Section 1. Introduction

This section specifies the sources of procedural information available to MTN-008 study staff, the responsibilities of MTN-008 Investigators of Record (IoR), and the process by which the study site is approved to begin implementation of MTN-008. 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-008 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-008 Management Team of any such inconsistencies.

Any study implementation questions that arise should be managed as follows:

- Questions related to interpretation and proper implementation of the MTN-008 protocol should be directed to the MTN CORE (FHI): Karen Isaacs at kisaacs@fhi.org.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC): Corey Miller at corey@scharp.org.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the MTN Network Laboratory (NL): Pamela Kunjara at pkunjara@mwri.magee.edu
- When in doubt as to whether questions pertain to protocol interpretation, data collection, or laboratory procedures, contact the MTN-008 Management Team at mtn008mgmt@mtnstopshiv.org.
- 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 Senior Pharmacist: Scharla Estep and Cindy Jacobson at sr72v@nih.gov and rosecj@mwri.magee.edu.

Current contact details for the above-listed contact persons and all MTN-008 colleagues and collaborators can be found in the MTN Directory at:

http://mtnstopshiv.org

1.2 Investigator Responsibilities

MTN-008 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).

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. These SOPs are located at:
http://www.niaid.nih.gov/labsandresources/resources/daidsclinrsrch/Pages/Default.aspx /.

MTN-008 must also 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. The site must file copies of all such regulations, policies, and guidelines in their MTN-008 essential document files (see also Section 3.1).

The IoR must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct MTN-008 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 site will keep copies of the protocol signature page and 1572 on site with their essential documents (See SSP Section 3).

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. The IoR may delegate his/her obligations and responsibilities for conducting MTN-008 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, the study site must obtain approval to conduct MTN-008 from all required regulatory authorities and IRBs/ECs. The site also must complete Protocol Registration procedures with the DAIDS Regulatory Support 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 steps can be found in Section 10 of the MTN MOP. The MTN CORE will issue a Site-Specific Study Activation Notice when all study activation requirements have been met. 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-008. 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.

The study site is encouraged to request that their IRB/ECs acknowledge receipt for all documents submitted to them, and to request that the IRBs/ECs note both the effective date and the expiry dates of all approvals. Before registering your IRB approval letter with the DAIDS Protocol Registration Office, ensure that your site approval letter includes a 45 CFR Part 46, subpart D pediatric risk designation. 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-008

Document	Written Approval Required*
MTN-008 Protocol, Version 1.0	Yes
Informed consent forms: • Screening for Pregnancy Cohort • Screening for Lactation Cohort • Enrollment for Mothers and Infants in Pregnancy Cohort • Enrollment for Women for Lactation Cohort • Screening and Enrollment for Infants in Lactation Cohort • Storage and Future Testing of Specimens	Yes
Investigator of Record current CV	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-008

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)	Yes
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.