

Section 3 Documentation Requirements

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Section 3 Documentation Requirements

Study site staff are responsible for the collection, storage, timely submission, and quality assurance of study data collected at their site. In addition, the site is responsible for maintaining all administrative and regulatory documentation critical to the conduct of the study, known as Essential Documents. This section contains a listing of required Essential Documents that each site must maintain and keep current throughout the study, as well as procedures for establishing adequate and accurate participant research records.

3.1 Essential Documents

The DAIDS Standard Operating Procedure (SOP) for Essential Documents (Appendix B) specifies the administrative and regulatory documents that HPTN study sites must maintain for DAIDS-sponsored studies, including HPTN 058. 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. However, documents must be stored in an organized manner for easy access and review.

Table 3-1 at the end of this section presents a suggested filing structure for HPTN 058 essential documents. The suggested structure incorporates guidance received from the DAIDS Prevention Science Branch Clinical Operations Group and the DAIDS Clinical Site Monitoring Group (PPD). Study sites are not required to adopt the suggested structure, but all sites are encouraged to consider the suggested structure when developing their filing approach for HPTN 058. All sites also are encouraged to establish an SOP to document their filing approach. Further clarifications of the suggested filing structure follows.

- Essential documents may be stored in files or in binders. The files/binders listed in Table 3-1 may be further divided, consolidated, or otherwise reorganized if desired.
- It is recommended that a contents sheet be inserted as the first page(s) of each file/binder. Within each file/binder, it is recommended that documents be filed in ascending date order.
- Study drug related essential documents will be filed in the study pharmacies. Details of other documents to be maintained in the pharmacies are provided in Section 9.
- Certain lab related essential documents will be stored with the other essential documents (see Table 3-1) to facilitate routine inspection of these documents by study monitors. Other lab related essential documents (e.g., lab SOPs not listed) may be filed in the lab.

The suggested filing structure assumes that:

- Individual HPTN 058 participant study records, including signed and dated informed consent forms, will be stored separately in the study clinic or data management area, not necessarily with the essential documents listed here.
- The HPTN 058 Screening and Enrollment Log, Participant Identification Number (PTID) - Name Link Log, and Clinic Randomization Logs will be stored in the study clinic(s) or data management area, not necessarily with the other essential documents listed here.

- Site- and study-specific quality management documentation will be maintained separately from study-specific essential documents.

3.2 Participant Research Records

US regulations and guidelines for Good Clinical Practices (GCP) require study site staff to maintain adequate and accurate participant “case history records” containing all information pertinent to the study for each HPTN study participant. All study data should be collected in accordance with applicable specifications of this manual and the DAIDS SOP for Source Documentation included in Appendix C.

3.2.1 Participant Research Record Content

Participant research records 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 (including Informed Consent Comprehension Quizzes for screening and enrollment)
- documentation that the participant provided written informed consent to store study specimens for future testing if allowed at site
- documentation that the participant met the study's eligibility criteria
- a record of the participant's randomization assignment
- a record of the participant's exposure to study drug
- a record of all contacts and attempted contacts with the participant, including all clinic visits, and all verbal and written contacts
- a record of all procedures performed by study staff during the study
- complete source documents; e.g., notes recorded by attending nurse or record of any visits to referral physicians, if available (certified copy of notes)
- a record of any adverse events (AEs) (not DataFaxed for this study, but collected in participant charts), serious adverse events (SAEs) and Expedited Adverse Events (EAEs) including onset and resolution dates, severity grading and relationship to study product
- study-related information on the participant's condition before, during, and after the study, including:
 - subjective data obtained directly from the participant (e.g., interview responses)
 - objective data ascertained by study staff (e.g., exam and lab findings)
 - objective data obtained from non-study sources (e.g., non-study medical records and death certificates)

In addition to the above, the DAIDS SOP for Source Documentation requires that all protocol departures/deviations/violations be documented as protocol deviations in the participant's study records, along with reasons for the departures and attempts to prevent or correct the departures, if applicable.

3.2.2 Concept of Source Documentation

The ICH guidance for GCP defines source data and source documentation as follows:

The term “source data” refers to all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

The term “source documents” refers to original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects’ diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, microfiche, photographic negatives, microfilm or magnetic media, x-rays, subject files, and records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the trial).

Source documents are commonly referred to as the documents —paper-based or electronic— upon which source data are first recorded. HPTN study sites must adhere to the standards of source documentation specified in the DAIDS SOP for Source Documentation in Appendix C. This SOP contains both requirements and recommendations. Study sites must comply with all requirements and are advised, but not required, to comply with all recommendations. Source documentation includes original documents and certified copies that include documentation pertaining to a subject while on study.

For each HPTN study, participant case history records typically consist of some or all of the following:

- narrative chart notes
- visit checklists or other study-specific flow sheets
- laboratory reports
- DataFax case report forms (CRFs) and non-DataFax forms provided by the HPTN Statistical and Data Management Center (SDMC)
- randomization log or other documentation pertaining to participants’ randomization assignments
- investigational product dispensing, accountability and chain of custody records
- Locator information and contact logs
- other source documents and non-DataFax study forms/questionnaires

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. Study staff must follow the specifications of this SOP consistently for all study participants throughout the study. It is the responsibility of the study site to determine the most appropriate source document for each required case history element listed in Section 3.2.1. Table 3-2 at the end of this section provides example source documents for each case history element for this study. Each site must complete a site-specific version of this table.

In the event that study staff is not able to record source data directly onto forms designated as source documents, the following procedures should be undertaken:

- 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 CRF
- enter a chart note stating the reason why an alternative source document was used.

Supplemental information on the use of chart notes and DataFax and non-DataFax forms as source documents is provided in sections 3.2.4 and 3.2.5.

3.2.3 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.

Study records must be stored in the same manner for all participants. All study-specific documents that are transmitted to an off-site location, including DataFax CRFs and 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 PTID to maintain confidentiality. Inclusion of more than one unique participant 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. Study records that contain participant names or other personal identifiers, such as locator forms and informed consent forms, are recommended to be stored separately from study records identified by PTID.

Regardless of whether a participant identifier on a particular document is the participant's name or PTID, 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 medical records obtained from a non-study medical provider bear the participant name, the original document must remain unaltered and should be stored with other study documents bearing the participant's name. A copy of the document could be added to the participant's chart, with the participant's name obliterated from the copy and his/her PTID entered onto the document. Likewise, if supporting documentation for an EAE Report that is to be submitted to DAIDS, such as x-rays 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 PTIDs to participant names or other personal identifiers should be stored securely in a location separate from records identified by either PTID or name. These documents should never be left unattended or easily accessible to unauthorized individuals when in use.

It is strongly recommended that each site designate a single place where completed DataFax forms will be stored prior to transmission and a single place where transmitted forms will be stored prior to filing and/or re-filing in participant charts. A similar system should be established for EAE Report Forms and other records (e.g., laboratory results forms) that are transmitted to off-site locations and then returned to the participant's file.

As a condition for study activation, each study site must establish an SOP for data management. This SOP minimally should contain the following elements:

- Procedures for assigning PTID numbers, linking ID numbers to participant names, and storing the name-number link log
- Procedures for establishing participant files/charts/notebooks
- During-visit participant chart and CRF review procedures
- Post-visit participant chart and CRF review procedures and timeframes
- Data transmission procedures, including timeframes, case report form storage locations before and after faxing, and mechanisms for identifying when forms have been transmitted
- Procedures for resolving data quality queries sent from the SDMC
- Procedures for handling and filing recruitment and retention workers' logs, worksheets, etc.
- Storage locations for blank CRFs
- Procedures for back-up of electronic study data
- Handling of participant study records for off-site contacts
- Confidentiality protections
- Other ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- Quality control/quality assurance (QC/QA) procedures related to the above (if not specified elsewhere)
- Procedures for attempting to collect data on participants lost to follow up with a particular emphasis on the primary endpoints (HIV-infection and death), including what types of information are acceptable locally (i.e. death certificate, relative word-of-mouth, etc.).

3.2.4 Chart Notes

Chart notes may be used to document the following:

- 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 the protocol deviation form or other source documents

All chart notes or other tools used as source documentation must document the PTID number and/or name of the study participant to whom they pertain, the identity of the study staff member who entered information, and the date of the entry. Study sites are strongly encouraged to adopt a

common format — such as the subjective-objective-assessment-plan (SOAP) format — for all chart notes, to help ensure adequacy and consistency of note content and maximize adherence to GCP standards. Further information and guidance on the SOAP format can be found in Appendix 11 of the HPTN Manual of Operations (MOP) available at: <http://www.hptn.org/MOP2007/HPTNMOP2007.htm>. Alternative standardized formats are acceptable and may be adopted by study sites.

3.2.5 DataFax and Non-DataFax Forms Provided by the SDMC

CRFs are designed for use with the DataFax data management system described in Section 7. The SDMC will provide these forms to each site taking part in the study. The SDMC may also provide some non-DataFax forms to each participating site.

3.3 Record Retention Requirements

All study-related regulatory and administrative documentation as well as participant research records related to each participant screened and/or enrolled in the study must be retained on-site throughout the study's period of performance and after the completion or termination of the trial.

Documents should be maintained for 3 years following the last participant visit. Prior to the destruction of any study documentation, the clinical site must request permission in writing from DAIDS.

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

- Study management information, including the protocol, clarification memos, letters of amendment, protocol amendments, the study-specific procedures (SSP) manual and associated memos, addenda, and bulletins.
- Regulatory documents, including IRB documentation, product safety information, and staffing documentation.
- Signed informed consent forms for each study participant.
- CRFs for each study participant labeled by PTID.
- Source documents such as clinic notes, pharmacy records, locator information, contact logs, and laboratory result reports.

The sponsor may provide further instructions for long-term storage of study records after the study is completed. No documents may be destroyed without written authorization from DAIDS.

3.4 Product Dispensing and Accountability Records

The receipt, dispensing, and final disposition of all study drug and supplies must be documented by designated study site staff in accordance with the *Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks*, as well as any supplemental instructions provided by DAIDS Pharmacy Affairs Branch (PAB), the study protocol and Section 9 of this SSP Manual.

3.5 Protocol Deviation Reporting

The HPTN has developed a policy to cover the reporting of protocol deviations, defined as individual incidents or omissions in study conduct that result in:

- Significant added risk to the participant
- Non-adherence to significant protocol requirements
- Significant non-adherence to the ICH E6: Guideline for Good Clinical Practice

Examples of protocol deviations that require formal documentation (Protocol Deviation Form) are:

- Enrolling an ineligible participant
- Not obtaining informed consent prior to performing protocol-specified procedures
- Deviating from study randomization procedures
- Not completing significant protocol-specified procedures or allowing a pattern of non-compliance (*Note: Participant non-compliance with the study protocol, including study treatment or visit scheduling specifications, is not considered a reportable protocol event.*)
- Breaching participant confidentiality
- Dispensing a larger dose of study drug than prescribed
- Failing to permanently discontinue a participant from study drug when indicated

Protocol deviations may be identified by site staff or representatives from the CORE, SDMC, DAIDS, or the Network Lab. Site staff should consult with the CORE Protocol Specialist and/or SDMC Project Manager if they are unsure whether an occurrence should be reported as a protocol deviation.

Protocol Deviation Forms must be completed with the following information:

- Occurrence date (*Note: If the event occurred over a period of time, the period between when the event started and ended should be specified.*)
- Awareness date on site
- Report date
- PTID of participants involved/affected (*Note: If more than one participant is involved in the event, the PTIDs for all participants can be included on one deviation form. If the event does not involve specific participant(s), this item will be left blank.*)
- Brief summary of deviation (description and location of occurrence if relevant)
- Steps taken to address this deviation
- Steps taken to prevent further occurrence
- Name, title and contact information of the person completing the reporting

In most cases, site staff will be asked to complete the Protocol Deviation Report Form and send a draft to the CORE before submitting to the full protocol event distribution list. All complete protocol deviation reports should be sent to the following distribution list and a copy kept at the site:

- 058ProtocolDeviations@HPTN.org (includes the Protocol Chair, DAIDS Medical Officer, DAIDS Clinical Operations Group Representative, DAIDS Protocol Pharmacist, CORE Protocol Specialist, SDMC Project Manager, and HPTN NL Representative)
- Investigator of Record at site

- Site Study Coordinator(s)

Refer to “Reporting of Protocol Deviations” in [section 16.2](#) of the HPTN Manual of Operations <http://www.hptn.org/HPTNMOP2007/HPTNMOP2007.htm> for the full policy and reporting form. A copy of this form is also available in Table 3-3 below.

3.6 Ancillary Studies

Ancillary studies (or sub-studies) are defined as secondary investigations conducted in conjunction with a primary 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 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 the Code of Federal Regulations and ICH GCP. The administrative and regulatory requirements for the conduct of ancillary studies can be found in Section 17 of the HPTN Manual of Operations. The Ancillary Study Application may be found in Table 3-4 of this document

3.7 Study Publications

All manuscripts, abstracts, posters or presentations based on the results or conduct of HPTN 058 must be prepared in accordance with the HPTN Manual of Operations, the HPTN Publication Policy (available at http://www.hptn.org/network_information/policies_procedures.htm), and the Clinical Trials Agreement (CTA).

Should you have any questions, please contact the CORE PS.

Table 3-1 Suggested Filing Structure for HPTN 058 Essential Documents

<p>File/Binder #1: HPTN 058 Protocol and Current Informed Consent Forms</p> <ul style="list-style-type: none"> • HPTN 058 Protocol (including copy of signed and dated protocol signature page): Current Version and any subsequent protocol Clarification Memos, Letters of Amendment, and Amendments. • Currently-approved site-specific HPTN 058 informed consent forms (original English, translations, back-translations and translation/back-translation verification statements)
<p>File/Binder #2: Regulatory Authority Documentation (if applicable)</p> <ul style="list-style-type: none"> • Regulatory Authority Correspondence/Authorization/Approval/Notification of Protocol (if applicable; if more than one regulatory authority has oversight responsibility for research performed at the study site, include subsections for each authority)
<p>File/Binder #3A: IRB/EC Documentation for (IRB/EC A)</p> <ul style="list-style-type: none"> • FWA documentation for IRB/EC A • Roster of IRB/EC A (if available) • Relevant IRB/EC A Submission Requirements/Guidelines/SOPs • IRB Correspondence for IRB/EC A: File complete copies of all correspondence to and from the IRB/EC; include all enclosures/attachments for all submissions, even if copies of the enclosures/attachments are filed elsewhere • IRB approval documentation; include stamped consents if approval letter does not reference which version of the consents were approved
<p>File/Binder #3B: IRB/EC Documentation for (IRB/EC B)</p> <ul style="list-style-type: none"> • FWA documentation for IRB/EC B • Roster of IRB/EC B (if available) • Relevant IRB/EC B Submission Requirements/Guidelines/SOPs • IRB Correspondence for IRB/EC B: File complete copies of all correspondence to and from the IRB/EC; include all enclosures/attachments for all submissions, even if copies of the enclosures/attachments are filed elsewhere • IRB approval documentation; include stamped consents if approval letter does not reference which version of the consents were approved
<p>File/Binder #4: Product Safety Information</p> <ul style="list-style-type: none"> • Product Safety Information/Reports/Memos (as provided by DAIDS) • Suboxone Package Insert: current version and any subsequent updates <p><i>Notes:</i></p> <ul style="list-style-type: none"> • Expedited adverse event reports will be stored in participant study notebooks. • Documentation of IRB/EC submission of above-listed documents (if applicable) will be maintained in the relevant IRB/EC Files/Binders (i.e., File/Binder #3A and #3B).
<p>File/Binder #5: HPTN 058 Study-Specific Procedures (SSP) Manual</p> <p>Final version 1.0 and any subsequent updates</p> <p><i>Notes:</i></p> <ul style="list-style-type: none"> • For the reference copy of the SSP Manual, do not discard out-dated pages or sections when updates are issued; retain all versions of all pages as a complete historical record. • The SSP Manual contains reference versions of all study CRFs; therefore additional (blank) copies of the CRFs need not be stored elsewhere in the essential documents files.
<p>File/Binder #6: HPTN 058 Study-Specific Standard Operating Procedures</p> <ul style="list-style-type: none"> • Final approved version and any subsequent updates of each SOP.

File/Binder #7: HPTN 058 Staffing Documentation

- FDA Form 1572 (original signed and dated form submitted to RCC for Protocol Registration, and any subsequent updates)
- HPTN 058 Investigator of Record CV (copy of CV submitted to RCC for Protocol Registration; it is recommended that CVs be updated as needed and signed and dated at least every two years)
- Financial Disclosure Forms (original signed and dated forms, and any subsequent updates)
- Study Staff Roster (submitted to FHI for study activation, and any subsequent updates)
- Study Staff Identification and Signature Sheet (if not combined with staff roster; original and any subsequent updates)
- Study Staff Delegation of Duties (if not combined with staff roster; original and all updates)
- CVs for key study staff other than the IoR including all subinvestigators, clinicians, study coordinator(s), and Pharmacist of Record (ensure that all CVs are current prior to initiating HPTN 058; it is recommended that CVs be updated as needed and signed and dated at least annually)
- Study Staff Job Descriptions
- Documentation of Study Staff Training (Good Clinical Practice and Human Subjects Research)

File/Binder #8: Local Laboratory Documentation

- Local Laboratory Certification(s), Accreditation(s) and/or Validation(s): File documentation current at time of study activation and all subsequent updates
- Local Laboratory Normal Ranges: File documentation of relevant normal ranges for all protocol-specified tests current at time of study activation and all subsequent updates
- Laboratory Manager CV (or cross-reference to CV contained in File/Binder #7)

Note:

- *It is recommended that a cross-reference be included in this file/binder specifying the storage location(s) of other lab-related essential documents filed in the local lab(s).*

File/Binder #9: Monitoring Visit Documentation

- Monitoring Visit Log
- Initiation and Monitoring Visit Reports and Documentation of Response to Visit Findings

File/Binder #10: Documentation of Other HPTN Site Visits

- (Non-Monitoring) Site Visit Log
- HPTN CORE (FHI) Site Assessment Reports and Documentation of Response to Visit Findings
- HPTN SDMC (SCHARP) Site Visit Reports and Documentation of Response to Visit Findings
- HPTN Network Lab Site Visit Reports and Documentation of Response to Visit Findings
- Other Site Visit Reports and Documentation of Response to Visit Findings

File/Binder #11: Study-Related Sponsor Communications

- Study-related communications to and from DAIDS
- Communications to and from the DAIDS RCC (includes emails acknowledging receipt or approving protocol registration from the DAIDS Protocol Registration Office)

Notes:

- *Communications related to individual study participants will be filed in participant study records.*
- *Product-related communications with DAIDS PAB (and its contractors) will be stored in the study pharmacy.*

File/Binder #12: Other Study-Related Communications

- Key study-related communications to and from HPTN CORE (FHI)
- Key study-related communications to and from HPTN SDMC (SCHARP)
- Key study-related communications to and from HPTN Network Lab (NL)
- Other key study-related communications

Notes:

- *Any documentation of agreements or significant discussions regarding study conduct, protocol deviations, or adverse event reporting should be filed.*
- *Communications related to individual HPTN 058 study participants will be filed in individual participant study records.*
- *Product-related communications with DAIDS PAB (and its contractors) will be stored in the study pharmacy.*

File/Binder #13: Study Site Staff Meeting Documentation

- HPTN 058 Staff Meeting Agendas, Participant Lists/Sign-In Sheets, and Summaries

File/Binder #14: Conference Call Documentation

- HPTN 058 Protocol Team Conference Call Summaries
- HPTN 058 Laboratory Group Conference Call Summaries
- HPTN 058 Protocol Safety Review Team Call Summaries
- HPTN 058 Counseling Call Summaries
- Summaries of Other HPTN 058 Conference Calls, such as site-specific calls

File/Binder #15: Reference Documentation

- DAIDS SOP for Source Documentation (Version 2.0 and any subsequent updates)
- DAIDS SOP for Essential Documents (Version 2.0 and any subsequent updates)
- DAIDS Protocol Registration Policy and Procedures Manual (August 2004 and any subsequent updates)
- Manual for Expedited Reporting of Adverse Events to DAIDS (Version 1.0, May 6, 2004 and any subsequent updates)
- US Regulations Applicable to Conduct of HPTN 058 (45 CFR 46; 21 CFR 50, 54, 56, and 312)
- HPTN Manual of Operations March 2007 (and subsequent updates)
- Any other relevant manuals or reference documents

File/Binder #16: Site-Specific Study Activation Documentation

- Site-Specific Study Activation Documents including Activation Notice

Table 3-2 Guide to Required Case History Elements and Source Documents for HPTN 058

HPTN 058 Required Case History Element	HPTN 058 Source Documents – [EXAMPLE TEXT, sites may have developed their own source documents for some elements- sites must specify the one source for each item in their source document SOP]	
Basic participant identifiers (e.g., name, date of birth)	<i>Demographics (CRF DEM-1)</i>	
Documentation that the participant provided written informed consent to participate in the study prior to initiation of any study procedures. ¹	<i>Signed and dated Informed Consent Forms; Informed Consent Comprehension Quizzes and Informed Consent for Enrollment Evaluation Survey (which is optional), signed and dated informed consent coversheet or chart notes stating that informed consent was obtained prior to initiating study procedures¹</i>	
If she/he chooses and if allowed at site, documentation that the participant provided written informed consent to storage and future use of samples ²	<i>Signed and dated Specimen Storage Consent Form; signed and dated chart note stating that storage consent was obtained (NOTE: this consent may be obtained at any point during study participation.)</i>	
Documentation that the participant met the study selection (eligibility) criteria:		
<ul style="list-style-type: none"> • At least 18 years old 		<i>Demographics (DEM-1)</i>
<ul style="list-style-type: none"> • HIV-uninfected 		<i>Local laboratory results (LLF-1)</i>
<ul style="list-style-type: none"> • Meets DSM-IV criteria 		<i>DSM-IV worksheets/chart notes</i>
<ul style="list-style-type: none"> • Positive urine test for opiates 		<i>Urine test results(UTR-1)</i>
<ul style="list-style-type: none"> • Injected at least 12 times in last 28 days 		<i>Screening assessment</i>
<ul style="list-style-type: none"> • If female, evidence of inability to become pregnant or self-reported willingness to use an effective method of contraception for the first twelve months of the study 		<i>Screening assessment, Medical History</i>
<ul style="list-style-type: none"> • Able to provide contact information and willing to be contacted by staff 		<i>Consent and study notes</i>
<ul style="list-style-type: none"> • Stated plans to be available for at least 2 years 		<i>Screening assessment</i>
<ul style="list-style-type: none"> • Has NOT currently, or within the last 12 weeks, received clinician-guided treatment for opioid dependence with methadone, LAAM, buprenorphine, naltrexone, or nalmefene 	<i>Screening assessment</i>	

¹ The DAIDS SOP for Source Documentation (Appendix C) provides detailed requirements and suggestions for documenting the informed consent process.

² Consent for long term storage is optional.

³ A study clinician must review all laboratory reports and document this review by signing and dating the reports.

Table 3-2 Guide to Required Case History Elements and Source Documents for HPTN 058

HPTN 058 Required Case History Element	HPTN 058 Source Documents – [EXAMPLE TEXT, sites may have developed their own source documents for some elements- sites must specify the one source for each item in their source document SOP]
<ul style="list-style-type: none"> NOT currently enrolled in another HIV prevention or drug use study 	Screening assessment
<ul style="list-style-type: none"> NO clinically-diagnosed allergy to buprenorphine or naloxone according to self-report 	Screening assessment
<ul style="list-style-type: none"> Does NOT meet DSM-IV criteria for dependence on alcohol or benzodiazepines; requiring immediate medical attention for dependence on other substances 	DSM-IV worksheets/chart notes
<ul style="list-style-type: none"> NOT currently injecting substances other than opiates more than twice in the last 28 days 	Screening assessment
<ul style="list-style-type: none"> NO psychological disturbance or cognitive impairment interfering with ability to comply with study procedures 	Study Notes and Physical Exam
<ul style="list-style-type: none"> NOT pregnant or lactating 	Medical History
<ul style="list-style-type: none"> NO acute or chronic renal failure 	Local laboratory results (LLF-1), Medical History
<ul style="list-style-type: none"> ALT NOT greater than 3 times ULN³ 	Local laboratory results (LLF-1)
<ul style="list-style-type: none"> Hemoglobin NOT less than 8g/dL for men, or less than 7g/dL for women³ 	Local laboratory results (LLF-1)
<ul style="list-style-type: none"> Platelet count NOT less than 50,000/mm³ 	Local laboratory results (LLF-1)
<ul style="list-style-type: none"> Total bilirubin NOT greater than 2.5 times the ULN³ 	Local laboratory results (LLF-1)
<ul style="list-style-type: none"> NO other medical or psychiatric condition that would make participation in study unsafe or otherwise interfere with the study objectives or interpretation 	Medical History and Physical Exam
A record of the participant's random assignment	HPTN 058 Randomization Envelope; Randomization Assignment Form (found inside each Randomization Envelope)
A record of the participant's exposure to the study product	Induction Record (IR-1); Weekly Dosing Record (DR-1); participant-specific pharmacy dispensing records; chart notes (signed and dated)
A record of the participant's eligibility for a second detoxification at 26 weeks (if applicable)	Eligibility checklist for Second Detoxification
A record of all contacts, and all attempted contacts, with the participant (e.g. home visits, telephone contacts, etc.)	Weekly Counseling Session Attendance (CAW-1); Chart Notes (signed and dated), telephone logs, and/or other worksheets or local documents if designated in local SOPs.

Table 3-2 Guide to Required Case History Elements and Source Documents for HPTN 058

HPTN 058 Required Case History Element	HPTN 058 Source Documents – [EXAMPLE TEXT, sites may have developed their own source documents for some elements- sites must specify the one source for each item in their source document SOP]
A record of all procedures performed by study staff	<i>All documents listed above in addition to Risk Assessment (RA-1-8); Acceptability Assessment (AA-1); Chart Notes (signed and dated) detailing (a) procedures performed in addition to scheduled procedures and/or (b) the reason why scheduled procedures were not performed;</i>
Information on the participant’s condition before, during, and after the study	<i>All documents listed above plus: Risk Assessment (RA-1); COWS; Adverse Experience Log(AE-1); Pregnancy Report and History (PR-1); Pregnancy Outcome (PO-1); Pre-Existing Conditions Log (PE-1); Social Impact Assessment (SIA-1); Missed Visit (MV-1); Participant Transfer; Termination (TM-1); End of Study Inventory; Chart Notes (signed and dated); objective information received from non-study sources (e.g., medical records and death certificates)</i>

¹ The DAIDS SOP for Source Documentation (Appendix C) provides detailed requirements and suggestions for documenting the informed consent process.

²Consent for long term storage is optional.

³A study clinician must review all laboratory reports and document this review by signing and dating the reports.

Table 3-3

3.3 HPTN Preparatory/Ancillary Investigation and Data/Specimen Request Application

Comment [p1]: This table and the next needs to be flipped and the numbers changed.

1. Application Date:	
2. Number and title of primary HPTN study to which the proposed ancillary study or activity is linked	HPTN 058: A Phase III randomized controlled trial to evaluate the efficacy of drug treatment in prevention of HIV infection and death among opiate dependent injectors
3. Name and contact information for proposing HPTN Investigator (include institutional affiliation/email/phone):	
4. Name and contact information for non-HPTN collaborating Investigator (institutional affiliation/email/phone):	<input type="checkbox"/> Not applicable <i>Note: All non-HPTN investigators using biological specimens from HPTN studies must complete an HPTN Materials Transfer Agreement. If applicable, please attach a copy of the signed agreement.</i>
5. Is the proposed activity/investigation prospective (to be done concurrently with all or part of the primary HPTN study) or retrospective (using specimens or data collected during an HPTN study after its completion)?	<input type="checkbox"/> Prospective only <input type="checkbox"/> Retrospective only <input type="checkbox"/> A combination of retrospective and prospective
6. Description of proposed activity/investigation including purpose/objectives, rationale, methods, assessments to be performed, necessary staff and other resources, where the activities will be carried out, if and how the primary study will be affected by the proposed investigation, etc.	
7. Will separate informed consent be necessary for this activity (in addition to the primary HPTN study IC)?	<input type="checkbox"/> Yes <input type="checkbox"/> No, specify reason _____ * <input type="checkbox"/> Not yet sure <i>The IRB/EC is ultimately responsible for determining whether separate consent must be obtained; documentation of this is determination is required</i>
8. How will data from the ancillary/preparatory study be managed and analyzed?	<input type="checkbox"/> Data to be managed/analyzed by HPTN SDMC (<i>prior agreement with SDMC required</i>) <input type="checkbox"/> Other; specify who is responsible and where the data will be managed and analyzed:
9. Are supplemental HPTN funds required for the proposed investigation?	<input type="checkbox"/> Yes ⇒ Please specify estimated amount and purpose of funds requested (e.g. specimen shipping and handling costs, site staff time) <input type="checkbox"/> No; specify source of funding

Table 3-3

3.3 HPTN Preparatory/Ancillary Investigation and Data/Specimen Request Application

Comment [p1]: This table and the next needs to be flipped and the numbers changed.

<p>10. Will the proposed investigation involve use of biological specimens from participants in a primary HPTN study?</p>	<p><input type="checkbox"/> Yes; leftover stored specimens to be used that are on-site <input type="checkbox"/> Yes; additional specimens or volume to be obtained from subjects specifically for the ancillary investigation. <input type="checkbox"/> No biological specimens involved</p>
<p>10 a. Where will the proposed laboratory testing be done?</p>	<p><input type="checkbox"/> At the local site lab(s) <input type="checkbox"/> HPTN CL (<i>advance agreement with CL required</i>) <input type="checkbox"/> Other, specify institution/lab name and location:</p>
<p>10 b. Type of assays to be performed</p>	
<p>10 c. Type and quantity of specimens to be used (e.g. 5 ml plasma from 6 time points)</p>	
<p>10 d. Will the results of the proposed testing be linked to data collected in the primary HPTN study for purposes of analysis (e.g., identifiers, demographics, HIV risk behaviors, clinical and lab outcomes)? Describe.</p>	
<p>10 e. Will results of the proposed testing be given to the participants who provided the specimens?</p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No; explain.</p>
<p>11. If the proposed investigation involves use of <u>stored</u> (leftover) specimens from primary HPTN study: Have the following been completed?</p> <ul style="list-style-type: none"> • All primary study endpoints confirmed by SDMC and CL • All primary protocol-specified testing involving the stored specimens at issue completed and results received (including QC/QA testing). 	<p><input type="checkbox"/> Not applicable (no stored biological specimens to be used) <input type="checkbox"/> Yes ⇒ Attach documentation. <input type="checkbox"/> No; primary study not yet completed. <input type="checkbox"/> No; explain</p>

Table 3-4: Protocol Deviation Form



Use this form to report Protocol Deviations (see HPTN Manual of Operations for the definition of a Protocol Deviation). This form is to be used by staff at the CTU sites, CORE, SDMC, and NL. Upon completion, email this form to the distribution list created for the study.

Deviation Information			
DAIDS Site Number:	<i>[Enter site number]</i>	Date Deviation Occurred	<i>[ddMMMyy]</i>
		Date of Site Awareness	<i>[ddMMMyy]</i>
Protocol Number		Date Event Reported	<i>[ddMMMyy]</i>
Participant ID <i>(if applicable)</i>	<i>[Enter participant ID]</i>	Was Event Reported to the IRB/IEC?	Yes <input type="checkbox"/> No <input type="checkbox"/>
Report Completed By:	<i>[Name and title of staff person]</i>		
	<i>Contact phone and/or email:</i>		
Brief Summary of Deviation (Description of deviation and location it occurred if relevant) <i>(Maintain all documentation in study files.)</i>			
Steps that have been taken to address this deviation			
Steps have been taken to prevent further occurrences			

PROTOCOL DEVIATION FORM
Instructions

Instructions

- **Participant ID:** If more than one participant has the same deviation, list the IDs for all of the affected participants. If the deviation does not involve specific participant(s), leave this item blank.
- **Date Deviation Occurred:** If the deviation occurred over a period of time, specify the date the deviation first started and when it ended or if it is ongoing at the time this report is completed.