

<b>4. MTN COMMITTEES, WORKING GROUPS, and PROTOCOL TEAMS .....</b>	<b>1</b>
<b>4.1 Committees .....</b>	<b>1</b>
<b>4.2 Working Groups.....</b>	<b>2</b>
4.2.1 Biomedical Science Working Group (BSWG).....	2
4.2.2 Behavioral Research Working Group (BRWG) .....	3
4.2.3 Community Working Group (CWG).....	4
<b>4.3 Resource Committees.....</b>	<b>4</b>
4.3.1 Manuscript Review Committee (MRC) .....	4
4.3.2 Study Monitoring Committee (SMC).....	5
4.3.3 Network Evaluation Committee (NEC) .....	6
<b>4.4 Protocol Teams.....</b>	<b>7</b>
4.4.1 Protocol Team Responsibilities .....	8
4.4.2 Protocol Team Chair Responsibilities .....	11
4.4.3 Relationship of EC and Protocol Team .....	13
4.4.4 Conflicts Between MTN Investigators and MTN Committees and/or Working Groups .....	13
4.4.5 Conflict Resolution .....	13

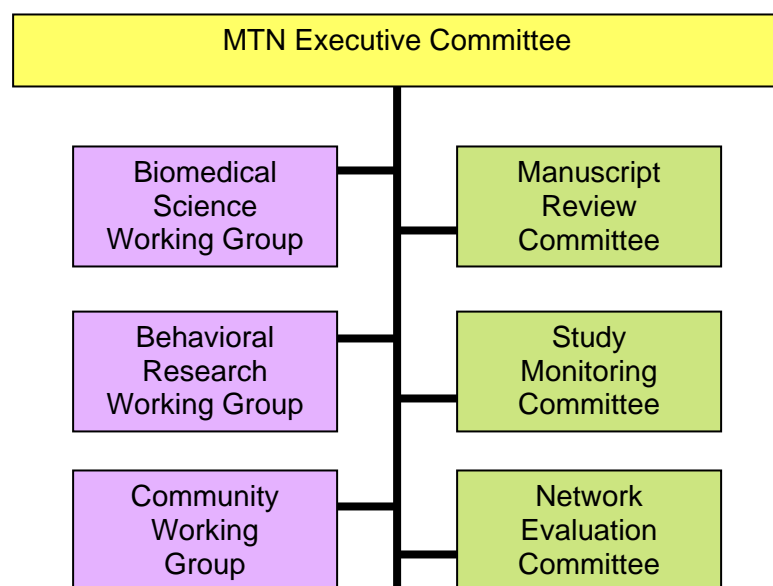
## **4. MTN COMMITTEES, WORKING GROUPS, AND PROTOCOL TEAMS**

### **4.1 Committees**

The Principal Investigator (PI) of the Microbicide Trials Network (MTN) serves as the Chair of the Executive Committee (EC). The EC membership consists of representatives from diverse fields and geographic regions, and includes MTN investigators, socio-behavioral and biomedical scientists, representatives of MTN Working Groups and staff members from the Coordinating and Operations Center (CORE), the Statistical and Data Management Center (SDMC), and the Network Laboratory (NL). The EC Chair recommends membership of the MTN Resource Committees and Working Groups (see Figure 4.1), subject to approval by the full EC. Committee and working group members serve for the duration of the cooperative agreement, and Chairs serve two-year terms, unless otherwise specified. Terms of committee Chairs may be extended with the approval of the EC Chair. Working groups appoint representatives to the EC.

- **Working Groups**
  - Biomedical Science Working Group (BSWG)
  - Behavioral Research Working Group (BRWG)
  - Community Working Group (CWG)
  
- **Resource Committees**
  - Manuscript Review Committee (MRC)
  - Study Monitoring Committee (SMC)
  - Network Evaluation Committee (NEC)

**Figure 4.1 MTN Committee Structure**



## **4.2 Working Groups**

The working groups provide scientific and community input for MTN protocols to maintain cutting-edge research. The BSWG provides input and innovative ideas to enhance understanding or monitoring of patient safety (e.g., biomarkers) and specimen collection. The BRWG provides input and innovative ideas to enhance understanding of behaviors before, during, and after microbicide use, and for collection of behavioral data. The CWG engages the community advisory boards at each site to provide input on MTN protocols and to provide feedback to the MTN regarding community experiences, best practices, and lessons learned.

### **4.2.1 Biomedical Science Working Group (BSWG)**

The BSWG is responsible for providing the EC with information and advice on a number of areas including, but not limited to, safety biomarkers, sexually transmitted infections and inflammation, antiretroviral resistance, and specimen collection. At least one member of the BSWG will be on each protocol development team as necessary to provide guidance on specimen collection and laboratory tests to be used.

The purpose of the MTN BSWG is to:

- provide the basic science and investigational science support for the development of MTN protocols, as necessary;
- develop innovative techniques/assays to test for safety biomarkers and antiretroviral resistance; and
- determine the best methods to collect samples for the techniques/assays developed by the BSWG.

*Membership:*

- BSWG Chair (EC member)
- NL PI
- Pharmacology Core PI or Designee
- Virology Core PI or Designee
- Immunology Core PI or Designee
- MTN Science Investigators

*Frequency of Meetings:*

Meetings will be held by teleconference every month, and there will be an annual face-to-face meeting at the MTN Annual Meeting. Summaries of calls and meetings of the full BSWG will be posted on the MTN website under restricted security access.

#### **4.2.2 Behavioral Research Working Group (BRWG)**

The BRWG is responsible for providing the EC with information and advice on a number of areas, including, but not limited to, measurement of behaviors relevant to the context of MTN trials (e.g., sexual behavior, other risk behaviors), product acceptability, and adherence. At least one member of the BRWG will be on each protocol development team that includes a behavioral component in order to provide guidance on methodology and data collection tools for behavioral assessment, especially acceptability and adherence to investigational product(s).

The purpose of the MTN BRWG is to:

- provide behavioral science input and support for the design and development of MTN protocols;
- develop innovative techniques (including new technologies) to capture critical behavioral data in clinical studies;
- develop the tools and instruments to capture quantitative and qualitative behavioral data in MTN protocols; and
- provide input and support for the development of innovative intervention programs to improve adherence and protocol compliance.

*Membership:*

- BRWG Chair (EC member)
- MTN Behavioral Scientists and affiliates
- U.S. National Institute of Mental Health (NIMH) Representative

*Frequency of Meetings:*

Meetings will be held by teleconference every month, and there will be an annual face-to-face meeting at the MTN Annual Meeting. Summaries of calls and meetings of the full BRWG will be posted on the MTN website under restricted security access.

### **4.2.3 Community Working Group (CWG)**

The main goal of the MTN CWG is to conduct community preparedness and engagement activities to ensure the successful conduct of MTN studies. Other goals include:

- ensuring community input into the scientific agenda and the research process of the MTN;
- building local community capacity to provide input into research at the site level; and
- developing mechanisms for sharing experiences, lessons learned, and best practices for community involvement in MTN research.

*Membership:*

Voting:

- CWG Co-Chairs (EC members)
- One Community Educator and one Community Advisory Board (CAB) member from each MTN CRS, if appropriate

Non-voting:

- CORE (FHI) Community Program staff
- Ethics Representative
- Global Campaign for Microbicides (GCM)
- International Rectal Microbicide Advocates (IRMA)
- African Microbicide Advocacy Group (AMAG)
- U.S. Division of AIDS (DAIDS) Prevention Sciences Program (PSP) Representative

The CRS PI appoints a community educator to serve on the CWG, and the local CAB elects a CAB member to serve on the CWG. Community educators and CAB members do not alternate participation in CWG conference calls, meetings and workshops, or other CWG activities.

*Frequency of Meetings:*

Meetings will be held by teleconference every month, and there will be an annual face-to-face meeting at the MTN regional meeting. These meetings will provide a forum for identifying any new and emerging issues, getting feedback from sites and representatives on Network leadership structures, monitoring progress, and building community capacity (see Section 6 for more information on community participation in the MTN).

## **4.3 Resource Committees**

### **4.3.1 Manuscript Review Committee (MRC)**

The primary role of the MRC is to ensure that manuscripts resulting from research conducted within MTN:

- reflect accurate reporting of the design, conduct, and analysis of studies;
- are developed in a collaborative fashion with the active participation of all investigators participating in the design and conduct of the study; are published expeditiously and are widely disseminated (abstracts that report the preliminary or highlighted results of a research study do not substitute for a full manuscript);

- protect confidentiality of medical, personal, and product information in accordance with the HIPAA Privacy Rule, the requirements for the protection of human subjects, and any applicable Clinical Trials Agreements; and
- meet all applicable National Institutes of Health (NIH) requirements, including, but not limited to, the NIH Public Access Policy.

The MRC is a core resource committee of the MTN. The major responsibility of the MRC is to review any publications or abstracts emanating from MTN studies prior to submission for publication that contain data or statistically related content. Either the MRC Chair will conduct the review, or the MRC Chair will identify committee members or other appropriate professionals to assist in the process (see Section 5: MTN Publication Policy for further information regarding MTN manuscripts and publication).

*Membership:*

- Manuscript Review Committee Chair
- SDMC (PI or designee)
- MTN Investigator(s)
- EC Chair
- NL (PI or designee)
- BRWG Representative
- BSWG Representative
- *Ad hoc* members (experts knowledgeable in the research area)

*Frequency of Meetings:*

Reviews are done as needed.

#### **4.3.2 Study Monitoring Committee (SMC)**

The SMC functions as an arm of the EC to provide peer review of the conduct of all MTN studies, with an emphasis on key performance indicators such as participant accrual and retention, protocol and intervention adherence, data quality, and laboratory quality (for the specific functions of the SMC, see Section 16.6).

The SMC is composed of at least seven voting members representing the CORE (FHI), CORE (University of Washington [UW]), SDMC (two representatives), NL, and DAIDS Microbicide Research Branch (MRB), together with one or more *ad hoc* voting members with relevant technical expertise. For each study, the composition of the SMC is maintained throughout the duration of each study, if possible. SMC members may not be directly involved with the study under review; if such a conflict of interest is identified, an alternate reviewer from the conflicted member's organization will be substituted.

The SDMC schedules SMC reviews and prepares study-specific data reports for review by the SMC. The CORE (FHI) prepares a written summary of each review that is shared with the Protocol Team. The EC is informed of SMC review outcomes, typically during routine EC conference calls.

*Membership:*

- SDMC Co-investigator (Chair)
- SDMC Co-investigator
- CORE (FHI) Representative
- CORE (UW) Representative
- NL Representative
- DAIDS MRB Chief or Designee
- External expert(s) designated by SMC Chair or SDMC PI

#### **4.3.3 Network Evaluation Committee (NEC)**

The NEC functions as an advisor to the Network Evaluation program. Evaluation contributes to improving services, policies, and programs, and provides evidence of MTN's ability to efficiently and effectively run clinical trials. Along with the NEC, the Evaluation Coordinator identifies objectives needed for successful protocol development and implementation, provides reports with comments and recommendations, and pinpoints areas for improvement.

Quantitative and qualitative measures are used to perform an ongoing evaluation of various levels of network function. The NEC develops performance metrics for components of the MTN, including associated clinical research sites (CRSs), to provide an annual review. Evaluation reports are shared with the MTN components and CRSs, the National Institute of Allergy and Infectious Diseases (NIAID), the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), and the NIMH, as appropriate. Being able to measure the quality and efficiency of the work done for MTN facilitates appropriate allocation of resources.

A primary component of network evaluation is the CRS Performance Report. This report focuses on critical aspects of study implementation, such as recruitment, retention, adherence, laboratory quality, regulatory issues, data quality, and community involvement. The report is used to identify opportunities to enhance efficiency, and may be used to modify funding strategies. It is expected that this evaluation will be performed annually to ensure that updates about major activities and milestones are made in a timely manner.

Depending on the direction of the NEC, one or more of the following metrics may be evaluated at the network level: protocol development timelines, community engagement, study trainings, communication with sites, and scientific impact.

The Data Communications Specialist and the Evaluation Coordinator at MTN CORE (University of Pittsburgh [PITT]) prepare the Evaluation Report, with input from the NEC. Data from the SDMC, as well as from monitoring reports, are included in the Evaluation Report. Once the draft report is prepared, it is submitted to the NEC for review, and then distributed to CRS personnel. Once the CRS personnel review the report and have time to ask questions, the report is revised if necessary and distributed to the EC members and Protocol Chairs.

*Membership:*

- NEC Co-chairs
- Evaluation Coordinator
- CORE (PITT) Representative

- CORE (FHI) Representative
- SDMC Representative
- NL Representative
- DAIDS/NIH Representatives
- Site Representatives

The NEC will meet monthly by teleconference and have a face-to-face meeting at the MTN Annual Meeting.

#### **4.4 Protocol Teams**

Protocol Teams assume primary responsibility for scientific leadership in the development, implementation, and day-to-day oversight of MTN studies. The Protocol Teams, along with CORE (FHI) and CORE (PITT), are responsible for dissemination of their results.

##### *Membership:*

Protocol Chairs play a key role in the successful execution of a clinical study. They are expected to contribute scientifically and programmatically to the development of a protocol, and to provide leadership as the protocol progresses through the DAIDS protocol review process.

The Protocol Chair will collaborate with CORE (PITT) during protocol development, and will help to draft responses to queries from the U.S. Food and Drug Administration (FDA). Persons eligible to serve as Protocol Chairs include members of the CORE, SDMC, NL, Working Groups, and Site Investigators. Selection of the Protocol Chair(s) will occur during the earliest stages of protocol development. The CORE, SDMC, NL, Working Groups, and Site Investigators will be polled for their interest in serving as Protocol Chair. If no member steps forward to volunteer as a Protocol Chair, the MTN leadership will solicit applications. Following submission of interest, the EC will select the Protocol Chair. Other Protocol Team members (except for positions assigned by the CORE, SDMC, NL, and NIH) will be invited to participate. Membership of each Protocol Team will vary according to the protocol, but should include:

- Protocol Chair
- Protocol Co-Chair or designated investigator from each participating study site
- CORE (FHI) Clinical Research Manager (CRM)
- CORE (FHI) Community Program Manager (CPM)
- CORE (PITT) Protocol Specialist (PS)
- CORE (PITT) Protocol Physician
- CORE (PITT) Protocol Safety Physician
- MTN Director of Pharmacy Affairs (if applicable)
- SDMC Protocol Statistician
- SDMC Project Manager (PM)
- NL Representative (if applicable)
- CWG Representative (if applicable)
- DAIDS Medical and/or Program Officer
- NICHD and/or NIMH Representative (if applicable)
- DAIDS Protocol Pharmacist (if applicable)
- Pharmaceutical or other Co-sponsor Representative (if applicable)

Additional members, as required for a specific protocol, may include members from the BSWG and/or BRWG.

Study-specific MTN CWGs are responsible for nominating one or more members to represent the group on protocol teams.

#### **4.4.1 Protocol Team 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. The CORE (PITT), CORE (FHI), SDMC, and NL provide technical and administrative support throughout the process. Although individual Protocol Team members have different roles in fulfilling specific Protocol Team responsibilities (see Figure 4.2), all members are expected to provide scientific, operational, or site-specific input to Protocol Team activities, as appropriate. Protocol Team responsibilities include:

- developing the study protocol, including responding to requests made by the Prevention Science Review Committee (PSRC) for revisions in the draft protocol;
- soliciting community input during protocol development and review;
- providing detailed estimates of the resources required to conduct the study, including site-specific study costs and requirements for NL and SDMC resources to the MTN Leadership, as requested;
- developing data collection instruments and instructions for the completion of these instruments;
- developing the Study-Specific Procedures (SSP) Manual with CORE (FHI);
- defining, in collaboration with CORE, SDMC and NL, protocol milestones for monitoring performance;
- overseeing accrual and retention of study participants and management of these individuals as specified in the protocol;
- monitoring participant safety in conjunction with the Protocol Safety Review Team (PSRT);
- conducting ancillary study review and, when necessary, advocating for additional resources
- Monitoring conduct of the study through reports produced by the SDMC concerning accrual, retention, data management quality, adherence to intervention, endpoint assessment completion, and safety;
- developing and carrying out corrective action plans for problems with study implementation;
- overseeing study conduct and implementation, including compliance with all applicable standards and requirements; and
- producing scientific publications and making presentations related to study findings in a timely manner.

The Protocol Chair plans and manages Protocol Team business in consultation with and with support from the CORE (PITT) PS during protocol development and the CORE (FHI) CRM after the study protocol has been finalized. Specifics of Protocol Team management vary according to the type of study (i.e., Phase I, II, or III, research area, etc.), the number and location of sites involved, and individual leadership and management approaches.

The Protocol Chair may identify working groups to address specific needs/activities during protocol development and study conduct. The Protocol Chair appoints Protocol Team members to these groups. Examples might include working groups to address:

- development and/or oversight of specialized behavioral procedures for a study;
- development and/or oversight of specialized clinical procedures for a study;
- development of specialized data collection modules (in collaboration with SDMC);
- ongoing monitoring of study participant safety data; and
- drafting and submission of manuscripts and presentations.

The CORE (PITT) PS and CORE (FHI) CRM facilitate and participate in the conference calls and meetings of these working groups. Where applicable, the PS and CRM provide summaries to the Protocol Team for these working group meetings and conference calls.

**Figure 4.2 Roles and Responsibilities of Key Protocol Team Members**

Team Member	Primary Roles and Responsibilities
Protocol Chair	<ul style="list-style-type: none"> <li>• Lead Protocol Team meetings and calls</li> <li>• Lead protocol development</li> <li>• Establish working groups of Protocol Team to complete specific activities, as needed</li> <li>• Monitor study implementation across sites</li> <li>• Participate in Data and Safety Monitoring Board (DSMB) meetings, if applicable</li> <li>• Develop, plan for, and lead writing of manuscripts and dissemination of study results</li> </ul>
Site Investigators	<ul style="list-style-type: none"> <li>• Provide site-informed input into protocol development and implementation plans</li> <li>• Provide detailed site estimates of costs for study implementation</li> <li>• Submit protocol and other required study documents to IRB/ECs</li> <li>• Review and comment on SSP Manuals and data collection forms</li> <li>• Manage and oversee the quality of study implementation at sites</li> <li>• Participate in manuscript development</li> </ul>
Community Representative(s)	<ul style="list-style-type: none"> <li>• Provide perspective of community and potential participants; facilitate communication with site CAB:               <ul style="list-style-type: none"> <li>◦ during development of protocol and informed consent forms</li> <li>◦ during study conduct, bringing community concerns and issues to the attention of the Protocol Team</li> </ul> </li> <li>• Work with CORE (PITT) Protocol Team and CAB to develop and implement a plan for dissemination of study results to the community</li> <li>• Lead study-specific CWG meetings and calls</li> <li>• Participate in manuscript development</li> </ul>
CORE Protocol Physician	<ul style="list-style-type: none"> <li>• Provide medical expertise during protocol development</li> </ul>
CORE Protocol Safety Physician	<ul style="list-style-type: none"> <li>• Provide safety monitoring guidance and language during protocol development and implementation</li> <li>• Collaborate with SDMC to ensure that safety monitoring is appropriate to the product under study, collected in a timely manner, and evaluated at regular intervals</li> <li>• Participate in manuscript development</li> </ul>
CORE (PITT) PS	<ul style="list-style-type: none"> <li>• Organize and document Protocol Team conference calls and meetings during protocol development</li> <li>• With Protocol Chair, provide scientific input to the protocol and coordinate development of protocol and informed consent forms</li> <li>• Submit protocol for required DAIDS reviews (e.g., PSRC, Regulatory, Medical Officer)</li> <li>• Develop and submit to relevant NIH agency any necessary protocol modifications</li> <li>• Maintain files documenting protocol reviews and approvals by DAIDS</li> <li>• Participate in manuscript development</li> </ul>
CORE (FHI) CRM	<ul style="list-style-type: none"> <li>• Contribute to protocol development, with the CORE (PITT) PS</li> <li>• Coordinate all aspects of study implementation</li> </ul>

Team Member	Primary Roles and Responsibilities
	<ul style="list-style-type: none"> <li>• Organize and document Protocol Team conference calls and meetings after the study protocol has been finalized</li> <li>• Contribute to CRF development, with the SDMC</li> <li>• Produce SSP Manual with input from SDMC, NL, and other team members</li> <li>• Provide study-specific training for the CTUs and coordinate development of the training plan and materials to provide on-site training</li> <li>• Coordinate and track site-study activation requirements</li> <li>• Provide technical assistance and oversight to CTUs during study conduct, enabling the sites to respond to problems and issues that arise during implementation of studies and dissemination of findings</li> <li>• Summarize SMC reviews and distribute as appropriate</li> <li>• Participate in manuscript development</li> </ul>
CORE (FHI) CPM	<ul style="list-style-type: none"> <li>• Contribute to protocol development, with the CORE (PITT) PS</li> <li>• Coordinate all aspects of community participation</li> <li>• Organize study-specific CWG calls and meetings</li> <li>• Provide technical assistance to CRS community education staff, to facilitate community education</li> </ul>
SDMC Lead Statistician	<ul style="list-style-type: none"> <li>• Provide design and statistical input during protocol development and throughout the conduct of the study</li> <li>• Develop the statistical components of the protocol</li> <li>• Develop the randomization and treatment allocation scheme, if needed</li> <li>• Conduct data analyses and generate DSMB reports</li> <li>• Participate in manuscript preparation</li> </ul>
SDMC PM	<ul style="list-style-type: none"> <li>• Collaborate in the development of the protocol and SSP Manual</li> <li>• Lead the development of data collection instruments and instructions</li> <li>• conduct data management and CRF training at sites</li> <li>• Develop a plan for and provide regular reports to Protocol Team and CTUs (i.e., regarding enrollment, retention, adherence, etc.)</li> <li>• Provide support for data collection and management and operational matters that may influence study data</li> <li>• Facilitate close-out of data collection and cleaning</li> </ul>
NL Representative	<ul style="list-style-type: none"> <li>• Define appropriate laboratory testing methods and materials</li> <li>• Develop the laboratory section of the SSP Manual</li> <li>• Provide training for CTU laboratories in protocol-specified laboratory tests, as needed</li> <li>• Coordinate and perform (as applicable) protocol-specified laboratory testing</li> <li>• Monitor technical quality of protocol test results; provide assistance to local laboratories, as needed</li> <li>• Provide laboratory expertise in CRF development</li> </ul>
MTN Director Pharmacy Affairs	<ul style="list-style-type: none"> <li>• Collaborate with DAIDS Protocol Pharmacist when applicable</li> <li>• Advise Protocol Team on all product-related issues; consult on available dosage forms and placebos</li> <li>• Interact with pharmaceutical companies to ensure product supply</li> <li>• Provide training for CRS pharmacists, as needed</li> <li>• Develop pharmacy/study-product-related documents</li> <li>• Provide product shipment to study sites</li> </ul>
DAIDS Medical Officer	<ul style="list-style-type: none"> <li>• Participate fully in Protocol Team discussions and decisions</li> <li>• Facilitate communication between the Protocol Team and DAIDS groups and staff</li> <li>• Monitor participant safety through membership in the PSRT and evaluation of expedited adverse event report forms</li> <li>• Provide oversight of the adequacy and appropriateness of site-specific safety monitoring systems/procedures</li> </ul>
DAIDS Protocol Pharmacist	<ul style="list-style-type: none"> <li>• Collaborate with CORE (PITT) Pharmacist</li> <li>• Advise Protocol Team on all product-related issues; consult on available dosage forms and placebos</li> <li>• Interact with pharmaceutical companies to ensure product supply</li> <li>• Provide training for CRS pharmacists as needed</li> </ul>

Team Member	Primary Roles and Responsibilities
	<ul style="list-style-type: none"> <li>• Develop pharmacy/study-product-related documents</li> <li>• Oversee study product shipments to study sites</li> </ul>
BRWG Representative	<ul style="list-style-type: none"> <li>• Provide design and behavioral input during protocol development and throughout the conduct of the study</li> <li>• Develop the behavioral components of the protocol</li> <li>• Lead the development of behavioral data collection instruments and instructions</li> <li>• Collaborate in the development of the SSP Manual</li> <li>• Provide support for behavioral data collection</li> <li>• Conduct behavioral data analyses</li> <li>• Lead manuscript preparation of behavioral outcomes</li> </ul>
BSWG Representative	<ul style="list-style-type: none"> <li>• Recommend biological samples for collection to help the evaluation of safety and efficacy of a product</li> <li>• Collaborate in the development of the SSP Manual</li> <li>• Provide support for manuscript development and/or be the lead in manuscript preparation dealing with sample collection or biological mediators</li> </ul>

#### 4.4.2 Protocol Team Chair Responsibilities

In addition to duties as a Protocol Team member, the Protocol Chair is responsible for:

- providing overall leadership and guidance to the Protocol Team throughout the development, implementation, and operation of the protocol;
- establishing and maintaining an efficient schedule of conference calls and meetings to develop and manage the study that includes all members of the Protocol Team and additional representatives from the SDMC and the NL, as appropriate;
- coordinating the establishment and dissolution of working groups to achieve efficiency in the development, implementation, and reporting of the study;
- monitoring participant safety through active membership in the PSRT;
- reporting on the status of the study at open sessions of the DSMB, together with the Protocol Statistician;
- facilitating final decision making within the Protocol Team to achieve agreement on scientific or operational issues brought before it (if no agreement can be reached, referring the issue to the EC for consideration);
- advocating for resources for study conduct (i.e., when MTN study-specific funding is limited, seeking additional funds from sources outside the MTN); and
- overseeing analysis and writing teams during manuscript preparation (i.e., designates writing team members, reviews schedules, monitors progress, communicates publication plans, responds to the MRC review, and advocates for additional resources, as required).

The Protocol Chair also acts as liaison between the Protocol Team and the following groups:

- EC, BSWG, BRWG, SMC, and MRC as appropriate
- CORE and DAIDS to facilitate development, review, approval, and implementation of the protocol in accordance with all applicable clinical studies requirements with available resources, and on dissemination of study results
- NL 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

#### **4.4.3 Relationship of EC and Protocol Team**

The EC monitors each MTN Protocol Team with regard to protocol development, implementation, analysis, and reporting. This oversight is accomplished through the MTN Study Operations Group, the SMC, and the MRC via formal review of key documents produced by the Protocol Teams (e.g., study protocol, study update reports, open reports to the SMC and DSMB, and primary and secondary manuscripts), as well as review of reports prepared by the SDMC and the CORE. Routine EC oversight includes:

- evaluation of study progress in relation to key implementation benchmarks;
- assistance to NIAID in determining the need for additional resources (i.e., because of unexpected costs associated with planned study procedures, or to support ancillary studies endorsed by the Protocol Teams; see Section 18);
- adjudicating conflicts that cannot be resolved within the Protocol Team. If all reasonable attempts to adjudicate conflicts within the Protocol Team fail, the EC may direct that the Protocol Team membership or its leadership be modified.

#### **4.4.4 Conflicts Between MTN Investigators and MTN Committees and/or Working Groups**

If an MTN investigator is not satisfied with a decision of an MTN Committee or Working Group, and the issue cannot be resolved through discussion and negotiation with the chair of that Committee or Working Group, the investigator or the Committee/Working Group Chair may refer the issue to the EC.

#### **4.4.5 Conflict Resolution**

The EC is the final arbitrator for all conflicts and/or disputed issues that cannot be resolved as described above within the MTN.