Section 1. Introduction

This section specifies the sources of procedural information available to MTN-012/IPM 010 study staff, the responsibilities of MTN-012/IPM 010 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN-012/IPM 010.

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN-012/IPM 010 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-012/IPM 010 Study Management Team (described below) of any such inconsistencies.

Study implementation questions that are not answered by the protocol, or this manual, should be directed to the MTN-012/IPM 010 Study Management Team. This group consists of representatives of the MTN Coordinating and Operations Center (CORE; FHI), Statistical and Data Management Center (SDMC), Network Laboratory (NL), and the MTN Pharmacist, and can be reached using the following email address:

mtn012mgmt@mtnstopshiv.org

Per the specifications of Section 8 of this manual, questions related to participant clinical eligibility, study product use management, adverse event reporting, and adverse event management should be directed to the MTN-012/IPM 010 Protocol Safety Physicians using the following email address:

mtn012safetymd@mtnstopshiv.org

1.2 Investigator Responsibilities

MTN-012/IPM 010 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. Copies of these regulations and guidelines are referenced in the MTN Manual of Operations (MOP) which can be accessed at:

http://www.mtnstopshiv.org/node/187

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:

http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch

MTN-012/IPM 010 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 essential document files (see also Section 3.1 of this manual).

The IoR at each site must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct MTN-012/IPM 010 in accordance with the study protocol and all applicable regulations, policies, and guidelines. The protocol signature page can be found in Section 2 of this manual. The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form. IoRs may delegate their obligations and responsibilities for conducting MTN-012/IPM 010 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 throughout the period of study implementation.

Consistent with the regulations, guidelines, and policies cited above, the IoR at each site must obtain and maintain institutional review board and/or ethics committee (IRB/EC) approval of MTN-012/IPM 010 throughout the period of study implementation. See Section 8.4 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 site must obtain approval to conduct MTN-012/IPM 010 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, FHI, SDMC, NL, and the MTN Pharmacist. Detailed information on the requirements of these pre-implementation steps can be found in Section 10 of the MTN MOP. On a site-by-site basis, the MTN CORE (FHI) 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.