Section 1. Introduction

This section specifies the sources of procedural information available to MTN-016 study staff, the responsibilities of MTN-016 Investigator of Record (IoR), and the process by which the study site is approved to begin implementation of MTN-016. Also included is information on required submissions to Institutional Review Boards and/or Ethics Committees (IRBs/ECs).

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN-016 protocol (see Section 2). 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-016 management team (mtn016mgmt@mtnstopshiv.org) 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-016 protocol should be directed to the MTN-016 management team.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC): Laura McKinstry at lmckinst@scharp.org.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the MTN Laboratory Center (LC): Urvi Parikh at ump3@pitt.edu and Pam Kunjara at kunjaranaayudhyarp@upmc.edu.
- When in doubt as to whether questions pertain to protocol interpretation, data collection, or laboratory procedures, contact the MTN CORE at mtn016mgmt@mtnstopshiv.org .

Current contact details for the above-listed contact persons and all MTN-016 colleagues can be in the MTN Directory at:

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

1.2 Investigator Responsibilities

MTN-016 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 Operations (MOP). The MTN MOP is located at:

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

The Division of AIDS (DAIDS) Standard Operating Procedures (SOPs) for Essential Documents and Source Documentation are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations. These SOPs are located under the 'Regulatory' and 'Clinical Site' links, respectively, at:

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

MTN-016 must also 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. Each site must file copies of all such regulations, policies, and guidelines in their MTN-016 essential document files (see also Section 3.1).

The IoR at each site must sign both a protocol signature page (PSP) and a DAIDS Investigator of Record Agreement Form (http://rcc.tech-res.com/forms.htm) to formally indicate his/her agreement to conduct MTN-016 in accordance with the study protocol, applicable US regulations, and MTN policies. 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 IoR agreement and 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. The IoR may delegate his/her obligations and responsibilities for conducting MTN-016 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 study implementation.

Current CVs for the IoR, PI, SC, and Pediatrician(s) for MTN-016 should be forwarded to MTN Regulatory.

1.3 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MTN-016 from all required regulatory authorities and IRBs/ECs. The site also must complete Protocol Registration procedures with the DAIDS Regulatory Compliance Center 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. No protocol-specified study procedures may be undertaken prior to issuance of the Site-Specific Study Activation Notice.

1.4 IRB/EC Submissions

Figures 1-1 and 1-2 list IRB/EC submission and approval requirements pertinent to MTN-016. Figure 1-1 lists IRB/EC requirements that must be met prior to study initiation. Figure 1-2 lists IRB/EC requirements that must be met during and following study implementation.

Each study site is encouraged to request their IRB/ECs acknowledge receipt for all documents submitted to them, and to request that the IRBs/ECs note the effective date and the expiry dates of all approvals. Procedures for IRB/EC communication must be documented in site-specific 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.

Figure 1-1
IRB/EC Submissions Required Prior to Initiation of MTN-016

Document	Written Approval Required*
MTN-016 Protocol	Yes
Informed consent forms (for Screening and Enrollment of Woman and Infant and for Infant Testing) and associated Comprehension Checklists, with translations and back-translations): *Note: Informed consent forms may contain information on participant incentive amounts and schedules; however incentives may be approved through submission of separate materials.*	Yes
Investigator of Record current CV	No
Participant recruitment materials (prior to use)	Yes
Other written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/EC	If required by IRB/EC

*Denotes approvals required by US regulations and GCP guidelines.

Figure 1-2
IRB/EC Submissions Required During and Following Conduct of MTN-016

Document	Written Approval Required*
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/ Comprehension Checklists (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) *Note: Informed consent forms may contain information on participant incentive amounts and schedules, however incentives may be approved through submission of separate materials. If incentive information is not presented in the informed consent forms, the supplemental materials must be updated, submitted, and approved prior to modification of the incentive amounts or schedules.*	Yes
New information that may affect adversely the safety of study participants or the conduct of the study (e.g., IND Safety Reports)§	No
Reports of adverse events, serious adverse events, and/or events meeting criteria for expedited reporting to DAIDS (per IRB/EC requirements)	No
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	No
Investigator of Record current CV (if Investigator of Record changes during study)	No
Updated/additional participant recruitment 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.
§Safety information will be distributed by the DAIDS RCC or the MTN CORE. All distributions will include instructions related to IRB/EC submission of the safety information.