

Section 1. Introduction

This section specifies the sources of procedural information available to MTN 001 study staff, the responsibilities of MTN 001 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN 001. Also included is information on required submissions to Institutional Review Boards and/or Ethics Committees (IRBs/ECs).

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN 001 protocol (see Section 2). The purpose of this manual is to supplement the protocol, not to replace or substitute for it. In the event that this manual is inconsistent with the protocol, the specifications of the protocol take precedence. Please alert the MTN Coordinating and Operations Center (CORE) of any such inconsistencies.

Any study implementation questions that arise should be managed as follows (see also Figure 1-1):

- Questions related to interpretation and proper implementation of the MTN 001 protocol should be directed to the MTN CORE: Kailazarid Gomez and Sherri Johnson.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC): Karen Patterson.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the MTN Network Laboratory (NL): Charlene Dezzutti and Edward Livant.
- Questions related to the investigational study products should be directed by the study site Pharmacist of Record to the DAIDS Protocol Pharmacist and the MTN CORE Pharmacist: Debra S. Mérés and Cindy Jacobson.
- Questions related to community involvement and/or the CWG should be directed to the Community Program Manager: Rhonda White
- When in doubt as to whether questions pertain to protocol interpretation, data collection, laboratory procedures, or product related, contact the MTN 001 Management Team: mtn001mgmt@mtnstopshiv.org.

Current contact details for the above-listed contact persons are found in Figure 1-1 as well as in the MTN Directory at: <http://mtnstopshiv.org/?q=search/user>

Figure 1-1: MTN-001 STUDY COMMUNICATION

Protocol Implementation and Procedural Related		
Kailazarid Gomez	919.544.7040 x11282	kgomez@fhi.org
Sherri Johnson	703-516-9779 x12127	sjohnson@fhi.org
Community Involvement Related		
Rhonda White	919.544.7040 x11515	rwhite@fhi.org
Data Management Related		
Karen Patterson	206-667-7052	karen@scharp.org
Laboratory Related		
Ted Livant	412.641.3772	livantew@upmc.edu
Product Related		
Debra Mérés,	301-451-2775	depayne@niaid.nih.gov
Cindy Jacobson	412.641.8913	cjacobson@mail.magee.edu
Clinical Management/PSRT Related		
Katherine Bunge	412.917.9936 (pager)	kbunge@mail.magee.edu
Nancy Connolly	206.523.1177	nancycsc@gmail.com
Ross Cranston	412.647.4007	cranstonr@dom.pitt.edu

1.2 Investigator Responsibilities

MTN 001 must be conducted in accordance with the United States (US) Code of Federal Regulations and the International Conference on Harmonization Consolidated Guidance for Good Clinical Practice (GCP). Copies of these regulations and guidelines are referenced in the MTN Manual of Operations (MOP) which is available at:

<http://www.mtnstopshiv.org/?q=node/398>

The Division of AIDS (DAIDS) Standard Operating Procedures (SOPs) for Essential Documents and Source Documentation are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations. Copies of these SOPs are provided in Section 16 of this manual.

At each site, MTN 001 also must be conducted in accordance with all site-specific regulations, policies, and guidelines applicable to human subjects research in general and/or the conduct of study procedures in particular. Each site should file copies of all such regulations, policies, and guidelines in their MTN 001 essential document files (see also Section 3.1).

The IoR at each study site must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct MTN 001 in accordance with the study protocol, applicable US regulations, and MTN policies. A copy of the protocol signature page can be found in the protocol in Section 2 of this manual. The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form itself, which can be found in Section 3.4.1 of the MTN MOP. IoRs may delegate their obligations and responsibilities for conducting MTN 001 to other study staff members, however delegation does not relieve the IoR of his/her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented throughout study implementation.

1.3 Study Activation Process

Prior to undertaking any study procedures, each study site must obtain approval to conduct MTN 001 from all responsible regulatory authorities and IRBs/ECs. Each site also must complete Protocol Registration procedures with the DAIDS Regulatory Compliance Center and Study Activation procedures with DAIDS and the MTN CORE, MTN SDMC, and MTN NL. Detailed information on the requirements of these pre-implementation procedures can be found in Section 10 of the MTN MOP. On a site-by-site basis, the MTN CORE will issue a Site-Specific Study Activation Notice when all study activation requirements have been met. At each site, no protocol-specified study procedures may be undertaken prior to issuance of the Site-Specific Study Activation Notice.

1.4 IRB/EC Submissions

Figures 1-2 and 1-3 list IRB/EC submission and approval requirements pertinent to MTN 001. Figure 1-2 lists requirements that must be met prior to study initiation. Figure 1-3 lists requirements that must be met during and following study implementation.

Each study site must submit all required documents to all responsible IRBs/ECs; however IRB/EC approval is not required for all documents. Documents requiring approval per US regulations and GCP guidelines are indicated in Figures 1-2 and 1-3. Additional approvals beyond those indicated in the figures may be required by individual IRBs/ECs; in such cases, all required documents must be submitted to and approved by the IRBs/ECs.

Study sites are encouraged to request an acknowledgement of receipt for all documents submitted to the IRBs/ECs, and to request that the IRBs/ECs note the effective and expiry dates of all approvals. Procedures for IRB/EC communication must be documented in site-specific SOPs. Documentation of all correspondence to and from all responsible IRBs/ECs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in on-site essential document files.

Figure 1-2
IRB/EC Submissions Required Prior to Initiation of MTN 001

Document	Written Approval Required*
MTN 001 Protocol, Version 1.0 MTN 001 Protocol, Version 2.0 <i>Note: Some sites will be required to submit only Version 2.0 of the protocol.</i>	Yes
Informed consent forms: -Screening -Enrollment -Specimen Storage <i>Note: Informed consent forms may contain information on participant incentive amounts and schedules; however incentives may be approved through submission of separate materials.</i>	Yes
Investigator of Record current CV	No
Tenofovir Disoproxil Fumarate (TDF) Investigator's Brochure	No
Tenofovir 1% Vaginal Gel (Tenofovir Gel) Investigator's Brochure	No
Participant recruitment materials (prior to use)	Yes
Other written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/EC	If required by IRB/EC

*Denotes approvals required by US regulations and GCP guidelines.

**Figure 1-3
IRB/EC Submissions Required During and Following Conduct of MTN 001**

Document	Written Approval Required*
Study status reports/updates (at least annually)	Yes
Protocol clarification memos (submission encouraged but not required by DAIDS)	No
Protocol amendments (including full amendments (to a new protocol version) and letters of amendment)	Yes
Amended informed consent forms (including forms that are amended due to protocol amendments as well as forms that are amended for site-specific reasons, e.g., to update participant incentive information or to update site contact information) <i>Note: Informed consent forms may contain information on participant incentive amounts and schedules; however incentives may be approved through submission of separate materials. If incentive information is not presented in the informed consent forms, the supplemental materials must be updated, submitted, and approved prior to modification of the incentive amounts or schedules.</i>	Yes
Tenofovir Disoproxil Fumarate (TDF) Investigator's Brochure updates	No
Tenofovir 1% Vaginal Gel (Tenofovir Gel) Investigator's Brochure updates	No
New information that may affect adversely the safety of study participants or the conduct of the study (e.g., IND Safety Reports) [§]	No
Reports of adverse events, serious adverse events, and/or events meeting criteria for expedited reporting to DAIDS (per IRB/EC requirements)	No
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	No
Investigator of Record current CV (if Investigator of Record changes during study)	No
Updated/additional participant recruitment materials (prior to use)	Yes
Updated/additional written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/EC	If required by IRB/EC
Final study report/closure report	No

*Denotes approvals required by US regulations and GCP guidelines.

[§]Safety information will be distributed by the DAIDS RCC or the MTN CORE. All distributions will include instructions related to IRB/EC submission of the safety information.