United States-Latin America-Caribbean HIV/HPV-Cancer Prevention Clinical Trials Network (ULACNet)

Study-Specific Monitoring Plan Guidance Document

Introduction

This document outlines the National Cancer Institute (NCI)/Division of Cancer Prevention (DCP) expectations of the Lead Academic Organizations (LAOs) Partnership Center (PC - study sponsors) role in defining monitoring activities at the Affiliate Organizations (AOs) conducting ULACNet trials. A study-specific monitoring plan should be submitted by the PC for each ULACNet trial.

Study Conduct Monitoring Purpose

The purpose of trial monitoring[1] is to verify

a) Human subjects' protection
b) That trial data is complete, accurately recorded and reported, and verifiable from source documents
c) That trial conduct is compliance with the currently approved protocol, with GCP, with the applicable regulatory requirement(s), and with ULACNet Guidelines.

Study Sponsor obligations for Monitor Selection and Qualifications

ICH-GCP-E6(R2) defines the sponsor obligations to monitor the conduct of study. LAOs, as the study sponsors, are responsible for the selection and qualification of study monitors or to delegate this responsibility to a CRO. If the LAOs delegate the Monitoring responsibility to a CRO, FDA regulations (21 CFR 312.52) require the written transfer of any obligations from a sponsor to a CRO and require the CRO to comply with the regulations. Although sponsors can transfer responsibilities for monitoring to a CRO(s), they retain responsibility for oversight of the work completed by the CRO(s) that assume this responsibility.[2]

a. The study sponsor (i.e., the Lead Academic Organization – LAO) may delegate monitoring responsibilities to to a CRO or an independent monitor (i.e., a monitor not otherwise affiliated with the LAO or accruing organization). If monitoring is to be performed by the LAO or an accruing organization, documentation of an independent monitoring office/team/person should be submitted with the monitoring plan. DCP/NCI reserve the right to deny the request or require additional monitoring by an external body if the study risk level is deemed high (e.g., as in a first-in-human vaccine trial).
b. Monitors should be qualified by training, having the scientific and clinical knowledge to monitor the trial.
c. Monitor qualifications and training records should be maintain by the LAO

d. Monitors should be thoroughly familiar with the investigational product(s), the protocol, written informed consent form and any other written information to be provided to participants, the sponsor's SOPs, GCP, and applicable regulatory requirement(s).

e. The LAO is responsible for selecting a qualified monitor who is able to communicate effectively with the site staff, preferably via the site's preferred language. If this is not possible, and language barrier(s) exist, a description of how the monitor will communicate with the site staff during visits must be outlined in the study-specific monitoring plan. For a study where each AO has a different preferred language, the monitoring plan should outline the communication approach for each language. In addition, each study-specific plan must outline a process for translation of all documents to be monitored.

Monitoring Plan Requirements

NCI/DCP expects the LAOs to have oversight of the study conduct through implementing monitoring activities. These activities should be outlined on a monitoring plan which meet the following requirements.

- Each ULACNet monitoring plan should be study specific.
- The study monitoring plan will outline the level of monitoring to be performed based on the study design and level of risk*, and ensure that the content of the plan aligns with ICH-GCP-E6(R2) and should consider the following:
    - IND required versus IND exempt studies
    - Trial type and/or safety of investigational product: Screening trials / precancer treatment trials / vaccine trials
    - Complexity of study design
    - Study size, duration, and number of accruing sites
    - Types of study endpoints
    - Geography of accrual site and strength of each site's infrastructure

- Each monitoring plan should include at least the following elements:
    - Plans for day-to-day study oversight (documentation of correspondence, monthly study calls, etc.)
    - Identify the person(s)/organization responsible for monitoring the study
    - Communication plan and document translation plan for sites where a language barrier exists
    - The frequency with which monitoring reviews will be performed
    - Monitoring visit type(s): on-site (or remote visits when on-site visits are not permitted)
    - Description of review of site processes, procedures, and records to ensure

the protection of study participants, and integrity of study data including:
  - Regulatory study site binder review
  - Informed consent verification
  - Adherence to protocol eligibility
  - Participant record review
  - Documentation of study agent accountability and administration, if applicable
  - Documentation of staff training
- Requirements for identifying and reporting adverse events or other issues that could potentially affect participant safety

- Outline for timely submission of monitoring visit reports and any action items/follow up to the National Cancer Institute (NCI)/Division of Cancer Prevention (DCP) and the Clinical Monitoring Research Program Directorate (CMRPD)/Leidos Biomedical Research, Inc. (Leidos Biomed)

* A risk-based approach should focus oversight activities on preventing or mitigating important and likely risks to data quality and to processes critical to human subject protection and trial integrity.

Documentation of Monitoring Activities / Follow-up of Action Items

- The monitoring plan should state that the ULACNet Monitoring Report template and Action Item Follow-up template may be used to document monitoring activities. If the monitor elects not to use the ULACNet templates, the plan should outline the content of the monitoring visit report which should include:
  - Date and type of visit
  - Name of monitor
  - Study number and title
  - Study staff present during the visit
  - Summary of monitoring activities / data reviewed
  - A description of findings, issues resolved during the visit, and outstanding action items.

NCI/DCP expectations of a monitoring activities

- Monitoring Plan Adherence
  - The monitor, LAO and Study Investigators are expected to adhere to the study's monitoring plan. Any deviation from the monitoring plan must be documented and reported to DCP.
  - If monitoring activities show that there is a problem at an AO, DCP reserves the right to request that Leidos perform a for-cause audit the AO.

Monitoring Plan NCI/DCP Submission and Approval

- A draft Monitoring plan written by the LAOs or their selected CRA/CROs must be submitted to DCP and Leidos via the DCP Protocol Information Office (PIO) no later than 30-days after a study is given *Approval on Hold*.
- Final study approval will not be granted unless a draft monitoring plan has been submitted.
- An approved monitoring plan should be in place no later than 30-days after the study activation date (i.e., study open to accrual) as documented on the ULACNet Study Status Update form.

Monitoring Activities Communication

- The LAOs or their selected CRA/CROs, should notify DCP and their contractor, Leidos Biomedical Research (LBR) of upcoming monitoring visits, and should be included in the calendar invitation for each visit. This will allow DCP to participate in the opening meeting and exit summary meeting for each visit, and better track monitoring visits and anticipated receipt dates for the resulting visit reports.

- The LAOs or their selected CRA/CROs, should send an exit summary meeting calendar invitation for each exit meeting to DCP.

- A monitoring visit report and action item list must be sent to the LAO PI, DCP ULACNet Staff, and the LBR team **within 30 calendar days of each monitoring visit**. An action item reportwith the status of each action item (i.e., resolved / pending resolution) will be submitted with the monitoring visit report. The action item report will be submitted to the organization being monitored, with a response from the organization due within 30 calendar days of receipt of the action item report.

References

1. GCP Network: Monitoring
2. FDA Guidance for Industry: Oversight of Clinical Investigations
3. ULACNet Audit Plan documents