# Section 1. Introduction



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This section specifies the sources of procedural information available to study staff, the responsibilities of Investigators of Record (IoR), and the process by which each site will be approved to initiate implementation of MTN-039.

### 1.1 Current Protocol Specifications

The table below documents the history of the MTN-039 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-039 Protocol, Version 1.0 | 06 March 2019 |
| Letter of Amendment #01 for Protocol Version 1.0 | 20 September 2019 |
| Letter of Amendment #02 for Protocol Version 1.0 | 23 March 2020 |
| Letter of Amendment #03 for Protocol Version 1.0 | 24 July 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-039 webpage (https://mtnstopshiv.org/research/studies/mtn-039). 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).

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, 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).

For each visit where modifications due to COVID-19 considerations result in a deviation from the protocol, a single protocol deviation should be reported with "COVID-19" written in the description field, followed by what was modified during the visit. As required, sites should communicate contingency plans and protocol deviations related to COVID-19 to IRBs/ECs/regulatory bodies.

## 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. 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-039 Study Management Team at mtn039mgmt@mtnstopshiv.org. The Management Team should also be consulted for general questions on protocol implementation or study procedures, including clinical, lab, product, behavioral assessments, and/or data or case report form completion 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) and study leadership (Protocol Chair and DAIDS Medical Officer).

## 1.3 Investigator Responsibilities

MTN-039 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). MTN-039 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 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. 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).

Each site IoR must sign an Investigator Signature Form (protocol signature page; PSP) and a U.S. Food and Drug Administration (FDA) Form 1572 to formally indicate his/her agreement to conduct MTN-039 in accordance with the study protocol, applicable US regulations and MTN policies. A copy of the PSP can be found in the MTN-039 protocol. A PSP must be signed by the IoR and uploaded to DPRS for all initial protocol versions, all full protocol amendments, and all Letter of Amendment (LoAs). The site will keep copies of the PSP and 1572(s) on site with their essential documents. The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 and PSP are listed on the forms themselves. Updates to the 1572 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 3 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.

The IoR may delegate his/her obligations and responsibilities for conducting MTN-039 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: 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 1572 is completed and submitted to DAIDS.

Staff regularly involved in the source documentation of safety data or are delegated to perform critical trial related procedures should be included on the 1572 as a sub-investigator. Such components may include, but are not limited to, adverse event (AE) assessment, provision of informed consent, 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 FDA Form 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 DoD 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. Additionally, sites should notify FHI 360, MTN Regulatory, and their OCSO Program Officer 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-039 throughout the period of study implementation. Detailed information on IRB/EC submission, review, approval, and documentation requirements is located 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 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MTN-039 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 the Study Management Team.

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.