# 18 CLINICAL RESEARCH SITE STUDY SPECIFIC CLOSE-OUT

The term "close-out" refers to procedures undertaken to fulfill administrative, regulatory, and human participant requirements after participant follow-up in an HPTN study has been completed at a Clinical Research Site (CRS). For the purposes of a Division of AIDS (DAIDS) Network, study close-out may be defined as the time when all participant visits have been completed, database has been locked, and all lab specimens are accounted for/reconciled. This definition is independent of the CRS study closure with their Institutional Review Boards/Ethics Committees (IRBs/ECs).

## 18.1 Responsibilities for CRS Study Specific Close-out

Study specific close-out at the CRS is separate from overall study closure (in the case of a multi-site study) and site closure, both of which involve Office of Clinical Site Oversight (OCSO). OCSO is not involved in CRS study specific close-out.

To facilitate planning for CRS study specific close-out, the Statistical and Data Management Center (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.

Projections initially will be made upon completion of accrual into the study. Thereafter, projections will be updated as needed depending on the study design and planned duration of participant follow-up.

The protocol team will begin planning for CRS study specific close-out prior to completion of participant follow-up at each participating study site. As part of this planning, the protocol team will:

- Provide input to the Leadership and Operations Center (LOC) Clinical Research Manager (CRM) regarding content of the study-specific close-out checklist
- If applicable, develop plans, procedures, and materials for unblinding the protocol team, study staff, and participants (see Section 12.1.7 for participant unblinding)
- Develop plans, procedures, and materials for release of study results to the protocol team, study staff, participants, and participant communities (see Section 12.6 for the release of HPTN data from the SDMC)
- 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 LOC, SDMC, Laboratory Center (LC), and DAIDS will facilitate planning for CRS study specific close-out as follows:

- The LOC CRM will develop a study specific closeout checklist
- The SDMC Protocol Statistician and Clinical Data Manger (CDM) will develop a plan for final study data submission, cleaning, database lock and analysis. For information about publications, see Section 21
- The SDMC CDM will provide technical assistance as needed to study sites wishing to access reports or data maintained at the SDMC to fulfill IRB/EC study close-out reporting requirements
- If applicable, the SDMC CDM will provide the LC with a listing of study participants who did not provide informed consent for post-study specimen

storage and possible future research testing, so that the LC may coordinate sample destruction (see section 18.3)

- The LC will develop a plan to complete all required post-study laboratory testing, including testing performed for verification of study endpoints. The LC also will inform study sites when all protocol-specified testing has been completed
- The DAIDS Prevention Sciences Program (PSP) 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 within-DAIDS communication to begin planning for the study closing at the site
- If applicable, the DAIDS Pharmaceutical Affairs Branch (PAB) Protocol Pharmacist will develop written instructions for final disposition of investigational study drugs/products and associated documentation
- As an HPTN study draws to a close, the SDMC staff will determine whether the number of outstanding data queries, particularly ones essential to analysis of protocol objectives, warrant a data quality control visit. When appropriate, the SDMC CDM will contact the study coordinator to arrange a visit
- The SDMC, LC, and CRS will work together to reconcile the database to each specific sample (type and number of aliquots) collected during the study, available on site, and available at LC

Each participating study site will begin planning for study specific closeout prior to completion of participant follow-up at that site. As part of this planning, the site will:

- Notify the responsible IRBs/ECs of CRS study closeout according to the IRBs/ECs' procedures
- If applicable, in consultation with site-specific study staff and community representatives, 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, tailor plans, procedures, and materials for release of study results to study staff, participants, and participant communities to suit local site needs
- Develop operational and staffing plans for completion of all required study close-out procedures as listed on the study specific closeout 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 specific closeout procedures as listed on the study specific closeout checklist. It is recognized that closeout procedures need not be completed in the order listed on the checklist, and that some procedures will require considerably more time (up to 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 closeout process.

Site staff will de-register the protocol through the DAIDS Protocol Registration System (DPRS) according to instructions on the Regulatory Support Center (RSC) website.

- Deregistration can occur when:
  - The CRS no longer has participants on study (all follow-up has been completed) and does not plan to enroll additional subjects

- If no participants were ever enrolled at the CRS and the study has closed to accrual

- The DAIDS deregistration process is independent of a CRS's closure/termination of a study at their IRB/EC. The IRB/EC's determination to close or terminate a study is NOT required for a CRS to deregister with DAIDS. Completion of the DAIDS deregistration process indicates that a CRS's participation in a study is complete but does not reflect the closure of a multi-center study at all CRSs participating in the study. Refer to the DAIDS Protocol Registration Manual for complete deregistration details

After all requirements have been met, the study site Investigator of Record will sign and date the checklist, file the signed original on site, and forward a copy to the LOC CRM. The LOC CRM will forward a copy to the DAIDS PSP Medical Officer.

All study records must be retained in accordance with the DAIDS Policy on Storage and Retention of Clinical Research Records.

## 18.2 Long-term Storage of Study Records

*Investigational New Drug Application (IND)*

For studies under an IND, investigators must retain study records for a period of at least two years following the date of approval of any labeling change for this licensed product and at least three years after the completion of research or as applicable. If no marketing application is filed, or if the application is not approved, the records must be retained for two years after the United States Food and Drug Administration (FDA) is notified that the IND is discontinued (21 CFR 312.62), or longer if needed to comply with local regulations.

Completion of a clinical research study occurs when the following activities have been completed:

- All research-related interventions or interactions with human subjects (e.g. when all subjects are off study)
- All protocol-required data collection of identifiable private information described in the IRB/EC-approved research plan
- All analysis of identifiable private information described in the IRB/EC-approved research plan
- Primary analysis of either identifiable private or de-identified information

*Non-IND Studies*

For studies not under an IND, investigators must retain study records for a minimum of three years after completion of the research, or longer if needed to comply with local regulations. Completion of a clinical research study occurs when the following activities have been completed:

- All research-related interventions or interactions with human subjects (e.g., when all subjects are off study)
- All protocol-required data collection of identifiable private information described in the IRB/EC-approved research plan
- All analysis of identifiable private information described in the IRB/EC – approved research plan

- Primary analysis of either identifiable private or de-identified information

For more information see DAIDS Policy on Storage and Retention of Clinical Research Records. For all studies, retention of study records must also be in accordance with local regulatory requirements as well as local IRB/EC policies and procedures. **No study records are permitted to be destroyed before the study to which the records relate are included on one of the lists entitled "List of Protocols having CRF/Pharmacy Records that will not be stored by DAIDS". There is one list for IND protocols and one list for non-IND protocols. These are studies for which DAIDS no longer has any regulatory obligation.** This information can be found on the DAIDS RSC website for CRF management.

### 18.3 Sample Destruction

Study site staff must store all specimens collected during a study. Specimens collected during the study may not be destroyed without prior permission of the LC unless specifically requested by study participant(s).

Study participants are asked to provide written informed consent for their specimens to be stored after the end of the study for possible future testing. If participants do not consent to long-term storage and additional testing of their specimens, study staff must destroy the specimens at the end of the study after all protocol-related and quality assurance testing has been performed, the data have been cleaned, and primary and secondary analyses are completed; the SDMC CDM will provide the LC with a listing of study participants who did not provide informed consent for post-study specimen storage and possible future research testing so that the LC may coordinate sample destruction. Study staff must obtain permission from the LC before destroying specimens.