Title: Site (LAO/AO) Preparations for Quality Assurance Audits

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REVISION HISTORY (most recent first)

Version	Effective Date	Summary of Changes
1.0	AUG-17-2020	Original version of document.

1. INTRODUCTION AND PURPOSE

The National Cancer Institute (NCI)/Division of Cancer Prevention (DCP) requires Quality Assurance (QA) audits of clinical trials data and processes at each Lead Academic Organization (LAO) and Affiliated Organization (AO). Audits are conducted by the Cancer Prevention-Clinical Trials Network (CP-CTNet) Data Management Auditing and Coordinating Center (DMACC).

Auditing is an independent quality assurance function for systematic evaluation of trial processes and documents to determine whether trial-related activities are conducted, and data are recorded, analyzed, and accurately reported according to the protocol, the sponsor's Standard Operating Procedures (SOPs), relevant Good Clinical Practice (GCP) guidelines, applicable regulatory requirements, federal regulations, and NIH/NCI/DCP policies. Audits are performed by the DMACC on a routine and ad hoc basis, and are a snapshot in time of the CP-CTNet sites' compliance with program requirements.

The specific purpose of the auditing program is as follows:

- to document the accuracy of data submitted to Medidata Rave, the Stars enrollment system, and DCP
- to verify Accrual Quality Improvement Program (AQuIP) data
- to verify investigator compliance with protocol and regulatory requirements
- to verify adherence to CP-CTNet policies and procedures
- to provide site staff with resources for a more thorough understanding of regulatory requirements, GCP, data collection and data management practices as necessary

Auditing also provides the opportunity for the sites, DCP, and DMACC to work together to identify areas for systemic and policy-level improvements in order to increase both efficiency and compliance, to better ensure the protection of human subjects, and to enhance the quality and integrity of CP-CTNet clinical trials. Additionally, audits provide sites the opportunity to address any questions or concerns about the CP-CTNet processes or related issues.

The major objectives of the audit program are to ensure compliance with the protocol and all federal and regulatory requirements, to verify accurate recording and reporting of study data that could affect the interpretation of primary study endpoints, and to ensure participant safety. The four main components of a study audit are:

- Regulatory documentation review and Investigator Site File completeness
- Policy and procedure review
- Pharmacy and drug accountability
- Participant case review

LAOs will be audited on-site annually, and as needed, remotely. AOs will be audited remotely on an annual basis, or on-site in any one of the following instances:

- The AO has accrued 10 or more participants across all studies in the previous 12 months
- Three years have elapsed since the AO's last on-site audit
- "For-cause" auditing is required or requested

Note that multiple studies may be audited during one audit visit or remote audit.

2. SCOPE

This document details the responsibilities of the LAO and AO Site Coordinators and Principal Investigators (PIs) regarding the conduct of a QA audit. The scope of the audit includes but is not limited to:

- Regulatory Documentation and Investigator Site File completeness
  - CIRB approvals
  - Informed consent
  - Delegation of tasks
  - Form 1572*
  - Biosketches*
  - GCP training certificates*
  - Clinical Laboratory Improvements (CLIA) Certification
  - College of American Pathologists (CAP) Certification
  - Lab Normal Values (LNV)
  - Financial Disclosure Form (FDF)*

    Note: This documentation should be in the sites' printed or electronic regulatory binder.

    * Documents marked with an asterisk can also be printed from the NCI Registration and Credential Repository (RCR).
- Policy and Procedure review
  - Assurance of participant confidentiality
  - Training and qualifications of staff
  - Communication between the LAOs and AOs, and between the LAOs, AOs and DMACC
  - Protocol compliance
  - AQuIP Accrual procedures (e.g., accrual rates on target, recruitment procedures in place, AQuIP recruitment journaling thoroughly documented, eligibility determination)
  - Deviation reporting (including to CIRB) and follow-up
  - Biomaterial collection, storage and submission
  - Trial-specific procedures
- Pharmacy/Drug Accountability
  - Completion and correctness of drug accountability
  - Records of satellite dispensing area (if applicable)
  - Return of study agent
  - Study agent storage
  - Recording of temperature excursion
  - Recording of drug expiration
  - Adequacy of security
  - Authorized prescriptions
- Participant Case Review
  - Informed consent
  - Eligibility
  - Investigational agent compliance (administration, dose modification, etc.)
  - Adverse Event (AE)/Serious Adverse Event (SAE) reporting
  - General data management quality (e.g., timely, complete and accurate RAVE data entry and query response)
  - Participant-specific AQuIP data (strategies, reasons not enrolled, etc.)
  - Specimen collection, processing, storage, shipment
  - Secure record storage

The Audit Team will randomly select 25% of the total number of participants enrolled or a minimum of seven participant charts (whichever is greater), including any chart with a reported SAE since the last audit visit.

3. SITE COORDINATOR RESPONSIBILITIES FOR LAO AND AO

1. Collaborate with the auditor and DCP to identify a mutually agreeable date for the on-site audit or remote audit to allow maximum participation by site staff.
2. Acknowledge receipt of the confirmation email, confirming the date and objectives of the audit.
3. Communicate audit logistics and objectives to site and pharmacy staff.
4. If on-site, ensure adequate workspace will be available for the auditor during the visit.
5. Ensure all relevant materials are available for review at the time of the audit. This should include:
    - Regulatory documents
    - A template of the locally utilized Informed Consent Forms, as well as the signed Informed Consent Forms for all participants.
    - All relevant DCP Investigational Agent forms
    - Complete medical records (or copies) for participants selected for case review, including any investigation reports, laboratory data, worksheets, etc. If the institution utilizes electronic medical records (EMRs) and/or scans, the records may be printed for viewing by the auditors, or computers with EMR access may be provided. Also, a staff member must be present to assist with navigating through the system. For remote visits, ensure identifiers are removed.
    - SAE documentation and protocol deviations (PDs) (refer to SOP 02-01: Reporting Serious Adverse Events and SOP 02-02: Reporting Protocol Deviations for requirements)
    - Logs and documentation for enrollment, screening, and monitoring/auditing visits

      Note: For remote/virtual audits, the auditor will contact the site coordinator in advance to arrange for access to the documentation.
6. Ensure all entries in Medidata, which holds the database of record, are current, complete and accurate.

4. SITE COORDINATOR RESPONSIBILITIES FOR LAO ONLY

1. Ensure documentation is accessible to support the tracking of the receipt of regulatory documents from the AO(s) and forwarding of those documents to the CP-CTNet regulatory contractor.
2. Ensure documentation is accessible to support methods of communicating information to the AO(s). Examples include: meeting minutes, email documentation or an active website link.
3. Ensure documentation is accessible to support methods of tracking staffing changes, accrual and retention patterns, PDs, SAEs, data entry, and query resolution at the AO(s).
4. Ensure the LAO-specific Data and Safety Monitoring Plans (DSMPs) are current and are approved by DCP.

5. Ensure documentation indicating that all AO(s) have adopted the most current CP-CTNet SOPs as written or have exceptions on file with CP-CTNet approval is accessible.

5. DOCUMENTATION REQUIREMENTS

The Audit Team will create an Audit Report, including findings and any necessary corrective and preventative actions, and will provide the report to the site within 15 business days of the audit. The LAO or AO Site Coordinator will respond to all action items identified during a QA audit within thirty (30) calendar days of receipt of the report using the *Action-Item Site Response Form*. This response will indicate either resolution of the action item or include a corrective action plan with a projected resolution date. For items with a projected resolution date, the CP-CTNet Auditor will follow-up on those items every 30 days until all items are resolved. The reports are reviewed by the Director of Auditing and a DCP study representative. Once all items are resolved, the final Audit Report should be signed by the PI.

If the site does not respond within the 30-calendar day timeframe, the Auditor will contact the site to clarify the issue. If the site does not respond or resolve the issue within 7 calendar days, the Auditor will document the site's noncompliance in an email to the site, with DCP Representatives copied, and will record this as a major violation in the Audit Report.

Action-Item Response Form:
To avoid any potential pitfalls during preparation of the Action-Item Response Form the following should be considered:

- Document every step of corrective and preventative action implementation (documentation of root cause analysis, development of new procedures, any training, etc.).
- Specify the timeframe for completion of the corrective and preventive actions

Adherence to and implementation of the agreed corrective and preventive action is critical and may be the scope of a future audit.

Sites are requested to review the Audit Reports and record agreement or disagreement with each audit finding. If you do not agree, a reason and if applicable additional supporting documentation should be provided to the Auditor. For example, if the findings cited no evidence of hematologic values or radiotherapy treatment in the patient's chart, but values exist or radiation was given, it is necessary to send copies of the reports, which confirm the values or treatment. Any supporting documentation provided to the Auditor must be anonymized prior to sending.

The Auditor will follow up with the site to obtain necessary confirmatory documentation. If the PI confirms the documentation is not available, the PI or designee should flag the data as unconfirmed in Rave. If these data are related to eligibility criteria, inability to provide appropriate documentation may render the patient ineligible.

If the audit of individual participant source documents indicates data have been entered incorrectly in RAVE, and the PI agrees with this assessment, the site will make the appropriate changes to the database based on the Audit Report.

Sites should retain all audit reports and correspondence available for future audits and/or monitoring (e.g., in Regulatory Binder or protocol Trial Master File).

All Audit Reports and Action-Item Site Response Forms will be distributed to:

- LAO PI and Site Coordinator
- AO PI and Site Coordinator (as applicable)
- Appropriate (per protocol) DCP Medical Monitor
- Appropriate (per protocol) DCP Scientific Lead
- DCP Nurse Consultant

Any Audit Reports that identify major deficiencies within the site should also be distributed to:

- DCP Program Director
- DCP Program Official

Note: The Audit Team will also notify the Regulatory Contractor of any unreported or misreported SAEs.

6. ADDITIONAL INFORMATION:

Refer to the **CP-CTNet Acronym List** to see the description of commonly used acronyms in this SOP.

Please send questions and comments to the DMACC at Audit_CP-CTNet@frontierscience.org

7. REFERENCES

- None

8. APPENDICES

- None