Section 1: Introduction

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1. Introduction

This section specifies the sources of procedural information available to study staff, the responsibilities of the Investigators of Record (IoR), and the process by which each site will be approved to initiate implementation of MTN-035.

1.1 Current Protocol Specifications

The table below documents the history of the MTN-035 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 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-035 Protocol, Version 1.0	15 June 2018
Letter of Amendment #01 for Protocol Version 1.0	06 January 2020

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-035 webpage: https://mtnstopshiv.org/research/studies/mtn-035. 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: https://mtnstopshiv.org/resources/manual-operational-procedures.

Note: In order to respond to the developing COVID-19 pandemic, sites may need to rapidly implement practices and procedures that are not in line with the protocol or SSP Manual (e.g., modified visit procedures in the interest of staff/participant safety, conduct of remote visits/procedures, etc.). Sites should communicate with the MTN-039 Management Team about this and document contingency plans related to COVID-19 proactively, to the best of their ability (and retrospectively, as needed).

1.2 Sources of 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.

Electronic versions of the SSP Manual, the MTN-035 protocol, and all other study implementation tools are available on the MTN-035 website: https://mtnstopshiv.org/research/studies/mtn-035

In the event study implementation questions are not adequately addressed by the study protocol or this Manual or if any inconsistencies between the two documents are identified, please notify the MTN-035 Management Team at mtn035mgmt@mtnstopshiv.org. The same group should be contacted for general questions on protocol implementation or study procedures, including clinical, lab, product, and/or CRF procedures. The Management Team should also be consulted for general questions on protocol implementation or study procedures, including clinical, lab, study product, behavioral assessments, and/or CRF and data management procedures. 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), the MTN Laboratory Center (LC), the Protocol Chair and DAIDS Medical Officer.

1.3 Investigator Responsibilities

MTN-035 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) and the International Conference on Harmonisation Consolidated Guidance for Good Clinical Practice (GCP). MTN-035 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 the sites' essential document files.

The Division of AIDS (DAIDS) policies, Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials and Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations.

Each site IoR must sign an Investigator Signature Form (protocol signature page; PSP) and a DAIDS IoR Form to formally indicate his/her agreement to conduct MTN-035 in accordance with the study protocol, applicable US regulations, and MTN policies. A copy of the PSP can be found in the MTN-035 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 hard-copies of the PSP and DAIDS IoR Form on site with their essential documents.

The obligations and responsibilities assumed by the IoR when signing the DAIDS IoR Form and PSP are listed on the forms themselves. Updates to the DAIDS IoR Form should be submitted to the DAIDS Protocol Registration Office (PRO), as well as to MTN Regulatory (mtnregulatory@mtnstopshiv.org) with a short summary of any updates that were made.

All IoRs are also required to complete IoR training every three years, offered by MTN LOC (http://www.mtnstopshiv.org/node/4536), either prior to study initiation or prior to assuming

responsibility for an ongoing study; documentation of this training should be filed in site essential documents.

Consistent with the regulations, guidelines, and policies cited above, the site IoR must obtain and maintain IRB/EC approval of MTN-035 throughout the period of study implementation. Detailed information on IRB/EC submission, review, approval, and documentation requirements is in the MTN MOP. All sites are encouraged to request an acknowledgement of receipt for all documents submitted to their 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 Delegation of Duties

The IoR may delegate his/her obligations and responsibilities for conducting MTN-035 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 on the site's Delegation of Duties (DoD) Log throughout study implementation. Note that no staff member should fulfill the IoR role in the IoR's absence. Full responsibility and authority over the protocol by anyone other than the IoR may only take place if an additional DAIDS IoR Form is completed and submitted to DAIDS.

If there is a change in IoR, a revised DAIDS IoR Form 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 DoD log that includes 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 all DoD entries. Additionally, sites should notify FHI 360, MTN Regulatory, and their OCSO PO of the change and complete any other documentation requested.

Generally, staff who are regularly involved in the source documentation of safety data or are delegated to perform critical trial-related procedures should also be included on the DAIDS IoR Form. Such components may include, but are not limited to, adverse event (AE) assessment, collecting participant safety information, confirming participant eligibility, or dispensing study product. Ultimately, inclusion as a sub-investigator on the DAIDS IoR Form is dependent on the responsibilities that have been delegated to staff and is at the discretion of the IoR.

1.5 Financial Disclosure Forms

Each clinical investigator listed on the DAIDS IoR Form must disclose any financial interests that may be affected by the outcome of the research or attest to the absence of relevant significant financial interests. Per 21 CFR 312.53, a financial disclosure must be completed prior to study involvement. A blank FDF is available on the MTN-035 webpage.

The IoR and Regulatory Coordinator must ensure that financial disclosure forms (FDFs) are completed (signed and hand dated) for all investigators/sub-investigators ***prior*** to study involvement and ***prior*** to completing and signing the DAIDS IoR Form. All items can be entered electronically except for the signature and date. The *'Study start date'* is date on the cover of the most current version of the protocol. The '*Study end date'* is the date of last

follow-up at the site; this section on the FDF form may be left blank until the end of follow-up at the site.

Investigators must submit a new FDF each time an investigator is added to or removed from the DAIDS IoR Form as well as at the completion of all study-specific activities (i.e. the date of the last participant follow-up visit at the study site).

At the beginning of the study and throughout study duration, whenever an FDF is completed, sites should upload the form to the DAIDS Protocol Registration System (DPRS), under the "Other" submission category. Training slides on the requirements for FDF completion may be found at http://www.mtnstopshiv.org/node/1639.

1.6 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MTN-035 from all required regulatory authorities and IRBs/ECs. The site also must complete protocol registration procedures with the DAIDS Regulatory Support Center (RSC) and study activation procedures with DAIDS and with DAIDS and the MTN LOC, the behavioral team, the MTN SDMC, and MTN Laboratory Center (LC). Detailed information on the requirements of these pre-implementation steps can be found in the MTN MOP.

The MTN LOC 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.