Section 1. Introduction

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This section specifies the sources of procedural information available to MTN 023/IPM 030 study staff, the responsibilities of MTN 023/IPM 030 Investigators of Record (IoR), and the process by which the study site is approved to begin implementation of MTN 023/IPM 030. Also included is information on required submissions to Institutional Review Boards and/or Ethics Committees (IRBs/ECs).

1.1 Protocol Specifications

The table below documents the history of the MTN 023/IPM 030 protocol, along with Clarification Memos, Letter of Amendments, and Full Amendments. These documents are considered Essential Documents. A copy of each document should be available to staff and a copy should be maintained in site essential files. It is not necessary for sites to file copies of the below-mentioned documents in this manual.

Document	Date
MTN 023/IPM 030 Protocol, Version 1.0	23 October 2013
Protocol Version 1.0, Letter of Amendment #01	15 April 2014
Protocol Version 1.0, Clarification Memo #01	19 May 2014
MTN 023/IPM 030 Protocol, Version 2.0	14 January 2015
Protocol Version 2.0, Letter of Amendment #01	16 February 2016

Sites are expected to operate under the protocol version and associated Clarification Memos and/or Letters of Amendment that are currently approved by the local ethics committee/institutional review board of the given site. To ensure this section reflects the current specifications of the protocol, upon issuance of any future protocol Clarification Memo (CM), Letter of Amendment (LoA), or Protocol Amendment, specifications listed above will be updated accordingly.

Further information on the content and required handling of protocol clarification memos, letters of amendment, and full amendments is available in Section 10.2 of the MTN Manual of Operational Procedures (http://www.mtnstopshiv.org/node/187).

1.2 Sources of Procedural Information

All study procedures must be conducted in accordance with the MTN 023/IPM 030 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 023/IPM 030 Management Team of any such inconsistencies.

Electronic versions of this manual, the MTN 023/IPM 030 protocol, and all other study implementation tools are available on the MTN 023/IPM 030 website:

http://www.mtnstopshiv.org/studies/5223

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 023/IPM 030 Management Team using the following alias list for general questions on protocol implementation or study procedures, including clinical, lab, product, and/or CRF procedures:

mtn023mgmt@mtnstopshiv.org

Current contact details for all MTN 023/IPM 030 colleagues and collaborators, as well as study alias lists, can be found in the MTN Directory at:

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

1.3 Investigator Responsibilities

MTN 023/IPM 030 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 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/node/4537.

MTN 023/IPM 030 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 023/IPM 030 essential document files (see also Section 2.1).

The IoR must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct MTN 023/IPM 030 in accordance with the study protocol, applicable US regulations, and MTN/ATN policies. A copy of the protocol signature page can be found in the protocol. The site will keep copies of the protocol signature page and 1572 on site with their essential documents (See SSP Section 2.1).

The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form itself, also outlined in 3.4.3 of the MTN MOP. ATN sites should submit updates on the 1572 to Westat Regulatory. MTN sites should submit updates to the DAIDS PRO, as well as to MTN Regulatory Department (mtnregulatory@mtnstopshiv.org) with a short summary of any updates that were made. The IoR may delegate his/her obligations and responsibilities for conducting MTN 023/IPM 030 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 log throughout study implementation.

1.3.1 Sub-Investigators Listed on the FDA Form 1572

Per the DAIDS Protocol Registration Procedures Manual all study staff at a CRS that are responsible for making a direct and significant contribution to the data must be listed as a sub-investigator on the FDA Form 1572. This includes site personnel who have more than minimal involvement with the conduct of the research (performing study evaluations or procedures or providing intervention) or more than minimal study conduct-related contact with study participants or confidential study data, records, or specimens. Individuals who will sign study medication prescriptions and physicians who submit SAE/EAEs to DAIDS must be listed on the Form FDA 1572. The DAIDS Protocol Registration Procedures Manual can be accessed via the DAIDS RSC website at the following: http://rsc.tech-res.com/protocolregistration/.

1.4 Study Activation Process

Prior to undertaking any study procedures, the study site must obtain approval to conduct MTN 023/IPM 030 from all required regulatory authorities and IRBs/ECs.

- MTN sites must complete Protocol Registration procedures with the DAIDS Regulatory Support Center.
- ATN sites must complete Protocol Registration procedures through Westat. Westat will confirm this process by registering the ATN sites in the DAIDS PRO system.

Study Activation procedures will be completed in conjunction with DAIDS or Westat and with the MTN LOC, MTN SDMC, and MTN LC. Detailed information on the requirements of these pre-implementation steps will be summarized in the Activation Checklist.

The MTN LOC will issue a Site-Specific Study Activation Notice for all sites 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.

1.5 IRB/EC Submissions

Figures 1-1 and 1-2 list IRB/EC submission and approval requirements pertinent to MTN 023/IPM 030. 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.

Detailed information on IRB/EC submission, review, approval, and documentation requirements is located in Section 9.4 of the MTN MOP. All sites must 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. 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. Documentation of all IRB/EC approvals must also be submitted to the MTN LOC and Westat.

Figure 1-1: IRB/EC Submissions Required Prior to Initiation of MTN 023/IPM 030

Documents to be submitted to IRB/EC	Written Approval Required*
MTN 023/IPM 030 Current Protocol Version	Yes
Informed consent forms: • Informed Assent & Parent/Guardian Permission Form (Screening, Enrollment, and Long -Term Storage) • *If not within the enrollment consent:* Consent for Storage and Future Testing of Specimens	Yes
Investigator of Record current CV	No
Dapivirine Vaginal Ring Investigator's Brochure	If required by the IRB/EC
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 023/IPM 030

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)	If required by the IRB/EC
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	If required by the IRB/EC
New information that may affect adversely the safety of study participants or the conduct of the study (e.g., IND Safety Reports)§	If required by the IRB/EC
Reports of adverse events, serious adverse events, and/or events meeting criteria for expedited reporting to DAIDS (per IRB/EC requirements)	If required by the IRB/EC
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	If required by the IRB/EC
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	If required by the IRB/EC

*Denotes approvals required by US regulations and GCP guidelines.
§Safety information will be distributed by the DAIDS RSC or the MTN LOC. All distributions will include instructions related to IRB/EC submission of the safety information.