Section 1. Introduction

This section specifies the sources of procedural information available to HPTN 059 study staff, the responsibilities of HPTN 059 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of HPTN 059. 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 HPTN 059 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 HPTN Coordinating and Operations Center (CORE) of any such inconsistencies.

Study staff should contact the HPTN CORE with all questions related to interpretation and proper implementation of the protocol. Questions related to data collection and management should be directed to the HPTN Statistical and Data Management Center (SDMC). Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the HPTN Central Laboratory (CL). When in doubt as to whether questions pertain to protocol interpretation, data collection, or laboratory procedures, contact the HPTN CORE. Site-specific contacts for the HPTN CORE, SDMC, and CL are listed below. Questions related to the investigational study products should be directed by the study site Pharmacist of Record to the DAIDS Protocol Pharmacist.

CORE Protocol Specialist	**Elena Cyrus** **ecyrus@fhi.org** **tel: 703.516.9779 extension 345**
SDMC Project Manager:	**Karen Patterson** **karenp@scharp.org** **tel: 206.667.7052**
Central Lab Representative:	**Sarah Dawson** **sdawson7@jhmi.edu** **tel: 410.502.0435**

Contact information for all other HPTN 059 team members can be found in the electronic HPTN directory at www.hptn.org.

Current contact details for all HPTN 059 colleagues and collaborators can be found in the HPTN Directory at http://www.hptn.org/network_information/network_directory.asp

1.2 Investigator Responsibilities

HPTN 059 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 17 of this manual.

At each site, HPTN 059 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 059 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 059 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 and Sample Document A in the SSPs. IoRs may delegate their obligations and responsibilities for conducting HPTN 059 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 059 from all responsible regulatory authorities and IRBs/ECs. Each site also must complete Protocol Registration procedures with the DAIDS Regulatory Compliance Center (RCC) and Study Activation procedures with DAIDS and the HPTN CORE, SDMC, and CL. 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 HPTN 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 1-1 and 1-2 list IRB/EC submission and approval requirements pertinent to HPTN 059. 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.

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 1-1 and 1-2. 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 1-1
IRB/EC Submissions Required Prior to Initiation of HPTN 059

Document	Written Approval Required*
HPTN 059 Protocol, Version 1.0 or 2.0	Yes
Informed consent forms: -Screening -Enrollment -CHBV Stored Specimen Storage *Note: HPTN informed consent forms typically 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
Tenofovir Disoproxil Fumarate Investigator's Brochure, 2 November 2004	No
Tenofovir Gel Investigator's Brochure, 31 March 2005	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 HPTN 059

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: HPTN informed consent forms typically 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
Tenofovir Disoproxil Fumarate Investigator's Brochure updates	No
Tenofovir Gel 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 HPTN CORE. All distributions will include instructions related to IRB/EC submission of the safety information.