

Section 1. Introduction

This section specifies the sources of procedural information available to MTN-007 study staff, the responsibilities of MTN-007 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN-007. Also included is information on required submissions to Institutional Review Boards.

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN-007 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:

- Study staff should contact the [MTN CORE \(FHI\) Clinical Research Manager](#) with all questions related to interpretation and proper implementation of the protocol.
- Questions related to data collection and management should be directed to the MTN CORE [Statistical and Data Management Center \(SDMC\) Project Manager](#).
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the [MTN Network Laboratory \(NL\) Representative](#).
- Questions related to the investigational study products should be directed to the [MTN CORE Pharmacist](#).
- Questions related to the administration of behavioral measures (Baseline Behavioral Questionnaire, the Adherence Questionnaire, and the Product Acceptability Questionnaire) should be directed to mtn007webtrouble@mtnstopshiv.org.

When in doubt as to whether questions pertain to protocol interpretation, data collection or laboratory procedures, contact the MTN-007 Management Team:

mtn007mgmt@mtnstopshiv.org

Site-specific contacts for the MTN CORE, SDMC, NL and study product are listed below.

FHI Clinical Research Manager:	Philip Andrew pandrew@fhi.org tel: 919.544.7040 extension 11213
SDMC Project Manager:	Missy Cianciola missy@ssharp.org tel: 206.667.7290
MTN Network Lab Representative:	Ratiya Pamela Kunjara Na Ayudhya pkunjara@mwri.magee.edu tel: 412.641.6393
MTN CORE Pharmacist:	Cindy Jacobson rosecj@mwri.magee.edu tel: 412.641.8999

Contact information for all other MTN-007 protocol team members can be found in the protocol document or in the MTN directory at <http://www.mtnstopshiv.org>.

1.2 Investigator Responsibilities

MTN-007 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/node/187>

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/ClinicalSite.aspx>

<http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSCLinRsrch/Pages/Regulatory.aspx>

At each site, MTN-007 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-007 essential document files (see also Section 3).

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-007 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 of the MTN MOP. IoRs may delegate their obligations and responsibilities for conducting MTN-007 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-007 from all responsible regulatory authorities and IRBs. Each site also must complete Protocol Registration procedures with the DAIDS Regulatory Support Center (RSC) and study activation procedures with DAIDS and the MTN CORE (FHI), SDMC and NL prior to participant screening procedures. MTN CORE (FHI), SDMC, and NL will assist the sites with pre-implementation activities required for activation. On a site-by-site basis, the MTN CORE (FHI) 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. For additional information, refer to the protocol registration documents located at <http://rsc.tech-res.com/protocolregistration/>. For questions regarding protocol registration, please email

protocol@tech-res.com, fax 1-800-418-3544 or 1-301-897-1701, or phone 1-301-897-1707. Protocol registration must occur as a condition for site-specific study activation. Detailed information on the requirements of these pre-implementation steps is also located in the MTN MOP.

1.4 IRB/EC Submissions

Figures 1-1 and 1-2 list IRB submission and approval requirements pertinent to MTN-007. Figure 1-1 lists requirements that must be met prior to study initiation. Figure 1-2 lists requirements that must be met during and following study implementation.

Each study site must submit all required documents to all responsible IRBs; however IRB approval is not required for all documents. Documents requiring approval per US regulations and GCP guidelines are indicated in Figures 1-1 and 1-2. Additional approvals beyond those indicated in the figures may be required by individual IRBs; in such cases, all required documents must be submitted to and approved by the IRBs. If your IRB does not require submission of certain documents, this must be documented and filed in your site Essential Document files.

Study sites are encouraged to request an acknowledgement of receipt for all documents submitted to the IRBs, and to request that the IRBs note the effective and expiry dates of all approvals. Submissions to your IRB should detail what documents are being forwarded for review. Similarly, replies from your IRB should list the documents that were reviewed and disposition for each document. Procedures for IRB communication must be documented in site-specific SOPs. Documentation of all correspondence to and from all responsible IRBs (i.e., complete copies of all submissions, responses, and approvals) must be maintained in your site Essential Document files.

**Figure 1-1
IRB Submissions Required Prior to Initiation of MTN-007**

Document	Written Approval Required*
MTN-007 Protocol, Version 2.0	Yes
Informed consent forms: -Screening -Enrollment -Storage and Future Testing of Specimens <i>Note: MTN informed consent forms typically contain information on participant incentive amounts and schedule; however, incentives may be approved through submission of separate materials.</i>	Yes
Investigator of Record current CV	No
Investigator's Brochures for Tenofovir gel and HEC placebo gel and the Package Insert for Nonoxynol-9	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	If required by IRB/EC

*Denotes approvals required by US regulations and GCP guidelines.

**Figure 1-2
IRB Submissions Required During and Following Conduct of MTN-007**

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: MTN informed consent forms typically 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
Investigator's Brochures for Tenofovir gel and HEC placebo gel and the Package Insert for Nonoxynol-9	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 CONRAD and the DAIDS MO (per IRB requirements)	No
Protocol departures/deviations/violations (per IRB 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	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 RSC or the MTN CORE. All distributions will include instructions related to IRB submission of the safety information.