

<b>19. STUDY CLOSE-OUT .....</b>	<b>1</b>
<b>19.1 Study Close-Out Responsibilities .....</b>	<b>1</b>
<b>19.2 Study Close-Out Procedures .....</b>	<b>1</b>
19.2.1. Data Quality Control Visits .....	3
19.2.2. Study Close-Out Visits .....	3
19.2.3. Long-Term Storage of Study Records .....	4
<b>19.3 Specimen Destruction .....</b>	<b>4</b>

## **19. STUDY CLOSE-OUT**

The term “close-out” refers to procedures undertaken to fulfill administrative, regulatory, data, laboratory, pharmacy, and human subjects requirements after participant follow-up in an Microbicide Trials Network (MTN) study has been completed. Responsibilities and procedures for study close-out are described below.

### **19.1 Study Close-Out Responsibilities**

MTN network partners have certain responsibilities for close-out of MTN studies. In general:

- MTN Protocol Teams are responsible for defining study-specific close-out milestones and requirements.
- MTN study sites are responsible for completing required study close-out procedures at each site. Ultimate responsibility for meeting all requirements rests with the study-specific Investigator of Record (IoR).
- U.S. National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS) and the MTN Coordinating and Operations Center (CORE), Statistical and Data Management Center (SDMC), and Network Laboratory (NL) are responsible for facilitating study sites completion of required study close-out procedures

Procedures for fulfilling these responsibilities are described in Section 19.2.

### **19.2 Study Close-Out Procedures**

To facilitate planning for study close-out, the SDMC will provide Protocol Teams with information on the projected, final, participant follow-up visit date for each participating study site and the study overall. Initially, projections will be made upon completion of accrual into the study. Thereafter, projections will be updated as needed depending upon the study design and planned duration of participant follow-up.

Each Protocol Team will begin planning for the study close-out approximately three months prior to completion of participant follow-up at any participating study site. As part of this planning, the Protocol Team will:

- provide input to the CORE (FHI) regarding content of the study-specific close-out checklist (see sample in Figure 19.1 below);
- develop plans, procedures, and materials for verification of primary study endpoints (if applicable);
- develop plans, procedures, and materials for unblinding the Protocol Team, study staff, and participants (if applicable);

- develop plans, procedures, and materials for release of study results to the Protocol Team, study staff, participants, and participant communities (if applicable); and
- develop plans for data analysis, manuscript preparation, and publication, taking into account that the primary manuscript should be submitted within eight months of the last participant scheduled follow-up visit.

In addition to taking part in the above-listed activities, designated Protocol Team members from the CORE (FHI), CORE (PITT), SDMC, NL, and DAIDS will facilitate planning for study close-out as follows:

- The CORE (FHI) Clinical Research Manager (CRM) will develop a study-specific closure checklist with input from the SDMC, NL, and pharmacy.
- The SDMC Protocol Statistician and Project Manager (PM) will develop a plan for final study data submission, cleaning, and analysis.
- The SDMC PM will provide technical assistance (as needed) to study sites that wish to access data maintained at the SDMC to fulfill Institutional Review Board/Ethics Committee (IRB/EC) study close-out reporting requirements.
- If applicable, the SDMC PM will provide study sites with a listing of study participants who did not provide informed consent for post-study specimen storage and possible future research testing.
- The NL will develop a plan to complete all required post-study laboratory testing, including testing performed for verification of study endpoints. The NL will inform study sites when all protocol-specified testing has been completed. The NL will inform the study sites to archive or destroy stored specimens.
- The DAIDS Medical Officer will inform all relevant parties at DAIDS of the projected end date for participant follow-up at each study site; at a minimum, this will include DAIDS communication to begin planning for conduct of final study monitoring visits and study close-out visits by the DAIDS Clinical Site Monitoring Group (CSMG).
- If applicable, the DAIDS Protocol Pharmacist or MTN Director of Pharmacy Affairs will develop written instructions for final disposition of investigational study drugs/products and associated documentation.

Each participating study site will begin planning for study close-out approximately three months prior to completion of participant follow-up at that site. As part of this planning, the site will:

- determine the study close-out reporting requirements of its responsible IRBs/ECs. Some IRBs/ECs require submission of a study close-out report upon completion of participant follow-up, whereas others do not consider a study “closed” until all study data analyses are completed and/or published. Each site will adhere to its IRB/EC requirements for report submission. In the event that IRB/EC guidelines do not specify the required content of study close-out reports, the reports should contain the following information:
  - The date when participant follow-up was completed
  - The number of participants enrolled in the study
  - The number of participants who completed the study
  - The number of participants who withdrew, or were withdrawn, from the study prior to completion
  - Information on the adverse experiences that occurred at the site during the study
  - If applicable, reference to all Investigational New Drug (IND) Safety Reports submitted to the IRB/EC during the study

- tailor plans, procedures, and materials for unblinding study staff and participants to suit local site needs in consultation with site-specific study staff and community representatives (if applicable);
- tailor plans, procedures, and materials for release of study results to study staff, participants, and participant communities to suit local site needs in consultation with site-specific study staff and community representatives (if applicable); and
- develop operational and staffing plans for completion of all required study close-out procedures as listed on the study-specific close-out checklist.

After participant follow-up has been completed, Protocol Teams and study sites will implement all plans listed above. Study sites will complete all required study close-out procedures as listed on the study-specific close-out checklist. It is recognized that close-out procedures need not be completed in the order listed on the checklist, and that some procedures will require considerably more time (i.e., as much as several months) than others. Study sites should complete each requirement in as timely a manner as possible and use the checklist to document progress toward meeting all requirements throughout the close-out process.

After all requirements have been met, the study site IoR will sign and date the checklist, file the signed original on site, and forward a copy to the CORE (FHI) CRM. Thereafter, all study records must be maintained in accordance with the DAIDS standard operating procedures (SOPs) for Essential Documents and Source Documentation, Good Clinical Practice (GCP) guidelines, the U.S. Code of Federal Regulations (CFR) 21 CFR 312.57 (if applicable), and other applicable DAIDS policies. See Section 19.2.3 for further information on record retention requirements.

#### **19.2.1. Data Quality Control Visits**

As an MTN study draws to a close, the SDMC staff will determine whether the number of outstanding data quality control (QC) notes, particularly ones essential to data analysis, warrant a Data Quality Control Visit. When appropriate, the SDMC PM contacts the clinic coordinator to arrange a visit. These visits are conducted by the SDMC PM.

#### **19.2.2. Study Close-Out Visits**

When requested by DAIDS, study close-out visits are conducted by the DAIDS CSMG. Typically, the visits take place within three months after site staff have resolved all outstanding data QC notes and queries, which should be within three to six months of the last participant's final follow-up visit.

### **19.2.3. Long-Term Storage of Study Records**

For MTN studies that are conducted under an IND application, all study records must be retained for at least two years after the U.S. Food and Drug Administration (FDA) approval or disapproval, IND withdrawal or study discontinuation as per US FDA 21 CFR 312.62 (c). For MTN studies that are not conducted under an IND, all study records must be retained for at least three years after completion of research as per HHS 45 CFR 46.115 (b). For both IND and non-IND studies, records must be retained in accordance with protocol-specified protections of participant confidentiality and with site IRB/EC policies and procedures. If the study record is subject to any other U.S. federal or state, country, or local laws, regulations, policies or other requirements, site staff should follow the strictest of any applicable laws, regulations, policies, or other requirements for study record retention. See DAIDS policy on *Storage and Retention of Clinical Research Records* for further information at:

<http://www3.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/ClinicalSite.htm>.

Study records must be maintained on site for the entire period of study implementation. Thereafter, guidance for long-term record storage will be provided by the CORE (FHI) in consultation with DAIDS. No records are permitted to be relocated off site, discarded, or destroyed without prior written authorization from DAIDS.

### **19.3 Specimen Destruction**

Study site staff must store all specimens collected during a study per protocol at least through the end of the study. Study participants may be asked to provide written informed consent for their specimens to be stored after the end of the study for possible future testing. The specimens of participants who do not consent to long-term storage and possible future testing must be destroyed after the study is completed; destruction will take place after all protocol-specified testing has been performed, relevant data have been cleaned, relevant data analyses have been completed; and permission to destroy the samples is obtained from the NL.

**Figure 19.1 Sample Study Close-Out Checklist**

**MTN XXX Study Close-Out Checklist**

- In accordance with IRB/EC requirements, inform all responsible IRBs/ECs of study closure; complete protocol de-registration with the DAIDS Protocol Registration Office.
- Compile lists of contacts related to study results and unblinding information.
- Complete and submit all required DataFax forms to the SDMC.
- Resolve all outstanding data QC notes.
- Ship any unused (unassigned) Clinic Randomization Envelopes to the SDMC.
- Resolve any pending monitoring findings/queries.
- Ship all pending biological specimens to the NL (or other designated laboratory).
- Collaborate with the SDMC and NL to resolve any discrepant laboratory test results and finalize endpoint-related documentation.
- In consultation with the SDMC and NL, after all protocol-specified laboratory testing is completed, archive or destroy all remaining stored specimens (specimens obtained from participants who did not provide informed consent for post-study specimen storage and possible future research testing must be destroyed).
- In accordance with instructions provided by the DAIDS Protocol Pharmacist (DAIDS Clinical Research Products Management Center) or MTN Director of Pharmacy Affairs, return or dispose of all investigational drug/product supplies.
- Review and assemble for long-term storage all required essential documents, including:
  - Administrative and regulatory documentation
  - Log linking participant names and ID numbers (which also serves as the completed participant identification code list required by ICH/GCP guidelines)
  - All study documents bearing participant names
  - All study documents bearing participant ID numbers
  - All study drug/product receipt, dispensing, accountability, and final disposition documentation
  - Updated financial disclosure forms (reflecting any relevant changes that occur during the course of the study and for one year following completion of the study)
  - Final report by investigator to IRBs/ECs and local drug regulatory authorities (where applicable)
- To the extent possible, organize and categorize all study documentation according to ICH/GCP guidelines (ICH E6, Section 9.4). Documents must be stored securely and with adequate protection of participant confidentiality. No study records may be discarded or destroyed without prior authorization from DAIDS. Prepare a written inventory of all documentation and storage locations; forward a copy to the CORE (FHI) CRM, the CORE (PITT) Regulatory Director, and the DAIDS OCSO Program Officer.
- If applicable, prepare for and take part in a study close-out visit performed by the DAIDS CSMG; resolve all visit findings/queries; and file all visit documentation with other study documentation.
- Complete, sign, and date this checklist. File original with other study documentation and provide a copy to the CORE (PITT) Regulatory Director and to the CORE (FHI) CRM.

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Investigator of Record Signature

Date

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Investigator of Record Name (Print)