4 HPTN SCIENCE COMMITTEES, WORKING GROUPS AND PROTOCOL TEAMS

Science Committees and Working Groups

The HPTN Executive Committee (EC) has provided general guidelines for the composition of HPTN science committees and working groups. Details are left to the individual groups, and membership of all groups should reflect the various expertise of the Network, including representatives from Central Resources Network operational components, Clinical Trials Units (CTUs)/Clinical Research Sites (CRSs), and community representatives as well as scientists and researchers.

4.1 Science Committees

The Science Committees (SCs) contribute to the development of and guide the scientific agenda of the HPTN. The SCs are:

- Adolescents at Risk
- Women at Risk
- Comprehensive Science
- Substance Use

Each SC is at minimum responsible for:

- Assessing research priorities considering new ideas and research opportunities
- Identifying gaps in current HPTN research agenda
- Ensuring inclusion and coordination of assessments utilized in HPTN studies that relate to the focus area or population for the scientific committee
- Reviewing relevant research concepts submitted to the HPTN
- Seeking collaboration across the scientific committees to advance the HPTN research agenda
- Assisting in dissemination of information regarding the HPTN Scientific Research Agenda

The SCs integrate scientific expertise into the development of the research agenda established by the committees through the inclusion of leaders in their respective fields (some who may not be affiliated with the HPTN) as group members.

The SC chair and co-chair attend HPTN EC meetings at least annually (and periodic conference calls as deemed appropriate by the committee) to report on activities of the committees and to discuss research priorities.

Membership

Each SC has a chair and co-chair, appointed by the HPTN EC Chair. The HPTN EC determines the composition of the committee within guidelines established by the HPTN EC. It is recommended that the SC committees have no more than 10 voting members, inclusive of the chairs. Non-voting membership in the SC includes liaisons to the Central Resources, Community Working Group (CWG), Ethics Working Group (EWG), and DAIDS.

4.2 Working Groups

HPTN working groups (WG) are cross-cutting groups that provide expertise to the Network as described below.

4.2.1 Community Working Group and Community Working Group Steering Committee

4.2.1.1 Community Working Group

The purpose of the HPTN Community Working Group (CWG) is to ensure that the principles of community involvement are the foundation of all community engagement activities at each clinical research site (CRS) and to facilitate community participation throughout the research process (concept development, study implementation, results dissemination, and post-trial access to interventions that are found to be effective).

Members of the Network CWG participate in quarterly calls, in-person (or virtual) meetings and workshops. Protocol-specific CWGs are established for many HPTN studies and are comprised of CWG members from the CRSs conducting the study. Protocol-specific CWG calls take place on a routine basis. Participation in protocol team and other network committee conference calls and meetings occur as appropriate.

The goals of the Network CWG are to:

- Assure that research conducted within the HPTN is done in partnership with trial site communities and integrates community perspectives
- Enhance community representatives of the research process so that more meaningful community participation and engagement can occur
- Increase HPTN researchers understanding and appreciation of the social context of participants in HIV prevention research
- Provide input in the science generation process

The goals of a protocol-specific CWG are to:

- Provide input into protocol development, adapting sample consent forms for local use and developing other study-related materials
- Participate in protocol-specific training and regional workshops
- Help to inform strategies for recruitment and retention, especially for populations deemed harder-to-reach
- Assist in monitoring any emerging issues in the community
- Facilitate the accurate and culturally appropriate dissemination of study results to the community

To meet these goals, the Network CWG and protocol-specific CWGs work to:

- Integrate participation of CWG members who represent study communities and their advocates into WGs, SCs, and protocol teams
- Promote understanding of community needs and issues among HPTN researchers and other Network members
- Provide leadership to CTU/CRS community engagement staff in addressing issues that cut across the populations, communities, and technical areas of the HPTN
- Support collaboration and partnership at the CTU/CRS, SC, WG, and Network levels
- Advise and advocate for Network efforts in research, evaluation, and training addressing community participation at all levels of HPTN research

Membership

The CWG Chair and Co-Chair are selected by the CWG and appointed by the HPTN EC Chair and serves a minimum three-year term, renewable at the discretion of the HPTN EC Chair. The CRS Leader or designee appoints a Community Educator (CE) to serve on the CWG and the local Community Advisory Board (CAB) will elect the CAB member to serve on the CWG. CWG members who serve on internal and external research teams and working group are selected by the CWG and appointed by the CWG Chair and Co-Chair. The CWG Chair, CWG Co-Chair and LOC community engagement program staff determine the composition of the CWG within guidelines established by the HPTN EC. This includes members both internal and external to the HPTN.

Standing membership in the HPTN CWG includes:

- Voting Member
- CWG Chair and Co-Chair (one each, US and non-US)
- From each HPTN CRS
  - 1 CAB Member
  - 1 CE
- Non-Voting Members
  - HPTN LOC Community Engagement Program and other staff
  - HPTN Principal Investigators
  - Division of AIDS (NIAID/NIH) Representative
  - *Ad-hoc* External Scientific Advisor and Advocacy Representatives

Membership in a protocol-specific CWG includes:

- Voting Members
  - HPTN CWG Chair and Co-Chair
  - Representative from each CRS
    - 1 CAB Member
    - 1 CE
- Non-Voting Members
  - HPTN LOC Community Engagement Program and other staff

4.2.1.2 Community Working Group Steering Committee

The HPTN CWG Steering Committee provides guidance and support to the HPTN CWG and advises HPTN Leadership on matters concerning community engagement in all aspects of the HPTN research agenda. The HPTN CWG Steering Committee serves as a conduit of information between the HPTN CWG, HPTN leadership and other HPTN working groups.

The HPTN CWG Steering Committee goals are to:

- Inform, facilitate and guide the development of a community-centered, relevant, effective and ethical research agenda
- Proactively identify challenges related to community engagement and/or research implementation to ensure the ethical and scientific rigor of HPTN research
- Inform the HPTN EC of the CWG's decisions, concerns and activities
- Advise the HPTN EC on strategies to address community related challenges and issues of concern
- Develop mechanisms for sharing experiences, lessons learned and best practices for community engagement in HPTN research

The membership of the CWG Steering Committee consists of the following:

- Voting Members
  - CWG Chair and Co-Chair
  - HPTN Performance and Evaluation Committee CWG Representative
  - HPTN Ethics Working Group CWG Representative
  - HPTN Science Review Committee CWG Representative
  - HPTN HANC Community Partners CWG Representatives
  - HPTN Science Committees CWG Representatives
- Non-Voting Members
  - HPTN LOC Community Engagement Program and other staff
  - Division of AIDS (NIAID/NIH) Representative

HPTN CWG Steering Committee members participate in routine conference calls and periodic face-to-face meetings.

4.2.2 Ethics Working Group

The goals of the EWG are to contribute to HPTN research by raising awareness of and engaging Network members in dialogue about ethical issues in HIV prevention research and to facilitate decision-making around ethical issues during the research process. The EWG membership represents a broad scope of ethical, scientific, research, and community expertise — internal and external to the HPTN and from all regions of the world.

The EWG's scope of work includes:

- Ensuring ethical input into and review of HPTN concepts and protocols by serving as non-voting members of the Science Review Committee (SRC), and ad hoc resources to protocol teams and SCs as determined by HPTN Leadership
- Developing and maintaining an ethics guidance document for the conduct of HPTN studies and for publication

The EWG developed guidelines to enhance HIV prevention research studies, HPTN Ethics Guidance for Research, which is posted on the HPTN website.

Membership

The Chair and the co-chair are appointed by the EC Chair. The EWG membership includes representatives from relevant fields and geographic regions, ethicists, social scientists, HPTN investigators, community representatives, and staff members from the LOC, SDMC, LC, National Institute of Allergy and Infectious Diseases (NIAID) and other collaborating National Institutes of Health (NIH) institutes.

The full EWG typically convenes via conference call at least quarterly and holds an in-person meeting at least annually. Subgroups of the EWG meet more frequently on an *ad hoc* basis.

4.2.3 Socio-Behavioral and Structural Working Group

The charge of the Socio-Behavioral and Structural Working Group (SBSWG) is to promote scholarly discussion within protocol teams or SCs regarding the best approach for the behavioral measurement of interventions in line with the populations that the Network serves.

SBSWG's scope of work includes:

- Provide expertise in intervention acceptability
- Discuss appropriateness of measures to include in a protocol, such as use of respondent driven sampling, financial incentives, peer navigation, etc.
- Review concepts that have socio-behavioral and/ or structurally applicable elements

Membership

The Chair and the co-chair are appointed by the EC Chair. The SBSWG membership includes representatives from relevant fields within behavioral research and may include HPTN investigators, community representatives, and staff members from the LOC, SDMC, LC, NIAID, and other collaborating NIH institutes.

The full SBSWG typically convenes via conference call at least quarterly. Subgroups of the SBSWG may meet more frequently on an *ad hoc* basis.

4.2.4 Biomedical Sciences Working Group

The Biomedical Sciences Working Group (BWG) is established to provide expertise on emerging HIV prevention modalities and technologies. Including antiretrovirals (ART) for prevention multipurpose technologies (MPTs) and broadly neutralizing antibodies (bnAbs). The BWG works directly with protocol teams and Science Committees to provide input that best serves the populations of the HPTN.

Membership

The Chair and the co-chair are appointed by the EC Chair. The BWG membership includes representatives from relevant fields who understand the evolution of HIV medical/pharmaceutical prevention modalities and new technologies in delivery systems for HIV prevention (injection, IV therapy, implants, etc.). The BWG may also include HPTN investigators, community representatives, and staff members from the LOC, SDMC, LC, NIAID and other collaborating NIH institutes.

The full BWG typically convenes via conference call at least quarterly. Subgroups of the BWG may meet more frequently on an *ad hoc* basis.

4.3 HPTN Oversight and Operations Committees

The HPTN EC Chair recommends, and the HPTN EC approves, chair(s) and membership of the HPTN committees. Committee members serve for the duration of the cooperative agreement, and chairs serve three-year terms unless otherwise specified. Terms of committee chairs may be extended with the approval of the HPTN EC Chair. In addition to the HPTN EC, SCs, and WGs, four key Network oversight and operations committees include:

- Science Review Committee (SRC)
- Study Monitoring Committees (SMC)
- Manuscript Review Committee (MRC)
- Performance Evaluation Committee (PEC)

4.3.1 Science Review Committee

The SRC ensures that study protocols are scientifically rigorous, accurate, consistent, complete and standardized to the extent possible relative to other HPTN protocols. The SRC will also review the protocol for operational feasibility, focusing on key issues such as site participation, infrastructure and capacity, relevance to the community and any ethical concerns.

Membership

The SRC membership for each protocol is composed of appointed and *ad hoc* members and includes representatives of relevant disciplines including prevention science, biostatistics, ethics, and clinical trial operations. The CTU/CRS investigators, EWG and community are also represented. Membership of the SRC, as proposed by the protocol team, is approved by the SRC Chair and is comprised of individuals who are not directly involved with the protocol.

Voting Members/ SRC conference call participants:

- SRC Chair (the HPTN Principal Investigator [PI] acts as designee in case of conflict of interest)
- SDMC Statistician (PI or designee)
- NIH Representative
- Ad hoc Scientific Reviewer (one or more voluntary experts knowledgeable in the research area)

Contributing Reviewers/from:

- SDMC Operations
- LOC
- LC
- CTU/CRS Investigator
- Site Coordinator
- CWG
- EWG

Note: the SRC may be observed by HPTN leadership.

The SRC convenes as needed. The SRC reviews are conducted via conference call with the voting members and the LOC CRM for the study.

As noted above, voting members are not directly involved with the protocol under discussion. If a voting member does have a conflict of interest with the protocol under consideration (e.g., is a protocol team member), a designee votes in the member's place.

Ad hoc members may include:

- Representatives (ex officio) from NIH institutes
- One or two research area experts external to the HPTN

Once an SRC is constituted for a protocol review, every attempt is made to maintain the same composition should the protocol need to be resubmitted for review.

A written review is provided to the team within 5 working days following the review. Refer to Section 9.2.2.1 for more details.

4.3.1.1 HVTN/HPTN Joint Science Review Committee

For concepts or protocols jointly led between the HVTN and the HPTN, the HVTN/HPTN Joint Science Review Committee (JSRC) ensures that the concepts or protocols have scientific merit, high public health impact, are scientifically rigorous, accurate, consistent, and standardized to the extent possible relative to other joint network protocols. As much as feasible, the majority of the protocol text for joint protocols are derived from the HVTN/HPTN mAb template for cross-protocol consistency and comparability.

Membership

The JSRC membership is a standing committee including representatives from both networks based on the positions below. Currently, the HPTN and the HVTN Laboratory Scientists who are voting members of the committee serve as the JSRC co-chairs.

JSRC Voting Members

- HPTN and HVTN Network PIs
- HPTN and HVTN Laboratory Scientists
- HPTN and HVTN Statisticians
- HPTN and HVTN Clinical Scientists
- HPTN and HVTN Community Representatives
- NIH Representatives

JSRC Observers

- Network LOC Directors
- NIH/DAIDS Medical Officers
- Protocol Operation Teams (Protocol Team Leads, Clinical Research Managers/Clinical Trials Managers, Clinical Trials Assistants)

Additional observers should be added as needed per protocol.

The JSRC convenes as needed and reviews are conducted via conference call with the voting members and observers.

4.3.2 Study Monitoring Committees

The SMC is delegated by the EC to provide a review of the conduct of all HPTN studies. Active HPTN studies are typically reviewed by a SMC approximately every six months during implementation, including prior to Data and Safety Monitoring Board (DSMB) reviews, if applicable (see Section 15.8). The SDMC PI in collaboration with HPTN leadership will determine the need for and frequency of SMC reviews for each study. Observational and feasibility studies that are not being reviewed by the DSMB and others that may be determined by HPTN leadership to not require this frequency of review will have a modified review frequency and process. Studies that may take less than a year to complete might not be reviewed by the SMC at the discretion of the EC.

The SMC reviews study conduct, such as enrollment and retention, quality/adherence to the implementation of the intervention, quality/adherence to the completeness and timeliness of data; safety, endpoint rates (only in aggregate, in closed session) and, as applicable, aggregate or by arm safety data (adverse events, abnormal laboratory results, product holds and discontinuations) in a closed session. Safety data and endpoint rates may be reviewed on the same time schedule as the scheduled SMC review of study conduct or may be more frequent, depending on the type of study (e.g., phase I/II studies of products not yet approved by the United States Food and Drug Administration (FDA)) and may be conducted by a subset of the SMC. The frequency of review of safety data by the SMC will be determined by the Protocol Chair, DAIDS MO, and SMC chair.

Membership

The PI, or designee, of each of the Central Resource components of the Network, the LOC, SDMC, and LC, as well as the DAIDS PSP Chief are members of this committee.

The voting members are not directly involved with the protocol under discussion. If a voting member has a conflict of interest with the protocol under consideration (e.g., is a protocol team member), a designee participates in the member's place. Deliberations in the closed SMC reviews remain confidential. SMC open reports are shared with the protocol team and other relevant bodies. The LOC works with the SDMC, LC, NIH Medical Officer(s) and protocol chair(s) to determine the composition of the SMC for each protocol.

Members:

- SMC Chair (a SDMC Senior Statistician)
- LOC Representative (PI or Designee)
- LC Representative
- SDMC Statistician
- One or two *ad hoc* members (expert from within or outside of the HPTN knowledgeable in the research field) not connected to the study and with no conflict of interest. If the SMC will review safety data, at least one *ad hoc* member must be a physician.
- PSP Chief or Designee

Observers:

- DAIDS Medical Officer
- DAIDS PAB Pharmacist
- LC Deputy Director or Designee
- LC QA/QC Coordinator
- SDMC Associate Director and/or Senior Clinical Data Manager (SCDM)
- SDMC CDM

- LOC Director
- LOC CRM and CTA
- LOC HPTN Network Pharmacist, as applicable
- Representative(s) from other collaborating NIH institutes
- Representatives from study partner organizations

A schedule of routine SMC reviews (based on the phase and need of the study) may be established in advance to maximize availability of voting members for initial and subsequent reviews. However, members may appoint designees from their organizations, as needed, to ensure a quorum for each review. A SMC quorum is defined as the SMC Chair and at least three (3) other members A SMC review call can only be scheduled if this minimum requirement is met. In exceptional situations, the SMC Chair may convene a call without the required quorum, or request that a review be carried out in their absence and identify a designee to serve as Chair in their stead.

Once a SMC is constituted for a study, every attempt is made to maintain the same membership throughout the study. Each study will develop a charter that outlines the membership and responsibilities as outlined above, specific to that study.

4.3.3 Manuscript Review Committee

The primary responsibility of the MRC is to ensure that abstracts, presentations, and manuscripts that contain data or statistically related content from HPTN studies are developed, reviewed and endorsed, according to the HPTN Publications Policy (Section 21) prior to submission for publication. Reviews are conducted mainly via email with written feedback provided to the submitting author(s).

Membership

Members of the MRC include:

- MRC chair(s)
- SDMC PI
- LOC representative
- Science reviewers
- LC representative

Further details of the MRC review process are found in the HPTN Publications Policy (Section 21).

4.3.4 Performance Evaluation Committee

The PEC is responsible for overseeing a continuous, comprehensive evaluation of clinical research sites conducting HPTN studies (see Section 19 for more information about the Network evaluation).

The primary purpose of the evaluation is to provide data to determine if the sites are contributing effectively to the protocols that they have undertaken and to elicit corrective action, if necessary, so that all sites are functioning at peak performance level.

Membership

The membership of the PEC includes:

- PEC Chair
- SDMC Associate Director
- LC representative
- LOC representative
- LOC Evaluation Coordinator
- CTU/CRS PI
- CTU/CRS Study Coordinator
- LOC Community Program representative
- DAIDS/PSP representatives
- Community representative

An LOC staff member serves as an Evaluation Coordinator and is responsible for compilation, production, and distribution of evaluation results as well as facilitation of the work of the PEC.

The PEC convenes routinely by conference call. A quantitative evaluation report is produced after May 31 each year and is submitted to the EC for review and action to NIAID prior to July 1.

4.4 Policy and Procedures Group

The Policies and Procedures Group (PPG), with membership from the LOC, SDMC, LC and DAIDS, is an operations committee tasked with developing and maintaining the HPTN Manual of Operations (MOP). The MOP is typically reviewed on an annual basis and revised, as necessary.

4.5 Protocol Teams

Protocol teams assume primary responsibility for scientific and operational leadership in the development, implementation, and day-to-day oversight of HPTN studies and dissemination of their results.

4.5.1 Membership

The Protocol Chair identifies protocol team members (except for those positions assigned by the LOC, SDMC, LC, and NIH). Membership of each protocol team will vary according to the protocol, but membership should include:

- Protocol Chair
- PI or a designated investigator from each participating CTU/CRS
- Community representative(s) (sites)
- LOC Community Engagement Program representative(s)
- LOC CRM
- SDMC lead statistician
- SDMC lead CDM
- LC QA/QC Coordinator (protocol specialist)

- LC Investigator
- DAIDS Medical and/or Program Officer
- DAIDS PAB Pharmacist (if applicable)
- NIAID collaborating institute representative (if applicable)
- LOC HPTN Network Pharmacist (if applicable, see Section 23)
- Pharmaceutical or industry representative (if applicable)

Additional members, as required for a specific protocol, may include a pharmacologist, virologist, behavioral scientist, immunologist, EWG representative, etc.

4.5.2 Protocol Chair Selection

Scientific priorities are decided by the HPTN EC. Concepts addressing these priorities are either generated centrally by the HPTN leadership or by investigators and scientific committees (see Section 9.1.1). For the concepts developed centrally, the protocol chair for approved concepts is selected by soliciting nominations for this leadership position. For the concepts developed by investigators or by the scientific committees, the concept teams can nominate the chair. Nomination and selection as a chair does not imply that the affiliated site (if any) will be selected for the study. Final approval as protocol chair is made by the HPTN EC.

4.5.3 Protocol Chair Responsibilities

The Protocol Chair will provide scientific leadership during the development, implementation, and reporting of the study and will assume responsibility for completion of protocol team responsibilities within the projected budget and timeline. In some instances, studies will identify a co-chair to whom the chair may delegate some specific areas of responsibility, but the ultimate responsibility for execution of the study and final decision-making authority rests with the designated chair.

Because of the time commitments necessary to successfully implement and oversee a protocol, **investigators cannot simultaneously chair or co-chair more than two HPTN studies**.

Protocol Chairs will need to familiarize themselves with the HPTN processes and adhere to them. All new protocol chairs must attend a protocol chair training to orient them to Network processes. An agreement outlining responsibilities will be provided to Protocol Chair(s), who will be required to sign it. First time Protocol Chairs/co-Chairs will be subject to specific training in Network processes and Chair/co-Chair responsibilities as outlined in Section 11.

Protocol team business is planned and managed by the Protocol Chair, in consultation and with the support of the LOC CRM and other core team members. Specifics of protocol team management vary according to the type of study (Phase I, II, III, research area, etc.), the number and location of sites involved, and individual leadership and management approaches.

In addition to duties as a protocol team member, the Protocol Chair and Co-Chair(s) are responsible for:

- Providing overall leadership to ensure that the protocol adheres to the projected budget and is completed by the projected timeline
- Working with the Central Resource partners, to provide detailed projections to the HPTN Leadership of the resources required to conduct the study, including site- specific study costs as well as costs associated with study drug and any potential outside contractors or vendors, where applicable

- Facilitating final decision making within the protocol team to achieve agreement on scientific or operational issues brought before it, including reviewing and approval of secondary and exploratory objectives; if agreement cannot be reached, referring the issue to the SC for consideration
- Participating as a member of the Clinical Management Committee
- Together with the lead protocol statistician, reporting on the status of the study at open sessions of the DSMB
- Coordinating the establishment and dissolution of working groups as necessary to achieve efficiency in the development, implementation, and reporting of the study
- Overseeing the establishment of writing teams during manuscript preparation (designates writing team members, reviews schedules, monitors progress, helps prioritize analysis, communicates publication plans, responds to the MRC review, and advocates for additional resources as required)
- Ensuring review and approval of all manuscripts, abstracts and presentations related to study endpoints.
- Providing status updates to HPTN leadership, as needed

The Protocol Chair(s) will act as a liaison between the team and the:

- SC, EC, and its standing committees with responsibilities for protocol oversight (SRC, SMC, MRC, and PEC)
- LOC and DAIDS to facilitate development, review, approval, and implementation of the protocol in accordance with all applicable clinical trials requirements with available resources
- LC in the development of the protocol design and its implementation, particularly regarding assay evaluation, protocol training and testing as needed, development and review of study-specific laboratory procedures, and establishment of quality assurance guidelines
- SDMC in the design, development, implementation, and reporting of the study

In addition, the protocol chair and team have the responsibilities outlined in the next section.

4.5.4 Protocol Team Responsibilities

The LOC CRM provides technical and operational support throughout the process. Although individual protocol team members have different roles in fulfilling specific protocol team responsibilities (see table below), all members are expected to provide scientific, operational, or site-specific input, as appropriate, to protocol team activities. Protocol team responsibilities include:

Roles of Key Protocol Team Members	
Team Member	**Primary Roles and Responsibilities**
Protocol Chair (see Section 4.4.3 for further details of chair responsibilities)	• Provide leadership in development of the protocol including judicious inclusion of secondary and tertiary objectives • Ensure that the protocol adheres to the projected budget and is completed by the projected timeline • Lead protocol team meetings and calls • Lead protocol development with LOC representative • Establish subcommittees and working groups of protocol team to complete specific activities, as needed • Monitor study implementation across sites • Participate in SMC and DSMB meetings, if applicable • Develop plan for and lead writing of manuscripts and dissemination of study results
Site Investigators (see Section 3.4.1.3 for further details of investigator responsibilities)	• Provide site-informed input into protocol development • Provide detailed site estimates of costs for study implementation • Submit protocol and other required study documents to Institution Review Boards/Ethics Committees (IRB/ECs) and relevant regulatory authorities, if necessary • Review and comment on all SSP manuals and data collection forms • Manage study implementation at sites • Participate in manuscript development
Community Representative(s)	• Provide perspective of community and potential participants; facilitate communication with site CAB: - during development of protocol and informed consent - during study conduct, bringing community concerns and issues to the attention of the protocol team - during manuscript development • Work with protocol team and CABs to develop and implement plans for dissemination of study results to the community, as needed

Roles of Key Protocol Team Members	
Team Member	**Primary Roles and Responsibilities**
LOC CRM (see Section 3.1.1 for further details of LOC responsibilities)	• With Protocol Chair, provide scientific and operational input to the protocol, coordinate and lead development of protocol • Organize protocol team conference calls and meetings and document key decisions after protocol is approved by HPTN SRC • Review study budget with sites and LOC financial staff • Submit protocol for required HPTN and DAIDS reviews (SRC, PSRC, Regulatory, Medical Officer) and manage response/revision process • Develop and produce SSP manuals with input from SDMC, LC and other team members • Provide onsite study-specific training with SDMC and LC counterparts and coordinate development of training plan and materials to provide onsite training, as needed • Provide technical assistance and oversight to CTUs/CRSs during study conduct, enabling the sites to respond to problems and issues that arise during implementation of studies and dissemination of findings • Track site progress on activation requirements and review-related Standard Operating Procedures (SOPs) • Assess the performance of CTUs/CRSs and report results, in conjunction with the SDMC, to the PEC, EC, and DAIDS • Summarize SRC and SMC reviews and distribute as appropriate • Collaborate with DAIDS Pharmaceutical Affairs Branch (PAB) and the pharmaceutical companies to meet study product supply needs • Collaborate with SDMC to develop Case Report Forms (CRFs) and test them in the field before implementation • Collaborate with LC to enable CTUs/CRSs to meet proficiency
SDMC Lead Statistician (see Section 3.2.1 for further details of SDMC responsibilities)	• Provide design, statistical and scientific input during protocol development and throughout the conduct of the study • Develop statistical components of the protocol • Develop Statistical Analysis Plan (SAP) • Develop randomization and treatment allocation scheme, if needed • Conduct data analyses and generate SMC and DSMB reports • Provide ongoing support for statistical questions • Participate in manuscript preparation

Roles of Key Protocol Team Members	
Team Member	**Primary Roles and Responsibilities**
SDMC Lead CDM	• Collaborate in development of protocol • Lead and collaborate in development and production of the data-related SSP manual • Lead the development of data collection instruments (e.g., CRFs, computer-based questionnaires) and instructions • Collaborate with CRM on review of site SOPs related to data management and randomization prior to activation • Collaborate with CRM and DAIDS PAB Pharmacist on study product distribution as it relates to randomization and data collection • Conduct data management and data collection instrument (e.g., CRF) training at sites • Develop plan for and provide regular reports to protocol team and CTUs/CRSs (enrollment, retention, adherence, specimen storage, data management quality) • Coordinate development and production of SMC and DSMB reports • Provide support for data collection and management • Collaborate with CRM to provide support for operational matters that may influence study data • Assess the data management quality of CTUs/CRSs and report results to protocol team • Conduct data management site visits as needed • Collaborate with LC on quality assurance testing of specimens • Facilitate closeout of data collection and cleaning

Roles of Key Protocol Team Members	
Team Member	**Primary Roles and Responsibilities**
LC QA/QC Coordinator (protocol specialist) (see Section 3.3.2 for further details of LC responsibilities)	• Provide laboratory input during protocol development • Define appropriate laboratory testing methods and materials to support study protocols • Lead and collaborate in development and production of the Laboratory SSP Manual • Provide training for CTU/CRS laboratories in protocol-specified laboratory tests, as needed • Coordinate and perform (as applicable) protocol-specified laboratory testing • Monitor technical quality of protocol test results; provide assistance to local laboratories, as needed • Provide laboratory expertise in eCRF development • Provide support to the study team as laboratory issues arise during implementation of the protocol • Ensure regulatory compliance for LC activities related for IND-enabling studies
LC Investigator	• Provide scientific input during protocol development, including drafting laboratory related study objectives and the design of sub-studies, as applicable • Provide input on laboratory-related issues of the protocol and direct development of the laboratory section of the protocol • Define appropriate laboratory testing methods and materials and sub-studies, as necessary • Monitor technical quality of specialized protocol test results • Provide assistance to local laboratories, as needed, for specialized tests
DAIDS Medical Officer	• Participate fully in protocol team discussions and decisions • Facilitate communication between protocol team and DAIDS groups and staff • Provide timely Medical Officer review • Provide oversight of safety monitoring

Roles of Key Protocol Team Members	
Team Member	**Primary Roles and Responsibilities**
DAIDS PAB Pharmacist (For HPTN Pharmacist role see Section 23)	• Provide expertise on all pharmaceutical and study product-related aspects of protocol development and conduct • Develop the study product/pharmacy section of the protocol and Pharmacy Study-Specific Procedure (SSP) Manual for each study • Coordinate and oversee the supply, management, and distribution of study products for DAIDS-sponsored studies • Collaborate with pharmaceutical companies and other external partners to ensure study product supply • Conduct protocol-specific training for CRS and pharmacy staff • Provide support to the protocol team and sites on protocol-specific pharmacy-related issues

4.5.5 Relationship of HPTN Executive Committee and Protocol Team

The HPTN EC monitors each HPTN protocol team with regards to protocol development, implementation, analysis, and reporting. This oversight is accomplished through the SC, the SMC, the PEC, and the MRC by a mixture of formal review of key documents produced by the protocol teams (study protocol, protocol summaries, open reports to the DSMB, and primary and secondary manuscripts) as well as review of reports prepared by the SC, the SDMC, the PEC, and the LOC.

In addition to oversight provided by the SMC or DSMB and the standing and *ad hoc* committees, routine EC oversight includes:

- Evaluation of study progress in relation to key implementation benchmarks established by the PEC and information from the protocol teams and SDMC (e.g., timeliness of enrollment and follow-up targets, routine reports to the DSMB, and progress in data analysis and reporting). The HPTN EC identifies and communicates recommended actions on delayed protocols and unexpected problems in protocol implementation
- Assistance to DAIDS in determining the need for additional resources, for example, because of unexpected costs associated with planned study procedures or in order to support ancillary studies endorsed by the protocol teams
- Adjudication of conflicts that cannot be resolved within the protocol teams and/or the relevant SC. If all reasonable attempts to adjudicate conflicts or address problems with the protocol team and the SC fail, the HPTN EC may direct that the protocol team membership or its leadership be modified

4.5.6 Conflict Resolution

Conflicts within the HPTN are handled by referring the issue in dispute to the next level of the HPTN organizational structure.

4.5.6.1 Conflicts within Protocol Teams

- If a conflict arises within a protocol team and cannot be resolved between the members involved, the issue is referred to the Protocol Chair
- If the issue cannot be resolved, it is referred to HPTN Leadership

4.5.6.2 Conflicts between HPTN Investigators and HPTN Committees

If an HPTN investigator is not satisfied with a decision of an HPTN committee (SRC, SMC) or a finding of the PEC, and the issue cannot be resolved through discussion and negotiation with the chair of that committee, the investigator or the committee chair may refer the issue to the HPTN EC.