Section 1. Introduction

This section specifies the sources of procedural information available to study staff, the responsibilities of Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN-013/IPM 026. Also included is information on required submissions to Institutional Review Boards (IRBs).

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN-013/IPM 026 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 Study Management Team of any inconsistencies found.

Study implementation questions that are not addressed by the protocol or within this manual, should be directed to the study management team using the designated email address below. This group consists of representatives of the MTN Coordinating and Operations Center (CORE; Family Health International (FHI360)), Statistical and Data Management Center (SDMC), MTN Core Pharmacist, and Network Laboratory (NL) and can be reached using the following email address:

mtn013mgmt@mtnstopshiv.org

Per the specifications of Sections 10 and 11 of this manual, questions related to participant eligibility, study product use management, adverse event reporting, and adverse event management should be directed to the Protocol Safety Review Team (PSRT) using the following email address:

mtn013psrt@mtnstopshiv.org

Questions related to investigational study product supply, accountability, and/or dispensing should be directed to the MTN Director of Pharmacy Affairs. Contact details for both the MTN Core Pharmacist as well as all of the above listed individuals are listed in the MTN-013/IPM 026 protocol and are available in the MTN Directory, which can be accessed at:

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

1.2 Investigator Responsibilities

MTN-013/IPM 026 must be conducted in accordance with the United States (US) 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 Operational Procedures (MOP) which is available at:

http://mtnstopshiv.org/node/187

The Division of AIDS (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 applicable regulations and guidelines in accordance with DAIDS expectations. Copies of these policies are located on the DAIDS Clinical Research Policies and Standard Procedures Documents webpage:

http://www.niaid.nih.gov/labsandresources/resources/daidsclinrsrch/pages/default.aspx

MTN-013/IPM 026 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.

The Investigator of Record (IoR) at each study site must sign both an *Investigator Signature Form* (protocol signature page) and a *FDA Form 1572* to formally indicate his/her agreement to conduct MTN-013/IPM 026 in accordance with the provisions of the study protocol, applicable US regulations, and MTN policies. A copy of the *Investigator Signature Form* can be found in the protocol as well as in Section 2 of this manual. IoRs may delegate their obligations and responsibilities for conducting MTN-013/IPM 026 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. The obligations and responsibilities assumed by the IoR when signing the *FDA Form 1572* are listed on the form itself, which is available on the DAIDS Regulatory Support Center (RSC) web site:

http://rsc.tech-res.com/Document/protocolregistration/Form_FDA_1572.pdf

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-013/IPM 026 throughout the period of study implementation. See Section 9.4 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 study site must obtain approval to conduct MTN-013/IPM 026 from their local regulatory authorities and IRBs/ECs. After receiving final approval from their local IRB/EC, each site also must complete protocol registration procedures with the DAIDS Regulatory Support Center Protocol Registration Office and study activation procedures with the MTN CORE (FHI360), SDMC, NL and the DAIDS. Detailed information on the requirements of these pre-implementation procedures can be found in Section 11 of the MTN MOP. On a site by site basis, MTN CORE (FHI360) will notify sites when all activation requirements have been met by issuing a *Site-Specific Study Activation Notice*. At each site, no protocol-specified study procedures may be undertaken prior to issuance of the Site-Specific Study Activation Notice.