4. NETWORK COMMITTEES, WORKING GROUPS AND PROTOCOL TEAMS

4.1 Working Groups and Resource Committees

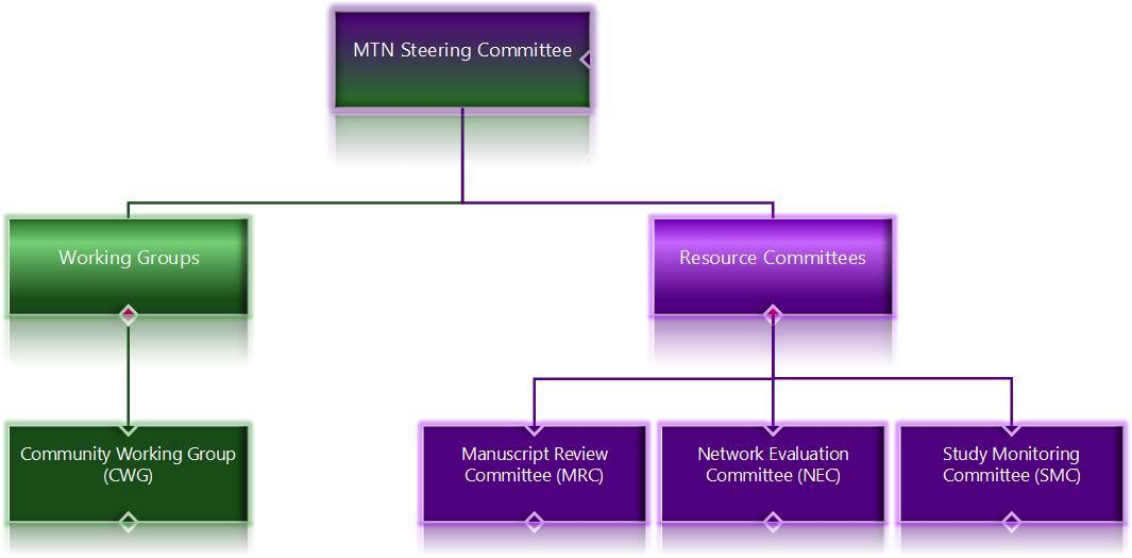
The primary governance body of the Microbicide Trials Network (MTN) is the Steering Committee (SC) [previously the MTN Executive Committee (EC)], which is responsible for the overall scientific direction, development and implementation of policy, procedural decisions and resource allocation. The SC is chaired by the MTN Principal Investigator (PI) and is supported by three resource committees and one working group (Figure 4.1).

4.2 Working Groups

Prior to Nov. 30, 2021, there were three MTN Working Groups. The Biomedical Sciences Working Group and the Behavioral Research Working Group are no longer required in these final stages of MTN operations and have been eliminated. The Community Working Group (CWG) has been streamlined. Normally, the CWG 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. (See Section 07 of this Manual.)

Figure 4.1 MTN Main Committee Structure



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 MTN publications (i.e., manuscripts, conference abstracts, posters and oral presentations containing MTN study data or statistically related content resulting from MTN studies or are funded by NIH through MTN) must conform to MTN and NIH standards prior to their submission for publication. The MRC Chair may personally conduct reviews or may identify committee members or other appropriate professionals to assist in the process. The MRC is responsible for developing policies and procedures related to MTN publications and for management of the MRC review step. (See Section 20 of this Manual for further information regarding MTN publications.)

The MRC review provides an independent review after thorough editing by the Co-Authors, and for publications related to a specific MTN protocol, approval by the Protocol Publications Committee (PPC) and review by the Product Developer (if applicable based on the relevant CTA). The PPC includes the DAIDS Medical Officer (MO) and, as applicable, additional U.S. National Institutes of Health (NIH) MOs and other key members of the protocol team. Publications are required to undergo the review steps listed above before submission for MRC review.

The MTN publications review process and MRC reviews are conducted to ensure that all MTN publications:

Reflect accurate reporting of the design, conduct and analysis of the studies
All publications are developed in a collaborative fashion with active participation by all investigators involved in the design and conduct 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 policies, 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
All manuscripts as well as abstracts and their related posters/oral presentations are published expeditiously and made available to the scientific community.

Beginning on Dec. 01, 2023, newly identified concepts for ancillary studies and data analyses, based on MTN studies that have completed follow-up, will be restricted (see Section 20 of this Manual). Such publications will only be given an abbreviated MRC review prior to publication to ensure standard Network acknowledgments.

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), CTU/CRS investigators as well as ad hoc MTN members or non-members who are experts knowledgeable in a relevant research area.

The MRC membership consists of:

- MRC Chair
- 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 Steering Committee (SC) 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 16.7 of this Manual for further information regarding the SMC's specific functions.)

The SMC is composed of voting members representing the LOC [FHI 360], 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 are chosen after recommendations by the Protocol Chair(s) and/or SC 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 SC is informed of the outcomes of the SMC review, typically during routine SC conference calls.

The membership of the SMC consists of the following:

SDMC Co-Investigator (Chair)
SDMC representative(s)
LOC (FHI 360) 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 16.7 of this manual for more information about SMC reviews.)

4.3.3 Network Evaluation Committee

The NEC functions as an arm of the MTN Steering Committee (SC). The NEC 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 SC. 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.

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.

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) collaborate with the MTN LOC (Pitt) during protocol development/modification, and 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) occurs during the earliest stages of protocol development; however, a replacement may occasionally be required. As no further new protocols are anticipated, only the selection of replacement Chairs is expected. MTN Leadership will solicit interest from qualified investigators, as needed. Following submissions of interest, the SC 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
LOC (FHI 360) Pharmaceutical Product Manager (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)
Behavioral Consultant
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)	• Lead protocol team meetings and calls • Lead protocol development and modification • Establish study-specific *ad hoc* 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	• Provide site-informed input into protocol development, modification 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)	• 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	• Provide medical expertise during protocol development
LOC (Pitt) Protocol Safety Physician	• Provide safety monitoring guidance and language during protocol development, modification 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
LOC (Pitt) Protocol Development Team representative	• Organize and document conference calls and meetings for the protocol team during protocol development • With the Protocol Chair(s), coordinate development and modification 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

Team Member	Primary Roles and Responsibilities
	• 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	• Contribute to protocol development and modification 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	• Contribute to protocol development and modification • 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	• Provide design and statistical input during protocol development, modification 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	• Collaborate in the development of the protocol and SSP manual • 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

Team Member	Primary Roles and Responsibilities
	• 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	• 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	• Contributes to protocol development and modification • Define appropriate laboratory testing methods and materials • Develop the laboratory section of the SSP manual • Oversee implementation of laboratory procedures • 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
LOC (FHI 360) Pharmaceutical Product Manager	• Contribute to protocol development and modification • 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	• Contribute to protocol development and modification • 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 • Provide oversight of the adequacy and appropriateness of site-specific safety monitoring systems and procedures
Behavioral Consultant	• Provide design and behavioral input during protocol development, modification, 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

Team Member	Primary Roles and Responsibilities
	• Provide support for behavioral data collection • Conduct behavioral data analyses • 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 SC 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 SC

The SC monitors each protocol team with regard to implementation, analysis and reporting. Reporting to the SC regarding protocol maintenance activities (clarifications and modification) is provided by the MTN LOC (Pitt) Director of Operations and Fiscal during SC meetings. Reporting regarding ongoing studies will be provided by the FHI 360 PI. SMC reviews study conduct, the NEC reviews site performance across studies and the MRC provides a formal review of publications and presentations will be reviewed as needed.

Routine oversight by the SC 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.
Adjudicating conflicts that cannot be resolved within the protocol team (if all reasonable attempts to adjudicate conflicts within the protocol team fail, the SC 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 SC.

4.4.6 Conflict Resolution

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