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-045.

1.1 Current Protocol Specifications

The table below documents the version history of the MTN-045 protocol, along with any Clarification Memos and Letters of Amendment, if applicable, all of which are considered Essential Documents. 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, the table will be updated accordingly. These documents are available on the MTN-045 webpage (https://mtnstopshiv.org/research/studies/mtn-045).

Document	Date
MTN-045 Protocol, Version 1.0	25 February 2019
Clarification Memo #01 for Protocol Version 1.0	27 May 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). A copy of each document should be available to staff and a copy should be maintained in site essential files. 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 (http://www.mtnstopshiv.org/MOP).

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., paused visit procedures in the interest of staff/participant safety, conduct of remote study activities such as transcription and QA/QC procedures, etc.). Sites should communicate with the MTN-045 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 Procedural Information

This 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-045 Study Management Team at mtn045mgmt@mtnstopshiv.org.

The MTN-045 Study Management Team consists of the Protocol Chairs and representatives

from the MTN Leadership and Operations Center (LOC)-University of Pittsburgh (Pitt) and FHI 360, Research Triangle International (RTI), the DAIDS Medical Officer, NIMH and the study sites. Sites should contact this group for general questions on protocol implementation or study procedures.

Contact details for the above-listed individuals are listed in the MTN-045 protocol and are also available in the MTN Directory, which is accessible via the MTN webpage (http://www.mtnstopshiv.org/people/directory).

1.3 Investigator of Record (IoR) Responsibilities

MTN-045 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-045 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 also available on the MTN website under 'Resources and Links' (http://www.mtnstopshiv.org/resources).

The IoR at each study site must sign an Investigator Signature Form (Protocol Signature Page [PSP]) and a DAIDS IoR Form to formally indicate his/her agreement to conduct MTN-045 in accordance with the provisions of the study protocol, applicable US regulations, and MTN policies. The obligations and responsibilities assumed by the IoR when signing the DAIDS IoR Form are listed on the form itself, which is available on the DAIDS Regulatory Support Center (RSC) website. 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. A PSP must be signed by the IoR and uploaded to DPRS for all initial protocol versions, all full protocol amendments, and all LOAs.

An IoR may delegate his or her obligations and responsibilities for conducting MTN-045 procedures to other study staff members. However, in doing so, this 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 the period of study implementation on the site's Delegation of Duties (DoD) Log. DoD Logs must meet standards as outlined in the DAIDS **Delegation of Duties Log Policy**. Sites must employ the DAIDS-provided DoD template and should reference the related instructions.

Consistent with the regulations, guidelines, and policies cited above, the site IoR must obtain and maintain IRB/EC approval of MTN-045 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 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 Leadership and Operation Center (LOC).

Note: Guidance outlined in the current DAIDS Protocol Registration Manual regarding which staff should be included on the DAIDS IoR form as sub-investigators should be followed. The manual outlines that staff who make a "direct and significant contribution to the data" should be included as sub-investigators. This includes "site personnel who have more than minimal involvement with the conduct of the research (performing study evaluations or procedures or providing intervention) or more than minimal study conduct-related contact with study

participants or confidential study data, records, or specimens." The CRS Leader should be included as a sub-investigator if this individual is not also the IoR at the site.

If there is a change in IoR after study activation, a revised DAIDS IoR Form and a new PSP should be submitted to the DAIDS Protocol Registration Office (PRO). Sites should follow guidance in the current DAIDS Protocol Registration Manual regarding procedures for a change in IoR with the DAIDS PRO. Incoming investigators should also complete IoR training and document the change in IoR on the study DoD log (per DAIDS' instructions). In addition, they may need to complete an electronic financial disclosure form via the HANC system; investigators who need to complete a HANC financial disclosure will be contacted by MTN Regulatory with additional guidance. Outgoing investigators sign off all DoD Log entries. Additionally, sites should notify FHI 360, MTN Regulatory, and their OCSO PO of the change and complete any other documentation requested.

1.4 Study Activation Process

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

- obtain approval to conduct MTN-045 from all required local regulatory authorities and IRBs/ECs,
- complete protocol registration procedures with the DAIDS RSC PRO, and
- complete study activation requirements, and be issued a Site-specific Study Activation Notice from MTN LOC.

Information on these procedures can be found in the MTN MOP. Detailed information on the requirements of pre-implementation steps are summarized in the MTN-045 Activation Checklist. FHI 360 will notify sites (on a site-by-site basis), when all activation requirements have been met by issuing a Site-Specific Study Activation Notice.

1.5 IRB/EC Submissions

Figure 1-1 lists IRB/EC submission and approval requirements pertinent to MTN-045. The study sites are encouraged to request that their IRBs/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. Procedures for IRB/EC communication must be documented in site-specific Standard Operating Procedures (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. Documentation of all IRB/EC approvals may also be requested by the MTN LOC.

Figure 1-1: IRB/EC Submissions Required for MTN-045

Documents to be submitted to IRB/EC	Written Approval Required*
Prior to study initiation:	
MTN-045 Protocol, Version 1.0	Yes
Informed Consent Forms: • Screening/Enrollment	Yes
Investigator of Record current CV	No
Participant pre-screening, recruitment plans and materials (prior to use)	Yes
Other written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/EC such as SOPs, CRFs, and interview questionnaires.	If required by IRB/EC

During and following conduct of the study:	
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
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	No
New information that may adversely affect the safety of study participants or the conduct of the study	No
Investigator of Record current CV (if IoR changes during study)	No
Updated/additional participant recruitment plans and 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.