Title: Preparations for Site Closeout

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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

Sites (LAOs and AOs) are responsible for meeting all study obligations as part of site closeout.

The DMACC (Data Management and Coordinating Center) will conduct a site closeout visit for all active Lead Academic Organizations (LAOs) and Affiliated Organizations (AOs) for each study after all study activities are complete, or at the discretion of Division of Cancer Prevention (DCP) study staff. An active LAO/AO is defined as an institution or clinical site that, after having completed regulatory and DCP requirements for study initiation, is responsible for study administrative oversight and/or has been approved to accrue study participants. The site closeout visit may be done on-site or remotely at the discretion of the DCP Medical Monitor.

1. DMACC will conduct a site closeout visit at an LAO/AO when:
    - All participants enrolled at the LAO/AO have completed study-related activities; and
    - All data have been entered into Medidata Rave and outstanding data discrepancies have been resolved.
2. If an active site fails to accrue participants, DCP study staff, the DMACC and the LAO (for AO site closure) may elect to close the site early.
    - The DMACC will inform the site of the intention to close, and will schedule the site closeout visit.
    - If the site has received study agent, agent return or disposal must be handled as outlined in the protocol.
3. If a proposed accrual AO has not been activated, a site closeout visit is not required.
    - The LAO will send a letter to the AO (with a copy to DCP study staff, DMACC, and the DCP regulatory contractor) stating that the site was not activated; therefore, a site closeout visit is not required.
    - Regulatory documents that have been collected will be managed as directed by the LAO and/or as required by institutional policy.
    - The DCP Regulatory Contractor will manage regulatory documents submitted to them by the site.

2. SCOPE

This document details the responsibilities of the DMACC regarding the conduct of the site closeout visit, and outlines the information and materials LAOs and AOs are expected to prepare and provide during the visit.

3. ROLES AND RESPONSIBILITIES

LAO and AO Responsibilities:

The Site Coordinator is responsible for coordinating the site closeout tasks below in a timely manner. **During the site closeout visit, the DMACC will verify these items have been completed or will determine the completion status:**

1. All regulatory documents, including all required IRB/CIRB approvals, are current and on file.
2. The local IRB has been notified that all participants are off study according to institutional requirements.
3. An original or a certified copy of the original, signed and dated informed consent form(s) is/are

on file for each participant.

4. All required logs and documentation for enrollment, screening, monitoring and/or auditing visits, protocol deviations, and Serious Adverse Events (SAEs) are current and available.
5. Documentation is present in each participant's record indicating that study participation has ended, and the participant is off study.
6. There are no Adverse Events (AEs) or SAEs that require further follow-up for any participant.
7. There is no evidence to suggest the study blind was compromised, if applicable. If unblinding occurred, there is sufficient documentation to explain the appropriateness of the unblinding.
8. All data entry, data queries, and quality assurance (QA) activities in Rave are complete.
9. All action items from previous audits have been resolved.
10. The research specimen log(s) and/or research specimen management system(s) is/are current.
11. All study analyses involving research specimens are complete or are in progress.
12. All unused investigational agent has been returned to the repository or destroyed according to the protocol.

DMACC Responsibilities:

1. Schedule the site closeout visit.
    1.1. Identify a mutually convenient date with the site Principal Investigator (PI) and the Site Coordinator.
        - The duration of the site closeout visit is typically one full day.
        - The visit will include an exit summary meeting with site, the LAO (for an AO visit), and DCP staff to discuss the site closeout and any outstanding issues.
    1.2. The DMACC will send an email confirmation to the PI and Site Coordinator, LAO (for an AO visit), and DCP study staff. The email will state the purpose and objectives of the visit, documents that will be reviewed, and the scheduled date(s) for the visit. The exit summary meeting invite should be distributed by the DMACC.
2. Prepare for the site closeout visit.
    2.1. Review the protocol and study materials.
    2.2. Review accrual numbers (enrollment, registration, randomization) for the site.
    2.3. Assess status of data entry and remaining queries in Medidata Rave.
    2.4. Review all action items and findings identified in the report from the last audit visit.
    2.5. Review regulatory documents due and submitted by the LAO, or by the AO to the LAO, since the last monitoring visit.
    2.6. For AO closeout visits, contact the LAO Site Coordinator to inquire if there are any specific questions or concerns that should be addressed with the AO during the site closeout visit.
3. Discuss the upcoming study closeout activities and confirm they will take place after site closeout (Study close out procedures will be defined in SOP 04-02 Study Closeout Activities which is in development). The DMACC will:
    3.1. Instruct the site to notify the CIRB/IRB of site closeout.

3.2. Confirm whether there are existing biospecimens for submission to Frederick National Laboratory for Cancer Research (FNLCR), and review the submission process with the site.

3.3. For those studies collecting genomic data, explain that data should be submitted in accordance with the National Cancer Institute (NCI) Genomic Data Sharing (GDS) policy.

3.4. If the site closeout visit is at the LAO, confirm with the PI that there are plans to submit the draft manuscript to DCP study staff.

3.5. Confirm the site understands the requirement for retention and access of study records as outlined in the study protocol.

4. Record findings.

4.1. Note all findings identified during the site closeout.

4.2. Report deficiencies identified during the site closeout. A deficiency is any incomplete, incorrect, or missing finding that is not in keeping with the protocol, study plan, federal regulations, CP-CTNet Standard Operating Procedures, CP-CTNet Guidance Documents or institutional requirements.

- DMACC 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.
- Examples of major deficiencies specific to a site closeout visit, include:
  - Regulatory Documentation
    - Failure to obtain CIRB approval for the protocol or informed consent form (ICF)
    - Interruption in the CIRB continuing review approval of the protocol
  - ICF Documentation
    - Missing ICF
    - Failure to obtain appropriate signatures on the ICF
    - Use of wrong ICF version
    - A staff member not listed on Delegation of Tasks Log (DTL) obtains the informed consent from study participant
  - Site Operations
    - Failure to comply with the CP-CTNet Master Data Management Plan
    - Screening and/or enrollment logs missing or incomplete
    - Specimen log and/or specimen management system data are missing or incomplete
    - Action items from previous site visit unresolved
    - Excessive delinquent data entry in database.
  - Pharmacy Operations
    - Excessive instances of failure to maintain documentation of agent order receipts and returns
    - Study blind compromised without sufficient documentation to support the appropriateness of the unblinding
- Major deficiencies that are corrected and/or appropriately documented by the site prior to the site closeout visit will be noted in the Site Closeout Visit Report (currently in development).

4.3. Note all action items identified during the site closeout on the Action Item Site Response Form. An action item is any action required of the site following the site closeout visit. Each action item should be written in a manner that clearly conveys the expected action or outcome.

4.4. Prepare and conduct a summary meeting with the DCP study staff, PI, Site Coordinator, LAO (for AO closeout visit) and other key study staff to review the findings of the site closeout visit. During the summary meeting the DMACC will:

- Summarize findings from the site closeout visit.
- Describe any major deficiencies and/or action items identified.

5. Document the site closeout visit.

5.1. Complete a Site Closeout Visit Report, including a description of all deficiencies and action items.

5.2. Distribute the completed report via email to all applicable DCP study staff.

5.3. Distribute the completed report via email to the site and LAO (if applicable).

5.4. Ensure the site resolves all action items within 30 calendar days of distribution of the report. Note: The site cannot be closed out until all action items are resolved.

5.5. Notify the site and the DCP study staff once the action item response is acceptable.

6. Important information on reporting scientific misconduct:

6.1. The DMACC must immediately notify the DCP Medical Monitor/Scientific Lead 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.

6.2. The notification will be conducted by phone to permit clarification and discussion of the issues. Documentation should be included in the Site Closeout Visit Report.

4. DOCUMENTATION REQUIREMENTS

Each site is responsible for maintaining all study records, including source documentation, System Variable Attribute Reports (SVARs), laboratory data, pharmacy documentation, regulatory documents, and study communications in a secure manner.

1. Study records will be accessible for inspection by authorized NCI/DCP representatives, DMACC auditors, the local IRB and CIRB, Food and Drug Administration (FDA) personnel, and/or any drug company supporting the study.
2. If the study is conducted outside of the United States, additional requirements may apply that are specific to the country of the site(s) participating in the study.
3. The study records must be maintained and accessible as specified in the study protocol.
4. The NCI/DCP study staff will be notified prior to the planned destruction of any study materials.

5. 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 Audit_CP-CTNet@frontierscience.org.

6. REFERENCES

- None

7. APPENDICES

- None