

<b>18</b>	<b>CLINICAL RESEARCH SITE (CRS) STUDY CLOSE-OUT .....</b>	<b>18-2</b>
18.1	Responsibilities for CRS Study Close-Out .....	18-2
18.2	Long-Term Storage of Study Records .....	18-4
18.3	Sample Destruction.....	18-4
18.4	Referenced Web Links .....	18-4

## 18 CLINICAL RESEARCH SITE (CRS) STUDY 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 CRS. For the purposes of Division of AIDS (DAIDS) Network, study close-out may be defined as the time when all participant visits have been completed, data base has been locked, and all lab specimens are accounted for/reconciled. This definition is independent of the CRS study closure with their Institutional Review Board(s) (IRBs).

### 18.1 Responsibilities for CRS Study Close-out

Study 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 close-out.

To facilitate planning for CRS study 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 close-out at least 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 Coordinating and Operations Center (CORE) Clinical Research Manager (CRM)/Protocol Specialist (PS) regarding content of the study-specific close-out checklist (See Section 18.4 for the link to the sample 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 and Section 12.6 for the release of HPTN data from the SDMC)
- Develop plans, procedures, and materials for release of study results to the protocol team, study staff, participants, and participant communities
- Develop plans for data analysis, manuscript preparation, and publication, taking into account that the primary manuscript must 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, SDMC, Network Laboratory (NL), and DAIDS will facilitate planning for CRS study close-out as follows:

- The CORE CRM/PS will develop a study-specific study-closure checklist
- Site staff will de-register the protocol through the DAIDS Protocol Deregistration System (DPRS) according to instructions on the Regulatory Support Center (RSC) website (see Section 18.4 for URL).
  - 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/Ethics Committee (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 pages 49-50 (<http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/prmanual.pdf>).

- The SDMC Protocol Statistician(s) and Project Managers(s) (PM) will develop a plan for final study data submission, cleaning, database lock and analysis. For information about publication, see *HPTN Operating Policy 011: HPTN Publication Policy*.
- The SDMC PM(s) will provide technical assistance as needed to study sites wishing to access data maintained at the SDMC to fulfill IRB/EC study close-out reporting requirements.
- If applicable, the SDMC PM(s) 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 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, or designated Vaccine and Prevention Research Program (VPRP) 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 quality control queries, particularly ones essential to analysis of protocol objectives, warrant a data quality control visit. When appropriate, the SDMC PM will contact the study coordinator to arrange a visit.
- The SDMC, NL, 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 NL.

Each participating study site will begin planning for study close-out at least three months 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 close-out according to the IRB/EC's 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 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 (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 close-out process.

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 CORE CRM/PS. The CORE CRM/PS 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 (see Section 18.4 for URL).

## 18.2 Long-term Storage of Study Records

For studies under an Investigational New Drug Application (IND), investigators must retain study records for a period of two years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until two years after the investigation is discontinued and the Food and Drug Administration (FDA) is notified (21 CFR 312.62). For studies not under an IND, investigators must retain study records for a minimum of three years. The three-year time period begins when the primary analysis has been completed. For more information see DAIDS Policy on Storage and Retention of Clinical Research Records (see Section 18.4 for URL). 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 without prior written authorization from DAIDS.**

## 18.3 Sample Destruction

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

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. 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 once all quality assurance testing has been performed, the data have been cleaned, and primary and secondary analyses are completed; the SDMC PM(s) 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. Study staff must obtain permission from the NL before destroying specimens.

## 18.4 Referenced Web Links

Investigator recordkeeping and record retention 21 CFR 312.62	<a href="http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=312.62">http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=312.62</a>
Regulatory Support Center Protocol Registration	<a href="http://rsc.tech-res.com/protocolregistration/">http://rsc.tech-res.com/protocolregistration/</a>
DAIDS Policy on Storage and Retention of Clinical Research Records	<a href="http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/recordretention.pdf">http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/recordretention.pdf</a>
<i>HPTN Operating</i>	<a href="http://www.hptn.org/network_information/policies_procedures.htm">http://www.hptn.org/network_information/policies_procedures.htm</a>

<i>Policy 011: HPTN Publication Policy</i>	
<i>Sample Closeout Checklist</i>	<a href="http://www.hptn.org/network_information/network_templates.htm">http://www.hptn.org/network_information/network_templates.htm</a>