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19 DATA ACCESS, PUBLIC RELEASE AND COMMUNICATIONS

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

19.1 Policy on Internal Network Access to Study Data

Study data for the majority of MTN studies resides at the Statistical and Data Management Center (SDMC) in Seattle, Washington. Study data is captured via the study clinical database, (which houses Case Report Form (CRF) data), as well as via other data streams that capture specific types of data, such as Audio/Computer Assisted Self-Interview (ACASI/CASI) data, the results of protocol-specified laboratory analyses and ancillary study data.

While a trial is ongoing, the SDMC routinely reports out to the Protocol Team on study-specific metrics, such as the number of participants who screen out of the study, the number of participants who enroll in the study, the retention rate, visit adherence and procedure completion. In addition, the SDMC routinely generates study-specific reports and listings to support other study activities related to the monitoring of study conduct, such as protocol deviation summary tables and listings. The Reporting Plan contained in each study's Study Specific Procedures (SSP) Manual provides details on the reports and listings that the SDMC will produce for a given study, including the individuals who will have access to the report, the data contained in the report, and how the SDMC will provision the data (e.g., via SCHARP's Atlas web portal).

19.1.1 Release of Data to Individual Clinical Research 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.

- While a trial is ongoing, sites will have access to view their site-specific CRF data via the study clinical database (e.g., iDataFax or Medidata Rave). Per site request, the SDMC may also provide data reports and listings as needed (e.g., for local Institutional Review Board/Independent Ethics Committees (IRB/IEC) submission). Further details are provided in the subsections below.
- After database lock and study unblinding, if applicable, the SDMC may provide site-specific datasets to sites per their request. 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.
 - Protocol Chair(s) or designee (MTN LOC [FHI] 360 Clinical Research Manager [CRM]) have confirmed and communicated to the Protocol Statistician and MTN PI and Co-PI that the team has published all intended manuscripts of the protocol's objectives.
 - Resources have been identified to allow the SDMC to prepare the requested data.
 - Permission has been obtained in writing from MTN Leadership.

Site staff should contact the SDMC (SCHARP) Clinical Data Manager (CDM) for a given study to request release of study-specific data. As needed, the CDM will follow up internally within the SDMC to determine the appropriateness of the request. After internal review, a designated member of the SDMC (e.g., study CDM, Program & Portfolio Manager, or study statistician) may solicit input and/or approval from external network colleagues and/or DAIDS as needed. Factors under consideration will include the nature of the request, the type of study, and the stage of the study (e.g., in follow up, closeout, post-database lock, before or after study unblinding, if applicable). A designated member of the SDMC (usually the study CDM or study statistician) may request that site staff complete a SCHARP Data Request Form and/or Data Transfer Plan to document specifications related to the request (e.g., for data releases while a study is ongoing, whether to include all available data or only "clean" data that is free of QCs).

Publication and presentation at conferences of site-specific data is generally done in collaboration with the SDMC and the MTN Manuscript Review Committee, as described in Section 20 of this manual.

Documentation of data release requests, approvals (if required) and releases will be created and maintained in accordance with the applicable SDMC (SCHARP) Standard Operating Procedures and Work Instructions and MTN Good Documentation Policy (see Section 9.2.1 of this manual).

19.1.1.1 Safety Studies

In Phase I, Phase II and Phase IIa studies, where the primary objective is to provide an early assessment of participant safety, a site will be granted access to most of its site-specific data via SDMC-generated reports and listings while the study is ongoing. However, unblinded data will remain unavailable to all but those identified in Section 19.1.6 of this manual, with the exception of emergency unblinding, (see Section 19.1.6.2 of this manual).

19.1.1.2 Clinical Effectiveness Studies and Comparative/Observational Studies

In Phase IIb, Phase III and Phase IIIb studies, where the primary objectives are (i) to assess clinical effectiveness and (ii) to obtain greater insight about acceptability and safety, most site-specific data which is collected from participants prior to randomization may be released to the site during the study via SDMC-generated reports and listings. A request for any data other than that specified in the SSP reporting plan requires a formal request from the site to the SDMC. However, data that are collected after randomization will not be released until after the study is unblinded and the primary manuscript has been accepted for publication. See Section 20, MTN Publication Policy, of this manual for site data requests for purposes of manuscript development and publication. See Section 19.1.1 above for site dataset requests for purposes other than conducting protocol primary and secondary endpoint analyses or manuscripts.

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

19.1.1.3 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.

19.1.1.4 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:

- Data by treatment arm, with the exception of unblinded SDMC staff as identified in Section 19.1.6 and in cases of emergency unblinding as described in Section 19.1.6.2
- For randomized studies, data that could potentially lead to unblinding unless approved by the MTN Protocol Chair(s) and Protocol Statistician
- 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)

19.1.2 Release of Study Data to Data Safety Monitoring Boards (DSMB), Study Monitoring Committees (SMC) and Endpoint Adjudication Committee (EAC)

Section 16, Study Oversight, of this manual provides details on SMC and DSMB oversight, including SDMC generation of reports to support these reviews. These reports are produced in accordance with the applicable SDMC (SCHARP) Standard Operating Procedures and Work Instructions. Section 14, Laboratory, of this manual provides details on the EAC process,

including SDMC provision of lab result data and data capture of member case decisions to support the endpoint adjudication review process.

Documentation of released data and generated reports should be created and maintained according to MTN Good Documentation Policy (see Section 9.2 of this manual).

19.1.3 Release of Data after Completion of a Study

19.1.3.1 Release of Final Data Analysis 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 that will be presented 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 primary endpoint data should be clean; that is, free of QCs (i.e., all data queries resolved) and not expected to change between the time of the meeting and the time of database lock. Ideally, the results should be provided to the Protocol Chair(s) approximately 1-2 weeks prior to the meeting. The meeting should occur prior to the data either 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) and/or product developer(s)
- The MTN Principal Investigator (PI) and co-PI
- The Study Protocol Chair(s)
- The MTN SDMC PI
- The MTN LC PI(s)
- NIH Medical Officer (MOs)
- The DAIDS Clinical Microbicide Research Branch (CMRB) Chief
- The Clinical Trials Unit (CTU) PIs and/or Investigators of Record (IoR) from participating CRSs
- The Study Protocol Statisticians
- Members of the study management team
- The Protocol 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, regardless of study type, will 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 obtains confidentiality agreements from meeting participants.

Documentation relevant to this meeting should be created and maintained according to MTN Good Documentation Policy (see Section 9.2 of this manual).

19.1.3.2 Release of Data to Other Institutions

Generally, no study data or interim analysis reports may be released by the SDMC to other institutions (other than an SMC or DSMB) 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 Product Developer, the Protocol Chair(s) and the SDMC.

Data releases (e.g., tables, listings, and figures) to regulatory agencies (e.g., EMA, FDA) may be required at any time, per their request, to support regulatory submissions.

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 the Product Developer, 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.

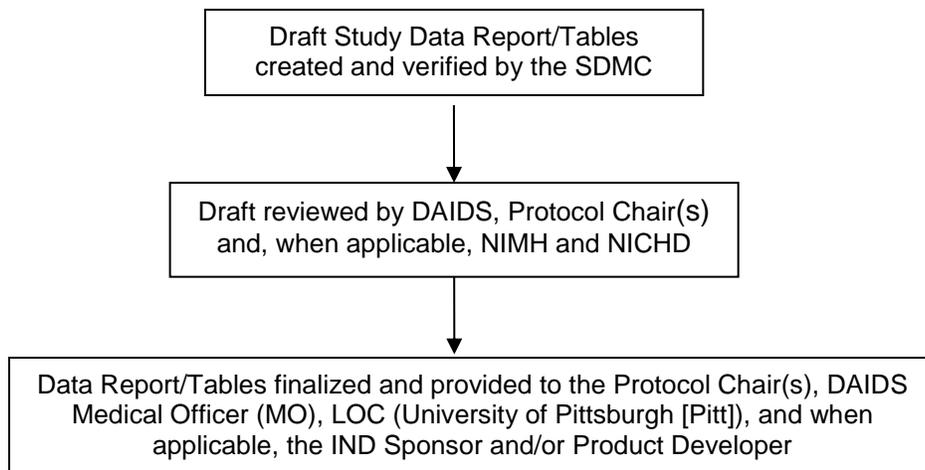
19.1.4 Preparation and Release of Final Study Data Reports and/or Tables

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 and may include a data narrative to explain the tables (similar to a Study Monitoring Committee [SMC] Report). In accordance with the applicable SCHARP Standard Operating Procedures and Work Instructions, both will be reviewed internally by SDMC staff for accuracy, completeness and internal consistency prior to release. Documentation of this review must be maintained (see Section 9.2.1 of this manual).

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. An additional, specific review and approval process that must occur prior to the finalization and release of these documents is presented in Figure 19.1. Documentation of this review must also be maintained (see Section 9.2.1 of this manual).

Figure 19.1 Review Process for Final Study Data Tables and Reports

Note: the number and content of the study data tables in the Final Study Report may be limited for studies in which a clinical study report is being developed.



19.1.5 Reporting Gender, Race and Ethnicity

To demonstrate compliance with 42 U.S.C. 282a-2, and NIH Policy and Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research (https://grants.nih.gov/grants/funding/women_min/guidelines.htm), MTN collects and reports gender, race and ethnicity information related to its study participants, in accordance with the Office of Management and Budget (OMB) 1997 Statistical Policy Directive No.15.

The overarching goal of these requirements is to ensure that women and minorities are appropriately included in clinical (biomedical and/or behavioral) research supported by NIH. These requirements are applicable to, and must be included in, 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.

19.1.6 Blinded / Unblinded 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 knowledge of their treatment assignment might adversely alter their behavior (such as behaviors that could increase their HIV risk). 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.

While a trial is ongoing, permissions to participant-specific treatment assignments are limited to those statisticians that comprise the study unblinded statistical team and are designated as such per SCHARP Work Instruction 0016 Implementation of Efficacy Trial Dual Statistical Team. Typically, members of a study's independent Data and Safety Monitoring Board (DSMB) have limited access to unblinded treatment assignments via closed session DSMB reports produced by the SDMC.

19.1.6.1 Formal Protocol Unblinding of Treatment Assignments

Except in the case of a medical emergency, unblinding of study participants and study site staff to individual participant treatment assignments occurs only after the Protocol Chair(s), NIAID, study co-sponsor(s) 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 receiving written approval from the Protocol Chair(s), the DAIDS MO [who consults with all relevant parties at DAIDS as needed, including the DAIDS Sponsors Authorized Representative (SAR) if DAIDS holds the IND] and MOs from other institutes, as applicable (when collaborations with other networks occur), Product Sponsor and the SDMC, the SDMC provides each study site with a list of participants' identification numbers and their respective treatment assignments. Documented approvals to unblind must be created and maintained according to MTN Good Documentation Policy (Section 9.2.1 of this manual).

Participants who complete the study prior to the formal unblinding must wait until the study is completely unblinded following the end of all study follow-up visits 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.

19.1.6.2 Emergency Unblinding

If the site IoR or designee determines that a participant has sustained a serious adverse event that necessitates unblinding in order to ensure proper management of the participant's condition, the site IoR or designee may decide to perform an emergency unblinding to learn the participant's study treatment assignment. Until the IoR or designee learns of the participant's unblinded treatment assignment, the participant's clinical management should proceed as if the participant were assigned to active study product. Emergency unblinding during the course of a trial has serious implications for study conduct and analysis. As such, site IoRs/designees should carefully consider whether or not emergency unblinding is warranted before proceeding. Simply removing the participant from the blinded treatment is often sufficient to provide effective clinical management of an event. The need for emergency unblinding is expected to be rare.

The study-specific mechanism for emergency unblinding will be specified in each applicable study's SSP Manual. In MTN studies, which utilize clinical databases that are set up in the Medidata Rave electronic data capture (EDC) system, site IoRs/designees may unblind themselves to a specific participant's treatment assignment via the EDC system. User-specific permissions to this unblinding feature in the EDC system are restricted to the IoR or designee at each CRS. Designated users will be required to undergo specific training by the SDMC on emergency unblinding procedures within the EDC system, including completion of an eLearning module, prior to being granted user permission to unblind within the EDC system. If and when an IoR or designee performs emergency unblinding of a participant in the EDC system, the audit trail of the request, including the user, date, time, and PTID, will be captured within the EDC system itself.

Once a specific participant is unblinded, the following steps must be taken:

1. The site IoR or designee must notify the Protocol Chair(s), Protocol Safety Review Team (PSRT), Protocol Statistician, MTN PI and co-PI, DAIDS MO, and protocol management team.
2. In a separate e-mail, the DAIDS MO will notify the product sponsor as agreed upon in the clinical trial agreement (CTA).
3. In a separate e-mail, the Protocol Statistician will notify the Fred Hutchinson Cancer Research Center's (FHCR) IRB (which is responsible for the SDMC) that the treatment information has been released.
4. The site IoR or designee must notify – in an expedited manner – all responsible IRBs/IEC for the site that unblinding has occurred.

19.1.6.3 Accidental Unblinding

Should an accidental unblinding occur at a trial site by any mechanism, the site IoR must notify the SDMC CDM, the MTN Director of Pharmacy Affairs and, if applicable, the DAIDS Protocol Pharmacist. The SDMC CDM notifies the Protocol Statistician, Protocol Chair(s), DAIDS MO, MTN PI and Co-PI, and the Fred Hutchinson Cancer Research Center (FHCR) IRB, which oversees the SDMC.

19.1.6.4 Protocol Extension and Unblinding

In the event that a study is extended, the MTN Executive Committee may decide to inform participants, who have not chosen to 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 those participating in the extension.

19.1.6.5 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 Sponsor and/or Product Developer need to know treatment-arm assignments earlier, in order to interpret laboratory analyses, he or she should petition the SDMC PI and Protocol Chair(s) for release of that information. Written approval signed and dated by the SDMC PI and Protocol Chair(s) and Co-Chair(s) is required and must be maintained (see Section 9.2.1 of this manual).

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 (WOCR) 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).

19.3 Release of Study Documentation for the Trial Master File (TMF)

All study documentation will be released to the Product Developer for inclusion in the TMF upon request, according to the CTA for the trial and DAIDS policies.

19.4 Release of Study Documentation to Regulatory or Approving Entities

Data tables, analyses and audit trail information will be prepared and released to regulatory agencies upon request and in a format useful to them, provided the release has been approved in writing by DAIDS, the SDMC PI, MTN PI and MTN Co-PI and the Product Developer. A listing or duplicate copy of all materials released should be maintained as per MTN Good Documentation Policy (section 19.1.2 of this manual).