## SOP 12: CLO Monitor Instructions for Conducting Monitoring Visits

### Overview:

1. The Consortium Lead Organization (CLO) is responsible for conducting monitoring visits at Participating Organizations (POs). These visits are conducted by the CLO Monitor to ensure compliance with Good Clinical Practice (GCP) Guidelines and with all applicable regulations pertaining to the conduct of cancer chemoprevention studies under contract with the National Cancer Institute (NCI)/Division of Cancer Prevention (DCP).
2. The CLO Monitor will conduct a monitoring visit at each active PO site for each study on an annual basis until the final participants complete the study. The first monitoring visit will occur once the fifth participant has enrolled at the PO site, or within 9 months of the first participant enrollment date (whichever occurs first). If no participants are enrolled at a site 9 months from PO activation, the monitor will discuss accrual issues and possible solutions with DCP Medical/Scientific Monitor, Nurse Consultant, and the study coordinator via conference call. The outcome of the call will be documented and distributed to call participants.
3. The CLO Monitor may conduct more frequent monitoring visits, or interim visits, as necessary to follow up with unacceptable deficiencies identified during the previous visit or concerns identified between visits. Other factors contributing to the need for an interim monitoring visit may include the complexity of the study, staff changes, number of subjects enrolled, and/or data quality concerns.

### Schedule the Monitoring Visit:

The CLO Monitor will:

1. Identify mutually convenient dates for an annual or interim site monitoring visit with the PO Site Coordinator.
   1. The duration of an annual visit is generally 2.5 days per study and the duration of an interim visit is generally between 1.5 and 2.5 days in duration.
   2. The visit will include a brief summary meeting with applicable PO staff to discuss the visit findings.
2. **(First monitoring visit** **at a PO** **for each study)** Randomly select five or more participant charts for monitoring review, including any chart with a reported Serious Adverse Event (SAE).
3. **(Subsequent monitoring visits)** Randomly select 25% of the unreviewed and partially reviewed number of participants enrolled by the PO or a minimum of seven participant charts (whichever is greater), including any chart with a reported SAE since the last monitoring visit.
   1. The charts selected for review will not include screen failures or charts that have been fully monitored previously. The exception can be the subset of records reviewed during a remote visit, when applicable: if deidentified records were provided during the previous remote monitoring visit, a subset of these records may be selected for review at the next onsite visit.
   2. Participant charts that have been partially reviewed during a previous visit may be selected for review again, if there is new data available.
   3. It may be appropriate at times to randomly select charts from specific time periods or staffing periods in order to optimize monitoring efforts.
   4. There is no penalty if the CLO Monitor is unable to complete the review of each selected chart during the visit. But if the CLO Monitor is unable to complete a sufficient review of charts due to the complexity of the study, high accrual rate, or barriers at the site (such as poorly organized records, poor data quality, missing records, etc.), this will be included in the report of findings and an interim visit will be scheduled.
   5. In specific situations involving an excessively high accrual pattern, it may be appropriate to select 25% of the total number of participant charts enrolled since the previous visit or to establish a cap for the total number of charts selected during a visit. In these situations, the CLO Monitor will receive DCP approval prior to the selection of charts for review.
4. Send an email confirmation to the PO Principal Investigator and Site Coordinator; and copy the DCP Help Desk.
   1. The email will state the purpose and objectives of the visit, documents that will be reviewed, duration of the visit, and date and time of the summary meeting (if confirmed).
   2. The email will also specify the participant identification number for each participant record (chart) selected for review during the visit.

### Prepare for the Monitoring Visit:

The CLO Monitor will:

1. Review the protocol and all study materials.
2. Review enrollment and randomization numbers for the PO, and compare with the Recruitment, Retention, and Adherence (RRA) Plan for the PO.
3. Review the history of staff changes at the PO since the last monitoring visit or study initiation meeting.
4. Review regulatory documents submitted by the PO to the CLO since the last monitoring visit or study initiation meeting.
5. Assess timely entry of study data into the database of record and ensure access to the database entries for all charts selected for review.
6. Review the most recent Minimum Data Set (MDS) submission and ensure access to the safety data entries for all charts selected for review.
7. Review all action items and findings identified during the last monitoring visit report, if applicable.
8. Review all DCP Consortia 2012 Standard Operating Procedures and DCP Guidance Documents.
9. Contact the CLO Site Coordinator to inquire if there are any specific questions or concerns that can be addressed during the monitoring visit.
10. For the remote visits, work with the site being monitored to ensure remote access to source data.

### Conduct the Monitoring Visit:

The CLO Monitor will:

1. Review the following, as outlined in detail in the [SOP 12a: Monitoring Visit Report](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/SOP12a-Monitoring-Visit-Report.docx) template:
   1. Regulatory documents at the PO to confirm that all documents that have been submitted to the CLO to date are current and complete.
   2. Review of the following documents:

* Annual Signatory Institution Worksheet content and approval letter
* Boilerplate language included in the Annual Signatory Institution Worksheet approval letter
* Annual Principal Investigator Worksheet content and approval letter
* Study-Specific Worksheet approval letter
  1. Informed consent forms to verify that a properly signed and dated form is on file for each study participant and that the site used the correct version of the form.
  2. Site operations to verify the site has adequate resources and procedures in place for successful conduct of the study and that all previously identified findings have been resolved, and to ensure that all staff participating in the conduct of the study have received adequate training from the PI, and have been informed of pertinent changes during study conduct, and receive additional training, as appropriate.
  3. Review all Protocol Deviations that occurred since last visit and ensure that they have been reported as per *DCP 2012 Consortia for Early Phase Prevention Trials SOP 4: Reporting Protocol Deviations*.
* Review all PDs with “CIRB reported - Yes” to verify documentation of CIRB notification.
  1. Screening and/or enrollment log(s) are current.
  2. Research specimen log and/or research specimen management system is current.
  3. Pharmacy operations and documentation to ensure compliance with all requirements.
* When a monitoring visit is conducted remotely, the monitor, in advance of the remote visit, will request a written response (email is acceptable) from the pharmacist on the below items:
* Investigational pharmacy is secure, and access is limited to appropriate staff
* Balance from DARF matches the balance in stock
* Outdated investigational agent is stored separately from active supply
* Investigational agent is stored separately from commercially available supply
* The monitor should use the pharmacist’s written response to complete the appropriate items on the Monitoring Report. The Monitor will use the comments column next to each item to document the pharmacist’s response, along with the pharmacist’s name, and correspondence date.
  1. Selected participant charts. For each chart, review from screening through the most current study week available and:
     1. Verify study participation occurred according to protocol requirements for inclusion/exclusion criteria, visit dates and windows, clinical and laboratory evaluations, use of concomitant medications, dose modifications, research specimen collection and tracking, and reporting of Adverse Events (AEs) including any SAEs.
     2. Verify that information captured in the source documentation has been transcribed accurately and completely to the paper Case Report Forms (if applicable), database of record, and most recent MDS submission.
     3. Confirm that protocol deviation forms are on file for any deviations from protocol requirements.
     4. Ensure missed visits or examinations are noted appropriately, and there is documentation of any attempts to locate and/or communicate with the study participant.
     5. Ensure the POs submit a copy of all source documentation (with identifiers removed) and CRFs for each participant selected for chart audit as applicable, and the materials are accessible and organized. Refer to [SOP 9: Site Preparation for Monitoring and Auditing Visits](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/SOP9-Site-Preparations-QA-Audits.docx).

1. Note all findings identified during the review. The [SOP 12a: Monitoring Visit Report](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/SOP12a-Monitoring-Visit-Report.docx) template includes prompts in italics for specific findings that will be recorded with each monitoring visit. Additional findings will be recorded in the comments section.
2. Note all deficiencies identified during the review. A deficiency is any incomplete, incorrect, or missing finding that is not in keeping with the study plan, federal regulations, DCP Consortia 2012 Standard Operating Procedures, DCP Guidance Documents or institutional requirements.
   1. The CLO Monitor is required to label a deficiency as ‘major’ if it is severe in nature or scope, compromises patient safety, or impacts data integrity. Minor deficiencies that are repetitive, process-related, or involve multiple participants may also be considered a major deficiency.
   2. Examples of major deficiencies by review category, include:
      1. Regulatory Documentation
         1. Failure to obtain IRB/CIRB approval for the protocol or informed consent form.
         2. Interruption in the IRB/CIRB continuing review approval of the protocol.
         3. Participant enrollment or study procedures prior to IRB/CIRB approval.
      2. Informed Consent Form (ICF) Documentation
         1. Missing ICF.
         2. Failure to obtain appropriate signatures on the ICF.
         3. Failure to obtain a signed and dated ICF prior to starting study procedures.
         4. Wrong version of the ICF was used.
         5. Failure to re-consent, if applicable.
      3. Site Operations
         1. Inadequate staffing, training, or facilities to conduct study.
         2. Failure to comply with Data Management Plan.
         3. Screening and/or enrollment logs missing or incomplete.
         4. Failure to store and/or secure study records appropriately.
         5. Action items from previous site visit unresolved.
      4. Pharmacy Operations
         1. Incorrect administration or dosing of study agent.
         2. Balance on Drug Accountability Record Form(s) (DARF)(s) does not match drug supply.
         3. Missing DARF(s), or failure to maintain DARF(s) correctly.
         4. Failure to store and/or secure study agent appropriately.
         5. Failure to maintain documentation of agent order receipts and returns.
      5. Participant records (charts)
         1. Unable to verify eligibility.
         2. Participant not eligible for study.
         3. Excessive study documentation missing.
         4. Recurrent missed study evaluations.
         5. Excessive failure to follow protocol plan.
         6. Delinquent data entry in database and/or MDS.
         7. Excessive transcription errors.
         8. Unreported AE, or the grade/date associated with an AE is missing or inaccurate.
         9. Failure to report an SAE appropriately.
         10. Recurrent under or over reporting of toxicities.
         11. Failure to collect or document collection of primary and/or secondary study endpoint data.
   3. Major deficiencies that are corrected and/or appropriately documented by the site prior to the monitoring visit may be down-graded to a minor deficiency at the discretion of the CLO Monitor.
3. Note all action items identified during the review. An action item is any action required of the site following the monitoring visit. Each action item should be written in a manner that clearly conveys the expected action or outcome.
4. Prepare and conduct a summary meeting with the PI, Site Coordinator, and other key study staff to review the findings of the monitoring visit. In advance of the meeting, the CLO Monitor will notify the DCP study staff of the Exit Summary Meeting details including date, time, and call-in number. During the summary meeting the CLO Monitor will:
   1. Summarize findings from the review of regulatory, informed consent documentation, site operations, pharmacy operations, and participant records.
   2. Describe all major deficiencies.
   3. Discuss problem areas and plans for improvement (when applicable).

### Document the Monitoring Visit:

The CLO Monitor will:

1. Establish and maintain a visit log at the PO site using [SOP 12b: Monitoring Visit Log](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/SOP12b-Monitoring-Visit-Log.docx)*.* This document, or an equivalent, is to be completed, dated and then signed by the CLO Monitor and a staff member from the PO site during each visit.
2. Complete the [SOP 12a: Monitoring Visit Report,](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/SOP12a-Monitoring-Visit-Report.docx) including source documentation (original, certified, etc.) accessible to the CLO Monitor at time of visit as well as a description of all deficiencies and action items. Any findings requiring a response from the site will be documented using the Action Item - Site Response Form. An itemized list of all findings/discrepancies resolved during the visit must be listed in the Visit Findings section.

When CLO monitor conducts both monitoring and closeout visits at the same time, separate reports should be completed - one for the monitoring visit and one for the closeout visit. Both reports should be sent to the site together. If any action items are identified during the visit, one Action Item Site Response Form can be sent with the reports, and:

1. If the action items result from the monitoring part of the visit, they should also be documented in the monitoring report.
2. If the action items result from the closeout part of the visit, they should also be documented in the closeout report.
3. If a finding applies to an item listed in both monitoring and closeout reports, “No” should be answered in both reports to this particular item, but it should be documented only once in the Action Item Site Response Form.
4. Distribute the completed report via email to the DCP Help Desk **within or 15 business days of the site visit date**. The DCP Help Desk will forward the report to all applicable DCP representatives.
5. Distribute the completed report via email to the PO site.
6. Ensure the PO site responds to all action items **within 30 calendar days of distribution of the report**. The PO response may be full resolution or a corrective action plan with a projected resolution date. Forward a copy of the PO response to the DCP Help Desk.
7. Notify the PO site and the DCP Help Desk once the action item response is acceptable, and again once the corrective action plan is completed (if applicable).

### Important Information on Reporting Scientific Misconduct:

1. The CLO Monitor must immediately notify the DCP Medical/Scientific Monitor of any findings that may suggest intentional misrepresentation of data and or disregard for regulatory safeguards for any of the components of the monitoring visit.
2. The notification will be conducted by phone to permit clarification and discussion of the issues. Documentation should be included in the site visit report.

### Additional Information:

Refer to the [DCP Acronym List](https://prevention.cancer.gov/sites/default/files/uploads/clinical_trial/DCP-Acronym-List.docx) to see the description of commonly used acronyms in this SOP.

**Please send questions and comments to the DCP Help Desk at**

**1-844-901-4357 or** [**dcphelpdesk@dcpais.com**](mailto:dcphelpdesk@dcpais.com)