Section 1. Introduction

This section specifies the sources of procedural information available to MTN 004 study staff, the responsibilities of MTN 004 Investigators of Record (IoRs), and the process by which each study site is approved to begin implementation of MTN 004. 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 004 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.

Study implementation questions that arise should be managed as follows (see Figure 1-1):

- Questions related to interpretation and proper implementation of the MTN 004 protocol should be directed to the MTN CORE (FHI): Kailazarid Gomez and Lisa Levy.
- Questions related to data collection and management should be directed to the MTN Statistical and Data Management Center (SDMC): Missy Cianciola.
- Questions related to the collection, processing, testing, storage, and/or shipment of laboratory specimens should be directed to the MTN Network Laboratory (NL): Charlene Dezzutti and Edward Livant.
- Questions related to the investigational study products should be directed to the MTN CORE Pharmacist: Cindy Jacobson.
- If questions pertain to more than one topic of protocol interpretation, data collection, laboratory procedures, and/or product, or if you are unsure of who to contact, email the MTN 004 Management Team: mtn004mgmt@mtnstopshiv.org.

Contact information for all other MTN 004 team members can be found in the electronic MTN directory at http://www.mtnstopshiv.org.

Figure 1-1: MTN-004 STUDY COMMUNICATION

Protocol Implementation and Procedural Related		
Kailazarid Gomez	919.544.7040 x11282	kgomez@fhi.org
Lisa Levy	919.544.7040 x11260	llevy@fhi.org
Data Management Related		
Missy Cianciola	206-667-7290	missy@scharp.org
Laboratory Related		
Ted Livant	412.641.3772	livantew@upmc.edu
Charlene S. Dezzutti	412. 641. 3462	rsicsd@mwri.magee.edu
Product Related		
Cindy Jacobson	412.641.8913	cjacobson@mail.magee.edu
Clinical Management/PSRT Related		
Katherine Bunge	412.917.9936 (pager)	kbunge@mail.magee.edu
Nancy Connolly	206.523.1177	nancycsc@gmail.com
Ross Cranston	412.647.4007	rdc27@pitt.edu

1.2 Investigator Responsibilities

MTN 004 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) which is available at:

http://www.mtnstopshiv.org.

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 at: http://www3.niaid.nih.gov/research/resources/DAIDSClinRsrch/Default.htm

At each site, MTN 004 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 MTN 004 essential document files (see also Section 3).

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 MTN 004 in accordance with the study protocol, applicable US regulations, and MTN 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 of the MTN MOP. IoRs may delegate their obligations and responsibilities for conducting MTN 004 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 MTN 004 from all responsible regulatory authorities and IRBs/ECs. The ATN sites must complete protocol registration procedures in compliance with NICHD study activation procedures and receive activation approval from Westat, in conjunction with NICHD and DAIDS, prior to participant screening procedures. The MTN site must complete protocol registration procedures with the DAIDS RCC Protocol Registration Office and receive activation approval from MTN CORE (FHI), prior to participant screening procedures. MTN CORE, SDMC, and NL will assist the sites with activities required for activation. Detailed information on the requirements of these pre-implementation steps can be found in the MTN MOP. Westat will issue a Site-Specific Study Activation Notice for ATN sites and MTN CORE (FHI) will issue a Site-Specific Study Activation Notice for the MTN Site, 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 MTN 004. 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. If your IRB/EC does not require submission of certain documents, this must be documented and filed in your site Essential Document files.

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. Submissions to your IRB/EC should detail what documents are being forwarded for review. Similarly, replies from your IRB/EC should list the documents that were reviewed and disposition for each document. 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 your site Essential Document files.

Figure 1-2
IRB/EC Submissions Required Prior to Initiation of MTN 004

Document	Written Approval Required*
MTN 004 Protocol, Version 1.0 and any subsequent versions (Versions 2.0 and 3.0)	Yes
Informed consent forms: -Screening -Enrollment -Storage and Future Testing of Specimens *Note: MTN 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
Investigator's Brochure for SPL7013 Gel (VivaGel™) Document & Version No. : CIB 001-07 ; Release Date : June 20, 2008	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 MTN 004

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: MTN 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
Investigator's Brochure for SPL7013 Gel (VivaGel™) 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.