

MTN Manual of Operational Procedures (MOP)

Section 4: Network Committees, Working Groups and Protocol Teams

4. NETWORK COMMITTEES, WORKING GROUPS AND PROTOCOL TEAMS	4-1
4.1 Working Groups and Resource Committees	4-1
4.2 Working Groups	4-2
4.2.1 Biomedical Science Working Group	4-2
4.2.2 Behavioral Research Working Group	4-3
4.2.3 Community Working Group and Community Resource Working Group	4-3
4.3 Resource Committees	4-5
4.3.1 Manuscript Review Committee	4-5
4.3.2 Study Monitoring Committee	4-6
4.3.3 Network Evaluation Committee	4-7
4.4 Protocol Teams	4-8
4.4.1 Protocol Team Membership	4-8
4.4.2 Protocol Team Responsibilities	4-9
4.4.3 Protocol Chair Responsibilities	4-13
4.4.4 Relationship between Protocol Team and EC	4-13
4.4.5 Conflicts between MTN Investigators and MTN Committees and/or Working Groups	4-14
4.4.6 Conflict Resolution	4-14

4. NETWORK COMMITTEES, WORKING GROUPS AND PROTOCOL TEAMS

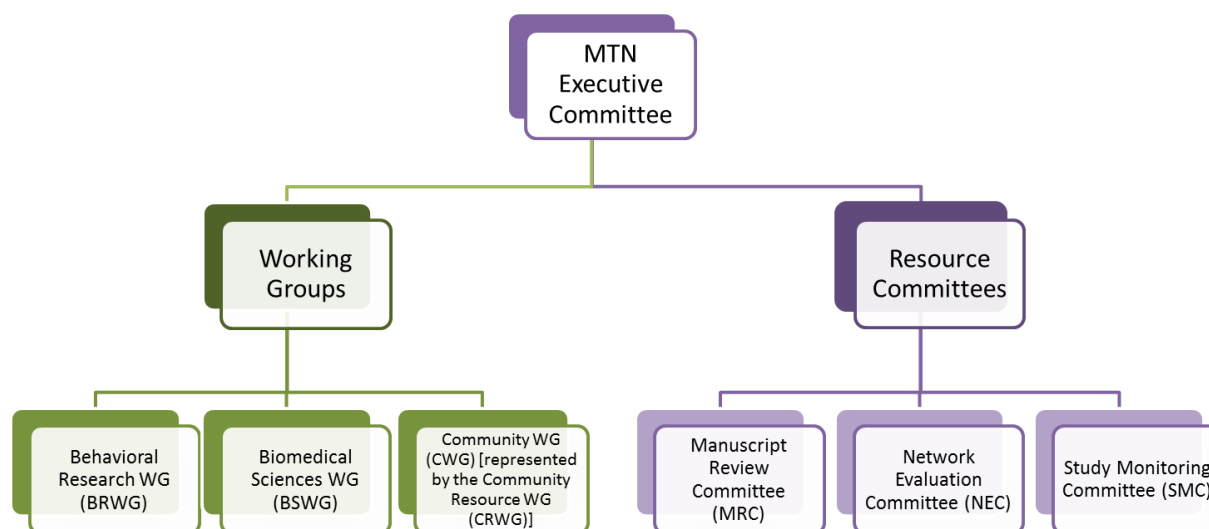
4.1 Working Groups and Resource Committees

The primary governance body of the Microbicide Trials Network (MTN) is the Executive Committee (EC), which is responsible for the overall scientific direction, development and implementation of policy, procedural decisions and resource allocation. The EC, which is chaired by the MTN Principal Investigator (PI), is supported by three resource committees and three working groups (Figure 4.1). Membership to the MTN Resource Committees and Working Groups is recommended by the EC Chair. Resource Committee and Working Group members serve for the duration of the cooperative agreement.

4.2 Working Groups

Working Groups ensure that scientific quality, innovation and community perspectives are the hallmarks of every study. The Biomedical Science Working Group (BSWG) provides input and innovative ideas to enhance the understanding and monitoring of participant safety (for example, biomarkers), drug pharmacokinetics and specimen collection. The Behavioral Research Working Group (BRWG) provides input and innovative ideas to enhance understanding of research participants' beliefs and behaviors before, during and after microbicide use, and for collecting behavioral data. The Community Working Group (CWG), along with the Community Resource Working Group (CRWG), ensures and facilitates site-level community engagement before, during and after studies, helping to communicate study results and next steps after study closure and seeking input on MTN protocols. The CWG also provides feedback to the MTN regarding community experiences, best practices and lessons learned. The CRWG serves as a conduit between the MTN CWG, MTN Leadership and other MTN Working Groups.

Figure 4.1 MTN Main Committee Structure



4.2.1 Biomedical Science Working Group

The BSWG is responsible for providing information and advice across several areas, including (but not limited to) biomarkers/bio-indicators, vaginal and rectal microflora, sexually transmitted infections and inflammation, antiretroviral drug resistance and specimen collection. The BSWG recommends the type of and manner in which specimens are collected, handled, stored and analyzed within each protocol. Resulting laboratory findings help inform the design of other protocols and define additional areas for inquiry by the MTN Laboratory Center (LC). 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 performed.

The purpose of the BSWG is to:

- Provide basic and investigational science support for the development of MTN protocols, as necessary

- Develop innovative techniques/assays to test for efficacy and safety biomarkers, product adherence and HIV exposure
- Determine the best methods to collect and store samples for the techniques and assays developed by the BSWG and LC

The membership of the BSWG consists of the following:

- BSWG Chair (EC member)
- LC PIs (one voting EC member; one non-voting EC member)
- LC Protocol Support Core leaders
- LC Pharmacology Core leaders
- LC Virology and Pharmacodynamics Core leaders
- MTN-affiliated Scientific Investigators

The BSWG meetings are held by teleconference quarterly or as needed. A face-to-face meeting takes place at the MTN Annual Meeting.

4.2.2 Behavioral Research Working Group

The BRWG is responsible for providing information and advice across several areas, including (but not limited to) measurement of behaviors relevant to the context of a particular MTN trial (for example, sexual behavior and other risk behaviors), product acceptability and product adherence. Every protocol with a behavioral component will include at least one member of the BRWG on the protocol development team to provide guidance on methodology and data collection tools for behavioral assessment, particularly in relation to participants' acceptability of and adherence to investigational product use.

The purpose of the BRWG is to:

- Provide behavioral science input and support in 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
- Provide input and support for the development of innovative intervention programs to improve adherence and protocol compliance

The BRWG membership consists of the following:

- BRWG Chair (EC member)
- MTN behavioral scientists and affiliates
- U.S. National Institute of Mental Health (NIMH) representative

Meetings are held by teleconference every month. A face-to-face meeting takes place at the MTN Annual Meeting.

4.2.3 Community Working Group and Community Resource Working Group

4.2.3.1 The MTN Community Working Group

The purpose of the MTN CWG as a collective is to ensure that the principles of community participation 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). Most MTN protocols will include a CWG representative on the protocol development team.

The goals of the MTN CWG are to:

- Help MTN researchers to better understand and appreciate the social context of research participants
- Enhance members understanding of the research process so that more meaningful community participation and engagement can occur
- Ensure that all research conducted within the MTN is done in collaboration with trial-site communities and integrates community perspectives

The CWG membership consists of the following:

Voting

- MTN CWG Co-Chairs (one voting EC member; one non-voting EC member)
- From each CRS:
 - One Community Advisory Board (CAB) member
 - One Community Educator (CE)
- Ethics representative

Non-voting

- Leadership and Operations Center ([LOC (FHI 360)] Community Engagement Program staff
- Advocacy representatives
- U.S. National Institutes of Health, National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS) community liaison

The CRS Leader or designee appoints a CE to serve on the CWG and, typically, the local CAB will elect the CAB member to serve on the CWG. Members of the full CWG participate in quarterly calls, face-to-face meetings and workshops. Protocol-specific CWGs are established for many MTN's studies and are comprised of CWG members from the CRSs conducting the particular study. Study-specific CWG calls take place on a routine basis. Participation in protocol team and other Network committee conference calls and meetings occur as appropriate.

4.2.3.2 MTN Community Resource Working Group

The MTN CRWG provides guidance and support to the MTN CWG and advises MTN Leadership on matters concerning community engagement in all aspects of the MTN research agenda. The MTN CRWG serves as a conduit of information between the MTN CWG, MTN Leadership and other MTN Working Groups.

The MTN CRWG's 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 MTN research with the goal of reducing new HIV infections
- Inform the MTN EC of the CWG's decisions, concerns and activities
- Advise the MTN EC on strategies to address challenges and issues of concern
- Seek opportunities that allow MTN CRS community staff to actively participate in the process of generating science as well as collaborate more closely with the BSWG, BRWG and protocol teams in supporting community-focused HIV prevention research
- Develop mechanisms for sharing experiences, lessons learned and best practices for community engagement in MTN research
- Collaborate with the MTN Network Evaluation Committee (NEC) to develop measurement criteria and tools for the evaluation of the MTN Community Engagement Program

The CRWG membership consists of the following:

Voting

- CWG Co-Chairs (2) (one voting EC member; one non-voting EC member)
- NEC CWG representative
- CWG Ethics representative
- At-large MTN Clinical Trials Unit (CTU)/CRS CAB members (2)
- CWG members named to represent MTN on Community Partners (4)

Non-Voting

- LOC (FHI 360) Community Engagement Program staff
- LOC [University of Pittsburgh (Pitt)] Communications and External Relations representative
- LOC (Pitt) representative
- DAIDS Community Liaison
- BRWG Liaison
- BSWG Liaison

CRWG members participate in routine conference calls and periodic face-to-face meetings.

(See Section 7 of this Manual for more information on the MTN CWG, CRWG, study-specific CWGs and community engagement in MTN.)

4.3 Resource Committees

The MTN is supported by three Resource Committees: Manuscript Review Committee (MRC), Study Monitoring Committee (SMC) and Network Evaluation Committee (NEC).

4.3.1 Manuscript Review Committee

The primary role of the MRC is to ensure that all abstracts, manuscripts, posters and oral presentations containing MTN study data or statistically related content resulting from MTN studies conform to MTN and NIH standards prior to their submission for publication. The MRC Chair(s) may personally conduct reviews or may identify committee members or other appropriate professionals to assist in the process. (See Section 20 of this Manual for further information regarding MTN publications.)

Manuscripts and abstracts must first receive approval from the study's Protocol Publications Committee, including the DAIDS Medical Officer (MO), and as applicable, by additional U.S. National Institutes of Health (NIH) MOs and/or the Investigational New Drug (IND) holder(s), and pharmaceutical collaborators (if applicable, based on the relevant CTA) before submission for MRC review.

MRC reviews are conducted to ensure that all materials:

- Reflect accurate reporting of the design, conduct and analysis of the study
- Protect the 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 Agreement
- Meet all applicable NIH standards and requirements, including (but not limited to) the *NIH Public Access Policy*
- Include a statement that acknowledges MTN and NIH's support for the work and references the applicable NIH cooperative agreement number(s), unless journal policy precludes such acknowledgement

The MRC also ensures that all articles and abstracts are published expeditiously and made available to the scientific community. Abstracts that report the preliminary results of an MTN research study do not substitute for a full manuscript.

The MRC will enlist a variety of persons across the MTN as reviewers. Reviewers may include persons from the Statistical and Data Management Center (SDMC), the Laboratory Center (LC), the BRWG, the Biomedical Science BSWG, CTU/CRS investigators as well as ad hoc MTN members or non-members who are experts knowledgeable in a particular research area.

The MRC membership consists of:

- MRC Chair(s)
- MTN LOC (Pitt) Manuscript Coordinator

The MRC determines the schedule for review meetings.

4.3.2 Study Monitoring Committee

The SMC functions as an arm of the EC to provide peer review of the conduct of MTN studies, with an emphasis on key performance indicators, such as participant accrual and retention, adherence to the protocol and the intervention, data quality and laboratory quality. (See Section 16.8 of this Manual for further information regarding the SMC's specific functions.)

The SMC is composed of voting members representing the LOC [FHI 360 and University of Washington (UW)], the SDMC, the LC, and DAIDS Prevention Sciences Program (PSP), together with *ad hoc* voting member(s) with relevant technical expertise, as needed. The *ad hoc* voting members will be sought after recommendations by the Protocol Chair(s) and/or EC members. SMC members must not be directly involved with the study under review (i.e., not members of the protocol team for the protocol under review). If such a conflict of interest is identified, an alternate reviewer will substitute for the conflicted member. The composition of the SMC is maintained throughout the duration of each study, if possible.

The SDMC schedules SMC reviews and prepares study-specific data reports for review by the SMC (see Section 19 of this Manual). The LOC (FHI 360) prepares a written summary of each review in compliance with MTN Good Documentation Policy (see Section 9.2 of this Manual) that is shared with the protocol team. The EC is informed of the outcomes of the SMC review, typically during routine EC conference calls.

The membership of the SMC consists of the following:

- SDMC Co-Investigator (Chair)
- SDMC representative(s)
- LOC (FHI 360) representative
- LOC (UW) representative
- LC representative
- DAIDS Deputy Director of PSP or designee
- External expert(s), as needed

The first review is typically scheduled approximately six months after the first enrollment. The SMC determines when/if future meetings and reviews are scheduled. (See Section 16.8 of this manual for more information about SMC reviews.)

4.3.3 Network Evaluation Committee

The NEC functions as an arm of the MTN EC and is responsible for developing a Network-wide evaluation program that will contribute to the improvement of processes and provide evidence of MTN's ability to run clinical trials efficiently and effectively. Quantitative and qualitative measures are used to perform ongoing evaluation of various network processes. The NEC develops performance metrics for MTN's components, such as the Working Groups, SDMC, LC, LOC, and MTN-associated CRSs.

As each evaluation is completed, the NEC, with support from the LOC (Pitt), develops a report that is submitted to the MTN EC. Evaluation reports are shared with the group whose work was evaluated, the NIAID, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) and the NIMH, as appropriate. Evaluation of the quality and efficiency of network processes helps in facilitating the appropriate allocation and/or reallocation of resources.

A primary component of the network evaluation is the Annual CRS Performance Report. This report focuses on critical aspects of study implementation, such as recruitment, retention, adherence, laboratory quality, regulatory compliance, data quality and community involvement.

At the request of the EC, the NEC may evaluate other areas of the MTN.

The membership of the NEC consists of the following:

- NEC Chair(s)
- Evaluation Coordinator/LOC (Pitt) representative
- LOC (FHI 360) representative
- SDMC representative
- LC representative

- DAIDS/NIH representatives
- Site representatives
- CWG representative

Meetings are held by teleconference and face-to-face.

4.4 Protocol Teams

Protocol teams assume responsibility for the development, implementation and day-to-day oversight of MTN studies. Protocol teams, along with the LOC (FHI 360 and Pitt) staff, are responsible for the dissemination of study results in accordance with the parameters and timelines set by NIAID and an overall communications plan that must consider protocol-specific CTA requirements and/or news embargo policies, should they exist (See Section 8 of this Manual).

4.4.1 Protocol Team Membership

Protocol Chair(s) play a key role in the successful execution of a clinical study. They contribute scientifically and programmatically to the development of a protocol and provide leadership as the protocol progresses through the DAIDS protocol review process.

Protocol Chair(s) will collaborate with the MTN LOC (Pitt) during protocol development, and will help draft responses to queries from the U.S. Food and Drug Administration (FDA), as applicable. Persons eligible to serve as Protocol Chair(s) include members of the LOC, SDMC, LC and Working Groups, as well as Site Investigators. Selection of Protocol Chair(s) will occur during the earliest stages of protocol development. The LOC, SDMC, LC, Working Groups and Site Investigators will be polled for their interest in serving as Protocol Chair/Co-Chair; MTN Leadership will solicit applications if there is no initial response. Following submissions of interest, the EC will select the Protocol Chair/Co-Chair.

The membership of each protocol team will vary according to the protocol, but may include the following:

- Protocol Chair(s)
- Investigators of Record (IoR) or designee
- LOC (FHI 360) Clinical Research Manager (CRM)
- LOC (FHI 360) Community Program Manager (CPM)
- LOC (Pitt) Protocol Development Team representative
- LOC (Pitt) Protocol Physician
- LOC (Pitt) Protocol Safety Physician
- MTN Director of Pharmacy Affairs (if applicable)
- SDMC Protocol Statisticians
- SDMC Clinical Data Manager (CDM) or Program & Portfolio Manager (PPM)
- SDMC Clinical Safety Associate (CSA)
- LC representative (if applicable)
- CWG representative (if applicable)
- BRWG representative (if applicable)
- BSWG representative (if applicable)
- DAIDS Medical and/or Program Officer

- NICHD and/or NIMH representative (if applicable)
- DAIDS Protocol Pharmacist (if applicable)
- IND Sponsor, Pharmaceutical Collaborator or other Co-sponsor representative (if applicable)

4.4.2 Protocol Team Responsibilities

Table 4.1 Roles and Responsibilities of Key Protocol Team Members

Team Member	Primary Roles and Responsibilities
Protocol Chair(s)	<ul style="list-style-type: none"> • Lead protocol team meetings and calls • Lead protocol development • Establish study-specific <i>ad hoc</i> working groups within the protocol team to complete specific activities, as needed • Monitor study implementation across sites • Participate in Data and Safety Monitoring Board (DSMB) meetings, if applicable • Develop, plan and lead the writing of manuscripts and dissemination of study results • Participate in communications planning for DSMB reviews (if applicable) and results dissemination with LOC (Pitt) • Serve as primary spokesperson in the dissemination of results • Coordinate and participate in the development of abstracts and manuscripts
Site IoR	<ul style="list-style-type: none"> • Provide site-informed input into protocol development and implementation plans • Provide detailed site estimates of the costs for study implementation • Submit protocol and other required study documents to the Institutional Review Boards/Independent Ethics Committees • Review and comment on Study Specific Procedures (SSP) manuals and data-collection forms • Manage and oversee the quality of study implementation at sites • Participate in the development of abstracts and manuscripts
CWG Representative(s)	<ul style="list-style-type: none"> • Provide the perspective of community and potential participants and facilitate communication with site CABs during the development of the protocol and informed consent forms • Bring community concerns and issues to the attention of the protocol team during study conduct • Work with the LOC (Pitt), protocol team and site CABs to advise on plans for disseminating study results to the community • Lead study-specific CWG meetings and calls • Participate in the development of abstracts and manuscripts
LOC (Pitt) Protocol Physician	<ul style="list-style-type: none"> • Provide medical expertise during protocol development
LOC (Pitt) Protocol Safety Physician	<ul style="list-style-type: none"> • Provide safety monitoring guidance and language during protocol development and implementation • Collaborate in the development of the SSP manual, as needed • Collaborate with the SDMC to ensure that safety monitoring is appropriate to the product under study and ensure that safety information or data is collected in a timely manner and evaluated at regular intervals • Document and archive minutes of PSRT meetings • Participate in the development of abstracts and manuscripts

Team Member	Primary Roles and Responsibilities
LOC (Pitt) Protocol Development Team representative	<ul style="list-style-type: none"> • Organize and document conference calls and meetings for the protocol team during protocol development • With the Protocol Chair(s), coordinate development of protocol and informed consent forms • Submit protocol for the required DAIDS reviews [such as Prevention Science Review Committee (PSRC), Regulatory and MO] • Develop and submit any necessary protocol modifications to the relevant NIH agency • Maintain files documenting protocol reviews and approvals by DAIDS • Serve as a member of study management teams • Participate in the development of abstracts and manuscripts • Collect and track site essential documents, including financial disclosures from investigators listed on the FDA Form 1572 • Respond to regulatory queries, as necessary
LOC (FHI 360) CRM	<ul style="list-style-type: none"> • Contribute to protocol development with the LOC (Pitt) Protocol/Regulatory Specialist • Coordinate all aspects of study implementation • Organize and document protocol team conference calls and meetings after the study protocol has been finalized • With the SDMC, contribute to case report form (CRF) development • Produce the SSP Manual with input from the SDMC, LC and other team members • Provide study-specific training for the CTUs/CRSs and coordinate development of the training plan and materials • Coordinate and track study-site activation requirements • Provide technical assistance and oversight to the CTUs/CRSs while the study is being conducted, enabling the sites to respond to problems and issues that arise during the implementation of studies and dissemination of findings • Conduct site-assessment visits, if applicable, after sites have been activated and provide written reports of their findings to the individual site and members of the protocol team • Summarize the SMC reviews and distribute, as appropriate • Participate in site preparation for DSMB reviews (if applicable) and results dissemination with LOC (Pitt) • Participate in the development of abstracts and manuscripts • Serve as a member on study management teams
LOC (FHI 360) CPM	<ul style="list-style-type: none"> • Contribute to protocol development • Coordinate all aspects of community engagement • Organize CWG calls and meetings • Provide technical assistance to the CTU/CRS community-education staff and/or CAB representatives as needed to facilitate community education • Participate in the development of abstracts and manuscripts
SDMC Protocol Statisticians	<ul style="list-style-type: none"> • Provide design and statistical input during protocol development and throughout the study • Develop the statistical components of the protocol • Develop the randomization and treatment allocation scheme, if needed • Conduct data analyses and generate the SMC, DSMB, IND, and other study-specific reports • Participate in the development of abstracts and manuscripts
SDMC CDM or PPM	<ul style="list-style-type: none"> • Collaborate in the development of the protocol and SSP manual

Team Member	Primary Roles and Responsibilities
	<ul style="list-style-type: none"> • Lead the development of data collection instruments and instructions • Lead the development of the study clinical database • Conduct study-specific data management training for CTUs/CRSs • Develop a plan for preparing regular reports regarding enrollment, retention, adherence, and for providing them to the protocol team and CTUs/CRSs • Provide site and team support for data collection and management and operational matters that may influence study data • Facilitate the close-out of data collection and cleaning • Track and facilitate SDMC work on the development of abstracts and manuscripts • Serve as primary liaison for SDMC on protocol-specific communications with protocol team and external partners (e.g., participate on protocol team calls) • Serve as a member on study management teams
SDMC Clinical Safety Associate	<ul style="list-style-type: none"> • Participate in protocol development, CRF and database design to ensure all required safety-related data are adequately represented and captured • Monitor clinical trial safety data for compliance in reporting, completeness, and accuracy • Assist in site safety data collection training as needed
LC Representative	<ul style="list-style-type: none"> • Contributes to protocol development • Define appropriate laboratory testing methods and materials • Develop the laboratory section of the SSP manual • Provide training for the 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 and provide assistance to the CTU/CRS laboratories, as needed • Provide laboratory expertise in protocol and CRF development • Participate in the development of abstracts and manuscripts • Serve as a member on study management teams
MTN Director of Pharmacy Affairs	<ul style="list-style-type: none"> • Contribute to protocol development • Advise the protocol team on all product-related issues and consult on available dosage forms and placebos • Interact with product manufacturer/developer to ensure product supply • Provide training for the CTU/CRS pharmacists and clinic staff, as needed • Develop documents related to pharmacy and study products • Provide product shipment to study sites • Collaborate with the DAIDS Protocol Pharmacist, when applicable • Participate in the development of abstracts and manuscripts • Serve as a member on study management teams
DAIDS MO	<ul style="list-style-type: none"> • Contribute to protocol development • Participate fully in the protocol team's discussions and decisions • Facilitate communication between the protocol team and DAIDS groups and staff • Monitor participant safety through membership in the PSRT and evaluation of expedited adverse-event report forms

Team Member	Primary Roles and Responsibilities
	<ul style="list-style-type: none"> • Provide oversight of the adequacy and appropriateness of site-specific safety monitoring systems and procedures
DAIDS Protocol Pharmacist	<ul style="list-style-type: none"> • Collaborate with the MTN Director of Pharmacy Affairs, when applicable
BRWG Representative	<ul style="list-style-type: none"> • Provide design and behavioral input during protocol development and throughout the conduct of the study • Provide behavioral component training to the sites • Develop the behavioral components of the protocol • Lead the development of behavioral data collection instruments and instructions • Collaborate in the development of the SSP manual • Provide support for behavioral data collection • Conduct behavioral data analyses • Participate in the development of abstracts and manuscripts
BSWG Representative	<ul style="list-style-type: none"> • Contribute to protocol development • Recommend biological samples for collection to evaluate product safety and efficacy • Propose testing to be used for primary, secondary and/or exploratory objectives • Collaborate in the development of the SSP manual, as needed • Participate in the development of abstracts and manuscripts

Although individual protocol team members have different roles in fulfilling specific protocol team responsibilities (see Table 4.1), all members are expected to provide scientific, operational and/or site-specific input to protocol team activities, as appropriate. Protocol team responsibilities include:

- Developing the study protocol, including making revisions in response to requests or comments from the PSRC, Regulatory Support Center (RSC), and Regulatory Affairs Branch (RAB)
- Soliciting, via the Study IoRs and the designated CWG team member, community input during protocol development and review
- Providing MTN Leadership with detailed estimates of the resources required to conduct the study, including site-specific study costs and requirements for the LC and SDMC resources, as requested
- Developing data-collection instruments and instructions for the completion of these instruments
- Developing the SSP manual with LOC (FHI 360) staff
- Defining protocol milestones for monitoring performance in collaboration with the LOC, the SDMC and LC staff
- Overseeing accrual and retention of study participants and managing these individuals as specified in the protocol
- Monitoring participant safety in conjunction with the PSRT
- Conducting ancillary study review and, when necessary, advocating for additional resources
- Monitoring the conduct of the study through SDMC reports on accrual, retention, data-management quality, adherence to intervention, endpoint assessment completion and safety
- Developing and carrying out corrective action plans for problems with implementing the study
- Overseeing study conduct and implementation, ensuring compliance with all applicable standards and requirements

- Producing scientific publications and making presentations related to study findings in a timely manner

4.4.3 Protocol Chair Responsibilities

Protocol Chair(s) will provide the primary scientific leadership during the development, implementation and reporting of the study, as well as assume responsibility for the completion of protocol team responsibilities.

Protocol Chair(s) plan and manage protocol team business in consultation with and support from LOC (Pitt) during the development of the protocol, and with LOC (FHI 360) staff after the protocol has been finalized (Version 1.0). The specifics of protocol team management vary according to the type of study (such as Phase 1, 2 or 3, research area), the number and location of the sites involved, and individual leadership and management approaches.

Protocol Chair(s) may identify study-specific working groups to address specific needs or activities during protocol development and study conduct. Protocol Chair(s) appoint protocol team members to these groups. Examples might include working groups to address the following:

- Developing and/or overseeing specialized behavioral procedures for a study
- Developing and/or overseeing specialized clinical procedures for a study
- Developing specialized data-collection modules (in collaboration with the SDMC)
- Ongoing monitoring of study-participant safety data
- Drafting and submitting manuscripts and presentations

Specific duties of the Protocol Chair(s) include:

- Establishing and maintaining an efficient schedule of conference calls and meetings (to include all members of the protocol team and additional representatives from SDMC and LC) to develop and manage the study, as appropriate
- Establishing study-specific working groups as needed to address study-related issues during protocol development, implementation and/or results dissemination
- Monitoring participants' 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 and, if no agreement can be reached, referring the issue to the EC for consideration
- Overseeing analysis and writing teams during manuscript preparation (such as designating writing-team members, reviewing schedules, monitoring progress and communicating publication plans, as required).

4.4.4 Relationship between Protocol Team and EC

The EC monitors each protocol team with regard to protocol development, implementation, analysis and reporting. Reporting to the EC regarding protocol development is provided by the MTN LOC (Pitt) Director of Operations during EC meetings and teleconferences. Reporting regarding studies approved for implementation occurs directly by Protocol Chair(s)/Co-Chair(s) for Phase 2b and Phase 3 trials and by FHI 360 CRMs for other studies. In addition, as arms of

the EC, the SMC reviews study conduct, the NEC reviews site performance across studies and the MRC provides a formal review of publications and presentations.

Routine oversight by the EC includes the following:

- Evaluating study progress in relation to key implementation benchmarks
- Assisting NIAID in determining the need for additional resources; for example, in the case of unexpected costs associated with planned study procedures, or to support ancillary studies endorsed by the protocol teams (See Section 21 of this Manual for further information regarding the process of developing, reviewing and approving ancillary studies.)
- 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 modification of the protocol team membership or its leadership).

4.4.5 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(s) of that Committee or Working Group, the investigator or the Committee/Working Group Chair(s) may refer the issue to the EC.

4.4.6 Conflict Resolution

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