

Section 1. Introduction

This section specifies the sources of procedural information available to MTN-015 study staff, the responsibilities of MTN-015 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN-015.

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN-015 protocol. 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-015 management team of any such inconsistencies.

Study implementation questions that are not answered by the protocol, or this manual, should be directed to the MTN-015 Study Management Team. This group consists of representatives of the MTN Leadership and Operations Center (LOC; FHI 360), MTN Statistical and Data Management Center (SDMC), and the MTN Laboratory Center (LC), and can be reached using the following email address:

mtn015mgmt@mtnstopshiv.org

Questions related to interpretation of study examination findings or laboratory test results, and/or clinical management of study participants, should be directed to the MTN-015 Clinical Management Group, using the following email address:

mtn015ClinMgt@mtnstopshiv.org

Current contact details for all MTN-015 colleagues and collaborators, as well as study alias lists, can be found in the MTN directory at:

<http://www.mtnstopshiv.org/people/directory>

1.2 Investigator Responsibilities

MTN-015 must be conducted in accordance with the United States 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 can be accessed on the MTN web site.

www.mtnstopshiv.org

The DAIDS policies on *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 regulations and guidelines in accordance with DAIDS expectations. These policies can be accessed at:

<https://www.niaid.nih.gov/research/daids-clinical-site-implementation-operations>

MTN-015 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. Copies of all such regulations, policies, and guidelines should be maintained in on-site MTN-015 essential document files (see also Section 3.1 of this manual).

The IoR at each study site must sign both a DAIDS Investigator of Record Agreement and Investigator Signature Page (protocol signature page) to formally indicate his/her agreement to conduct MTN-015 in accordance with the study protocol and applicable regulations, guidelines, and policies. A copy of the protocol signature page (PSP) can be found in the MTN-015 protocol. Effective 1 August 2017, 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). Sites will be contacted by the management team with additional guidance regarding retrospective uploading of PSPs for ongoing protocols to DPRS. The site will keep copies of the protocol signature page(s) and DAIDS IoR Agreement forms on site with their essential documents.

The obligations and responsibilities assumed by the IoR when signing the DAIDS Investigator of Record Agreement and protocol signature page (PSP) are listed on the forms. Updates to the DAIDS IoR Agreement should be submitted to the DAIDS Protocol Registration Office (PRO), as well as to MTN Regulatory Department (mtnregulatory@mtnstopshiv.org) with a short summary of any updates that were made. All IoRs are required to complete IoR training offered by MTN LOC (<https://vimeo.com/175516381>); documentation of this training should be filed in site essential documents. IoRs may delegate their obligations and responsibilities for conducting MTN-015 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 Authority (DoA) log throughout the period of study implementation.

If there is a change in IoR, a revised DAIDS IoR Agreement 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 sign off all DoA entries. Additionally, sites should notify FHI 360, MTN Regulatory, and their OCSO PO of the change and complete any other documentation requested.

Consistent with the regulations, guidelines, and policies cited above, the IoR at each study site must obtain and maintain institutional review board and/or ethics committee (IRB/EC) approval of MTN-015 throughout the period of study implementation. See Section 10 of the MTN MOP for detailed information on IRB/EC submission, review, approval, and documentation requirements. 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.

1.3 Study Activation Process

Prior to undertaking any study procedures, each study site must obtain approval to conduct MTN-015 from all responsible regulatory authorities and IRBs/ECs. Each site also must complete protocol registration procedures with the DAIDS Regulatory Support Center Protocol Registration Office and study activation procedures with DAIDS and the MTN CORE, MTN SDMC, and MTN LC. Detailed information on the requirements of these pre-implementation steps can be found in Section 12 of the MTN MOP. On a site-by-site basis, the MTN CORE 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.