

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 MTN Coordinating and Operations Center (CORE) staff at Family Health International (FHI) of any such inconsistencies.

Any study implementation questions that arise should be managed as follows:

- Questions related to interpretation and proper implementation of the MTN-015 protocol should be directed to the MTN CORE (FHI) Clinical Research Manager: Lisa Levy.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC) Project Manager: Missy Cianciola.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the MTN Network Laboratory (NL) representative: Edward (Ted) Livant.
- When in doubt as to whether questions pertain to protocol interpretation, data collection, or laboratory procedures, contact the MTN CORE (FHI) Clinical Research Manager.
- 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 the above-listed persons and all MTN-015 colleagues and collaborators can be found in the directory on the MTN web page:

www.mtnstopshiv.org/people/directory

Several reference documents and curricula that MTN-015 study staff may find useful are listed in Figure 10.1 below. Many of these documents were provided to all sites during study-specific training; please contact the MTN CORE if assistance is needed to obtain additional copies.

Figure 1-1
Reference Documents Applicable to MTN-015

Case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children (WHO, 2006)

Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings: recommendations for a public health approach (WHO, 2006)

Antiretroviral therapy for HIV infection in adults and adolescents in resource-limited settings: towards universal access: recommendations for a public health approach (WHO, 2006)

Addendum to 2006 guidelines on antiretroviral therapy for HIV infection in adults and adolescents: new dosage recommendations for stavudine (WHO)

Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access: recommendations for a public health approach (WHO, 2006)

HIV and infant feeding (WHO/UNAIDS/UNICEF, 2007)

HIV, nutrition, and food: a practical guide for technical staff and clinicians (Family Health International, 2008)

Nursing care of patients with HIV (training curriculum; Family Health International, 2008)

Family planning: a global handbook for providers (WHO/USAID/Johns Hopkins Bloomberg School of Public Health, 2007)

Medical eligibility criteria for contraceptive use (WHO, 2004)

Contraception for Women and Couples with HIV (training curriculum; Family Health International, 2008)

Hormonal contraception and HIV (Family Health International, 2007)

Sexually transmitted diseases treatment guidelines: cervical cancer screening for women who attend STD clinics or have a history of STD (CDC, 2006)

2006 consensus guidelines for the management of women with abnormal cervical cancer screening tests (Wright et al, AJOG, 2007)

The 2001 Bethesda system: terminology for reporting results of cervical cytology (Solomon et al, JAMA, 2002)

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:

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

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 a DAIDS Investigator of Record Agreement to formally indicate his/her agreement to conduct MTN-015 in accordance with the study protocol and applicable regulations, guidelines, and policies. The obligations and responsibilities assumed by the IoR when signing the DAIDS Investigator of Record Agreement are listed on the form. 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 throughout the period of study implementation.

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 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 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 Compliance Center Protocol Registration Office and study activation procedures with DAIDS and the MTN CORE, MTN SDMC, and MTN NL. 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 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.