15 STUDY CLOSE-OUT and RECORDS RETENTION

The term *close-out* refers to procedures undertaken to fulfill administrative, regulatory, data, laboratory, pharmacy, and human participants requirements after participant follow-up in an IDCRC study has been completed. Responsibilities and procedures for study close-out are described below.

15.1 Study Close-Out Activities

Overall study-specific closeout (in the case of a multi-site study) is separate from site closure.

To facilitate planning for study close-out, the Data Coordinating Center (DCC)[1] (Emmes/SDCC or SCHARP/SDSU) will provide protocol teams with information on the projected final participant follow-up visit date for each participating study site and the study overall. Initial timeline projections will be made upon completion of accrual into the study. Thereafter, projections will be updated as needed based on the study design and planned duration of participant follow-up.

The protocol team will begin planning for overall study closeout prior to completion of participant follow-up. This early planning should permit sites to close out in an orderly fashion and allow overall study closeout in a timeframe that meets potential external reporting requirements (e.g., posting of results to ct.gov within 12 months of achieving primary outcome). Activities related to closeout and reporting should be part of each protocol's timeline. On average, each protocol will have a funding period of 6 months for closeout.

Closeout planning will include the following:

- FHI 360 will customize the overall study-specific closeout checklist with input from the core/management team and DMID on the closeout milestones and requirements
- If applicable, plans, procedures, and materials will be developed (in alignment with the protocol) for unblinding the protocol team, study staff, and participants
- The DCC, in coordination with the monitoring group, DMID PVG, LOU and FHI 360, will develop a plan for final data cleaning of the clinical and laboratory data in preparation to the data lock.
- The DCC, in coordination with the monitoring group, DMID, LOU and FHI 360, will develop a plan for database lock of the clinical data and lock of the laboratory data (noting that these may occur separately).
- The DCC, under the direction of the protocol statistician, will produce the Statistical Analysis Plan (SAP) prior to data lock and prior to unblinding. For IND studies, the SAP may be submitted to FDA one month prior to data lock. For studies with interim statistical

[1] The Emmes Company serves as DMID's Statistical and Data Coordinating Center (SDCC) for most IND studies conducted under the IDCRC. The Statistical Center for HIV/AIDS Research and Prevention (SCHARP) at the Fred Hutchinson Cancer Center works under the direction of the Statistics and Data Sciences Unit (SDSU) for the IDCRC to serve as the data coordinating center on non-IND studies under the IDCRC and some IND studies when requested by DMID.

monitoring of primary endpoints or analysis of primary and/or secondary endpoints intended to be conducted prior to the end of the study, the SAP should be finalized prior to conducting statistical analyses.

- The protocol team will develop plans for conducting and reporting of data analysis, and manuscript preparation and publication, considering that the primary manuscript should be submitted for IDCRC Review within 12 months of the study database lock date. If extenuating circumstances prevent meeting this deadline, the Protocol Chair (PC) should discuss this with IDCRC Leadership. For more information about publications, see Section 21.
- Identification of the study close-out reporting requirements for single Institutional Review Board (sIRB). The DCC may be asked to provide technical assistance or reports (e.g., number of PDs, AE listings) as needed to fulfill IRB/EC study closeout reporting requirements.
- If applicable, during the period of protocol closeout the DCC will provide study sites and/or the LOU with a listing of study participants who did not provide informed consent for post-study specimen storage and possible secondary or exploratory research testing. See Section 16 for further information.
- The LOU will develop a plan to complete all required laboratory testing, including testing performed for verification of study endpoints. The LOU will also inform study sites and labs as appropriate when all protocol-specified testing has been completed and when study sites may archive or destroy stored specimens (if applicable). See Section 16 for more details.
- For studies that have had routine clinical monitoring visits, the Clinical Project Manager (CPM) may begin planning for final closeout study-monitoring visit(s).
- The CPM will develop instructions for final disposition of investigational study drugs/products and associated documentation (if applicable) in collaboration with DMID Product Support Team (PST).
- The DCC will develop plans, procedures, and materials for verification of primary study endpoints (if applicable).
- The DCC will perform a final review of the database(s) to confirm all research specimens have been entered and shipped to the final destination (DMID CMS, other repository, or testing laboratory, as applicable) and that all discrepancies (e.g., missing specimens, unexpected specimens, collection date queries) have been resolved.
- The DCC will provide tables, listings, and figures (TLFs) for a Final Study Report (FSR) or Clinical Study Report (CSR), as needed/appropriate for Non-IND and IND studies, respectively, and as described in the protocol.
- Protocols containing exploratory outcomes (funded or not) may be closed out assuming appropriate language is contained in the Objectives/Endpoints and Statistical Sections:
    - Exploratory objectives/endpoints: Assays for exploratory endpoints may be performed and the data provided if available from the research laboratory
    - Statistical: The final FSR or CSR will be completed when all primary and secondary safety, clinical, and immunological endpoint data are available. Any available data from the exploratory endpoints at the time of compilation of the final FSR or CSR may also be included. Additional exploratory endpoint data may be included in an addendum , publication of manuscript(s), or other report.

IDCRC VTEU clinical sites or protocol specific non-VTEU sites are responsible for completing required study close-out procedures. Ultimate responsibility for ensuring that all site requirements are met rests with the site's study specific Investigator of Record (IoR). Each

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

- Identify the study close-out reporting requirements for local Institutional Review Board/Independent Ethics Committee (IRBs/IECs)
- Develop operational and staffing plans for completion of all required study close-out procedures as listed on the study site specific close-out checklist
- *International sites only*: Develop timeline and plans for return/destruction/disposal/reallocation of site supplies and equipment procured for the purposes of IDCRC protocol(s); for example, computers, participant-tracking databases, educational and training models, and supplies

After participant follow-up has been completed, protocol teams and study sites will implement the plans as listed above. Study sites will complete all required study close-out procedures as listed on the site study-specific close-out checklist. Close-out procedures need not be completed in the order listed on the checklist, and some procedures may require considerably more time (as much as several months) than others. Study sites should complete each requirement as soon as possible and use the checklist to document progress toward meeting each requirement 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 email a copy to FHI 360 PS.

It is important to ensure that no IRB be closed before full discussion within the team to ensure that all appropriate steps/processes have been completed. For example, it is critical that IRBs (single site or sIRB) remain active until all data has been received, cleaned, data queries resolved/closed and there be no further need for a site to access data.

Please note that activities may differ for fast-track protocols.

15.2 Record Retention Requirements

All study records must be retained on-site throughout the study's period of performance and thereafter for a defined period in accordance with the protocol. No records will be destroyed without authorization from the COU and/or DMID per instructions in each the protocol.

15.3 Laboratory Specimen Storage and Shipping

Prior to study closure, the protocol team determines if additional laboratory testing is needed to complete the protocol-specified primary and secondary analyses, consistent with the protocol and statistical analysis plan(s). Each protocol should minimally provide an indication of when stored specimens are planned to be tested; details regarding specimen processing, storage, shipping, and testing are specified in the LOU Central Assay Plan (CAP).

Specimens must be retained for the duration of a study. During the study, the preferred location for specimen management and storage will be Fisher Services, however exceptions may be made. The decision on storage during the study will be discussed by the protocol team and the LOU. While specimens do belong to the VTEU the IDCRC expectation is that all specimens be maintained at Fisher both during and after a study. Exemptions to use of Fisher, in either instance (during or end of study) must be approved by the LOU and the appropriate exception approval received from NIH.