summary of Key Points

- Quality Assurance (QA) consists of planned, systematic activities conducted to ensure that a trial is performed—and that trial data are generated, documented, and reported—in compliance with the protocol and with Good Clinical Practice (GCP) and all other applicable regulatory requirement(s).
- QA is the responsibility of every member of the research team. The role of QA staff is to support and assist members of the research team in adhering to high quality standards.
- The purposes of monitoring are to verify that:
 - The rights and well-being of human participants are protected.
 - Reported trial data are attributable, legible, contemporaneous, original, accurate, and complete.
 - The trial is conducted in compliance with the currently approved protocol (including any amendments), as well as with GCP and all other applicable regulatory requirement(s).
- Monitoring can occur on-site and/or remotely (via centralized monitoring), and it is required before, during, and after completion of a trial.