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3 HPTN OPERATIONAL COMPONENTS

The following groups operationalize HPTN trials and are funded through cooperative agreements with the United States (US) [National Institutes of Health](#) (NIH):

- HPTN Leadership and Operations Center (LOC)
- Statistical and Data Management Center (SDMC)
- Laboratory Center (LC)
- Clinical Trials Units (CTUs)

3.1 HPTN Leadership and Operations Center

The HPTN LOC is responsible for the Network's scientific agenda and plays a key role in facilitating and managing all phases of science generation including:

- Creation of an overarching scientific agenda
- Concept Development
- Concept Review
- Protocol Development
- Protocol Review
- Protocol Implementation and Study Conduct
- Result Dissemination (Conference Calls, Posters, Presentations and Publications)

The HPTN LOC is responsible for facilitating and managing HPTN network-wide meetings and for smaller leadership gatherings. The HPTN LOC is responsible for logistical, administrative support, and management of all Network activities. The HPTN LOC also, in conjunction with the LC and SDMC, is responsible for scientific and technical network activities.

Staff from the HPTN LOC work closely with Network leadership; protocol teams; staff from the SDMC, LC, and CTUs/Clinical Research Sites (CRSs); [Division of AIDS](#) (DAIDS) and NIH; Science Committees (SCs); and CTU/CRS community programs on all aspects of the HPTN research program, as described in Section 3.1.1. The HPTN LOC is located at FHI 360.

3.1.1 HPTN LOC Responsibilities

The HPTN LOC's specific operational responsibilities include but are not limited to:

- Leadership and Governance
 - Convene and chair the HPTN Executive Committee (EC)
 - Serve on and provide technical, scientific, logistical and administrative support for the HPTN EC, SCs, Study Monitoring Committees (SMC), Science Review Committees (SRC), Manuscript Review Committee (MRC), Policy and Procedures Group (PPG), and Performance Evaluation Committee (PEC)
 - Oversee the HPTN Scholars Program
 - Organize and convene Network-wide meetings, including the HPTN Annual Meeting
 - Produce regular and *ad hoc* Network reports (e.g., Study Operations Reports, Performance Evaluation Reports)
 - Review, revise and retain key Network policies and procedures
 - Maintain version control of key Network policies and procedures

- Research Management
 - Appoint an HPTN LOC Clinical Research Manager (CRM) to each protocol
 - Participate in and coordinate support for Clinical Management Committees (CMCs) and other protocol-related groups
 - Lead the study-specific site selection and activation processes in accordance with Section 20 and Section 10, respectively, of the HPTN Manual of Procedures (MOP)
 - Collaborate with Protocol Chairs and protocol team members to lead the development of protocols, letters of amendment, clarification memos, Study-Specific Procedures (SSP) manuals, and other study implementation materials
 - Coordinate submission of protocols and modifications to the HPTN and NIH/DAIDS review groups and lead in the development of response to any review comments
 - Conduct pre-study operational walk-throughs with study staff, in collaboration with the SDMC and LC, if needed
 - Organize and coordinate development of materials and study-specific training, as required in collaboration with the SDMC, LC, and CRSs
 - Provide guidance and offer to review materials developed by CRSs for DAIDS protocol registration and study-specific site activation and/or study implementation, in collaboration with the SDMC and LC
 - Facilitate communication between the study CRSs, SDMC, LC and DAIDS entities
 - Coordinate study-related submissions to the contracted single Institutional Review Board (IRB) and facilitate communication between CTU/CRSs and the single IRB
 - Develop and maintain study electronic Trial Master Files, as needed
 - Register non-Investigational New Drug (IND) studies in ClinicalTrials.gov and maintain the record by updating key information such as study status, related dates in, such as study status and related dates.
- Quality Management
 - Support the establishment and implementation of reliable and efficient Quality Control (QC) and Quality Assurance (QA) processes and good documentation practices for the delivery of quality services, in compliance with applicable regulations
 - Support the development and implementation of effective monitoring and quality control systems for process performance; implement appropriate quality and process improvements, variability reduction, and innovation; and ensure the execution of quality study management activities
- Assistance to CTUs and CRSs with Study Conduct
 - Provide guidance to CTUs/CRSs in interpretation of study protocols and regulatory requirements, as well as in achieving protocol-specified targets for accrual and retention of study participants
 - Respond to inquiries from CTU/CRS investigators and DAIDS staff concerning procedures and implementation of HPTN studies in collaboration with the SDMC and LC
 - Assess performance of CTUs/CRSs during study implementation and report results to the HPTN EC and DAIDS through site assessment visits and regular communication with and reporting from CRSs

- Community Programs
 - Facilitate broad community involvement in all Network activities (see Section 5)
 - Assist CTUs/CRSs in developing and implementing community education efforts associated with HIV prevention trials
- Communication and Information Dissemination
 - Develop and maintain the HPTN website and social media accounts, including relevant information on CTUs/CRSs and HPTN studies
 - Develop and maintain email alias lists and directories for the HPTN communication system
 - Maintain databases that provide key Network information to HPTN leadership, DAIDS, and committees
 - Assist protocol teams by developing study-specific branding and recruitment/retention materials
 - Collaborate with protocol teams in manuscript development and dissemination of study results
 - Coordinate HPTN dissemination of study results in collaboration with NIH and other partners
 - Disseminate key Network policies and procedures to Network members
 - Support the National Institute of Allergy and Infectious Diseases (NIAID) Clinical Research Management System (CRMS) by maintaining compatible databases and web services systems and ensuring that current information and documents are provided in real time
- Financial Management and Support
 - Evaluate the adequacy of financial resources provided to CTUs/CRSs, as necessary
 - Assist NIH Grants Management Branch (GMB), DAIDS Prevention Sciences Program (PSP), Office of Clinical Site Oversight (OCSO), and HPTN leadership in analysis of CTU/CRS funding requests and all other Network financial matters
 - Provide guidance to CTUs/CRSs in preparing site-specific budgets as necessary, including provision of site-specific budget templates
 - Develop an annual funding plan based on the needs of the scientific agenda implemented during the funding cycle
 - Develop, negotiate, and execute agreements with participating CRSs for study-specific activation
- Product Management and Support (in certain cases – see Section 23)

3.2 Statistical and Data Management Center

The HPTN SDMC is responsible for helping to shape the network's technical and scientific agenda. It plays a key role in all phases of science generation, protocol development and study implementation. The SDMC is responsible for all aspects of data collection, reporting, and statistical analysis for HPTN trials following the principles of Good Clinical Data Management Practices (GCDMP) as well as Good Clinical Practices (GCP). The SDMC creates and manages the HPTN study databases and guides protocol teams on both the statistical components of study design and the collection and analyses of study data. The SDMC is located at the [Fred Hutchinson Cancer Center](#) (FHCC, Fred Hutch), and is comprised of faculty statisticians in the Vaccine and Infectious Disease Division (VIDD) and the Statistical Center for HIV/AIDS Research and Prevention (SCHARP).

3.2.1 SDMC Responsibilities

The SDMC's specific operational responsibilities, by functional area, include but are not limited to:

- Leadership and Governance
 - Serve on the HPTN EC, Leadership Group (LG), SCs, SRC, PEC, SMCs, PPG, and MRC
 - Participate in the management of the HPTN and the establishment of the HPTN scientific agenda
 - Participate in the review of concepts, ancillary studies, and other related study proposals
 - Participate in the development of HPTN protocols
 - Convene and chair study SMCs
 - Provide reports to the HPTN EC, SMC, PEC, and DAIDS on the status of CTU/CRS performance, including participant data management quality, accrual, retention, specimen collection, and adherence
- Scientific Leadership and Statistical Support
 - Appoint a SDMC faculty statistician to serve as lead protocol statistician for each HPTN protocol
 - Develop appropriate statistical methodologies for the conduct and analysis of HPTN trials including modelling if needed
 - Develop statistical and data management components of HPTN concept plans and protocols, including statistical analysis plans (SAP), interim monitoring plans, data management plans (DMP), and Study Progress, Data, and Safety Monitoring Plan (SPDSMP).
 - Provide regular reporting to the protocol team and HPTN leadership to facilitate monitoring of CRS data management quality, recruitment, retention, and adherence
 - Contribute to assessments of CRS performance regarding data management quality, enrollment, retention, and adherence to Network leadership and to the PEC
 - Develop and implement randomization and treatment allocation schemes for HPTN protocols
 - Conduct data analyses and generate open and closed reports for SMC reviews; chair and participate in SMC reviews
 - Conduct data analyses and generate open and closed reports for the Data and Safety Monitoring Board (DSMB); participate in the presentation and interpretation of those reports to the DSMB

- Contribute to abstract, presentation and manuscript preparation
- Provide data tables to fulfill IND reporting requirements
- Provide study data and reporting to pharmaceutical partners under the terms of the Clinical Trials Agreement (CTA)
- Provide needed information to the DAIDS Clinical Site Monitor to assist with site-monitoring visits
- Ensure timely and accurate entry of study results into ClinicalTrials.gov, in compliance with NIH and US Food and Drug Administration (FDA) requirements, specifically for results reporting, and maintenance of study records throughout the trial lifecycle in collaboration with the HPTN LOC
- Clinical Data Management
 - Design and maintain the study databases
 - Develop and implement centralized data management, QC, and validation systems
 - Collaborate with protocol team members in developing protocols, data-related SSP manuals and other study materials
 - Lead the development of study electronic Case Report Forms (eCRFs) or other means of data capture (e.g., computerized questionnaires) and procedures for collecting data from CTUs/CRSs
 - Conduct operational walkthroughs of eCRFs and other study materials and procedures, with HPTN LOC and LC, as needed
 - Conduct data collection and management training for CTU/CRS staff
 - Provide support to CTU/CRS staff regarding data collection and management during study operations
 - Identify problems in data collection and propose remedial changes in study procedures to CTU/CRS or protocol team
 - Provide timely data management performance reports to each CTU/CRS and to the PEC
 - Review and provide input in development of the CTA when the study involves an investigational product and fulfill SDMC responsibilities
 - Create and post deidentified datasets approximately two years after last study visit
- Laboratory Data Management
 - Provide operational assistance to CTUs/CRSs and the LC in regard to Laboratory Data Management System (LDMS) reports of LDMS entry errors and discrepancies between LDMS and study databases
 - Provide Data Transfer Plans (DTP) for laboratory results data submitted by the LC and other central laboratories
 - Receive LC data; assure quality and matching of laboratory data to study data
 - Select specimens for QA testing by the LC
 - Work with LC to provide data and adjudication tools if an HPTN Endpoint Adjudication Committee is convened (see Section 13.10) and capture the endpoint adjudication results used in the analysis

- Information Technology Support
 - Develop and maintain hardware and software systems and related procedures for transmitting, receiving, processing, analyzing, and storing study data and meeting reporting requirements
 - Assist CTUs/CRSs with data collection and management systems
 - Provide an accrual information data feed of participant level information to the NIAID CRMS
- Clinical Safety Data Management
 - Provide review of relevant laboratory and safety data for accuracy, consistency, and completeness
 - Provide QC and coding of adverse event (AE) and concomitant medications data
 - Verify completeness of expedited adverse event (EAE) reporting through reconciliation of AEs reported to DAIDS as EAEs and those reported to the SDMC
 - For studies of products not approved by the FDA for any indication, the SDMC may engage one or more Independent Safety Reviewers, who, in addition to the DAIDS Medical Officer (MO), will review monthly reports of safety data (see Section 14)

3.3 Laboratory Center

The HPTN LC is responsible for shaping the Network's scientific agenda in collaboration with the HPTN LOC and SDMC. Further, the LC plays a key role in all phases of science generation, protocol development, and study implementation. The LC oversees all laboratory-related activities, including specimen collection, testing, and reporting of results for testing performed at CRSs. The LC also performs QA/QC testing and specialized testing for HPTN protocols to advance the scientific agenda of the network and the field. The LC evaluates and validates assays for use in HPTN protocols and develops novel assays and laboratory methods to achieve study objectives. The LC assists in the development and quality assessment of CRSs, including building laboratory expertise and capacity at non-US CRSs, primarily in resource-limited settings. The LC plays a leadership role in cross-network activities by updating, harmonizing and streamlining laboratory procedures used in other networks and groups. The LC is centralized at the Johns Hopkins University School of Medicine.

3.3.1 Laboratory Center Composition

The LC includes an Administrative Core, a Protocol Operations Core, five Laboratory Cores, two Working Groups, and Consultants. The Administrative Core is responsible for administrative, regulatory, and financial operations. The Protocol Operations Core (Quality Assurance/Quality Control) is responsible for coordinating laboratory-related activities in HPTN protocols and for providing support and oversight to study sites. The Laboratory Cores are supported by Clinical Laboratories, Research Laboratories, and laboratories that perform both clinical and research testing. This includes QA testing, protocol testing, testing for ancillary studies, and laboratory-based research related to the mission of the network. The Laboratory Cores also develop, evaluate, and validate assays relevant to the HPTN research agenda. The LC includes Key Personnel who oversee activities in LC laboratories, lead ancillary studies and research sub-studies, and provide laboratory expertise to the HPTN. Working Groups help guide the LC. Consultants may provide additional expertise in Virology, Pharmacology, and other areas, as needed.

3.3.2 Laboratory Center Responsibilities

The responsibilities of the LC include but are not limited to:

- Serve on the HPTN EC, LG, SCs, SRC, PEC, SMC, PPG, and CMC
- Participate in management of the HPTN and establishment of the HPTN scientific agenda
- Provide laboratory-based scientific leadership and consultation to the HPTN
- Participate in development of HPTN protocols
- Review and define appropriate laboratory testing methods and materials to be used in HPTN studies
- Participate in the review of concepts, ancillary studies, and other related study proposals
- Release laboratory data from HPTN studies, after approval by HPTN leadership, for presentation, publication, or ancillary studies. The LC will provide input about feasibility and regulatory laboratory-related issues as needed and will inform the HPTN EC if there are any issues relevant to release of laboratory data
- Release/use of specimens, after approval of HPTN leadership, for ancillary studies or other work proposed by investigators outside of the LC, or for work beyond what is specified in the protocol
- Provide input about laboratory-related regulatory issues related to data release and inform the HPTN EC if there are any issues relevant to release of laboratory specimens
- Provide each protocol with an LC QA/QC Coordinator (Protocol Specialist) and one or more LC investigator(s)
- Draft the laboratory sections of protocols and the Laboratory Manual
- Provide training for CTU and CRS laboratories, as needed, for specimen tracking (using the LDMS), processing, testing, storage, and shipping; provide training for specialized testing, as appropriate
- Provide support to study teams as laboratory issues arise during design and implementation of protocols
- Assist with the design, implementation, and/or monitoring of QA procedures for local laboratory testing
- Provide support to the local laboratories related to the external proficiency testing
- Review a study-specific specimen management plan (processing, storage and retrieval guidelines) for specimens at both US and non-US CRSs
- Perform and/or coordinate the performance of protocol-specified laboratory testing in support of HPTN studies
- Use the LDMS to track the disposition of samples sent to the LC, including distribution to repository contractors or any other HPTN collaborator
- Use the LDMS and other systems to facilitate sample management and communication of test results between the LC, SDMC, and CTU/CRS investigators
- Develop a work plan that summarizes the protocol-specified laboratory testing, including details on the timing of specimen shipment and transmission of testing results to the SDMC; share the work plan with SDMC within a month after protocol go-live date
- Respond to inquiries from CTU/CRS investigators, the HPTN LOC, the SDMC, or DAIDS staff related to laboratory issues

- Collaborate with other DAIDS-sponsored HIV clinical trial networks to harmonize laboratory methods and maximize the efficiency of protocol development, implementation, and analysis
- Provide guidance when necessary for specimen processing, assay performance, and specimen-related result reporting for testing performed at CTU/CRS laboratories; this guidance is often provided during study training and site visits
- Provide training and support in laboratory quality assessment, assay performance, and specimen shipping procedures at CTU/CRS laboratories; this is often provided during study training and site visits
- Ensure regulatory compliance for LC activities as required for IND-enabling studies
- Maintain an LC Quality Management Plan for Clinical Laboratories and Research Laboratories within the LC
- Work with the HPTN LOC, SDMC and DAIDS on the provision of materials required for trial master file documents
- Provide opportunities to enhance expertise and build infrastructure through technology transfer, particularly to non-US laboratories
- Perform novel and routine immunologic, virologic, pharmacologic and other testing for HPTN protocols
- Work with DAIDS, the [Office of HIV/AIDS Network Coordination](#) (HANC), cross-network groups, and quality assessment partners to harmonize laboratory procedures across DAIDS-sponsored networks, whenever feasible and appropriate (see Section 13)
- Develop QA/QC and training tools and materials for use in US and non-US laboratories across DAIDS-sponsored networks
- Develop, standardize, or evaluate laboratory assays relevant to HIV prevention, with particular emphasis on assays that can be used in HPTN trials. These may include (but are not limited to) assays that:
 - Determine HIV status
 - Screen for and confirm sexually transmitted infections
 - Detect and/or quantify antiretroviral drugs
 - Measure hematologic and/or biochemical toxicities
 - Characterize HIV in study samples
 - Diagnose or characterize other related pathogens (e.g., hepatitis viruses, HSV-2)
 - Evaluate HIV incidence
 - Characterize the immune response to HIV infection
 - Detect drugs of abuse
 - Transfer LC test data to the SDMC including collaboration with SDMC on communication of testing plans, data transfer agreements, etc.
- Participate in preparation of presentations and publications that report results from HPTN studies
- Present and publish work performed at the LC, including work related to assay development/evaluation and pathogenesis-based studies

The LC staff maintains regular communication with CRSs, primarily through the CTU/CRS Principal Investigators (PIs) and laboratory managers, and confirms that CRSs are able to do study-required laboratory procedures and tests prior to site activation. The LC staff may also visit CRSs, as necessary, to assess laboratory facilities and procedures.

HPTN LC International QA/QC Coordinators (protocol specialists) may be based outside of the US. The responsibilities of these individuals include:

- Review and monitor the technical quality of all protocol test results
- Implement and monitor appropriate QA/QC functions of pre-analytical functions (specimen drawing, labeling, processing, test requisitions), analytical functions (testing), and post-analytic functions (test reporting, specimen storage, shipping) to assure validity of results and chain of custody of specimens
- Design and help implement appropriate policies and procedures to meet applicable guidelines for protocol testing
- Train technologists in specific test procedures and QA procedures to be used in protocol testing
- Assess competency of technologists performing protocol testing
- Provide expertise in troubleshooting general laboratory problems or specific assay problems
- Train personnel in how to establish reference intervals and write standard operating procedures (SOPs), then subsequently assure that SOPs and reference intervals are established
- Rarely, it may be necessary for a member of the LC to perform bench work at CRSs

3.4 Clinical Trials Units/Clinical Research Sites

HPTN research requires access to both study participants and research sites with experienced staff, adequate space, and equipped facilities.

HPTN studies are typically conducted by staff of NIH-funded CTUs, which will include an administrative component and one or more CRS. A CTU may have multiple CRSs in the US, outside the US, or both. NIAID provides resources to fund research infrastructure and study conduct through cooperative agreements with the primary CTU grantee through the HPTN LOC.

CRSs in certain circumstances may need to add additional locations (AL). With justification from the CTU PI and support from the Network leadership group, DAIDS will consider requests for an AL if 1) it does not compromise safety of study participants and integrity of the study, and 2) it is cost-effective when considering transportation costs, staff time, and other resources. Sufficient resources (personnel, supplies and fiscal) must be available at the CTU to provide to both the CRS and AL for appropriate conduct of any study-related procedures. Accrual at an AL will be attributed to the CRS.

CTU/CRS investigators and staff participate in the development and implementation of the research agenda, including leadership, concept and protocol development, participant recruitment and retention, intervention delivery, data collection and maintenance, and results reporting and publication.

3.4.1 CTU Investigators

Active participation of CTU investigators is critical to the HPTN scientific mission. Investigators may fulfill one or more role in the HPTN. These are described below.

3.4.1.1 CTU Principal Investigators

The CTU PI is the individual with legal and financial responsibility for a CTU cooperative agreement with NIAID. The institution that was awarded the cooperative agreement is considered the CTU administrative site. CTU investigators are expected to contribute to the HPTN scientific mission from initiation of study concepts through protocol development, implementation, and reporting of study findings in scientific reports, presentations, and manuscripts of studies in which their CRSs are participating. The CTU PI may delegate responsibilities to other investigators affiliated with the CTU but is expected to play a leadership role for the CTU and the Network.

Specifically, CTU PI responsibilities include but are not limited to:

- Execution of the Network research agenda
- Coordination and collaboration with the HPTN LG to ensure performance monitoring and evaluation of CRSs
- Knowledge, acceptance and compliance by all CTU/CRS component parts with the policies, procedures, and bylaws of the HPTN policies and procedures for the collection, recording, storage, and reporting of clinical trial data; sharing of research data and research resources; the research priorities of the HPTN; and performance standards established by the HPTN
- Ensuring that the CTU/CRS has investigators and appropriately qualified staff with demonstrated expertise in conducting HIV multi-center clinical trials
- Ensuring implementation of clearly defined organizational and communication plans and SOPs to ensure close supervision and oversight of the day-to-day activities of the CRS (and protocol-specific (PS) sites, if applicable)
- The receipt and appropriate administration of core funding to establish and maintain a minimal level of clinical research activities
- The receipt and appropriate administration of protocol funding provided by either NIAID or the HPTN. The CTU/CRS PIs will ensure that timely and accurate financial reports for all CTU/CRS component parts are provided to the NIAID and the HPTN. This information must be part of the annual progress report, or as requested, to NIAID, and sent to the HPTN LOC
- Ensuring compliance with all Federal regulations for human subjects, investigational agents and devices, and NIH and NIAID policies and procedures. HPTN-sponsored clinical research cannot be initiated at any CRS without prior approval by NIAID. All CRSs are also required to complete [Protocol Registration](#) for all clinical protocols in accordance with current NIAID policy and procedures prior to study initiation
- Ensuring compliance with the NIAID and HPTN standards
- Developing and implementing strategies at each CRS (and PS sites, if applicable) for the recruitment, screening, enrollment, retention and long-term follow-up of study participants appropriate to the conduct of the proposed research
- Ensuring that the CTU/CRS develops, implements, and oversees a comprehensive Quality Management Plan for all parts of the CTU/CRS in order to continually assess the quality of the research records and activities to ensure compliance with all Federal regulations, International Council for Harmonisation of Technical Requirements for

Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) guidelines, and NIH policies regarding participant safety, data completeness, accuracy, and quality assurance

- Ensuring cooperation with the NIAID Clinical Site Monitoring/Auditing representatives, and any other NIAID authorized groups. The purpose will include but not be limited to the review of research records and activities to verify compliance with protocol requirements, all applicable US Federal regulations, ICH GCP guidelines, and NIH policies on participant safety, data completeness and accuracy, and quality control. All performance problems identified through clinical monitoring must be evaluated in a timely manner and a plan for resolution developed, implemented, and documented, with emphasis on ensuring that the issue should not recur
- Implementation of a plan to achieve meaningful community partnership in CTU/CRS activities. This must include one or more Community Advisory Board (CAB) to represent the local population(s) impacted by HIV. The CTU/CRS must have procedures to ensure the community is engaged in the research process; provide financial and technical assistance from appropriately trained, culturally sensitive and experienced staff to support CAB activities and training; foster a partnership between researchers and the community, including the sharing of research results with the community, and develop ways to assess these efforts
- Compliance with all AE reporting requirements designated by NIAID and the HPTN, including, but not limited to, the established policies and procedures delineated in the [Manual for Expedited Reporting of Adverse Events to DAIDS](#)
- Ensuring that the CTU/CRS provides information requested by NIAID or the HPTN in a timely manner. In addition to clinical trial data, routine and *ad hoc* reports may be required. These reports may include, but are not limited to, participant recruitment and retention rates, summary demographic profiles of study participants, timeliness and completeness of all data, completeness and quality of laboratory data, and administrative and financial reports
- Ensuring effective leadership, clear lines of authority, strong communication pathways, and appropriate oversight for all parts of the CTU/CRS

The CTU PI may or may not also serve as the Investigator of Record (IoR) (see Section 3.4.1.3) for HPTN studies.

At the discretion of the CTU PI, some of these responsibilities may be delegated to or shared with other investigators affiliated with the CTU.

3.4.1.2 CRS PI or CRS Leader

The terms “Site PI” or “Site Leader” are often used — sometimes interchangeably — for investigators present at CRSs (although the official terms are CRS PI and Site PI). For some CTUs, an onsite counterpart to the CTU PI will have general oversight responsibility at the CRS; this investigator is referred to as the Site PI or Site Leader. These terms are also often used to refer to the onsite lead investigator or IoR for a specific study.

3.4.1.3 Investigator of Record

The IoR is the investigator who is responsible for the conduct of a study at a CRS. The IoR signs the [FDA Form 1572](#) (for studies conducted under an IND) or [DAIDS Investigator of Record Form](#) (for non-IND studies), as well as the protocol-specific Investigator Signature Page form, and thereby obligates the IoR, and by delegation, all study staff, to conduct the study in accordance with the responsibilities enumerated on the forms and in the list below. The FDA Form 1572 and the DAIDS Investigator of Record Form, as well as instructions for completing these forms, can be found on the RSC website. An IoR must be onsite.

The IoR for an HPTN research study must also:

- Ensure an adequate and well-trained study staff are in place prior to the initiation of an HPTN study
- Organize materials for protocol registration and activation including, signed FDA 1572/IoR Forms, financial disclosures for studies under IND, IRB/Ethics Committee and other applicable regulatory approvals of protocols and informed consent forms, Delegation of Duties log, Curriculum Vitae (CVs) of CRS staff, finalization of DAIDS and study-specific site SOPs for CRSs, etc.
- Implement study protocols, including the enrollment and follow-up of participants; timely data collection, submission, and cleaning; and local data management
- Conduct the trial in accordance with ICH GCP guidelines, DAIDS procedures, and relevant local and international regulatory requirements
- Delegate the responsibilities of study product management to a licensed/registered Pharmacist of Record and provide oversight of the site pharmacy and study product related activities of the protocol per DAIDS requirements
- Report safety information as required by the protocol, ICH GCP, DAIDS and responsible IRBs/Ethics Committees
- Serve on publication writing teams and take a leadership role in the conceptualization and preparation of manuscripts
- Maintain documentation, during and following a study, according to ICH GCP standards and DAIDS requirements
- Comply with HPTN Conflict of Interest policy for IND studies and the HANC policy for non-IND studies (see Section 8)

3.4.2 CTU or CRS Staff

Specific staffing for each CTU/CRS may vary according to the location and structure of the CTU, number of affiliated CRSs, number and type of studies conducted, and local requirements. Some CTU/CRS staff members may have more general CRS functions, while other staff members have study-specific responsibilities. However, CTU/CRS staff generally includes but is not limited to:

- PI
- In-country or Site IoR (as required and designated by the PI)
- Sub-investigators
- Coordinator (Site, Study, Clinic, as appropriate)
- Administrative/financial staff
- Community program staff
- Site QA/QC staff
- Data Manager
- Laboratory Manager and staff
- Laboratory QA/QC staff
- Research clinicians
- Pharmacists
- Recruitment and retention staff (often outreach workers)

Additional staff may include interviewers, counselors, outreach workers, laboratory technicians, data management staff, and computer and software support. Each CRS must have a clear staffing plan for the CRS and each study. The CRS must have SOPs for all key aspects of CRS operations, including clinical, pharmacy, and laboratory components before activation (see Section 10 for a list of required SOPs). Duties and responsibilities for studies must be clearly articulated, delegated, and documented, as specified in the DAIDS SCORE Manual: [Clinical Research Site Personnel Qualifications, Training and Responsibilities](#) and [Essential Documents](#).

3.4.2.1 CRS Staff Responsibilities

The following are general responsibilities that, collectively, staff of each CRS must fulfill. Satisfactory completion of these responsibilities will be reviewed by DAIDS OCSO and the HPTN LOC.

OCSO Requirement Examples:

- Conduct studies according to local and US federal regulations regarding the conduct of research using human subjects, including but not limited to Title 45 CFR [§46](#), [§160](#), and [§164](#) (where applicable), [Title 21 CFR §312](#), ICH GCP, and relevant local regulatory requirements
- Ensure that all required staff have participated in an appropriate research ethics training and GCP training in accordance with NIH and DAIDS policies
- Organize materials for protocol registration and activation including, signed FDA 1572/IoR Forms, IRB/Ethics Committee approvals of protocols and informed consent forms, CVs of CRS staff, finalization of DAIDS and study-specific site SOPs for CRSs
- Participate in a CRS QA program, DAIDS Clinical Site Monitor site visits, and audits as required by the HPTN and DAIDS
- Respond to DAIDS Clinical Site Monitor reports in a timely manner
- Establish and support a CAB/Community Advisory Group (CAG), or other approved process of community consultation, that advises the CRS regarding conduct of HPTN studies
- Assess the need for HIV prevention education; educate local communities in HIV prevention research

HPTN Requirements:

- Adhere to protocol and SSP-specified schedules and procedures, HPTN policies and procedures, and this HPTN MOP
- Submit research protocol and protocol amendments to, and receive approval from all appropriate IRBs/Ethics Committees and other applicable regulatory authorities, where necessary; comply with all IRB/Ethics Committee periodic review requirements; promptly submit any safety reports to the IRB/Ethics Committee; maintain files of outgoing and incoming correspondence with IRB/Ethics Committee; and obtain and file current rosters for these committees
- Recruit and enroll eligible participants into HPTN-supported trials, and obtain and document written informed consent
- For studies with investigational products, administer the study products according to the prescribed regimen; provide medical monitoring, collection of specimens, and prompt reporting of adverse events and referral for inter-current events

- Maintain confidentiality of all participant records
- Collect and manage all participant data, including completion of eCRFs in the order and manner specified in the SSP manual; review data; transfer to the SDMC central database in a timely manner; respond (within two weeks of original notification) to data queries from the SDMC
- Store study products according to protocol requirements; maintain complete and accurate inventory and accountability records
- Collect, process, label, inventory, ship, and transfer clinical specimens, and perform laboratory assays as specified in protocols. Data and specimens not specified in an approved study protocol may not be collected from study participants without prior review by the protocol team or its designees, written approval from the DAIDS MO, approval of the responsible IRB/Ethics Committee, and written informed consent from the participant
- Attend scheduled meetings and conference calls
- Participate in HPTN committees, teams, and working groups
- Establish and support a CAB/CAG, or other approved process of community consultation, that advises the CRS regarding conduct of HPTN studies
- Facilitate community representative participation on protocol teams, SCs, and other HPTN organizational components
- Assess the need for HIV prevention education; educate local communities in HIV prevention research