

## Section 1. Introduction

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### 1.1 Overview of Section 1

This section specifies the sources of procedural information available to HPTN 061 study site staff, the responsibilities of the Site Investigator, and the process by which each site will be approved to implement HPTN 061.

### 1.2 Sources of Procedural Information

All study procedures must be conducted in accordance with the study protocol and this Study-Specific Procedures (SSP) manual. 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) Clinical Research Manager (CRM) of any such inconsistencies.

In instances where there is an urgent need for a change to the SSP, and when a full revision of the SSP is not imminent, the CORE may distribute an email containing a “Notification of Interim Change” to the current version of the SSP. The “Notification of Interim Change” will also be posted on the HPTN 061 website. These interim changes will be considered an official part of the SSP, and should be considered official by the monitoring agent.

HPTU staff are encouraged to contact the HPTN Coordinating and Operations Center (CORE) Protocol Specialist with all questions related to interpretation and proper implementation of the protocol. HPTU staff should contact the Statistical Center for HIV/AIDS Research and Prevention (SCHARP) Protocol Operations Coordinator with questions related to data collection. HPTU staff should contact the HPTN Network Lab (NL) Manager with questions related to the collection, processing, and storage of local and central lab specimens.

**CORE Protocol Specialist:**

Sam Griffith  
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Tel: 919-544-7040 x 11571

**SCHARP Protocol Operations Coordinator:**

Lynda Emel  
[lemel@scharp.org](mailto:lemel@scharp.org)  
Tel: 206-667-5803

**Network Laboratory (NL) Representative:**

Vanessa Cummings  
[vcummin1@jhmi.edu](mailto:vcummin1@jhmi.edu)  
Tel: (410) 502-5296

**Laboratory Data Management System (LDMS)**

[ldmshelp@fstrf.org](mailto:ldmshelp@fstrf.org)  
Tel: 716-834-0900 ext 7311

Contact information for all other HPTN 061 protocol team members can be found in the electronic HPTN directory at [www.hptn.org](http://www.hptn.org).

### 1.3 Investigator Responsibilities

HPTN 061 must be conducted in accordance with the US Code of Federal Regulations (CFR) and the International Conference on Harmonization (ICH) Consolidated Guideline for Good Clinical Practice (GCP). Copies of the regulations governing the conduct of this study (45 CFR 46 and 21 CFR 11, 50, 54, 56, and 312) and the ICH guideline can be requested from the CORE or found online at [www.gpoaccess.gov/cfr/index.html](http://www.gpoaccess.gov/cfr/index.html) and <http://www.ich.org/cache/compo/276-254-1.html>, respectively. The *DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-RA-03.00)* and the *DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00)*, which are useful for interpreting and operationalizing these regulations and guidelines, can be downloaded from: <http://www3.niaid.nih.gov/research/resources/DAIDSCLinRsrch/Regulatory.htm> and <http://www3.niaid.nih.gov/research/resources/DAIDSCLinRsrch/ClinicalSite.htm>, respectively.

HPTN 061 also must be conducted in accordance with all local regulations, policies, and guidelines applicable to human subjects research in general and/or the conduct of study procedures in particular.

The Investigator of Record at each site participating in HPTN 061 is required to sign the protocol signature page, to formally indicate his/her agreement to conduct the study in accordance with the protocol; this SSP manual; all applicable US regulations, policies, and guidelines; and HPTN policies.

Investigators may delegate work involved in conducting the study to other study staff members; however, delegation does not relieve the Investigator of his/her ultimate responsibility for all study procedures performed and all study data collected. Additional guidance can be found in the US Food and Drug Administration's *Information Sheet Guidances: Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors* available at <http://www.fda.gov/oc/ohrt/irbs/default.htm>.

### 1.4 Study Activation Process

Prior to undertaking any study procedures, each study site must obtain approval to conduct the study from all responsible Institution Review Board/Ethics Committee (IRBs/ECs). Thereafter, sites must complete Protocol Registration with the DAIDS RCC, and Study Activation procedures with the HPTN CORE. The remainder of this section outlines the steps required to complete these procedures. These procedures are also described in the HPTN Manual of Operations (MOP) which can be found at <http://www.hptn.org/MOP%20NEW%20CD/MOP%20CD/HPTNMOP2008.htm>.

HPTN 061 study procedures may not be conducted prior to completing all of these steps and receipt of a site-specific study activation notice from the HPTN CORE. Note that study activation is not complete and the study may not begin at your site until DAIDS has granted final approval.

#### **1.4.1 Protocol Distribution**

The CORE CRMs will distribute the final implementation version of the protocol to the study sites.

#### **1.4.2 Development and CORE Review of Site-Specific Informed Consent Forms: English Language Version**

Site staff will adapt the sample informed consent forms appended to the study protocol to reflect local procedures and IRB/EC requirements and forward the forms for review by the CORE CRM. Approval of the site-adapted informed consent forms must be obtained prior to submission to IRBs/ECs or translation into another language (if applicable).

#### **1.4.3 Development and CORE Review of Site-Specific Informed Consent Forms: Foreign Language Version(s) (if applicable)**

If the site will be using a foreign language version of the informed consent forms, they should translate the CORE CRM-approved English forms into that language, and then obtain an independent back-translation of the forms. The site should then submit the translated forms and back-translations for review by the CORE CRM. The CRM will provide review comments to site staff as quickly as possible.

***Note:** The site is required to submit a Local Language Informed Consent Verification Statement document where the translator attests to the accuracy of the translation in writing for each translated consent form.*

***Note:** HPTN 061 procedures are intended to be conducted in English. The CRFs and ACASI data collection instruments will not be translated into any other languages. Particularly with regard to the ACASI instrument, which the participant will complete without the assistance of a counselor, it will be important that the participant be very comfortable understanding and responding in English. Sites may use non-English consent forms in order to be culturally respectful of the communities in which they are working, but sites should establish procedures to ensure that all enrolled participants can complete study procedures with full comprehension.*

#### **1.4.4 IRB/EC Review**

After incorporating review comments received from the CORE CRM, site staff will submit the study protocol, site-specific informed consent forms, the current curriculum vitae (CV) of the Investigator of Record, and any other study-related materials for review by all responsible IRBs/ECs. Any participant information sheets, pre-screening forms, focus group guides, individual interview questionnaires, promotional materials, or advertisements used during the study must be reviewed and approved by all responsible IRBs/ECs prior to use.

In the event that either the site and/or IRBs/ECs request changes to the submitted informed consent forms, it is the responsibility of the Investigator of Record to incorporate all such comments into a single final version of the study informed consent forms, and to obtain approval of this final version from all responsible IRBs/ECs. This may require multiple submissions to the responsible IRBs/ECs. If a foreign language consent form is being used, the final English back-translation must reflect the approved informed consent forms that will be used at the site.

An overview of IRB/EC submissions required before and during HPTN 061 is included in Table 1-1.

**Table 1-1: IRB/EC Submissions Required Prior to Study Initiation and During Study Conduct**

Document	IRB/EC Approval Required?*		Source of Document: HPTN CORE or CRS
	Prior to Study Initiation	During Study Conduct	
Protocol, (Current Version at Study Start)	yes	NA	CORE
Protocol amendments (including letters of amendment) and any other changes increasing risk to participants and/or affecting significantly the conduct of the study.	If applicable	yes	CORE
Protocol clarification memos (submission to IRB/EC encouraged but not required by DAIDS)	NA	no	CORE
Protocol departures/deviations/violations (per IRB/EC requirements and/or as directed by DAIDS)	NA	no	CRS
Informed consent forms, (Current Version at Study Start) Enrollment Informed Consent; Informed Consent for the Storage of Specimens Obtained While Participating in a Research Trial; Focus Group Informed Consent; Qualitative Interview Informed Consent	yes	NA	CRS
Amended informed consent forms (Spanish language(s) and back translations, if applicable)	If applicable	yes	CRS
Current CV for Investigator of Record	no	NA	CRS
Revisions to current CV for Investigator of Record (if Investigator of Record changes during study)	NA	no	CRS
Focus group guides and individual interview questionnaires	yes	yes	CORE
Participant recruitment materials (pre-screening form, posters, flyers, advertisements, etc.)	yes	NA	CRS
Updated/additional participant recruitment materials (pre-screening form, posters, flyers, advertisements, etc.)	NA	yes	CRS
Other written information for study participants	yes	NA	CRS
Updated/additional written information for study participants	NA	yes	CRS
Other documentation required or requested by the IRB/EC	no	no	CRS
Study status reports/updates (at least annually) This approval documents continuing review.**	NA	yes	CRS
New information that may affect adversely the safety of study participants or the conduct of the study	NA	no	DAIDS through CORE
Final study report/closure report	NA	no	CRS

DAIDS: Division of AIDS; EC: ethics committee; HPTN CORE; HIV Prevention Trials Network Coordinating and Operations Center; CRS: Clinical Research Site; IRB, Institutional Review Board; NA: not applicable.

\* Based on US regulations and GCP guidelines. Local regulatory authorities and/or responsible IRBs/ECs may require additional approvals. If so, the required approvals must be obtained and filed.

\*\* Guidance from the US Office for Human Research Protections (OHRP) on continuing review can be found at: <http://www.hhs.gov/ohrp/policy/index.html#continuing>.

Note: All documents must be submitted to all IRBs/ECs responsible for oversight of study implementation at the performance site. Documentation of all submissions to and approvals from all responsible IRBs/ECs must be maintained in the Essential Document files at the local performance site

## 1.4.5 Protocol Registration

*Note:* Additional details on the protocol registration process can be found in the Division of AIDS (DAIDS) Protocol Registration Policy and Procedure Manual (located at <http://rcc.tech-res.com/forms.htm>) and the HPTN MOP (located at [www.hptn.org/network\\_information/policies\\_procedures.htm](http://www.hptn.org/network_information/policies_procedures.htm))

Upon obtaining approval from all responsible IRBs/ECs, site staff will submit the following documents to the Protocol Registration Office (PRO) at the RCC. These documents may be sent electronically to [protocol@tech-res.com](mailto:protocol@tech-res.com). Site staff will also submit a copy of the submission documents to the CORE CRM:

- Current, signed, and dated CV of the Investigator of Record, in English
- Documentation of approval from all responsible IRBs/ECs of the study protocol and the informed consent forms.

*Note:* Documentation of IRB/EC approval must reference the exact protocol number, title, version number, and date as listed on the cover page of the protocol. If the approval documentation is provided by the IRB/EC in a language other than English, the document must be translated into English, and both the local language version and the English language version must be submitted.

- A copy of the approved site-specific (local language) informed consent forms

*Note:* The approved informed consent forms must include the exact protocol number, title, version number, and date as listed on the cover page of the protocol. Pages should be numbered 1 of x, 2 of x, etc. When an IRB/EC approves a single informed consent form that will be used at multiple sites, and the approved form contains blank spaces for site contact information, a memo specifying the relevant information for each site must be submitted together with the approved form.

*Note:* The site is required to submit a Local Language Informed Consent Verification Statement document where the translator attests to the accuracy of the translation in writing for each translated consent form.

Some sites may have additional site-specific documents to be included with the protocol registration package (e.g. additional information requested by DAIDS). These documents should be submitted to the RCC and a copy should be submitted to the CORE CRM.

DAIDS regulatory staff will communicate their review findings to the site staff, who will coordinate any required re-submissions.

#### 1.4.6 Certificate of Confidentiality

A Certificate of Confidentiality (COC) is a certificate issued by NIAID that protects the privacy of participants in health research projects by protecting investigators from being forced to release information that could be used to identify participants. The COC allows investigators to refuse to disclose identifying information in any civil, administrative or legislative proceeding whether at the US state, Federal or local level.

If sites have included language in their ICFs indicating that they will obtain a COC, they must apply for and obtain this COC prior to site activation. The site should notify FHI CORE after they have received IRB approval for all ICFs that they are ready to obtain the COC. The following must be submitted as part of the COC application:

- All IRB approved ICFs (stamped by the IRB, if applicable).
- The IRB approval notice which delineates all items which were submitted and approved.
- A signed cover letter (template provided by FHI CORE) including the name, address and credentials of the CTU PI and CRS IoR (if different), as well as relevant study information (protocol number, name and CTU/CRS DAIDS ID) and the assurance note below:

##### *Assurances*

*This institution agrees to use the Certificate of Confidentiality to protect against the compelled disclosure of personally identifiable information and to support and defend the authority of the Certificate against legal challenges. The institution and personnel involved in the conduct of the research will comply with the applicable Federal regulation for the protection of human subjects or, if no such Federal regulation is otherwise applicable, they will comply with 45 CFR Part 46. This Certificate of Confidentiality will not be represented as an endorsement of the project by the DHHS or NIH or used to coerce individuals to participate in the research project. All subjects will be informed that a Certificate has been issued, and they will be given a description of the protection provided by the Certificate. Any research participant entering the project after expiration or termination of the Certificate will be informed that the protection afforded by the Certificate does not apply to them.*

#### 1.4.7 Study Activation

The HPTN MOP specifies requirements that must be met in order to activate a site to begin HPTN study operations. These requirements have been adapted for HPTN 061 and are listed below.

- US Federal Wide Assurance (FWA) number on file with OHRP for the study site institution(s)
- IRB/EC approval of the current study protocol, and any other site-specific approvals if applicable
- Approved current site-specific informed consent forms (including translation and back translation into Spanish if applicable)
- Signed Investigator of Record (IoR) Agreement
- Signed IoR Protocol Signature Page
- Signed and dated CV of the IoR
- Completion of human subjects training within the last three years for all “key” study staff (as defined by US NIH policy)—(key personnel include all individuals responsible for the design and conduct of the study)
- Completion of good clinical practices training within the last three years for all “key” study staff (as defined by US NIH policy)-(key personnel include all individuals responsible for the design and conduct of the study).
- Completion of good clinical laboratory practices training for the appropriate laboratory staff
- Completion of study-specific training
- Resolution of any other finding/action items identified during site preparation activities
- DAIDS RCC Registration
- Certificate of Confidentiality obtained, if the site-specific informed consent has indicated that one will be in place
- Source Documentation of Participant Eligibility Table
- Individual Participant Eligibility Verification Checklist
- CRF Source Documentation Tables
- Study staff signature sheet, roster, and delegation of duties
- Final approval for site activation per FHI procedures

**SCHARP approval of site readiness for data management**

- Installation of required data relay equipment and/or validation of existing equipment
- Internet access with connections for data relay devices (DataFax and ACASI)
- Availability of CRFs
- Data Management SOP

**HPTN Network Lab approval of local lab readiness, including approval/confirmation of:**

- CLIA certification for laboratory protocol-related tests and CLIA Waiver certificates for in clinic protocol-related tests
- Local laboratory back-up arrangements
- LDMS set up including computer, printer, and scanner, and appropriate LDMS training
- Exporting LDMS data to FSTRF
- Freezer storage capacity
- IATA specimen shipping certification (for all site and laboratory personnel involved in shipping and transportation of samples)

**Table 1-2: Required SOPs for HPTN 061**

<b>Category</b>	<b>SOP</b>
<b>Data Management</b>	On-site data management including: QA/QC procedures; computer room hardware and data security; system user account maintenance; data acquisition; entry and processing; data queries and data error correction; data collection training; data quality management; and data storage
<b>Specimen Processing</b>	Local Specimen handling and chain of custody, including: results reporting, specimen acquisition, processing, tracking, and storage, lost, broken, and leaking samples, receipt and processing all samples, specimen transport, shipping specimens
<b>Laboratory</b>	LDMS reconciliation
	Biohazard safety and containment and occupational safety
	SOP for lab assays performed in-clinic; such as rapid HIV tests
<b>Clinical Management</b>	Safety and social harms monitoring, assessment and reporting for clinical study participants
	Referrals
	Explicit SOP for each clinical procedure (includes specimen handling): phlebotomy, rectal swab, urine collection, circumcision confirmation
<b>Administrative and Regulatory</b>	Source Documentation
	Essential Documents
	Community Involvement Plan
	IRB Communication
	SAE and Social Harms Reporting
	Informed Consent Process
	Staff Roles and Responsibilities (including CVs for on-site

Category	SOP
	staff)
	Staff training and certification documentation
	Study File Management
	SOP development, review and version control
	Participant Confidentiality
	Staff Safety Plan
	Audits and Inspections (including review and follow-up to monitoring and findings)
<b>Counseling</b>	HIV/STI voluntary Counseling and Testing, risk reduction counseling
<b>Study Specific</b>	Participant Eligibility Determination
	Participant Transfer
	Qualitative Research
	Peer Health Navigation
	Recruitment, Follow-up, and Retention

The required elements of the SOPs listed in Table 1-2 may be grouped together in single SOPs (e.g., one SOP to include source documentation and essential documents) or split among several SOPs (e.g., information about staff training may be added to each SOP.)

Once all study activation requirements are met at a site and documented, the HPTN CORE Clinical Research Manager/Protocol Specialist (CRM/PS) will issue a site-specific Study Activation Notice (see Section 10.11) confirming that all requirements have been met and indicating that the site may initiate study implementation. No study procedures may be undertaken before the activation notice is received. After issuing the site-specific Study Activation Notice, the CORE CRM/PS will provide to site staff a copy of the documentation upon which activation was based.

#### 1.4.8 Abbreviated Study Activation for Protocol Amendments

When a full protocol amendment is implemented after study initiation, sites are not required to repeat the entire site-specific study activation process. However, a subset of these activities must be conducted in order to prepare for the changes to study conduct based on full protocol amendments. If a protocol is amended prior to study implementation, all materials must reflect the amended protocol and both the amended protocol and Informed Consents must be approved by the IRB. The list below outlines the required activities and/or items that must be in place before a site can begin study conduct under a full protocol amendment. Not all items will apply for each amendment.

- Protocol amendment registration approval from DAIDS/RCC based on the following:
  - Approvals from all responsible IRBs/ECs for the amended protocol and site-specific ICFs
  - IRB/EC-approved informed consent forms (including local language and back translation where applicable)
- A Certificate of Confidentiality should be obtained or amended (if already issued) based on the amended protocol.
- Sites should review, and if necessary revise, the CV for the IoR, the CRF and Eligibility Source Documentation Tables, and all study-related SOPs.
- The IoR must sign the “Investigator of Record Signature Page” included in the protocol amendment
- Completion of study-specific training for (remote or on site) the latest version of the protocol
- The current CRFs must be on site
- The site must have a current IATA specimen shipping certification for at least one study staff member
- If any of the following laboratory-related SOPs are revised, they must be reviewed and approved by the network laboratory.
  - SOP for laboratory QA/QC procedures
  - SOP for chain of custody related to testing primary study endpoints
  - SOP for local laboratory back-up arrangements

## **1.5 Continuing Review**

Throughout the course of the study, all sites are required to submit annual progress reports to the IRB(s)/EC(s) overseeing study conduct and receive annual approval. The submission sent to the IRB(s)/EC(s) for annual review should include the following:

- The full protocol
- The current ICFs
- An annual report which includes:
  - The number of subjects accrued

- A summary of SAEs and any unanticipated problems involving risks to participants
- The number of participants who have withdrawn and any complaints about the research since the last IRB/EC review
- A summary of any modifications or amendments since the last IRB/EC review
- Any other relevant information, especially information about risks associated with the research

Additional information and guidance about continuing review can be found at the Office of Human Research Protection (OHRP) website:  
<http://www.hhs.gov/ohrp/policy/index.html#continuing>.