Section 3. Documentation Requirements

3.1 Overview of Section 3

This section contains a listing of required administrative and regulatory documentation, commonly referred to as "Essential Documents", which each study site must maintain and keep current throughout the study, as well as procedures for establishing adequate and accurate study participant source documentation records.

3.2 Essential Documents

The DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials (https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf) specifies the administrative and regulatory documents that HPTN study sites must maintain for DAIDS-sponsored studies. Based on this DAIDS Policy, the documentation listed below must be maintained for HPTN 074. When required documents are modified or updated, the original and modified/updated versions must be maintained. Although all required documentation must be available for inspection at any time, all documents need not be stored together in one location.

- Protocol (implementation version and any subsequent amendments, letters of amendment, clarification memos, and translated versions)
- Informed Consent Forms (all IRB-approved versions, all signed and dated forms from screened/enrolled study participants), as well as any updates such as "Dear Participant" Letters (all IRB-approved versions) for all screened/enrolled participants, translated and back-translated
- Investigator of Record Agreement
- Protocol Signature Page
- Documentation of OCSO site approval (if applicable)
- Documentation of approved protocol registration from DAIDS
- Documentation of study activation from the HPTN LOC CRM
- Documentation of local regulatory authority correspondence, authorization, and/or approval of the protocol if applicable
- Federal Wide Assurance (FWA) number(s) and expiration date
- IRB/EC roster(s)
- Relevant local IRB/EC submission requirements or guidelines
- All correspondence to and from the local IRB/EC, including documentation of all reviews and approvals and copies of site-specific interim and annual reports
- All IRB-approved participant informational/educational materials as well as subsequent updates
- Screening and enrollment logs
- Referral logs
- Participant identification code list (linking PTID to names)
- Study staff roster, signature sheet, and delegation of duties, including Investigator responsibilities

- Signed and dated CV and financial disclosure for each key study staff member, current within the last year
- Documentation of staff members' human subjects training
- Documentation of staff members' study-specific training
- Documentation of staff members' GCP training
- Local laboratory accreditations/certifications
- Local laboratory normal values/reference ranges for protocol-specified testing, if required
- Key study-related correspondence with the HPTN LC, SCHARP, the HPTN LOC, the RSC, and DAIDS, as well as other significant study-related communication
- Documentation of study-related conference calls and meetings
- Applicable local public health reporting requirements pertinent to study procedures; documentation of exemptions from requirements
- Final, approved version of each local site- and study-specific SOP that will be used for HPTN 074 and all subsequent updates
- DAIDS reference materials including: 1) DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (and subsequent updates), 2) DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials (and subsequent updates), 3) DAIDS Protocol Registration Policy and Procedures Manual (April 2010 and any subsequent updates)
- Study-specific procedures (SSP) manual, original versions and all updates, bulletins, clarifications, and communiqués
- Monitoring visit log, reports, and site response to visit findings (contract monitor, HPTN LOC, SDMC, HPTN LC, and other site visits)
- A complete, blank copy of the case report forms (CRFs) (original and all revisions, translated and back-translated)
- All completed CRFs, initialed and dated
- Record of stored specimens
- Source documentation tables (see Table 3-1 to 3-2)
- All source documents for each participant
- Signed agreements related to the study

3.3 Participant Research Record

The study site must maintain an accurate and complete participant research record containing all information pertinent to the study for each study participant. As defined by the *DAIDS Policy* for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials *(DWD-POL-CL-04.00,*https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf), , the research record consists of the following: original subject-signed informed consent form(s), participant source documents and case report forms (CRFs).

3.3.1 Concept of Source Documentation

A source document is defined as the first document on which study-related information is recorded. The study site must adhere to the standards of source documentation specified in the DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf) and the standards outlined in this manual. For HPTN 074, participant source documents will consist of narrative notes, qualitative materials, laboratory reports and forms provided by SCHARP (DataFax and non-DataFax). As a condition for study activation, the site must establish an SOP for source documentation that specifies the use of these documents as source documents.

3.3.2 Source Documentation

Participant source documentation should contain all of the following elements:

- Basic participant identifiers
- Documentation that the participant provided informed consent to participate in the study prior to the conduct of any study procedures (See Coversheet in 4-2)
- Documentation that the participant met the study's selection (eligibility) criteria
- Documentation of randomized assignment
- A record of all contacts, and attempted contacts, with the participant
- A record of all procedures performed by study staff during the study
- A record of Social Impacts/Benefits possibly related to study procedures and/or participation in the study
- Study-related information on the participant's condition before, during, and after the study, including:
  - Data obtained directly from the participant (e.g., interview responses)
  - Data ascertained by study staff (e.g., lab findings)
  - Data obtained from non-study sources (e.g., medical records)

Note: *In addition to the above, the DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf) requires that all protocol departures/deviations/violations be documented in participant's study records, along with reasons for the departures and/or attempts to prevent or correct the departures, if applicable. See Section 3.4.*

3.3.3 Examples of Source Documentation

3.3.3.1 Chart Notes

Study staff must document every contact with a study participant in a signed and dated note that will be retained in the participant record specifying the date, type, purpose, location of the contact, and the general

status of the participant.

Chart notes also may be used to document the following:

- The informed consent process. See Consent Coversheet in Section 4, Table 4.2, which is an example of documenting informed consent process.
- Procedures performed that are not recorded on other source documents, such as referral for substance use treatment.
- Pertinent data about the participant that are not recorded on other source documents.
- Protocol departures/deviations/violations that are not otherwise captured on other source documents. Note that the DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (https://www.niaid.nih.gov/sites/default/files/daids-sourcedocpolicy.pdf) requires that all protocol departures, deviations, or violations be recorded in participants' study records, along with reasons for the departures and/or attempts to prevent or correct the departures, if applicable.

3.3.3.2 Case Report Forms

SCHARP will provide the DataFax case report forms (CRFs) to each site. Each study site must document the source documentation for each CRF item by completing Table 3-1, submitting a copy to the HPTN LOC CRM, and maintaining the original document in the site's administrative and regulatory files. The comments section of Table 3-1 should be modified to accurately reflect the source documentation for each CRF item at the site. Table 3-1 will be finalized and signed prior to site activation. Site staff must follow the designations in Table 3-1 consistently for all study participants throughout the study.

In the event that it is not possible to record data directly onto forms designated as source documents, the following procedures should be followed:

- Record the data onto an alternative source document.
- Retain the alternative source document in the participant's research record.
- Transcribe the data from the alternative source document onto the appropriate case report form.
- Enter a chart note stating the relevant study visit code and date and the reason why an alternative source document was used.

Table 3-1: Example: HPTN 074 Source Documentation for All Items
(NOTE: A Source Document Table must be completed prior to activation. Modify the template below to fit your needs)

CRF Name	Acronym	Source			Comments
		Yes	No	Mixed	
Adverse Experience Log	AE			X	Depending on the situation and source of information, all or some could be source.
Agency Contact	ACL	X			CRF is source for all items.
Baseline Behavior Assessment	BBA	X			CRF is source for all items.
CD4+ Count and Viral Load	CDF		X		Lab reports are source for all items.
Demographics and Demographics by country	DEM, DVI, DIN, DUK	X			CRF is source for all items.
Follow-up Behavior Assessment	FBA	X			CRF is source for all items.
Follow-up Substance Use Treatment	FSU	X			CRF is source for all items.
Follow-up Visit	FUV	X			CRF is source for all items.
Index ART Initiation	IAI			X	CRF will be source unless documentation is provided for any or all items
Index Follow-up HIV Care and ART	IFH	X			CRF is source for all items.
Index Baseline HIV Care and ART	IBH	X			CRF is source for all items.
Index Enrollment	IE		X		Informed consent/informed consent cover sheet is source for items 1 and 2. Randomization email from SCHARP is source for item 3.
Index Network Status	INS		X		Social network interview is source for items 1, 2 and 4. Partner enrollment is source for item 3.
Index PTID Tracker	IPT		X		Fingerprint or other tracking database is the source for all items.
Index Screening Outcome	ISO		X		Informed consent is source for item 1. Item 2 chart notes. Item 3 Index Enrollment CRF. Item 4 chart notes and eligibility checklist.
Index Treatment Belief Questionnaire	ITB	X			CRF is source for all items.
Missed Visit	MV		X		Retention logs are source for all items unless retention logs are electronic in which case chart note may be source.
Partner Enrollment	PE			X	Informed consent is source for items 1 and 2. CRF is source for item 3.
Partner HIV Test Results	PHT		X		Lab reports are the source for all items.
Partner Screening Outcome	PSO		X		Informed consent is source for item 1. Item 2 Partner Enrollment CRF. Chart notes and eligibility checklist will be source for item 3.
Protocol Deviation Log	PDL			X	
Psychosocial Encounter	PSY			X	CRF is source for all items except item 4. Item 4 will be FBA or chart notes.
Social Impact Assessment	SIA	X			CRF is source for all items.
Social Impact Log	SIL		X		Social Impact Assessment CRF is source for all items.
Specimen Storage	SS		X		Lab requisition forms will be source for all items.
Social Support and Stigma Questionnaire	STG	X			CRF is source for all items.

CRF Name	Acronym	Source			Comments
		Yes	No	Mixed	
Study Extension CRF	EXT			X	ICF is source for item 1 and CRF is source for item 2.
Study Extension Termination CRF	ETM			X	CRF is source, unless an AE Log is filled out as well.
Substance Use Treatment Initiation	SUT			X	CRF will be source unless documentation is provided for any or all items.
Systems Navigator Encounter	SNE			X	CRF is source for all items except items 5, 6 and 7. Item 5 will be IAI CRF, Item 6 will be SUT and Item 7 will be FBA or chart notes.
Termination	TM		X		Chart notes will be source for all items.
Urine Drug Screen	UDS		X		Lab reports will be source for all items.
Social Network Interview **(NON-CRF)**		X			Although this item is not a CRF sent to SCHARP, information is collected from enrollment on for all participants and sent to UNC.

[1]A designated study staff member must review all study laboratory reports, as well as reports of information pertinent to the study from non-study providers, and sign and date the reports to document his/her review.

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Signature of Investigator of Record Date

3.3.3.3 Eligibility Criteria

It is essential that source documentation be provided to demonstrate that each inclusion and exclusion criteria contained in the protocol has been met before enrolling a participant. Failure to document that the criteria have been met may result in an enrollment violation. The site is encouraged to use Table 3-2 to show how they will document that all eligibility criteria have been met for each enrolled participant. As with Table 3-1, Table 3-2 should be modified to accurately reflect the source documentation being used at the site and it should be signed and dated by the Investigator of Record, included in the regulatory files, and followed consistently for all participants throughout the study. These example tables are reflective of the inclusion/exclusion criteria in Version 1.0 of the protocol (Sections 3.1 and 3.2).

Index participants will be approached after the study has ended, in order to determine whether or not they would like to re-enroll in the study extension (for an additional 9-12 months of follow-up). *There are no re-enrollment eligibility criteria for indexes to re-enroll in the study extension, except for previously being an index in the main study and undergoing HIV testing at re-enrollment. Partners are not eligible for the study extension.

Table 3-2: HPTN 074: Source Documentation for Eligibility Criteria (EXAMPLE)	
Eligibility Requirements	**Source Document**
Potential INDEX participants who meet all of the following criteria are eligible for inclusion in the study:	
Age 18-60 years at the Screening visit	Chart notes and eligibility checklist.
Able to provide informed consent	Informed consent form and cover sheet.
Active injection drug user, defined as self-report of: a) injecting drugs at least 12 times in the past three months and at least 6 times in the past month	Chart notes and eligibility checklist.
b) A PWID in the opinion of site staff	Chart notes and eligibility checklist.
Reports sharing needles/syringes or drug solutions at least once in the last month	Chart notes and eligibility checklist.
HIV-infected based on a study-defined testing algorithm	Local laboratory results and eligibility checklist.
Viral load ≥1,000 copies/mL at Screening	Local laboratory results.
CD4 > 50 cells/mm3 at Screening	Local laboratory results.
Willing and able to identify, recruit, and have enrolled at least one HIV-uninfected network injection partner (see eligibility requirement below)	Chart notes and eligibility checklist.
Have no plans to move outside the study area for at least one year after study enrollment	Chart notes and eligibility checklist.
Willing to participate in intervention activities, including regular phone contact	Chart notes and eligibility checklist.
Exclusion Criteria for Potential INDEX participants	
Current participation in any HIV prevention study	Chart notes and eligibility checklist.
Previous or current participation in an HIV vaccine trial	Chart notes and eligibility checklist.
Appearance of psychological disturbance or cognitive impairment that would limit the ability to understand study procedures, as determined by the investigators	Chart notes and eligibility checklist.
Any other condition that, in the opinion of the investigators, would make participation in the study unsafe, or otherwise interfere with the study activities	Chart notes and eligibility checklist.
Prior screening as a potential network member of another index participant in this study (NOTE: Screened partners who fail screening because they have one or more reactive/positive HIV test(s) may screen as an Index participant only if the original referring Index participant does not enroll).	Partner screening outcome
Currently or previously a partner of an index participant	fingerprint or other tracking database
Potential HIV-UNINFECTED NETWORK INJECTION PARTNERS who meet all of the following criteria are eligible for inclusion in the study:	
Age 18-60 years at the Screening visit	Chart notes and eligibility checklist.
Able to provide informed consent	Informed consent form and cover sheet.
Active injection drug user, defined as self-report of: a) injecting drugs at least 12 times in the past three months and at least 6 times in the past month	Chart notes and eligibility checklist.
b) A PWID in the opinion of site staff	Chart notes and eligibility checklist.
Confirmed injection partner, using referral identification cards or other means of identification from the index participant	Chart notes and eligibility checklist.

HIV-uninfected based on the study-defined testing algorithm	Local laboratory results and eligibility checklist.
Have no plans to move outside the study area for at least one year after study enrollment	Chart notes and eligibility checklist.
Exclusion Criteria for Potential HIV-UNINFECTED NETWORK INJECTION PARTNERS	
Current participation in any HIV prevention study	Chart notes and eligibility checklist.
Previous or current participation in an HIV vaccine trial	Chart notes and eligibility checklist.
Any reactive or positive HIV test at Screening or Enrollment, even if the individual is confirmed to be HIV-uninfected	Local laboratory results and eligibility checklist.
Appearance of psychological disturbance or cognitive impairment or any other condition that in the opinion of the investigator would limit the ability to understand study procedures, would make participation in the study unsafe, or otherwise interfere with the study activities	Chart notes and eligibility checklist.
Previously named and enrolled as a partner of another index participant	fingerprint or other tracking database

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Signature of Investigator Date

3.3.4 Document Organization

Study staff must make every effort to keep all research records – individual participant records as well as logs and documents pertaining to all participants – confidential and secure. All records should be securely stored in an area with access limited to authorized staff only.

All study-specific documents and biological specimens that are transmitted to an off-site location, including DataFax CRFs, and all biological specimens processed in any way by non-study staff or transferred to an off-site location must be identified only by the participant's study identification number (PTID) to maintain confidentiality. Inclusion of more than one identifier on other study records that are accessible only to authorized study staff is not prohibited by DAIDS; however, such records must be stored securely with limited access. Regardless of whether the participant identifier on a particular document is the participant's name or PTID number, the original identifier may not be obliterated or altered in any way, even if another identifier is added. When necessary to maintain confidentiality, identifiers may be obliterated or altered on copies of original source documents. For example, if supporting documentation of study eligibility that is to be submitted to the HPTN LOC, such as chart notes or lab reports, contains a participant's name, this should be obliterated on the copy transmitted off-site, but not on the original.

All local databases will be secured with password-protected access systems.

Log books, appointment books, and any other listings that link participant PTID numbers to participant names or other personal identifiers should be stored securely in a location separate from records identified by either participant ID or name. These documents should never be left unattended or easily accessible to unauthorized individuals when in use.

3.4 Reportable Protocol Deviations

The HPTN has established a reporting system to describe individual incidents, trends or omissions that result in significant added risk to the participant, non-adherence to significant protocol requirements and significant non-adherence to GCP. These are referred to as reportable protocol deviations. (More information about reporting a protocol deviation can be found at https://www.hptn.org/sites/default/files/inline-files/Entire%20MOP_March2017_1.pdf.)

Reportable protocol deviations are closely related to what the Clinical Site Monitor (i.e.,PPD) identifies as protocol non-adherence and violations, but there is not a one-to-one correlation. Protocol deviations reported by the protocol team are only those incidents that will affect patient safety and the outcome of the study. Non-adherence events and violations encompass every infraction of the protocol. For example, if a blood specimen is drawn for a CD4 cell count, but is not processed by the laboratory, it is a non-adherence event according to the Clinical Site Monitor but it is not a reportable

protocol deviation. If, however, a CD4 is to be drawn at each index participant visit and is not being done at all, this is both a protocol violation as well as a reportable protocol deviation. Other examples of reportable protocol deviations are:

- Enrollment of an ineligible patient.
- Informed consent not obtained prior to performing protocol-specified procedures.
- Protocol-specified procedures not followed.
- Breach of participant confidentiality.
- A site specific laboratory assay is deliberately added to protocol requirements by the investigator to be conducted for all participants.

Note: Participant non-compliance with the study protocol, including treatment specifications, is not considered a reportable protocol deviation.

All deviations that meet the above criteria, and any others not outlined above that are deemed as meeting the criteria for protocol deviations, will be reported using the Protocol Deviation Log Case Report Form. Protocol deviations that meet the above criteria that are identified by site staff or staff from LOC, SDMC, PPD and LC must be documented within 30 calendar days of awareness. The protocol deviation should be documented in an email to 074protdev@hptn.org containing the following information:

- Date that the protocol deviation occurred.
- Date of site awareness of the protocol deviation.
- Date protocol deviation reported.
- Identification (ID) numbers of participant(s) involved/affected.
- Brief summary of deviation (description of event, location it occurred, if relevant).
- Steps taken to address the deviation.
- Steps taken to prevent further occurrences of the deviation.
- Name, title and contact information of the person completing the report.

A copy of the email should be maintained at the site and the appropriate CRF should be completed (do not send the completed CRF to the 074 protocol deviations email alias list).

The site should follow the IRB/EC policies for reporting protocol deviations to the IRB/EC.

3.5 Record Retention Requirements

All study-related regulatory and administrative documentation as well as participant research records must be retained on-site throughout the study's period of performance and for at least three years after the completion or termination of the trial.

The study-related records include but are not limited to the following:

- Study management information, including the protocol, clarifications, letters of amendment, protocol amendments, the SSP manual and associated errata, addenda, and bulletins.
- Signed informed consent forms for each study participant.

- Audio files and written transcripts of qualitative interviews.
- CRFs for each study participant labeled by PTID.
- Source documents such as chart notes and laboratory result reports.

3.6 Ancillary Studies

Ancillary studies or "sub-studies" are defined as secondary investigations conducted in conjunction with a primary or "main" HPTN study. The investigator proposing the ancillary study is responsible for ensuring that all necessary approvals are obtained and that all relevant HPTN and DAIDS procedures are followed. All ancillary studies (sub-studies) using HPTN funding and/or data or biological specimens from a primary HPTN study are subject to HPTN administrative approval and, if applicable, to DAIDS regulatory approval.

The purpose of the review and approval process is to ensure that site and central Network resources are being used appropriately and that the rights and well-being of human subjects are protected in accordance with 45 CFR 46. The administrative and regulatory requirements for the conduct of ancillary studies can be found in the HPTN Manual of Operations (MOP) at https://www.hptn.org/sites/default/files/inline-files/Section%2017.pdf.

3.7 Study Publications

All manuscripts, abstracts, posters or presentations based on the results or conduct of HPTN 074 must be prepared in accordance with the HPTN MOP, and the HPTN Publication Policy (available at https://www.hptn.org/sites/default/files/inline-files/Section%2021%20July%202017_0.pdf).