

## Section 3. Documentation Requirements

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### 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 (DWD-POL-RA-03.00)* and *ICH E6 Good Clinical Practice: Consolidated Guidance* specify 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 052. 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, and clarification memos).
- Informed Consent Forms (all IRB-approved versions, local language and back-translations, all signed and dated forms from screened and enrolled study participants).
- Package Insert for each antiretroviral agent provided for the study. If the drug is not yet approved in the site’s country, the Investigator’s Brochure should also be maintained.
- FDA Form 1572, signed and dated by the Investigator of Record. The site must submit the original of this document to DAIDS; the site maintains a copy in their regulatory files.
- Documentation of approved protocol registration from DAIDS.
- Documentation of study activation from the HPTN CORE CRM.
- Documentation of local regulatory authority correspondence, authorization, and/or approval of the protocol if applicable.
- CTU 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 and advertisements for participant recruitment, as well as subsequent updates.
- Screening, enrollment, and randomization logs.
- Participant identification code list.
- Expedited Adverse Event (EAE) Reports.
- Product safety reports issued by DAIDS.
- Pharmacy accountability records, including a sample of the labels attached to investigational product containers and shipping records.
- Study staff roster, signature sheet, and delegation of duties, including Investigator responsibilities.
- Signed and dated CV for each study staff member, current within the last year.
- Financial disclosure forms (the original forms are maintained by the site).
- Documentation of staff members' humans 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.
- Key study-related correspondence with the HPTN Central Lab, SCHARP, the HPTN CORE, the RCC, or DAIDS, as well as other 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 SOPs that will be used for HPTN 052 and all subsequent updates.

- DAIDS reference materials including: 1) *DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00 and subsequent updates)* 2) *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 subsequent updates)*, 3) DAIDS Protocol Registration Policy and Procedures Manual (August 2004 and any subsequent updates), and 4) Manual for Expedited Reporting of Adverse Events to DAIDS (May 6, 2004 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 (for PPD, HPTN CORE, SCHARP, HPTN NL, and other site visits).
- A complete, blank copy of the case report forms (CRFs) (original and all revisions).
- All completed CRFs, initialed and dated.
- Record of stored specimens.
- Source documentation table (see Section 3.3.3.3, Table 3-1).
- Source documents.
- Signed agreements related to the study (e.g., between IoR and affiliated sites).

### **3.3 Participant Research Record**

Study sites 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)*, the research record consists of the following: original subject-signed informed consent form(s), participant source documents, pharmacy records, 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. Study sites 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 (DWD-POL-CL-04.00)* and the standards outlined in this manual.

For HPTN 052, participant source documents will consist of narrative chart notes, visit checklists, medical records, laboratory reports, pharmacy records, and forms provided by SCHARP (DataFax and non-DataFax). As a condition for study activation, each 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 written informed consent to participate in the study prior to the conduct of any study procedures.
- Documentation that the participant met the study's selection (eligibility) criteria.
- 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 the participant's randomization assignment.
- A record of the participant's exposure to the study products.
- A record of any AEs and EAEs.
- Complete source documents.
- 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., exam and 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 (DWD-POL-CL-04.00) 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.*

### 3.3.3 Examples of Source Documentation

#### 3.3.3.1 Clinic Notes

Study staff must document every contact with a study participant in a signed and dated clinic note specifying the date, type, purpose, location of the contact, and the general status of the participant. Clinic notes also must be used to document the following:

- The informed consent process
- Procedures performed that are not recorded on other source documents
- 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 (DWD-POL-CL-04.00)* 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.

One way that clinic notes can be structured is by using the SOAP method. The acronym SOAP stands for Subjective, Objective, Assessment, and Plan and the following information is included in each section:

**S:** Subjective information that includes what the patient tells you about how he/she is feeling or his/her symptoms. For example how he/she is sleeping or eating or if he/she is experiencing pain or having trouble urinating or defecating.

**O:** Objective information including vital signs, pertinent physical exam findings, and the most recent laboratory test results.

**A:** The assessment describes your diagnosis of the symptoms. The assessment also includes a summary of how the patient is doing and what has changed from the previous visit.

**P:** The plan includes how each diagnosis or problem will be addressed. This section will include information about new or changes to existing medication, laboratory tests to order, and consults to obtain.

Below are two examples of clinic notes using the SOAP method:

**Sample Clinic Note for a Screening Visit:**

**22 JAN 2004:** Participant presented for HPTN 052 screening at study site. Obtained written informed consent for screening before initiating any procedures. Procedures were completed per the visit checklist and site SOPs.

**S:** Participant reported no current health problems.

**O:** HIV test positive. Long-term partner identified and willing to come to clinic for testing.

**A:** Participant is eligible for the study thus far.

**P:** Test partner for HIV. Draw blood and collect urine to determine eligibility.

{staff signature/date}

**Sample Clinic Note for an Enrollment Visit:**

**30 JAN 2004:** Participant presented for HPTN 052 enrollment visit at study site. Obtained written informed consent for enrollment before initiating any procedures. Participant was not willing to consent for specimen storage for future research. Procedures were completed per the visit checklist and site SOPs.

**S:** Participant reported headaches during the past week.

**O:** Blood work results for CD4+ cell count, hemoglobin, platelet count, creatinine, AST, ALT, alkaline phosphatase, and total bilirubin. Physical exam and genital exam conducted. No laboratory abnormalities or clinical evidence of STDs found.

**A:** Participant is eligible for the study. Recent headaches are not indicative of more serious illness.

**P:** Enrollment completed. Patient randomized to treatment arm A and given ART (Combivir and nevirapine). Two week visit scheduled for 13 FEB 2004.

{staff signature/date}

### 3.3.3.2 Visit Checklists

The checklists provided in Section 6 of this SSP manual may be used as a convenient tool for study staff to ensure that all study procedures are performed at each visit. The checklists are not designed to serve as source documentation in their current format; however, they may be modified to serve this purpose as described in Section 6. If a site modifies the checklists to serve as source documents, individual study staff members must initial *only* those procedures that they complete to fulfill the source documentation requirement of identifying responsibility. In addition, if procedures listed on a single checklist are completed across multiple dates, the date upon which each procedure is completed must be clearly noted.

Even with modification, the checklists alone may not be sufficient for documenting all procedures. For example, chart notes may be required to document procedures performed at unscheduled study visits or to explain why procedures in addition to those specified on a checklist have been performed. Chart notes may also be required to document the content of counseling sessions and/or other in-depth discussions with participants (*e.g.*, related to adherence to protocol requirements).

### 3.3.3.3 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 CORE 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 your site. Table 3-1 will be finalized and signed at each site 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.
- Enter the alternative source document into the participant's study chart.
- 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: HPTN 052 Source Documentation for All CRF Items**

**(NOTE: This table is an example document. Each site must complete a site-specific table during protocol-specific training.)**

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.

CRF Name	Acronym	Source			Comments
		Yes	No	Mixed	
Index Enrollment	IEN-1		X		Clinic notes are the source for item 2. The informed consent forms are the source for items 3 and 3a. The Randomization Assignment Envelope and Envelope Tracking Record are the source for item 4 and 4a. Counseling checklists and clinic notes are the source for items 5 and 6.
Partner Enrollment	PEN-1			X	The informed consent forms are the source for items 1 and 5. Counseling checklists and clinic notes are the source for items 2, 3, 6, 6a1-6a5, and 6b. This CRF is the source for items 4 and 4a.
Index/Partner Demographics (Note: Add the relevant CRFs: IDZ-1, IDI-1, IDW-1, IDT-1, IDB-1 and PDZ-1-PDI-1, PDW-1, PDT-1, PDB-1)	IDM-1, PDM-1	X			This CRF is the source for all items.
Index Complete Hematology	ICH-1			X	Local laboratory reports <sup>1</sup> are the source for all items, except the AE Severity Grade, for which this CRF is the source, and the AE Log page #, for which another CRF is the source.
Index Complete Chemistries	ICC-1			X	Local laboratory reports <sup>1</sup> are the source for all items, except the AE Severity Grade, for which this CRF is the source, and the AE Log page #, for which another CRF is the source.
Index Enrollment CD4/Viral Load Results	IEV-1		X		Local laboratory reports <sup>1</sup> are the source for all items.
Index Enrollment Pregnancy Report and History	IPR-1 IPR-2		X		Local laboratory reports <sup>1</sup> are the source for items 1 and 2. Clinic notes are the source for items 5 – 7 and 7a-7j.
Index Pre-exiting Conditions	IPRE-1		X		Clinic notes are the source for all items.
Index/Partner STDs	IST-1, PST-1		X		Local laboratory reports <sup>1</sup> are the source for all items except item 2, for which clinic notes are the source.
Index/Partner Symptomatic STDs	ISS-1, PSS-1		X		Clinic notes are the source for all items.
Index/Partner Sexual History Assessment	ISX-1, PSX-1	X			This CRF is the source for all items.
Index/Partner Circumcision Assessment	ICA-1 PCA-1		X		Clinic notes are the source for all items.
Index QOL	IQL-1, IQL-2, IQL-3, IQL-4	X			This CRF is the source for all items.
Index Concomitant Medications Log	ICM-1			X	Clinic notes and pharmacy records are source for all items except for the question “Taken for a reported AE,” for which this CRF is the source and “Record AE Log pages” for which other CRFs are the source.

CRF Name	Acronym	Source			Comments
		Yes	No	Mixed	
Index Pill Count	IPC-1		X		Pharmacy records and notes are the source for all items.
Index ART Treatment Regimen Log	ITX-1			X	Clinic notes and pharmacy records are the source for all items except for item 8, for which this CRF is the source, and item 8a, for which other CRFs are the source.
Index Treatment Adherence	ITA-1, ITA-2, ITA-3	X			This CRF is the source for all items.
Index AE Log	IAE-1			X	This CRF is the source for items 3a, 8, 10a.-10d, and 10a1-10d1. Clinic notes are the source for items 1, 1a, 2, 3, 4, 6, 6a, 7, and 9. Pharmacy records are the source for item 5.
Index Pregnancy Report	IP-1		X		Clinic notes are the source for all items.
Index Pregnancy Outcome	IPO-1		X		Clinic notes are the source for all items.
Index/Partner Specimen Collection	ISC-1, PSC-1		X		Specimen collection, lab requisition, or specimen transfer forms are the source for all items.
Index CD4/Viral Load Results	IFV-1		X		Local laboratory reports <sup>1</sup> are the source for all items except item 3b, for which clinic notes are the source.
Index Immunologic/Virologic Failure	IVA-1		X		Local laboratory reports <sup>1</sup> are the source for all items except item 3, for which clinic notes is the source.
Partner CD4/Viral Load Results	PVL-1		X		Local laboratory reports <sup>1</sup> are the source for all items.
Partner HIV Test Results	PHT-1			X	Local laboratory reports <sup>1</sup> are the source for all items except item 4a, for which this CRF is the source.
Partner Complete Hematology Results	PCH-1		X		Local laboratory reports <sup>1</sup> are the source for all items.
Partner Complete Chemistries	PCC-1		X		Local laboratory reports <sup>1</sup> are the source for all items.
Index When-to-Start	IWT-1 IWT-2 IWT-3 IWT-4			X	Clinic notes are the source for items 1a – 1d, 1f – 1i, 1il, 4a, 5a-d (relationship of diagnosis to medication), 6, 6a, 6a1-6a6, 7, and 7a. Local laboratory reports <sup>1</sup> are the source for items 3, 3a – 3f, 4, 4b-4g Pharmacy records are the source for items 5, 5a-d (action taken with medication) This CRF is the source for items 1, 1e, 2, and 5a-d (drug code)
Index Follow-up Visit	IFU-1 IFU-2		X		Clinic notes are the source for items 3, 4a, 4b, 4d, 5d, 5f1, 5f2, 5g, and 6. Counseling checklists and clinic notes are the source for items 5b and 5c. Local laboratory results <sup>1</sup> are the source for items 1, 5d1, and 5e. Pharmacy records are the source for items 4c and 5f.
Partner Follow-up Visit	PFU-1		X		Clinic notes are the source for items 1, 2c, 2c1, 4, 5, 5a, and 5b. Counseling checklists and clinic notes are the source for items 2b and 3a-d.
Index/Partner Interim Visit	IIV-1, PIV-1		X		Other CRFs are the source for all items.
Couples Status	CPS-1		X		Clinic notes are the source for all items except item 4, for which the randomization assignment envelope is the source.
Couples Missed Visit	CMV-1		X		Clinic notes are the source for all items.

CRF Name	Acronym	Source			Comments
		Yes	No	Mixed	
Couples Receipt	CR-1			X	This CRF is the source for items 1 and 2. Informed consent forms are the source for items 3-6a.
Couples Transfer	CT-1			X	This CRF is the source for all items, except 3 for which clinic notes are the source.
Couples End of Study Inventory	CES-1		X		Other CRFs are the source for all items except items 6 and 6a – 6c, for which the randomization assignment form is the source.
Index Death Narrative	IDN-1		X		Clinic notes are the source for all items.
Couples Termination	CTM-1		X		Clinic notes are the source for all items.
Index Termination	ITM-1			X	This CRF is the source for all items except 2b, 2b1 and 2b2, for which clinic notes are the source and item “Record Index AE Log page” for which another CRF is the source.
Partner Termination	PTM-1			X	This CRF is source for items 1, 2a, 2c, 2d, 2e, 2f, 2g, 2i, 2j, 2k, 2l, and 2m. Clinic notes are the source for item 2b, 2b1, 2b2, and 2n. Local laboratory results <sup>1</sup> are the source for item 2h.

\_\_\_\_\_  
Signature of Investigator of Record

\_\_\_\_\_  
Date

#### **3.3.3.4 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. Sites are encouraged, but not required, 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.

If a site chooses to use Table 3-2, 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. This example table is reflective of the inclusion/exclusion criteria in Version 3.0 of the protocol.

**Table 3-2: HPTN 052: Source Documentation for Eligibility Criteria (EXAMPLE)**

Eligibility Requirements	Source Document
<b>Index</b>	
Positive HIV serology obtained within 60 days of enrollment	HIV test results
Sexual partner without HIV willing to participate	Clinic notes, informed consent form
Plans to maintain sexual relationship with identified partner	Clinic notes
Sexual activity ( $\geq 3$ times in past 3 months)	Clinic notes
Willing to be randomized if pregnant or breast-feeding	Clinic notes
CD4 count (must be between 350-550 cells/mm <sup>3</sup> )	Lab results
Hemoglobin (must be $\geq 7.5$ g/dL)	Lab results
Platelet count (must be $\geq 50,000/\mu\text{L}$ )	Lab results
AST, ALT, ALK Phos (must be $\leq 5$ x ULN)	Lab results
Total bilirubin (must be $\leq 2.5$ x ULN)	Lab results
Creatine clearance $\geq 60$ mL/min	Lab results
Absolute neutrophil count $\geq 750$ mm <sup>3</sup>	Lab results
Age ( $\geq 18$ years old)	Clinic notes or screening log
Willing to disclose HIV test results to partner	Index Eligibility Checklist or clinic note
Location/relocation (anticipates staying in area)	Clinic notes
No current or previous use of ART (none except for MTCT)	Clinic notes
No documented or suspected hepatitis within 30 days of enrollment	Clinic notes
No current or previous AIDS defining illness	Clinic notes
No injection drug use (none within last 5 years)	Index Eligibility Checklist or clinic note
No experimental HIV vaccine	Index Eligibility Checklist or clinic note
No current or anticipated incarceration	Index Eligibility Checklist or clinic note
No acute therapy for serious illness within 14 days of enrollment	Clinic notes
No radiation or chemotherapy within 45 days of enrollment	Clinic notes
No active drug or alcohol dependency	Clinic notes
No immunomodulator or investigational therapy within 30 days of enrollment	Clinic notes
No vomiting or inability to swallow such that the participant cannot take the study drug	Index Eligibility Checklist or clinic note
No need for a prohibited medication as listed in the protocol	Clinic notes
No allergy/sensitivity to any study drugs or their formulations	Clinic notes
Any other condition that may affect study participation	Clinic notes
<b>Partner</b>	
Negative HIV serology within 14 days prior to enrollment	HIV test results
Sexual partner with HIV willing to participate	Clinic notes, informed consent form
Plans to maintain sexual relationship with identified partner	Clinic notes
Sexual activity ( $\geq 3$ times in past 3 months)	Clinic notes
Age ( $\geq 18$ years old)	Clinic notes or screening Log
Willing to disclose HIV test results to partner	Index Eligibility Checklist or clinic note
Location/Relocation (anticipates staying in area)	Clinic notes
Injection drug use (none within last 5 years)	Index Eligibility Checklist or clinic note
No experimental HIV vaccine	Index Eligibility Checklist or clinic note
No current or anticipated incarceration	Index Eligibility Checklist or clinic note
Any other condition that may affect study participation	Clinic note

\_\_\_\_\_  
Signature of Investigator of Record

\_\_\_\_\_  
Date

### **3.3.4 Document Organization**

Study staff must make every effort to keep all research records - both 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, EAE Report Forms, 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 for an EAE Report is to be submitted to DAIDS, such as x-rays or lab reports, contain 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.

The receipt, dispensing, and return of all study product (antiretroviral therapy provided for the study) will be documented by HPTU pharmacists in accordance with Section 8 of this SSP manual. Separate accountability records must be maintained for each study product. As with source documentation, all study product inventory records must be stored securely at the HPTU.

## **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.

Reportable protocol deviations are closely related to what the Clinical Site Monitor (e.g. 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 ALT, 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, an ALT is to be drawn at each patient 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
- non-compliance with study randomization and blinding 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

*Participant non-compliance with the study protocol, including treatment specifications, is not considered a reportable protocol deviation, but should be discussed by the Protocol Team.*

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 a protocol deviation form found in the HPTN MOP. Study staff or other protocol team members will work jointly with DAIDS to assess the deviation's severity. Protocol deviations that meet the above criteria that are identified by site staff or staff from CORE, SDMC and NL must be documented within 30 calendar days of awareness. The protocol deviation should be documented in a report 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 all reports for each study, regardless of author, should be maintained at the site and the distribution list for the reports should include:

- Protocol Chair (Myron Cohen)
- Site Investigator of Record
- Site Study Coordinator
- Site Quality Assurance/Quality Control Coordinator(s)
- CORE Clinical Research Managers/Protocol Specialist (CRMs/PS)  
(Theresa Gamble, Marybeth McCauley, Jackie Talley)
- SDMC Project Manager (PM) (Leslie Cottle)
- NL representative (Estelle Piwowar-Manning)
- Member of the DAIDS Prevention Sciences Branch (PSB) or Office of Clinical Site Oversight (OCSO)
- DAIDS Medical Officer (Vanessa Elharrar)
- If the deviation involves an investigational product, the DAIDS protocol pharmacist should be included in the distribution list. (Ana Martinez)

### **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 after the completion or termination of the trial.

As this study is being conducted under IND, the study-related records must be maintained for 2 years after the marketing application is approved for the drug(s); or, if an application is not approved for the drug(s), until 2 years after shipment and delivery of the drug(s) for investigational use is discontinued and the FDA has been so notified (21 CFR 312.57).

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.
- CRFs for each study participant labeled by PTID.
- Source documents such as clinic notes, pharmacy records, 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).

### **3.7 Study Publications**

All manuscripts, abstracts, posters or presentations based on the results or conduct of HPTN 052 must be prepared in accordance with the HPTN MOP, and the HPTN Publication Policy (available at [http://www.hptn.org/network\\_information/policies\\_procedures.htm](http://www.hptn.org/network_information/policies_procedures.htm)). Publications may also need to be reviewed by the companies who have donated drug to the study; such terms will be spelled out in the Clinical Trials Agreement (CTA) with each company.