Section 1: Introduction

1.1 Overview of Section 1

This section includes specifics on study conduct including the sources of procedural information available to HPTN 091 study site staff, the responsibilities of the site Investigators, and the process by which each site will be approved to implement HPTN 091.

1.2 Current Protocol Specifications

The Table 1.1 documents the history of the HPTN 091 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.

Table 1.1: Protocol Documents

Document	Date
HPTN 091 Protocol, Version 1.0	13 April 2020
Letter of Amendment #1 to Protocol Version 1.0	26 May 2021
Letter of Amendment #2 to Protocol Version 1.0	27 July 2021
Letter of Amendment #3 to Protocol Version 1.0	5 October 2022

Note: Clarification Memos and Letters of Amendment are incorporated into subsequent full versions of the protocol. A Clarification Memo may also be incorporated into a subsequent Letter of Amendment.

Sites are expected to operate under the protocol version and associated Clarification Memos and/or Letters of Amendment that are currently approved by the 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. These documents are available on the HPTN 091 webpage: https://www.hptn.org/research/studies/185.

1.3 Source of Procedural Information

All study procedures must be conducted in accordance with the study protocol and this study specific procedures (SSP) manual. Unless instructed by the HPTN Leadership and Operations Center (LOC), if there is inconsistency between this manual and the protocol, the specifications of the protocol take precedence. Please alert the HPTN Leadership and Operations Center (LOC) of any such inconsistencies.

In instances where there is an urgent need for a change to the SSP manual, and when a full revision of the SSP is not imminent, the LOC may distribute an email containing a "Notification of Interim Change" to the current version of the SSP manual. These interim changes will be considered an official part of the SSP manual and should be considered official by any monitoring agents.

Study site staff are encouraged to contact the HPTN LOC Clinical Research Managers (CRMs) with all questions related to interpretation and proper implementation of the protocol. Questions related to community education and outreach should be directed to the HPTN LOC Community Program Manager. Questions related to data management and data collection should be directed to the HPTN Statistical and Data Management Center (SDMC) Protocol Manager. Questions related to the collection, processing, and storage of local and central lab specimens should be directed to the HPTN Laboratory Center (LC) study representatives. Questions regarding pharmacy issues should be directed to the protocol pharmacist at the Division of AIDS (DAIDS) Pharmacy Affairs Branch (PAB). The persons to contact for these types of questions are:

HPTN LOC Clinical Research Managers	Kailazarid Gomez-Feliciano Tel: 1-919-321-3486 Email: kgomez@fhi360.org Cell: 919-884-9672 Busola Akingbade Tel: 1-919-321-3344 Email: bakingbade@fhi360.org
HPTN LOC Clinical Trial Assistant	Maxine Awekey Tel: 1-202-884-8072 Email: mawekey@fhi360.org
HPTN LOC Community Program Managers	Jonathan Paul Lucas Tel: 1-919-321-3574 Email: jlucas@fhi360.org
HPTN SDMC Protocol Manager	Ian Bell Tel: 1-206-667-7061 Email: ibell@scharp.org
HPTN Laboratory Center (LC) Representatives	Vanessa Cummings Tel: 410-614-0479 Email: vcummin1@jhmi.edu Mark Marzinke Tel: 443-287-7516 Email: mmarzin1@jhmi.edu
Laboratory Data Management System (LDMS)	Tel: 716-834-0900, ext. 7311 Email: ldmshelp@fstrf.org
DAIDS Protocol Pharmacist	Justine Beck Phone: 301-761-5288 Email: justine.beck@nih.gov Cindy Parker Phone: 301-761-7199 Email: cindy.parker@nih.gov

Contact information for all other HPTN 091 protocol team members can be found in the protocol roster in the HPTN 091 protocol.

1.4 Sites Participating in HPTN 091

Table 1-2
Participating HPTN 091 Sites by Region

Region	CRS Name	CRS ID	City	State/ Country
Latin America	Instituto de Pesquisa Clinica Evandro Chagas (IPEC) CRS	12101	Rio de Janeiro	Brazil
US	Bridge HIV CRS	30305	San Francisco	California
US	Harlem Prevention Center CRS	30276	New York	New York
US	Penn Prevention CRS	30310	Philadelphia	Pennsylvania
US	Houston AIDS Research Team CRS	31473	Houston	Texas

1.5 Investigator Responsibilities

HPTN 091 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 HPTN LOC or found online at https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR and http://www.ich.org/home.html respectively. The DAIDS Site Clinical Operations and Research Essentials (SCORE) Manual which is useful for interpreting and operationalizing these regulations and guidelines, can be found online at https://www.niaid.nih.gov/research/daids-score-manual.

HPTN 091 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 (IoR) at each site is the person responsible for the conduct of the clinical trial at the clinical research site. This person is the signatory for the FDA Form 1572 which must be signed prior to site activation, to formally indicate their agreement to conduct the study in accordance with the protocol; this SSP manual; all applicable US and in country 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 their 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 Guidance: Information Sheet Guidance for Institutional Review Boards (IRBs), Clinical Investigators, and Sponsors available at https://www.fda.gov/science-research/guidance-

documents-including-information-sheets-and-notices/information-sheet-guidance-institutional-review-boards-irbs-clinical-investigators-and-sponsors.

1.6 Study Activation Process

Prior to undertaking any study procedures, each study site must obtain approval to conduct the study from all responsible US and local Institution Review Board/Ethics Committee (IRBs/ECs) and any other local regulatory bodies. Thereafter, sites must complete Protocol Registration with the DAIDS Regulatory Support Center (RSC), as well as Study Activation procedures with the HPTN LOC. These procedures are also described in the HPTN Manual of Operations (MOP) available at: https://www.hptn.org/resources/manual-of-operations. HPTN 091 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 LOC.

1.6.1 Protocol Distribution

The HPTN 091 Clinical Research Manager (CRM) will distribute the final implementation version of the protocol electronically to the study sites.

1.6.2 Development and HPTN LOC Review of Site-Specific Informed Consent Forms: English Language Versions

Site staff will adapt the informed consent form (ICF) template to reflect local procedures and IRB/EC requirements. For US sites, the ICF template will be submitted by the LOC to the sIRB for the study. Once the sIRB approves the ICF template, the study CRM will distribute to all US sites to adapt for local needs. If sites make substantial changes to the ICF from the approved template, sites must submit the updated form to the study CRM.

1.6.3 Development and HPTN LOC Review of Site-Specific Informed Consent Forms: Local Language Version(s) and Back-translation(s)

For the initial version of the protocol, after incorporating review comments from the HPTN LOC CRM, if applicable, site staff will translate the informed consent forms into all applicable local languages and then submit the translated forms, back-translations of the forms, and a certificate of translation for review by the HPTN LOC. Please note back-translations are not required if local language is Spanish. The HPTN LOC CRM will provide review comments to site staff as quickly as possible. The back-translation need not be completed by a certified translator; however, it is recommended that two different individuals translate the document(s) and then review each other's work to prepare a composite. The back-translation should be completed by an individual who did not participate in the translation process.

1.6.4 IRB/EC Review

For US sites: The HPTN LOC will submit the protocol and other general study documents to the sIRB for approval. Sites are responsible for submitting their site-specific documents, including ICF, current curriculum vitae (CV) of the IoR and any other study-related materials, to the sIRB for approval.

For Brazil site: staff will submit the study protocol, site-specific informed consent forms, the current curriculum vitae (CV) of the IoR, and any other study-related materials for review by all responsible local IRBs/ECs. Any participant information sheets, flip charts, promotional materials, or advertisements used during the study must be reviewed and approved by all responsible IRBs/ECs prior to use.

In the event either the site and/or local IRBs/ECs request changes to the submitted informed consent forms, it is the responsibility of the IoR 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. The final English back translation of the ICFs submitted to the DAIDS RSC must accurately and entirely reflect the approved local-language informed consent forms that will be used at the site.

1.6.5 Protocol Registration

Upon obtaining approval from all responsible IRBs/ECs, sites will complete the Protocol Registration process as described in the Division of AIDS (DAIDS) Protocol Registration Policy and Procedure Manual (located at https://rsc.niaid.nih.gov/clinical-research-sites/daids-protocol-registration-policy-and-procedures-manual).

For initial protocol registration only, site staff will also submit a copy of the submission documents to the HPTN LOC.

If the site deletes or makes any substantive change to basic and/or additional elements as presented in the ICFs, the IoR must provide written documentation to explain the deletions/change(s) at the time of initial protocol registration with the DAIDS RSC.

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

1.6.6 Study Activation

The HPTN has specified requirements that must be met in order to activate HPTN study operations. The activation requirements for HPTN 091 are outlined in the HPTN 091 Activation Checklist. The Activation Checklist is distributed to sites in advance of expected study activation. The study management team, as outlined in Section 1.3 above, will ensure all activation requirements are met prior to stie activation. General HPTN study-specific site activation requirements can be found in Table 1 of Section 10 of the HPTN MOP https://www.hptn.org/sites/default/files/2016-05/Section10_23Jul14.pdf.

If there is an inconsistency between the items in this SSP manual and the HPTN MOP for study-specific site activation, contact the HPTN 091 CRM for clarification.

1.6.7 Abbreviated Study Activation for Protocol Amendments

When a full protocol amendment is implemented, 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. 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. Sites should submit for DAIDS protocol registration within 14 days after receiving IRB/EC approval for the protocol and site specific-ICFs. The list below applies to any version after Version 1.0.

- Approvals from all responsible IRBs/ECs for the protocol and site-specific ICFs
- Sites should review, and if necessary, revise the CV for the IoR, the CRF and Eligibility Source Documentation Tables, and all study-related SOPs
- Completion of study-specific training (remote or on site) for the latest version of the protocol, if necessary
- 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

1.7 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. Documentation of this approval must be submitted to the RSC. See https://rsc.niaid.nih.gov/clinical-research-sites/daids-protocol-registration-policy-and-procedures-manual for more information.

Additional information and guidance about continuing review can be found at the Office of Human Research Protection (OHRP) website: http://www.hhs.gov/ohrp/regulations-and-policy/guidance/guidance-on-continuing-review-2010/.