Section 1. Introduction

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This section specifies the sources of procedural information available to MTN-020 study staff, the responsibilities of MTN-020 Investigators of Record (IoR), and the process by which the study site is approved to begin implementation of MTN-020. 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-020 protocol and this manual. 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-020 management team of any such inconsistencies.

Electronic versions of this manual, the MTN-020 protocol, and all other study implementation tools are available on the ASPIRE website:

http://www.mtnstopshiv.org/studies/3614

Note that all study documents can be searched electronically for key words and phrases using the "find" feature (CTRL+F). Sites are encouraged to become familiar with electronic searching to make specific guidance easier to locate in the study documents.

Please contact the MTN-020 management team using the following alias list for general questions on protocol implementation or study procedures, including clinical, lab, product, and/or CRF procedures:

mtn020mgmt@mtnstopshiv.org

Current contact details for all MTN-020 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-020 must be conducted in accordance with the United States (US) Code of Federal Regulations (CFR) 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 Division of AIDS (DAIDS) policies *Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials* and *Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials* are useful for interpreting and operationalizing the applicable regulations and guidelines in accordance with DAIDS expectations. These policies are posted on the MTN website under *Resources and Links*: http://www.mtnstopshiv.org/resources.

MTN-020 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. The site must file copies of all such regulations, policies, and guidelines in their MTN-020 essential document files (see also Section 3.1).

The IoR must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct MTN-020 in accordance with the study protocol, applicable US regulations, and MTN policies. A copy of the protocol signature page can be found in the MTN-020 protocol. The site will keep copies of the protocol signature page and 1572 on site with their essential documents (See SSP Section 3.1).

The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form itself, also outlined in 3.4.4 of the MTN MOP. Updates to the 1572 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 CORE, either prior to ASPIRE activation or upon assuming this role; documentation of this training should be filed in site essential documents. The IoR may delegate his/her obligations and responsibilities for conducting MTN-020 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.

1.2.1 Sub-Investigators Listed on the FDA Form 1572

Staff who are regularly involved in the source documentation of safety data, or are delegated to perform critical trial related procedures should also be included on the FDA Form 1572. Such components may include, but are not limited to, Adverse Event (AE) assessment, collecting participant safety information, confirming participant eligibility, or dispensing study product. See Operational Guidance #3 for additional information.

1.3 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MTN-020 from all required regulatory authorities and IRBs/ECs. The site also must complete protocol registration procedures with the DAIDS Regulatory Support Center (RSC) and study activation procedures with DAIDS and the MTN CORE, MTN SDMC, and MTN Laboratory Center (LC). Detailed information on the requirements of these pre-implementation steps can be found in Section 11 of the MTN MOP. 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-020. Figure 1-1 lists requirements that must be met prior to study initiation. Figure 1-2 lists requirements that must be met during and following study implementation.

The study site is encouraged to request that their IRB/ECs acknowledge receipt for all documents submitted to them, and to request that the IRBs/ECs note both 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-020

Documents to be submitted to IRB/EC	Written Approval Required*
MTN-020 Protocol, Version 1.0	Yes
Informed consent forms: • Consent for Screening • Consent for Enrollment • *If not within the enrollment consent:* Storage and Future Testing of Specimens, Off-Site Visits, IDIs and Focus Group Discussions (if applicable)	Yes
Investigator of Record current CV	No
Dapivirine Vaginal Ring Investigator's Brochure	No
Participant pre-screening, recruitment plans and materials (prior to use)	Yes
Other written information for study participants (prior to use)	Yes
Other documentation required/requested by the IRB/EC such as SOPs, CRFs, and interview questionnaires.	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-020

Document to be submitted to IRB/EC	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 (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)	Yes
Dapivirine Vaginal Ring Investigator's Brochure updates	No
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 plans and 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 RSC or the MTN CORE. All distributions will include instructions related to IRB/EC submission of the safety information.