19 DATA ACCESS, PUBLIC RELEASE AND COMMUNICATIONS

This section describes the policies and procedures regarding access to and release of data that are collected as part of a Microbicide Trials Network (MTN) study, and outlines the policies and procedures for the communication of study results and outcomes of interim study data and safety reviews. (See also Section 8 for a comprehensive overview of public communication policies and procedures.)

19.1 Policy on Access to Study Data

The central database for the majority of the studies conducted by MTN resides at the Statistical and Data Management Center (SDMC). This database includes case report form (CRF) data, Audio/Computer Assisted Self-Interview (ACASI/CASI) data, the results of protocol-specified laboratory analyses, and ancillary study data.

19.1.1 Release of Data During a Study

19.1.1.1 Release of Site-Specific Study Data to Study Sites

The SDMC is responsible for releasing site-specific study data to Clinical Research Sites (CRS) participating in that study when appropriate and when resources are available. Publication and presentation at conferences of site-specific data is generally done in collaboration with the SDMC, as described in Section 20 of this manual. As part of each study's Protocol Publications Committee (PPC), the SDMC reviews all abstracts and manuscripts that contain or report on data collected by the SDMC.

19.1.1.2 Safety Studies

In Phase I, Phase II and Phase IIa studies, the primary objective is to provide an early assessment of participant safety. For these studies, a site can access most of its site-specific data while the study is ongoing. For blinded studies, data are provided in a blinded fashion.

19.1.1.3 Clinical Effectiveness Studies and Comparative/Observational Studies

In Phase IIb, Phase III and Phase IIIb studies, the primary objectives are (i) to assess clinical effectiveness and (ii) to obtain greater insight about acceptability and safety. In such studies, most site-specific data collected from participants prior to randomization may be released to the site during the study, but data that are collected after randomization will not be released during the study.

A comparative or observational study with prospective data collection is handled in the same way as a Phase IIb or Phase III study.

19.1.1.4 Other Studies

For non-comparative cohort studies, natural history studies and comparative studies with retrospective data collection (for example, case-control), all data submitted from a site may be released to that site during the study.

19.1.1.5 Data Not Available During a Study (Regardless of Study Type)

Some categories of data will not be available to the protocol team (including study sites) during the study, regardless of study type. These data types include the following:

- Coding (for example, by MedDRA) of adverse events or concomitant medications
- Non-CRF laboratory data (that is, laboratory data that are sent directly to the SDMC from one of the laboratories that is affiliated with the MTN Laboratory Center [LC])
- Non-CRF data captured electronically (for example, ACASI/CASI)
- Non-CRF data with participant identifiers where the participant has an expectation of confidentiality (for example, in-depth interview data)
- For randomized studies, data that could potentially lead to unblinding unless approved by the MTN Protocol Chair(s) and Protocol Statistician

19.1.2 Release of Data after Completion of a Study

19.1.2.1 Release of Data to MTN Investigators

After completion of the last protocol-specified study visit, the Protocol Chair(s) and/or Protocol Statistician may lead a closed meeting for the protocol team, either in-person or via teleconference, to report the results of protocol-specified analyses. Prior to the meeting, the Protocol Chair(s) and Protocol Statistician will discuss and come to consensus on the specific analyses to present at the meeting, as well as who will be presenting. Scheduling of the meeting will take into account the specific analyses and the SDMC time needed to complete these analyses once the data is available. The meeting itself may occur prior to locking the study database, but the relevant data should be clean; that is, stable enough that the results are not expected to change between the time of the meeting and the time of database lock. Ideally, and dependent upon SDMC recommendation, the results should be provided to the Protocol Chair(s) approximately 2 weeks prior to the meeting. The meeting should occur prior to data being publicly presented at a scientific meeting and/or published. Participation in these confidential meetings is generally limited to the following:

- The study sponsor representative(s)
- The MTN Principal Investigator (PI) and co-PI
- The MTN Protocol Chair(s)
- The MTN SDMC PI

- The MTN LC PI
- NIH medical officer(s)
- The DAIDS Clinical Microbicide Research Branch (CMRB) Chief
- The Clinical Trials Unit (CTU) PIs and/or Investigators of Record (IoR) from participating CRSs
- The Protocol Statisticians
- Members of the study management team
- The protocol's Working Group representatives

For Phase I, II, and IIa studies, the Protocol Chair(s) and the Protocol Statistician(s) will make the final determination regarding who may participate in the meeting. The SDMC CDM will create the initial list, solicit feedback, finalize the list, and schedule the meeting.

For Phase IIb or higher trials, the MTN PI and co-PI, and the MTN SDMC PI, in consultation with the Protocol Chair(s) and Protocol Statistician(s), will develop the list of meeting participants and make the final determination regarding who may participate in the meeting.

All participants may be asked to sign a confidentiality agreement asking them not to disclose the results shared at the meeting until such time that the data are publicly presented at a scientific meeting and/or published. The SDMC PI (or designee) makes the final determination regarding whether a confidentiality agreement must be in place for the meeting.

Site-specific data sets, as well as the complete study data set, may be released to CTU and/or CRS investigators who contribute data to a study after the following:

- The study database has been cleaned and locked by the SDMC.
- All manuscripts reporting results of the protocol's primary and secondary objectives have been accepted for publication.
- Resources have been identified to allow the SDMC to prepare the requested data.

To release the data to interested MTN CTU and/or CRS investigators, the Protocol Chair(s) or designee (MTN LOC [FHI] 360 Clinical Research Manager [CRM]) must confirm and communicate to the Protocol Statistician and MTN PI and co-PI that the team has published all intended manuscripts of the protocol's objectives.

19.1.2.2 Release of Data to Other Institutions

Generally, no study data or interim analysis reports may be released by the SDMC to other institutions during the conduct of the study. When applicable, release of data and/or data reports to the study's Investigational New Drug (IND) Sponsor and/or Product Developer either during or after study completion, is governed by the terms set forth in the study-specific Clinical Trials Agreement (CTA). Exceptions noted in the protocol will be negotiated among National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS), the Protocol Chair(s) and the SDMC.

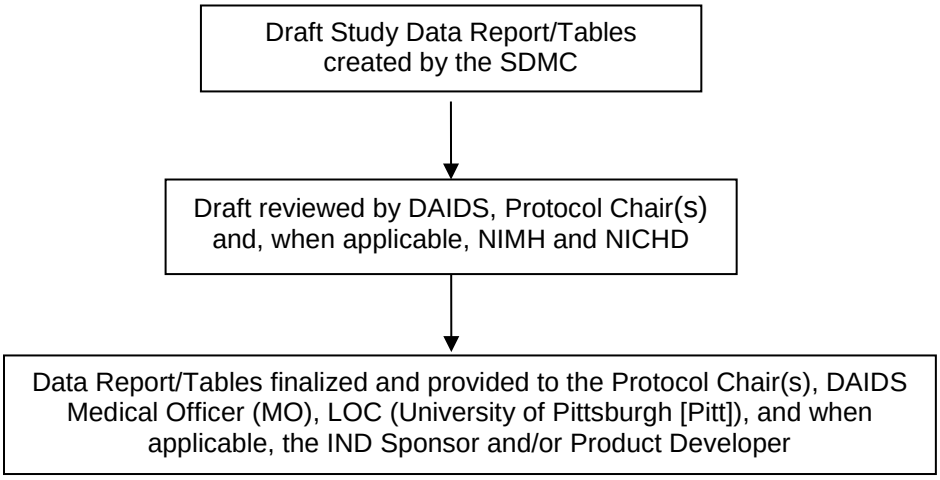
Any request to release data or data reports to other institutions or investigators during a study requires the approval of the Protocol Chair(s) and Protocol Statistician in consultation with NIAID/DAIDS and, when applicable, the National Institute of Mental Health (NIMH) and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD). Please refer to Section 21.3, Request for Datasets, for additional information.

19.1.3 Preparation and Release of Final Study Data Reports/Tables

The SDMC is responsible for preparing final study data tables that address the objectives of the protocol. For Phase I, Phase II and Phase IIa studies, the final study data tables will be provided in the form of a Final Study Data Report. This data report will include data tables as well as a data narrative to explain the tables (similar to a Study Monitoring Committee [SMC] Report).

For Phase IIb, Phase III or Phase IIIb studies, in which a closed results meeting may occur prior to public release of any study results, it may be that only final data tables are provided, with no accompanying data narrative. Regardless of whether a Final Study Data Report or final study data tables are generated, there is a specific review and approval process that must occur prior to the release of these documents (see Figure 19.1).

Figure 19.1 Review Process for Final Study Data Tables and Reports



19.1.4 Reporting Gender, Race and Ethnicity

The MTN collects gender, race and ethnicity information of its study participants, in compliance with NIH requirements (1997 OMB Directive 15). This requirement applies to all new applications and proposals, annual progress reports, competing continuation applications, competing supplement applications for research grants and contracts, and intramural projects as of January 10, 2002.

19.1.5 Blinded Data

MTN's randomized studies typically are double-blinded, which means neither study participants nor study-site staff have access to specific treatment assignments. Participants are blinded to reduce the chance that they may alter behaviors (such as those that could increase their HIV risk) based on knowledge of their treatment assignment. Study site staff, including clinical and laboratory study staff members, are blinded to avoid bias in their clinical and laboratory assessments. Only the CTU/CRS Pharmacy staff, MTN Director of Pharmacy Affairs, DAIDS Protocol Pharmacist (if applicable), Protocol Statistician(s) and SDMC CDM(s) may have access to coded randomization assignments. All SDMC MTN Statisticians may have access to unblinded treatment assignments for ongoing MTN studies. Typically, members of a study's

independent Data and Safety Monitoring Board (DSMB) have limited access to unblinded treatment assignments.

19.1.5.1 Formal Protocol Unblinding of Treatment Assignments

Unblinding of participants and study site staff to individual participant treatment assignments occurs only after the Protocol Chair(s), NIAID, study co-sponsor and the SDMC have approved the decision to unblind the study. As a rule, unless otherwise requested by the DSMB, a study is not unblinded until after the study database has been locked. In a multicenter study with geographically separated study sites, unblinding may occur on a site-by-site basis after the study database has been locked.

Prior to formal unblinding, the SDMC notifies all parties of the intention to unblind the study. After approval, the SDMC provides each study site with a list of participants' identification numbers and their respective treatment assignments.

Participants who complete the study prior to the formal unblinding must wait until the study is unblinded to be informed of their treatment assignments. This policy should be made clear to participants at the time of recruitment and when they exit the study. While the manner in which participants are unblinded is at the discretion of the site IoR, it is recommended that unblinding take place in person.

19.1.5.2 Emergency Unblinding

If the site IoR or designee determines that a participant has sustained an event that necessitates unblinding, the site IoR or designee may request that the SDMC reveal the participant's study treatment assignment. Until unblinded product assignment information is received from the SDMC, the participant's clinical management should proceed as if the participant were assigned to active study product. The need for emergency unblinding is expected to be rare.

To request unblinding for a specific participant, the following steps must be taken:

1. The site IoR or designee requesting the unblinded treatment assignment must contact the Protocol Safety Review Team (PSRT).
2. If the PSRT rules that unblinding is required, the PSRT will send the unblinding request to the Protocol Statistician and copy the site IoR or designee. The MTN PI and co-PI should also be copied on this request.
3. The Protocol Statistician will provide the participant's treatment assignment directly to the site IoR or designee.
4. In a separate email, the Protocol Statistician will notify the MTN PI and co-PI, the DAIDS MO, the protocol management team and Protocol Chair(s) and the Fred Hutchinson Cancer Research Center's (FHCRC) Institutional Review Board (IRB) (which is responsible for the SDMC) that the treatment information has been provided.
5. The site IoR or designee must notify – in an expedited manner – all responsible IRBs/Independent Ethics Committees (IEC) for the site that unblinding has occurred.

19.1.5.3 Accidental Unblinding

Should an accidental unblinding occur at a trial site by any mechanism, the site IoR must notify the SDMC Clinical Data Manager, the MTN Director of Pharmacy Affairs and the DAIDS Protocol Pharmacist, if applicable. The SDMC Clinical Data Manager notifies the Protocol Statistician, Protocol Chair(s), DAIDS MO, MTN PI and co-PI, and the FHCRC IRB.

19.1.5.4 Protocol Extension and Unblinding

In the event that a study is extended, the MTN Executive Committee may decide to inform participants who do not participate in the extension of their treatment assignment after they have completed their study follow-up. In this situation, any participants who are not involved in the extension should be unblinded by a staff member who is not involved in the follow-up of participants in the extension.

19.1.5.5 Unblinding IND Sponsor/Product Developer

Once the decision is made to unblind study participants, the SDMC will, upon the IND Sponsors' and/or Product Developers' request, provide them with a list of the participants' identification numbers and their respective treatment-arm assignments. If an IND Sponsors and/or Product Developer needs to know treatment-arm assignments earlier to interpret laboratory analysis of specimens, he or she should petition the SDMC PI and Protocol Chair(s) for release of that information.

19.2 Public Release of Study Data, DSMB Outcomes and Study Results

The MTN LOC (Pitt) Communications and External Relations Team, in conjunction with the NIAID Office of Communications and Government Relations (OCGR) News and Public Information Branch and the DAIDS Workforce Operations, Communications and Reporting Branch (WOCRB) manages all aspects of public information and public release of MTN study-related data, including DSMB outcomes and study results. These activities are performed in collaboration with DAIDS Leadership, the MTN PI and co-PI, SDMC PI, Protocol Chair(s) and other relevant parties, including a study's IND Sponsor and/or Product Developer (please see Section 8 for more information).