Section 1. Introduction

This section specifies the sources of procedural information available to HPTN 035 study staff, the responsibilities of HPTN 035 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of HPTN 035. Also included is information on required submissions to Institutional Review Boards and/or Ethics Committees (IRBs/ECs).

NOTE: Effective with Version 2.0 of this section, prior references to the HIV Prevention Trials Network (HPTN) have been replaced where applicable with references to the Microbicide Trials Network (MTN).

1.1 Sources of Procedural Information

All study procedures must be conducted in accordance with the HPTN 035 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 Coordinating and Operations Center (CORE) of any such inconsistencies.

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

- Questions related to interpretation and proper implementation of the HPTN 035 protocol should be directed to the MTN CORE: Anne Coletti, Kailazarid Gomez, and Robbyn Lewis.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC): Missy Cianciola and Corey Leburg.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the HPTN Network Laboratory (NL), Estelle Piwowar-Manning, and MTN NL, Lorna Rabe.
- When in doubt as to whether questions pertain to protocol interpretation, data collection, or laboratory procedures, contact the MTN CORE.
- Questions related to the investigational study products should be directed by the study site Pharmacist of Record to the DAIDS Protocol Pharmacist: Scharla Estep.

Current contact details for the above-listed contact persons and all HPTN 035 colleagues and collaborators can be found in the HPTN Directory at:

http://www.hptn.org/network_information/network_directory.asp

A listing of frequently asked questions for HPTN 035 can be found on the HPTN web site at:

http://www.hptn.org/research_studies/HPTN035QuestionsAndAnswers.htm

1.2 Investigator Responsibilities

HPTN 035 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 HPTN Manual of Operations (MOP) which is available at:

http://www.hptn.org/network_information/policies_procedures.htm

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. Copies of these SOPs are provided in Section 16 of this manual.

At each site, HPTN 035 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. Each site should file copies of all such regulations, policies, and guidelines in their HPTN 035 essential document files (see also Section 3.1).

The IoR at each study site must sign both a protocol signature page and an FDA Form 1572 to formally indicate his/her agreement to conduct HPTN 035 in accordance with the study protocol, applicable US regulations, and HPTN policies. A copy of the protocol signature page can be found in the protocol in Section 2 of this manual. The obligations and responsibilities assumed by the IoR when signing the FDA Form 1572 are listed on the form itself, which can be found in Section 3.4 of the HPTN MOP. IoRs may delegate their obligations and responsibilities for conducting HPTN 035 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 study implementation.

1.3 Study Activation Process

Prior to undertaking any study procedures, each study site must obtain approval to conduct HPTN 035 from all responsible regulatory authorities and IRBs/ECs. Each 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 HPTN and MTN NLs. Detailed information on the requirements of these pre-implementation steps can be found in Section 10 of the HPTN 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.

1.4 IRB/EC Submissions

Figures 1-2 and 1-3 list IRB/EC submission and approval requirements pertinent to HPTN 035. Figure 1-2 lists requirements that must be met prior to study initiation. Figure 1-3 lists requirements that must be met during and following study implementation.

Each study site must submit all required documents to all responsible IRBs/ECs; however IRB/EC approval is not required for all documents. Documents requiring approval per US regulations and GCP guidelines are indicated in Figures 1-2 and 1-3. Additional approvals beyond those indicated in the figures may be required by individual IRBs/ECs; in such cases, all required documents must be submitted to and approved by the IRBs/ECs.

Study sites are encouraged to request an acknowledgement of receipt for all documents submitted to the IRBs/ECs, and to request that the 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.

Figure 1-2
IRB/EC Submissions Required Prior to Initiation of HPTN 035

Document	Written Approval Required*
HPTN 035 Protocol, Version 2.0	Yes
Informed consent forms: -Screening Phase II/IIb (with/without colposcopy as applicable) -Screening Phase IIb -Enrollment II/IIb (with/without colposcopy as applicable) -Enrollment IIb -Specimen Storage *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
BufferGel Investigator's Brochure	No
PRO 2000/5 Gel (P) Investigator's Brochure	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 1-3
IRB/EC Submissions Required During and Following Conduct of HPTN 035

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 (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
BufferGel Investigator's Brochure updates	No
PRO 2000/5 Gel (P) 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 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.