Section 1. Introduction

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This section specifies the sources of procedural information available to study staff, the responsibilities of the Investigator of Record (IoR) and the process by which each site will be approved to initiate implementation of MTN-033.

1.1 Current Protocol Specifications

The table below documents the history of the MTN-033 protocol, along with any Clarification Memos, Letters of Amendment, and Full Amendments, if applicable, all of which are considered Essential Documents. A copy of each document should be available to staff and a copy should be maintained in site essential files. It is not necessary for sites to file copies of the below-mentioned documents in the SSP Manual itself.

Document	Date
MTN-033/IPM 044 Protocol, Version 1.0	28 April 2016
MTN-033 Protocol, Version 2.0	08 December 2017
Letter of Amendment #01 for Protocol Version 2.0	26 July 2018

Sites are expected to operate under the protocol version and associated Clarification Memos and/or Letters of Amendment that are currently approved by the local institutional review board/ethics committee (IRB/EC). To ensure this section reflects the current specifications of the protocol, upon issuance of any future protocol Clarification Memo (CM), Letter of Amendment (LoA), or Protocol Amendment, specifications listed above will be updated accordingly. These documents are available on the MTN-033 webpage (http://www.mtnstopshiv.org/node/7333). Further information on the content and required handling procedures for these documents is available in the Microbicide Trials Network (MTN) Manual of Operational Procedures (MOP), which is located on the MTN webpage under 'Resources' (http://www.mtnstopshiv.org/MOP).

1.2 Procedural Information

The Study Specific Procedures (SSP) Manual serves to supplement the protocol. It does not replace or substitute the protocol or its contents. In the event this manual is inconsistent with the information and guidance provided in the protocol, the specifications in the protocol will take precedence. In the event study implementation questions are not adequately addressed by the study protocol or this manual or if inconsistencies between the two documents are identified, please notify the MTN-033 Study Management Team at mtn033mgmt@mtnstopshiv.org.

This group consists of the MTN Director of Pharmacy Affairs and representatives from the Behavioral Research Working Group (BRWG), the Leadership and Operations Center (LOC) – University of Pittsburgh (Pitt) and FHI 360, the Statistical and Data Management Center (SDMC), and the MTN Laboratory Center (LC).

Contact details for all of the above listed individuals are listed in the MTN-033 protocol and are also available in the MTN Directory (http://www.mtnstopshiv.org/people/directory), accessible via the MTN webpage.

1.3 Investigator of Record (IoR) Responsibilities

MTN-033 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonization Consolidated Guidance for Good Clinical Practice (GCP). In addition, MTN-033 must be implemented 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. Copies of all such regulations, policies, and guidelines should be maintained in on-site essential document files.

The Division of AIDS (DAIDS) policies '*Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials*' and '*Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials*' are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations. These resources are available on the NIAID website (https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations) as well as on the MTN website under 'Resources and Links' (http://www.mtnstopshiv.org/resources).

The IoR at the study site must sign a Protocol Signature Page (PSP; Investigator Signature Form) and a U.S. Food and Drug Administration (FDA) Form 1572 to formally indicate his or her agreement to conduct MTN-033 in accordance with the provisions of the study protocol, applicable regulations, and MTN policies. A copy of the PSP can be found in the study protocol. For this protocol, a PSP must be signed by the IoR and uploaded to DPRS for all initial protocol versions, all full protocol amendments, and all letters of amendment (LOAs). The site will keep copies of the PSP(s) and 1572(s) on site with its essential documents.

An IoR may delegate his or her obligations and responsibilities for conducting MTN-033 to other study staff members. However, in doing so, this delegation does not relieve the IoR of his or her ultimate responsibility for all study procedures performed and all study data collected. Delegation of IoR responsibilities must be formally documented throughout the period of study implementation on the site's Delegation of Authority (DoA) log.

The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form itself, which is available on the DAIDS Regulatory Support Center (RSC) website. Updates to the 1572 should be submitted to the DAIDS Protocol Registration Office (PRO), as well as to the MTN Regulatory Department. The IoR is required to complete IoR training every three years, offered by MTN LOC (http://www.mtnstopshiv.org/node/4536), prior to study initiation or prior to assuming responsibility for an ongoing study. Documentation of this training should be filed in site essential documents.

Full responsibility and authority over the protocol by anyone other than the IoR may only take place if an additional 1572 is completed and submitted to DAIDS. Staff regularly involved in the source documentation of safety data or who are delegated to perform critical trial-related procedures should be included on the FDA Form 1572 as a sub-investigator. Such

components may include, but are not limited to, adverse event (AE) assessment, collection of participant safety information, confirmation of participant eligibility, or dispensation of study product.

The IoR is also responsible for managing the process and ensuring that financial disclosure forms are completed (signed and hand dated) for all investigators/subs investigators prior to completing the 1572.

If there is a change in IoR, a revised Form FDA 1572 and a new PSP should be submitted to the DAIDS PRO. Sites should follow guidance in the current Protocol Registration Manual regarding procedures for a change in IoR with the DAIDS PRO. Incoming investigators should also complete IoR Training as well as a new, complete DoA including all study staff. In addition, they may need to complete an electronic financial disclosure via the HANC system; investigators who need to complete a HANC financial disclosure will be contacted by MTN Regulatory with additional guidance. Outgoing investigators should complete the end of study financial disclosure paper form and sign off on all DoA entries. Additionally, the site should notify FHI 360, MTN Regulatory, and its OCSO PO of the change and complete any other documentation requested.

Consistent with the regulations, guidelines, and policies cited above, the site IoR must obtain and maintain IRB/EC approval of MTN-033 throughout the period of study implementation. Detailed information on IRB/EC submission, review, approval, and documentation requirements is in the MTN MOP. The site is encouraged to request an acknowledgement of receipt for all documents submitted to its IRBs/ECs and to request that IRBs/ECs note the effective and expiry dates of all approvals. 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. Documentation of all IRB/EC approvals may also be requested by the MTN LOC.

1.4 Study Activation Process

Prior to commencing active recruitment activities and undertaking any study procedures, the study site must complete the following:

- obtain approval to conduct MTN-033 from all required local regulatory authorities and IRBs/ECs,
- complete protocol registration procedures with the DAIDS RSC Protocol Registration Office (PRO), and
- complete study activation requirements in collaboration with DAIDS, MTN LOC and LC, and the SDMC and be issued a Site-Specific Study Activation Notice.

Detailed information on these procedures can be found in the MTN MOP. MTN LOC will notify the site when all activation requirements have been met by issuing a Site-Specific Study Activation Notice.