United States-Latin America-Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network (ULACNet), Audit Plan for Lead Academic Organizations (LAOs)
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The National Cancer Institute (NCI)/Division of Cancer Prevention (DCP) requires Quality Assurance (QA) audits of clinical trial data and processes at each Lead Academic Organization (LAO). The Frederick National Laboratory (FNL) Clinical Monitoring Research Program Directorate (CMRPD)/Leidos Biomedical Research, Inc. (Leidos Biomed) will support ULACNet by conducting audits at each LAO.

Auditing is an independent QA function for the systematic evaluation of clinical trial processes and documentation. It is used to determine whether trial-related activities are conducted—and data recorded, analyzed, and accurately reported—according to the protocol, ULACNet Program Guidelines, relevant Good Clinical Practice (GCP) guidelines, and other applicable regulatory requirements. This audit plan is a living document that will be updated ad hoc to meet the NCI/ULACNet program needs.

Each LAO audit will be protocol specific, reviewing protocol-specific requirements and the LAO's management of the protocol being audited. The protocol-specific auditing plan will be outlined on the audit confirmation letter.

This document outlines: the audit overview, scope, and frequency of the audit; the person who will be responsible for conducting the audit; reference documents required for the audit; and timelines for audit reporting, corrective action, and resolution of any audit findings.

Each protocol that an LAO oversees will be audited at least annually, and ad hoc.

Audit Overview

Each LAO provides oversight of its Administrative and Coordinating Core, Data Management and Statistical Core, Central Laboratory Core, and Clinical Trials Program, including all studies and AOs within the Partnership Center. An LAO audit will evaluate the LAO support provided to the AOs in conducting ULACNet studies according to GCP guidelines, the approved protocol, ULACNet Program Guidelines, and applicable US and international regulatory requirements. During an audit, pre-study and study initiation activities, study database of record, computerized systems (e.g., regulatory file management systems), monitoring programs, study supply logistics, staff training, documentation of meeting minutes, and other support provided to the sites will be reviewed.

While the focus of an LAO audit will be on the overall management of a specific protocol, it is possible that during a single visit from the Clinical Trials Manager (CTM) auditor, more than one protocol will be scheduled for an audit. If multiple audits are conducted during one visit, the scheduling letters, confirmation letters, follow-up letters, and audit reports will be generated separately for each protocol.

The Audit Scope

Site Start-Up Process

- IRB Approval/In-Country Regulatory Approval and Tracking
- Essential Documentation Collection Process
- Protocol and Study Manuals Training
- Regulatory File Set Up
- Central Laboratory Logistics
- Drug Shipment Logistics (if applicable)
- Equipment/Supply Acquisition (if applicable)
- Site Training
- Program Processes (e.g., Minimum Data Set Quality Control)
- Processes for Ensuring any Action Items are Resolved

Site Continuous Monitoring Program

- Study-Specific Monitoring Plan/Monitoring Schedule
- Monitor Training
- Monitoring Visit Report Review/Approval, Site Follow-Up
- ICF Tracking Tool (to ensure correct ICF version is used)
- Drug Accountability Tracking Tools (if applicable)
- AEs/SAE Tracking Tools
- IRB/ Regulatory Authority Continuous Review
- Site Action Item Resolution Records
- Deviation Reporting (to ULACNet Leadership) and Follow-Up
- Data Management System
- Trial Master File Maintenance
- Document Control Processes
- Minimum Data Set Process
- Participants Enrollment Tracking-AQuIP Accrual Procedures
- Blinding/Unblinding Process (if applicable)
- Center/Site Close-Out Process
- Audit of Accrual to US site(s) (if applicable)

Audit Frequency

Audits will be conducted off-site/remotely or in-person at each LAO at least annually, and ad hoc. Audits may be conducted any time between the date a study is approved and the date a study is completed.

The Auditor

The CMRPD Clinical Trials Manager (CTM) will conduct audits on behalf of the National Cancer Institute (NCI) and ULACNet Leadership.

CMRPD Audit Preparation

In preparation for an audit, the auditor will:

- Contact the LAO six to eight weeks prior to the audit to schedule an agreed-upon audit date and time.
- Specify how the audit will be conducted (i.e., remote or in-person).
- Prepare an audit confirmation letter detailing the audit scope, the documents to be reviewed, the personnel required to be present throughout the audit (i.e., during the opening meeting, the course of the audit itself, and the closing meeting). The audit confirmation letter and audit agenda will be sent to the LAO and DCP ULACNet staff two to four weeks prior to the audit.
- Prepare for the audit by reviewing data and documents, including but not limited to:
    - Study Initiation Visit reports generated from LAO monitoring of the AO(s), including any action items, close-out visit reports, the current IRB approved protocol, and LAO and/or LAO-designated Clinical Research Organization (CRO)/Clinical Research Associate (CRA) correspondence with the AO.
    - LAO and AO regulatory documents, including documents uploaded to the NCI Registration and Credential Repository (RCR), 1572s, Delegation of Tasks Logs (DTLs), AQuIP recruitment data, MDS data, eCRF data queries, and specimen management tracking for storage, shipping, analysis, and reporting.
    - Investigational drug shipping records, staff training documentation.

LAO Audit Preparation

In preparation for an audit, the LAO should:

- Collaborate with the auditor to identify a mutually agreeable date and time for the audit to allow maximum participation by site staff.
- Acknowledge receipt of the confirmation email, including the audit date(s) and objectives.
- Review the scope of the audit described in the confirmation letter; prepare documents; ensure that investigational agent distribution and specimen storage systems are up to date (if applicable); and schedule time for the audit participants to meet with the auditor.
- [For in-person audits] Reserve space for the opening meeting, closing meeting, and the auditor to work on reviewing documents. Arrange for a facility tour, if applicable.
- [For remote audits] Gather all required documents to be shared with the auditor via a secure data transfer system, and schedule time for auditor to meet with site staff.
- Request that the auditor be granted access to the necessary electronic systems (if applicable).

Post-Audit Expectations

At the end of the audit, the auditor will hold a closing meeting with LAO staff to review audit findings, including items corrected during the audit and items pending correction for which a corrective and preventative action plan (CAPA) is recommended, and to discuss the timing of the next audit.

The auditor will send an email to ULACNet staff within 48-hours of the visit outlining the overall audit findings. For major findings, the auditor may elect to call ULACNet staff in addition to sending the post-audit email.

The auditor will prepare an audit report outlining items audited, audit findings, and recommended corrective and preventative actions (CAPAs) that need to be taken. The finalized audit report is an internal report that will be send to ULACNet Leadership. A detailed follow-up letter will be sent to the LAO's study Principal Investigator, Study Coordinator, and ULACNet Leadership. Both action items addressed during the audit and action items pending resolution will be included in the letter. Responses to all pending action items, including CAPAs, if applicable, are expected within thirty (30) calendar days of receipt of the follow-up letter. Action items related to monitoring activities should be forwarded to and addressed by the LAO-designated CRO/CRA. The CRO/CRA will need to provide written corrective actions/resolutions to the sponsor and auditor. The LAO will collect and submit all responses to the auditor, including responses from the CRO/CRA.

CMRPD will send a letter to the LAO PI and ULACNet staff if the LAO does not address action items within 30 days.

AUDIT COMMNUNICATION FLOW