**HPTN XXX**

**Study Title**

**A Study of the HIV Prevention Trials Network (HPTN)**

**Sponsored by:**

Division of AIDS (DAIDS), United States (US) National Institute of Allergy and Infectious Diseases (NIAID)

US National Institutes of Health (NIH)

(Other agencies if applicable)

**Co-Sponsored by:**

If applicable

**IND #:** XXXXXX (if applicable)

**Protocol Chair:**

Name  
Affiliation

Location (City, State (if applicable), Country)

**Protocol Co-Chair:**

Name  
Affiliation

Location (City, State (if applicable), Country)

**DAIDS Protocol #:** XXXXX

**(DRAFT/FINAL) Version X.X**

**Version Date: Day Month Year**

**HPTN XXX**

**Study Title**

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# LIST OF ABBREVIATIONS AND ACRONYMS

AE Adverse Event

AIDS Acquired immunodeficiency syndrome

ART Antiretroviral therapy

ARV Antiretroviral

CAB Community Advisory Board

CBC Complete blood count

CDC Centers for Disease Control and Prevention

CFR Code of Federal Regulations

CI Confidence intervals

CLIA Clinical Laboratory Improvement Act of 1988

Cmax Maximum plasma concentration that a drug achieves after dosing

CMC Clinical Management Committee

CPQA Clinical Pharmacology Quality Assurance

CRF Case Report Form

CRM Clinical Research Manager

CRPMC (DAIDS) Clinical Research Products Management Center

CRS Clinical Research Site

CT *Chlamydia trachomatis*

CTA Clinical trials agreement

DAERS DAIDS Adverse Experience Reporting System

DAIDS Division of AIDS

DHHS US Department ofHealth and Human Services

DNA Deoxyribonucleic Acid

DOT Directly Observed Therapy

DSMB Data and Safety Monitoring Board

EAE Expedited Adverse Event

EC Ethics Committee

EQA External Quality Assurance

FDA (United States) Food and Drug Administration

FTC/TDF Emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF); Truvada®

GC *Neisseria gonorrhoeae*

GCP Good Clinical Practices

GLP Good Laboratory Practices

HIV Human Immunodeficiency Virus

HPTN HIV Prevention Trials Network

IB Investigator Brochure  
IATA International Air Transport Association

ICF Informed consent form

IM Intramuscular

IND Investigational New Drug

INR International normalized ratio

IoR Investigator of Record

IQA (DAIDS) Immunology Quality Assurance

IQR Interquartile range

IRB Institutional Review Board

IS Injection site

ITT Intention to treat

IUD Intrauterine device

LC (HPTN) Laboratory Center

LDMS Laboratory Data Management System

LL Local laboratory

LOC Leadership and Operations Center

NIAID (United States) National Institute of Allergy and Infectious Diseases

NIH (United States) National Institutes of Health

PRO Protocol Registration Office

pSMILE Patient Safety Monitoring and International Laboratory Evaluation

RE Regulatory entity

RNA Ribonucleic acid

ROC Regulatory Operations Center

RSC Regulatory Support Center

SAE Serious Adverse Event

SDMC (HPTN) Statistical and Data Management Center

SMC Study Monitoring Committee

SUSAR Suspected, Unexpected Serious Adverse Reaction

STI Sexually transmitted infection

SOP Standard Operating Procedures

SSP Study Specific Procedures

UK NEQAS United Kingdom National External Quality Assessment Service

US United States

VQA (DAIDS) Virology Quality Assurance

**HPTN XXX**

**Study Title**

# PROTOCOL TEAM ROSTER

|  |  |
| --- | --- |
| **Chair:**  Name, Degree(s)  Title, Affiliation  Address 1  Address 2  City, State Zip (If applicable), Country  Phone: xxxxxxxxxxx, Ext. xxxxx  Fax: xxxxxxxxxxxxxx  Email: | **Co-Chair:**  Name, Degree(s)  Title, Affiliation  Address 1  Address 2  City, State Zip (If applicable), Country  Phone: xxxxxxxxxxx, Ext. xxxxx  Fax: xxxxxxxxxxxxxx  Email: |
| Rest of Team (Alphabetically) |  |
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**HPTN XXX**

**Study Title**

# SCHEMA

(Must meet the Objectives listed in Section 2)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| |  |  | | --- | --- | | **Purpose:** |  | | **Design:** |  | | **Study Population:** |  | | **Study Size:** |  | | **Treatment Regiment:** |  | | **Study Duration:** |  | | **Primary Objective(s):** | (Must match Section 2.1) | | **Secondary Objectives:** | (Must match Section 2.2) | | **Exploratory Objective:** | (Must match Section 2.3) | | **Study Sites:** |  | |  |
|  |  |

**(SAMPLE)**

**HPTN XXX**

**Study Title**

**OVERVIEW OF STUDY DESIGN AND RANDOMIZATION SCHEME**



# PROTOCOL SIGNATURE PAGE

**HPTN 0xx:**

**Full Name**

**A Study of the HIV Prevention Trials Network (HPTN)**

**Sponsored by:**

Division of AIDS, US National Institute of Allergy and Infectious Diseases

US National Institutes of Health

**Support Provided by:**

Add any other partners

The signature below constitutes approval of this study in full accordance with the provisions of this protocol and the attachments. I agree to conduct this study in compliance with the protocol, in-country and local regulatory requirements, applicable United States (US) Code of Federal Regulations (CFR) and ICH Good Clinical Practices (E6).

I agree to maintain all study documentation for at least two years following the date of marketing approval for the study product for the indication in which it was studied, unless otherwise specified by DAIDS, or the HPTN Leadership and Operations Center (LOC). If no marketing application is filed, or if the application is not approved, the records will be retained for two years after the US Food and Drug Administration (FDA) is notified that the Investigational New Drug (IND) is discontinued. Publication of the results of this study will be governed by HPTN policies. Any presentation, abstract, or manuscript will be submitted to the HPTN Manuscript Review Committee (MRC), and DAIDS for review prior to submission.

I have read and understand the information in the Investigator's Brochure(s) (IB), including the potential risks and side effects of the products under investigation, and will ensure that all associates, colleagues, and employees assisting in the conduct of the study are informed about the obligations incurred by their contribution to the study.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Name of Investigator of Record (print name)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Signature of Investigator of Record Date (MM/DD/YYYY)

# Introduction

## Background and Prior Research

[Describe pertinent background information (e.g., the epidemiology of HIV/AIDS in the target study population) and the results of relevant prior studies of the study treatment/product/intervention. Use additional subsection headings to organize all relevant available information.]

## Rationale

* + 1. [Describe the rationale for the study overall and its relevance to the HPTN research agenda. If applicable, describe the rationale for the study treatment/product/intervention dose regimen and the rationale for the control condition. If applicable, describe the applicability of the intervention to the study population post-study.]**More information**

Text

* + 1. **More information**

Text

# study objectives and design

## Primary Objective(s)

The primary objectives of this study are to:

[Be sure to state the objectives in terms of measurable outcomes.]

## Secondary Objectives

The secondary objectives of this study are to:

[Be sure to state the objectives in terms of measurable outcomes.]

## Exploratory Objectives

The exploratory objectives of this study are to:

## Study Design

[Provide a 1-2 page description of the study design. Reference the design figure and Appendices as applicable. Be sure to address the following: phase of study; single- or multi-center; participating study sites; study treatment arms; randomization scheme, blinding procedures; schedule of study visits and procedures, and a summary of the major endpoint(s). For primary endpoints ascertained via a laboratory testing algorithm (i.e., HIV antibody testing), specify the testing algorithm in an appendix. HIV antibody testing algorithms that have been approved for use in adult HPTN studies by the HPTN Network Lab are appended to this document (and are available as PowerPoint files on FHI/HPT shared drives). If a Protocol Team would like to specify an alternative HIV testing algorithm, prior approval of the alternative algorithm should be sought from the Network Lab.]

# study population

### [type of participants (e.g., HIV-uninfected injection drug users)] will be included in this study. Participants will be selected for the study according to the criteria in Section 3.1 and 3.2 [and the guidelines in Section 3.4]. They will be recruited, screened, and enrolled as described in Section 3.3 [and assigned to a study treatment/product/intervention group as described in Section 7.4]. Issues related to participant retention and withdrawal from the study are described in Sections 3.5 and 3.6, respectively.

## Inclusion Criteria

[Type of persons (e.g., men, women, adults, adolescents)] who meet all of the following criteria are eligible for inclusion in this study:

## Exclusion Criteria

[Type of persons (e.g., men, women, adults, adolescents)] who meet any of the following criteria will be excluded from this study:

## Recruitment Process

[Describe the strategy/process by which participants will be recruited, screened, and enrolled in the study.]

## Co-Enrollment Guidelines

[Describe applicable allowances/restrictions on enrollment in other research studies, if any.]

## Participant Retention

[Tailor as needed:]

Once a participant enrolls in this study, the study site will make every effort to retain him/her for [xx] months of follow-up in order to minimize possible bias associated with loss-to-follow-up. [Optimally, participant retention procedures will be established such that loss rates do not exceed the incidence rate of the primary study outcome.] Study site staff are responsible for developing and implementing local standard operating procedures to target this goal. Components of such procedures include:

[Thorough explanation of the study visit schedule and procedural requirements during the informed consent process and re-emphasis at each study visit.

Thorough explanation of the importance of all [number] study treatment groups to the overall success of the study.

Collection of detailed locator information at the study Screening Visit, and active review and updating of this information at each subsequent visit.

Use of mapping techniques to establish the location of participant residences and other locator venues.

Use of appropriate and timely visit reminder mechanisms.

Immediate and multifaceted follow-up on missed visits.

Mobilization of trained outreach workers or “tracers” to complete in-person contact with participants at their homes and/or other community locations.

Regular communication with the study community at large to increase awareness about HIV/AIDS and explain the purpose of HIV prevention research and the importance of completing research study visits.]

## Participant Withdrawal

[Be careful in this section not to confuse discontinuation of treatment/product/ intervention with withdrawal from the study. The protocol should make clear that participants who discontinue treatment shall be maintained in follow-up as originally scheduled whenever possible.]

Regardless of the participant retention methods just described, participants may voluntarily withdraw from the study for any reason at any time. The Investigator also may withdraw participants from the study in order to protect their safety and/or if they are unwilling or unable to comply with required study procedures after consultation with the Protocol Chair, DAIDS Medical Officer, SDMC Protocol Statistician, and Leadership and Operations Center (LOC) Clinical Research Manager (CRM). [If applicable, describe any study-specific withdrawal and/or replacement criteria here.]

Participants also may be withdrawn if the study sponsor, government or regulatory authorities, or site Institutional Review Boards/Ethics Committees (IRBs/ECs) terminate the study prior to its planned end date.

Every reasonable effort will be made to complete a final evaluation (as described in Section 5.x) of participants who terminate from the study prior to [planned termination time period, e.g., Day 21, Month 24], and study staff will record the reason(s) for all withdrawals from the study in participants’ study records.

# study treatment/product/intervention

[Tailor this section as needed to reflect the specific study treatment/product/intervention. Eliminate this section for observational studies.]

## Treatment/Product/Intervention Formulation/Content

Text

## Treatment/Product/Intervention Regimen(s)

Text

## Treatment/Product/Intervention Administration

Text

## Treatment/Product/Intervention Supply and Accountability

[If applicable:] The site pharmacist must maintain complete records of all study drugs/products received from the NIAID Clinical Research Products Management Center (CRPMC) [and/or the drug/product manufacturer] and subsequently dispensed to study participants. All [used/unused/both] supplies must be returned to the NIAID Clinical Research Products Management Center after the study is completed or terminated.

## Adherence Assessment

[If applicable, describe how adherence to the study treatment/product/intervention will be assessed/measured. State study-specific definitions of adherence and describe replacement “rules,” if any.]

## Toxicity Management

[If applicable, describe how treatment/product/intervention regimen(s) will be modified in response to observed side effects/AEs. State criteria for withdrawal from treatment.]

## HIV Seroconversion

[If applicable, describe how often participants will be followed after HIV seroconversion is confirmed, what assessments will be performed, and whether product use will continue.]

## Concomitant Medications

[This section is not likely applicable for behavioral studies.]

[Note whether any concomitant medications are exclusionary for the study. For example, “Enrolled study participants may continue use of all concomitant medications — except those listed under criteria for exclusion or treatment discontinuation — during this study.” Or “Use of the following concomitant medications is not be permitted by enrolled study participants: …”]

All concomitant medications [taken or received by participants within the X weeks prior to study enrollment] will be reported on applicable study case report forms (CRFs). In addition to prescribed and over-the-counter medications [tailor as needed: vitamins, herbal remedies, and other traditional preparations will be recorded. Alcohol and recreational or street drug use will be recorded in clinical progress notes if needed for interpretation/documentation of observed participant health status.] Medications used for the treatment of AEs that occur during study participation also will be recorded on applicable study CRFs.

# study procedures

An overview of the study visit and procedures schedule is presented in Appendix I. Presented below is additional information on visit-specific study procedures. Detailed instructions to guide and standardize all study procedures across sites will be provided in the study-specific procedures manual.

## Screening Visit

Text and Bullets

## Enrollment Visit

Text and Bullets

## Week 4

Text and Bullets

## Week 8

Text and Bullets

## Final Visit/Exit

Text and Bullets

## Procedures for Participants with Suspected or Confirmed HIV Infection

The Clinical Management Committee (CMC) must be notified of any reactive or positive HIV test result identified at Enrollment or follow-up. Individuals who have one or more reactive or positive HIV tests at Screening or Enrollment are not eligible to participate in this study. Furthermore, at the Screening and Enrollment (at Enrollment, prior to randomization), individuals with any signs or symptoms consistent with acute (pre-seroconversion) HIV infection will not be enrolled. Signs and symptoms consistent with acute HIV infection will be included in the SSP Manual. Participants who have any reactive or positive HIV test result during follow-up visits will be referred for care. These participants will have further testing to confirm infection, as described in the SSP Manual. [Samples from participants with confirmed HIV infection may be sent to a local laboratory for resistance testing to assist with clinical management; results from resistance testing performed in local laboratories will not be reported to the HPTN Statistical and Data Management Center (SDMC)]. The participant will not receive additional doses of study drug if they have a reactive or positive HIV test, even if further testing indicates that they do not have HIV infection.

## Pregnancy

[Modify as needed]

Because this is an investigational agent, receipt of study product by female study participants of reproductive potential requires use of an effective method of contraception, including an IUD, hormonal contraception, or sterilization. All participants should also use male or female condoms for prevention of HIV and other sexually transmitted infections (STIs). As needed, study staff will provide contraceptive counseling to enrolled participants throughout the duration of study participation and will facilitate access to contraceptive services through direct service delivery and/or active referrals to local service providers. Study staff also will provide participants with male and/or female condoms and lubricant and counseling on use of condoms.

Female participants of reproductive potential will have pregnancy testing performed as outlined in the Schedule of Evaluations and Procedures. Participants will be encouraged to report all signs or symptoms of pregnancy to study staff.

In the event that a female participant has a positive pregnancy test at Weeks (X), study product will be discontinued and the participant will be followed approximately every 12 weeks starting at the Week (X) visit until pregnancy outcome is reached. Once pregnancy outcome is reached, the participant will be terminated from the study. See the SSP Manual for details regarding visit procedures and specimens to be collected at follow-up visits in the event of pregnancy.

The site Investigator of Record (IoR) or designee will counsel any participants who become pregnant regarding possible risks to the fetus according to site-specific SOPs. Participants may not enroll if they are currently breastfeeding and study product should be discontinued if any participant identifies that she is breastfeeding after enrollment. The site IoR or designee also will refer the participant to all applicable services; however, sites will not be responsible for paying for pregnancy-related care.

Participants who are pregnant at their last study visit will continue to be followed (if they agree) until the pregnancy outcome is ascertained or it is determined that the pregnancy outcome cannot be ascertained. All pregnancy outcomes will be reported on relevant CRFs. Outcomes meeting criteria for expedited adverse event (EAE) reporting also will be reported.

## Interim Contacts and Visits

[Modify as needed] Interim contacts and visits (those between regularly scheduled follow up visits) may be performed at participant request or as deemed necessary by the investigator or designee at any time during the study. All interim contacts and visits will be documented in participants’ study records and on applicable CRFs.

Some interim visits may occur for administrative reasons. For example, the participant may have questions for study staff. Interim visits at which no data are collected are not documented on CRFs. Other interim contacts and visits may occur in response to AEs experienced by study participants. When interim contacts or visits are completed in response to participant reports of AEs, study staff will assess the reported event clinically, record the event on the CRF, and provide or refer the participant to appropriate medical care.

## Criteria for Early Termination of Study Participation

[Modify as needed] Participants may voluntarily withdraw from the study for any reason at any time. Site IoRs may, with the approval of the CMC, withdraw participants before their scheduled termination visit to protect their safety, and/or if participants are unable or unwilling to comply with study procedures. Participants also may be withdrawn if the study sponsors, government or regulatory authorities (including the OHRP and US FDA), or site IRBs terminate the study prior to its planned end date. Study staff will record the reason(s) for all withdrawals in participants’ study records.

# safety monitoring and adverse event reporting

## Safety Monitoring

Close cooperation between the Protocol Chair, study site Investigator(s), DAIDS Medical Officer, LOC CRM, SDMC Biostatistician, SDMC Clinical Affairs Staff, HPTN Laboratory Center (LC), and other study team members will be necessary in order to monitor participant safety and to respond to occurrences of toxicity in a timely manner. The team will have regularly scheduled conference calls during the period of study implementation, and additional ad hoc calls will be convened if required.

The study site Investigators are responsible for continuous close monitoring and management of AEs in conjunction with IoRs. Sites are required to have detailed SOPs describing methods for AE reporting and toxicity management to ensure that AEs are reported and managed in accordance with the protocol and for alerting the Clinical Management Committee (CMC – outlined below) if unexpected concerns arise.

A sub-group of the Protocol Team, including the Protocol Chair, DAIDS Medical Officer, site clinicians, and the SDMC Clinical Affairs Safety Associate will serve as members of the CMC. The CMC provides support to site clinicians regarding individual participant clinical management (e.g., questions related to eligibility, toxicity management, clinical holds of study drug, permanent discontinuations, etc.). In addition, for trials such as this with no DSMB oversight, the HPTN Study Monitoring Committee (SMC) may also review safety data in aggregate.

## Clinical Data Review

A multi-tiered safety review process will be followed for the duration of this study. The study site investigators are responsible for the initial evaluation and reporting of safety information at the participant level, and for alerting the CMC if unexpected concerns arise.

Participant safety is also monitored by the SDMC Clinical Affairs staff (SMC reviews), who review incoming safety data for completeness and consistency on an ongoing basis. Events identified as questionable, inconsistent, or unexplained will be queried for verification.

AE reports submitted in an expedited manner to the DAIDS Safety Office will be forwarded to the DAIDS Medical Officer for review.

The SDMC will prepare routine study conduct and safety reports for the SMC, which will meet by conference call approximately every 6 months and will review safety data by study arm (unblinded) during a closed meeting. More frequent or ad hoc reviews of safety reports may be conducted by the SMC as needed. A recommendation to stop the trial may be made by the SMC at any such time that the team agrees an unacceptable type and/or frequency of AEs has been observed. If at any time a decision is made to discontinue the study product in all participants, DAIDS will notify the US FDA, as well as the site IoRs, who will notify the responsible IRBs expeditiously.

## Adverse Event Definition and Reporting

An adverse event (AE) is defined as any untoward medical occurrence in a clinical research participant administered an investigational product and which does not necessarily have a causal relationship with the investigational product. As such, an AE can be an unfavorable or unintended sign (including an abnormal laboratory finding, for example), symptom or disease temporally associated with the use of an investigational product, whether or not considered related to the product.

Study participants will be provided a 24-hour telephone number and contact information and instructed to contact the study clinician to report any AEs they may experience. For life-threatening events, they will also be instructed to seek immediate emergency care. Where feasible and medically appropriate, participants will be encouraged to seek evaluation where the study clinician is based, and to request that the clinician be contacted upon their arrival. With appropriate permission of the participant, whenever possible, records from all non-study medical providers related to AEs will be obtained and required data elements will be recorded on study CRFs. All participants reporting an AE will be followed clinically, until the AE resolves (returns to baseline) or stabilizes.

Study site staff will document in source documents and the appropriate CRF all AEs (Grade 1 and higher) reported by or observed in enrolled study participants regardless of severity and presumed relationship to study product. AE severity will be graded per the DAIDS Table for Grading Adult and Pediatric Adverse Events, Version 1.0, December 2004 (Clarification dated August 2009), or most current version.

Relatedness is an assessment made by a study clinician of whether or not the event is related to the study agent. The relationship of all AE to study product will be assessed as specified in Version 2.0, January 2010 (or most current version) of the DAIDS Expedited Adverse Event (EAE) Reporting Manual.

## Expedited Adverse Event (EAE) Reporting

Requirements, definitions, and methods for expedited reporting of adverse events are outlined in Version 2.0 *(or latest version)* of the DAIDS EAE Manual, which is available on the DAIDS Regulatory Support Center (RSC) website at http://rsc.tech-res.com/safetyandpharmacovigilance.

## Reporting to DAIDS

The DAIDS Adverse Event Reporting System (DAERS), an internet-based reporting system, must be used for EAE reporting to DAIDS. In the event of system outages or technical difficulties, EAEs may be submitted via the DAIDS EAE form.

This form is available on the DAIDS RSC website at <http://rsc.tech-res.com/safetyandpharmacovigilance/>.

For questions about DAERS, please contact NIAID CRMS Support at [CRMSSupport@niaid.nih.gov](mailto:DAIDS-ESSupport@niaid.nih.gov). Please note that site queries may also be sent from within the DAERS application itself.

For questions about expedited reporting, please contact the DAIDS RSC Safety Office at ([DAIDSRSCSafetyOffice@tech-res.com](mailto:DAIDSRSCSafetyOffice@tech-res.com)).

## Reporting Requirements for this Study

* The Serious Adverse Event (SAE) or Suspected Unexpected Serious Adverse Reactions (SUSAR) Reporting Category, as defined in Version 2.0 *(or latest version)* of the DAIDS EAE manual, will be used for this study.
* The study products for which expedited reporting are required are: [Insert generic or non-proprietary names of study products here. Note that all placebos/controls administered as study products must be listed, and only products listed in this section will have expedited reporting. For example, “The study products for which expedited reporting are required are abacavir/lamivudine and placebo for abacavir/lamivudine."].

*[In this section, clarify if an abbreviation is used. For example: zidovudine (zdv) or VRC hivadv014-00-vp (vrcrad5)].*

* In addition to the [SAE or SUSAR] Reporting Category identified above, other adverse events that must be reported in an expedited manner are:[Insert additional AEs here. For example, “all cancers,” “all myopericarditis events,” “all hepatic failures,” “all autoimmune diseases,” etc.].

## Grading Severity of EAEs

[Specify that the most current Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events (DAIDS AE Grading Table) is used and is available on the DAIDS RSC website at http://rsc.tech-res.com/safetyandpharmacovigilance/.]

[If the study MOP contains a copy of the current DAIDS AE Grading Table, note here.]

[Protocol teams which have developed protocol-specific EAE grading criteria not found in the DAIDS AE Grading Table should define those additional or modified parameter(s) here or in an appendix noted here. For example, “non-fasting lipid levels will be graded according to the values for fasting triglycerides provided in this protocol.”]

## EAE Reporting Period

The EAE reporting period for this study is [insert reporting period here. For example, “as per the DAIDS EAE Manual.” If additional reporting is required beyond that specified in the DAIDS EAE Manual, then state the additional reporting period, the (SAE or SUSAR) reporting category and the study products (using generic/non-proprietary names)].

After the protocol-defined EAE reporting period, unless otherwise noted, only SUSARs as defined in Version 2.0 of the DAIDS EAE Manual will be reported to DAIDS if the study staff become aware of the events on a passive basis (from publicly available information).

## Social Impact Reporting

It is possible that participants' involvement in the study could become known to others, and that a social impact may result (i.e., because participants could be perceived as being HIV-infected or at "high risk" for HIV infection). For example, participants could be treated unfairly, or could have problems being accepted by their families and/or communities. These are social impact events. Social impacts events are those negative events that a participant reports as affecting them as a result of being involved in a research study. It is not the researcher’s opinion of how they perceive an event has affected a participant. A social impact that is reported by the participant and judged by the IoR/designee to be serious or unexpected will be reported to the responsible site’s IRBs at least annually, or according to their individual requirements. Social impacts will be collected and reported on CRFs during regular visits. In the event that a participant reports a social impact, every effort will be made by study staff to provide appropriate care and counseling to the participant as necessary, and/or referral to appropriate resources for the safety of the participant. Each site will provide such care and counseling in accordance with standardized guidance in the SSP Manual. While maintaining participant confidentiality, study sites may engage their Community Advisory Board (CAB) in exploring the social context surrounding instances of social impacts, to minimize the potential occurrence of such an impact.

# statistical considerations

## Review of Study Design

[Re-state the study design in 1-2 sentences (consider using the design statement from the Schema).]

## Endpoints

[List the endpoint(s) to be measured for each study objective. Endpoints should be described in terms of measurable outcomes observed in participants over the course of the study (e.g., HIV infections, STI infections, grade 3 adverse events, episodes of unprotected sex, and episodes of needle sharing). Typically, the study data analysis plan will specify that calculations be performed on the number of endpoints observed (e.g., HIV infection rates, proportion of participants who report unprotected sex), and that study effect measures will be based on these calculations (e.g., relative risks of HIV infection). These calculated measures should not be listed as endpoints per se, however their use for purposes of statistical analysis should be described in detail in Section 7.6 below.]

## Primary Endpoints

Consistent with the primary study objective to [summarize objective], the following endpoint(s) will be assessed:

Consistent with the primary study objective to [summarize objective], the following endpoint(s) will be assessed:

[If only one endpoint is specified, the above should be collapsed into a single sentence without bullets.]

## Secondary Endpoints

Consistent with the secondary study objective to [summarize objective], the following endpoint(s) will be assessed:

Consistent with the secondary study objective to [summarize objective], the following endpoint(s) will be assessed:

## Accrual, Follow-up, and Sample Size

[State the overall sample size and site-specific accrual targets, if any. Describe the accrual plan (e.g., number of participants expected per week or month) and reference replacement rules, if any, in Section 4.5. Note any caps on the total number of participants to be accrued (overall and by site) as well as any plans to adjust site-specific accrual targets during the accrual period.]

[Present the statistical power of the study, along with assumptions used to arrive at the power calculations.]

## Random Assignment/Study Arm Assignment

[If applicable, describe the study randomization scheme (e.g., stratified, blocked) and procedures (e.g., using envelopes, via telephone system) or the procedures for assigning participants to study arm.]

## Blinding

[If applicable, describe the measures that will be undertaken to blind study participants and/or study staff from participant treatment assignments. State when unblinding is expected and if/when participants will be told their assignments. Note plans to handle early unblinding to protect participant safety, if any.]

## Data Analysis

* + 1. **Primary Analyses**

[Describe the analyses to be undertaken to assess each primary study objective. If applicable, describe interim as well as final analyses.]

* + 1. **Secondary Analyses**

[Describe the analyses to be undertaken to assess each secondary study objective. If applicable, describe interim as well as final analyses.]

# human subjects considerations

## Ethical Review

[The HPTN Ethics Working Group (EWG) developed the [Ethics Guidance for Research](http://hptn.org/web%20documents/EWG/HPTNEthicsGuidanceV10Jun2009.pdf), a network-wide ethical principles document, which is suitable for further elaboration and tailoring for each study.

This protocol and the template informed consent form(s) (ICF) contained in Appendix (II) —— will be reviewed and approved by the HPTN Scientific Review Committee and NIAID Prevention Science Review Committee with respect to scientific content and compliance with applicable research and human subjects regulations.

The protocol, site-specific ICF, participant education and recruitment materials, and other requested documents — and any subsequent modifications — also will be reviewed and approved by the ethical review bodies responsible for oversight of research conducted at the study site.

Subsequent to initial review and approval, the responsible IRBs/ECs will review the protocol at least annually. The Investigator will make safety and progress reports to the IRBs/ECs at least annually, and within three months of study termination or completion. These reports will include the total number of participants enrolled in the study, the number of participants who completed the study, all changes in the research activity, and all unanticipated problems involving risks to human subjects or others. [In addition, all open DSMB reports will be provided to the IRBs/ECs.] Study sites will submit documentation of continuing review to the DAIDS Protocol Registration Office, in accordance with the current DAIDS Protocol Registration Manual.

## Informed Consent

Written informed consent will be obtained from each study participant (or the parents or legal guardians of participants who cannot consent for themselves). Each study site is responsible for developing a study ICF for local use, based on the template in Appendix II, which describes the purpose of the study, the procedures to be followed, and the risks and benefits of participation, in accordance with all applicable regulations. The study site also is responsible for translating the template form into local languages, and verifying the accuracy of the translation by performing an independent back-translation.

Literate participants will document their provision of informed consent by signing their informed consent forms. Non-literate participants [if applicable to this protocol] will be asked to document their informed consent by marking their ICFs (e.g., with an X, thumbprint, or other mark) in the presence of a literate third party witness. (Further details regarding DAIDS requirements for documenting the informed consent process with both literate and non-literate participants are provided in the DAIDS Standard Operating Procedure for Source Documentation.) Any other local IRB/EC requirements for obtaining informed consent from non-literate persons also will be followed.

Participants (or their parents or legal guardians) will be provided with a copy of their ICFs if they are willing to receive them.

## Risks

[Describe all reasonably foreseeable risks to participants, including those associated with the study treatment/product/intervention, and those associated with study procedures (e.g., phlebotomy, pelvic exams). Also describe potential social impacts, e.g., “Participants may become embarrassed, worried, or anxious when completing their HIV risk assessment and/or receiving HIV counseling. They also may become worried or anxious while waiting for their HIV test results. Trained counselors will be available to help participants deal with these feelings.

Although study sites will make every effort to protect participant privacy and confidentiality, it is possible that participants' involvement in the study could become known to others, and that social harms may result (i.e., because participants could become known as HIV-infected or at "high risk" for HIV infection). For example, participants could be treated unfairly or discriminated against, or could have problems being accepted by their families and/or communities.”]

[The risks described in this section must correspond with the risks statement in the sample ICF.]

## Benefits

Describe any reasonably foreseeable benefits to the participant, and to “society.” Diagnostic and treatment services available to participants as research procedures may be considered benefits, however, benefit cannot be claimed from the receipt of (unproven) prevention interventions. Sample text is provided below:

“There may be no direct benefits to participants in this study, however, participants and others may benefit in the future from information learned from this study. Specifically, information learned in this study may lead to the development of a safe and effective [intervention] that prevents HIV infection.

In addition, participants will receive HIV counseling and testing as part of the study screening process, as well as [e.g., pelvic exams and Pap smears.] Participants also will be screened for a number of sexually transmitted infections (STI), and provided STI treatment if applicable. (See also Section 8.5.)”

[The benefits described in this section must correspond with the benefits statement in the sample ICF.]

## Incentives

Pending IRB/EC approval, participants will be compensated for their time and effort in this study, and/or be reimbursed for travel to study visits and time away from work. Site-specific reimbursement amounts will be specified in the study ICFs.

## Confidentiality

All study-related information will be stored securely at the study site. All participant information will be stored in locked file cabinets in areas with access limited to study staff. All laboratory specimens, reports, study data collection, process, and administrative forms will be identified by a coded number only to maintain participant confidentiality. All local databases will be secured with password-protected access systems. Forms, lists, logbooks, appointment books, and any other listings that link participant ID numbers to other identifying information will be stored in a separate, locked file in an area with limited access.

Participant’s study information will not be released without the written permission of the participant, except as necessary for monitoring by the NIAID and/or its contractors; [the manufacturer of the study treatment/product]; representatives of the HPTN LOC, SDMC, and/or LC; [the US Food and Drug Administration], other government and regulatory authorities, and/or site IRBs/ECs.

[If a Certificate of Confidentiality will be obtained for this study, include information on the certificate in this section, i.e., “A Federal Certificate of Confidentiality will be sought for this study. The Certificate will apply to all study sites, and will protect study staff from being compelled to disclose study-related information by any Federal, State or local civil, criminal, administrative, legislative, or other proceedings.”]

## Communicable Disease Reporting Requirements

[Include if applicable: Study staff will comply with all applicable local requirements to report communicable diseases identified among study participants to local health authorities. Participants will be made aware of all reporting requirements during the study informed consent process.]

## Study Discontinuation

The study also may be discontinued at any time by NIAID, the HPTN, [list as applicable: the treatment/product manufacturer, and/or the US Food and Drug Administration, other government or regulatory authorities], and/or site IRBs/ECs.

# laboratory specimens and biohazard contaimnemt

Laboratory procedures are described below, Appendices (X), and Section 5.0; additional tests to be performed at a subsequent visit for participants who have a reactive or positive HIV test result are described in Appendix (X).

## Local Laboratory Specimens

[Tailor as needed to reflect study procedures]

As described in Section 5, the following types of specimens will be collected for testing at the local laboratory (LL): [list, use bullets as needed].

Local laboratories will perform Chemistry, Hematology, and pregnancy tests as indicated in Appendix I. Laboratories performing these tests will be monitored by Patient Safety Monitoring and International Laboratory Evaluation (pSMILE) and must demonstrate successful participation in the relevant External Quality Assurance (EQA) programs.

Local laboratories may also perform CD4 cell count testing and quantitative HIV RNA (viral load) testing as indicated in Appendix I. Laboratories performing these tests will be monitored by the Immunology Quality Assurance (IQA) and /or Virology Quality Assurance (VQA) programs and must demonstrate successful participation in the relevant EQA programs.

Each study site will adhere to standards of Good Clinical Laboratory Practice (GCLP), and local standard operating procedures for specimen management including proper collection, processing, labeling, transport, and storage of specimens to the LL. Specimen collection, testing, and storage at the LL will be documented using the HPTN Laboratory Data Management System (LDMS) as described in the study-specific procedures manual.

## Laboratory Center Specimens

[Tailor as needed to reflect study procedures]

As described in Section 5, the following types of specimens will be collected for testing at the HPTN Laboratory Center (LC) [list, use bullets as needed].

Each study site will adhere to standards of good clinical laboratory practice and the HPTN Laboratory Center Manual for proper collection, processing, labeling, and transport of specimens for the LC. All specimens will be shipped in accordance with IATA specimen shipping regulations. All shipments will be documented using the HPTN LDMS as described in the study-specific procedures manual.

## Quality Control and Quality Assurance Procedures

The clinical sites will document that their clinical laboratories are certified under the Clinical Laboratory Improvement Act of 1988 (CLIA-certified) and/or participate in DAIDS sponsored EQA programs. LC staff will conduct periodic visits to each site to assess the implementation of on-site laboratory quality control (QC) procedures, including proper maintenance of laboratory testing equipment and use of appropriate reagents. LC staff will follow up directly with site staff to resolve any QC or quality assurance (QA) problems identified through proficiency testing and/or on-site assessments. Throughout the course of the study, the HPTN LC will select a random sample of stored specimens to test for QA purposes. LC staff will follow-up directly with site staff to resolve any QA problems identified through this process. All of the assays to be used in this study have been approved for use in HPTN studies by the cross-network CPQA program. The quality of the assays is also continuously evaluated by a twice yearly proficiency testing program administered by the CPQA. Satisfactory scores are required for the laboratory to be able to continue to use assays in support of HPTN studies. The Pharmacology

Lab will adhere to Good Clinical Laboratory Practice (GCLP) for processing all samples.

[Describe laboratory QA procedures to be undertaken for the study, if any. The following is an example: “Throughout the course of the study, on a quarterly basis, the HPTN LC will select a random sample of stored specimens to test for quality assurance (QA) purposes. The total number of specimens undergoing QA testing will represent xx percent of all specimens collected.

The LC will inform site staff of the samples selected for quality assurance testing, and site staff will ship the selected specimens to the LC. The LC will test the specimens for HIV antibody and compare the results of their tests with the results obtained by the local labs. LC staff will follow-up directly with site staff to resolve any quality assurance problems identified through this process.”]

## QC for HIV Diagnostic Testing

The HPTN LC will perform HIV diagnostic testing for QC. Before performing HIV diagnostic testing, all sites must validate their testing algorithm, and the validation study must be approved by the HPTN LC. LL will perform testing for HIV diagnosis at Screening, Enrollment, and other scheduled visits. Algorithms for HIV diagnostic testing are provided in the SSP Manual.

Participants will be tested for HIV infection status using two HIV rapid tests, one of which must be FDA-cleared. Participants with one or two reactive HIV rapid test results at Screening or Enrollment will not be eligible for enrollment, regardless of subsequent test results. In those cases, HIV infection status will be confirmed using local HIV testing guidelines. Participants who have one or two reactive

HIV rapid test results at any other study visit will be further tested using an FDA cleared *(insert as applicable*: *Western blot or the GenAptima HIV RNA test*). Further testing will be based on the results of the confirmatory testing, as described in the SSP Manual. In addition, if a participant has signs or symptoms consistent with acute HIV infection, or expresses a concern about recent HIV acquisition, testing will be performed using the *(insert as applicable:* *GenAptima HIV RNA test).* Regardless of whether HIV RNA testing is used for diagnostic testing, HIV infection must be confirmed in all cases using two independent samples collected on different days.

## QC for HIV RNA Monitoring

Quantitative HIV RNA (viral load) testing will be performed at local laboratories to monitor HIV infection in any subject with confirmed HIV infection. Viral load testing will be performed in HIV-infected participants at the visit when HIV infection is confirmed, and at subsequent study visits. Note that this is distinct from use of qualitative HIV RNA testing that is performed to determine HIV Infection status (see above). Local laboratories must participate in the DAIDS Virology QA (VQA) program, with EQA results that are deemed satisfactory by the HPTN LC.

## QC for CD4 Cell Count Determination

For participants who become HIV-infected during the study, CD4 cell count testing will be performed at the time when HIV infection is confirmed and at subsequent study visits. Non-US laboratories performing CD4 cell count testing must be enrolled in the United Kingdom National External Quality Assessment Service (UK NEQAS) program through the DAIDS IQA program.

## Specimen Storage and Possible Future Research Testing

[Tailor as needed to reflect study procedures and include language regarding all countries that will perform any protocol-related testing or store left over samples. The following is an example: “Study site staff will store all [type of specimens] collected in this study at least through the end of the study. In addition, study participants will be asked to provide written informed consent for their [type of specimens] to be stored after the end of the study for possible future testing. The specimens of participants who do not consent to long-term storage and additional testing will be destroyed at the end of the study.]

## Biohazard Containment

As the transmission of HIV and other blood-borne pathogens can occur through contact with contaminated needles, blood, and blood products, appropriate blood and secretion precautions will be employed by all personnel in the drawing of blood and shipping and handling of all specimens for this study, as currently recommended by the United States Centers for Disease Control and Prevention. All infectious specimens will be transported in accordance with United States regulations (42 CFR 72).

# administrative procedures

## Protocol Registration

Initial Registration of the protocol by the DAIDS Protocol Registration Office (PRO) is required prior to implementation of this protocol. As part of this process, each site must have the protocol and protocol ICF(s) approved, as appropriate, by their local institutional review board (IRB)/ethics committee (EC) and any other applicable regulatory entity (RE). Upon receiving final approval, sites will submit all required protocol registration documents to the DAIDS PRO at the Regulatory Support Center (RSC). The DAIDS PRO will review the submitted protocol registration packet to ensure that all of the required documents have been received. In the case of Initial Registration, site-specific ICFs WILL be reviewed and approved by the DAIDS PRO. Sites will receive an Initial Registration Notification from the DAIDS PRO that indicates successful completion of the protocol registration process. A copy of the Initial Registration Notification should be retained in the site's regulatory files.

Following Initial Registration, any full protocol amendments require submission of a protocol registration packet to the DAIDS PRO as described above; however, the DAIDS PRO **WILL NOT** review and approve site-specific ICFs. Sites will receive a Registration Notification when the DAIDS PRO receives a complete registration packet.

For additional information on the protocol registration process and specific documents required for initial and amendment registrations, refer to the current version of the DAIDS Protocol Registration Manual, which can be found at http://rsc.tech-res.com/protocolregistration/.

## Study Activation

Pending successful protocol registration and submission of all required documents, the HPTN LOC staff will “activate” a site. Study implementation may not be initiated until a study activation notice is provided to the site by the HPTN LOC. (In some cases, DAIDS has provided activation approval via email, which is also acceptable documentation of activation.) In addition, if study “activation” is determined to be necessary for any subsequent amendments, study implementation may not be initiated until a study activation notice is provided to the site by the HPTN LOC.

## Study Coordination

[If applicable, include a paragraph regarding the study IND and sponsorship arrangements. The following is an example: “DAIDS holds the Investigational New Drug (IND) application for this study (#XXXXX). Copies of all regulatory documents submitted to this IND by DAIDS will be forwarded to [company] for cross-referencing with the company’s other INDs for the study product. Assignment of all sponsor responsibilities for this study will be specified in a Clinical Trials Agreement (CTA) executed by DAIDS and [company].”]

Study implementation will be directed by this protocol as well as the SSP manual. The SSP manual — which will contain links to the Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials, as well as the DAIDS Manual for Expedited Reporting of Adverse Events to DAIDS, Version 2.0, dated (Month Year) and the DAIDS Toxicity Tables — will outline procedures for conducting study visits; data and forms processing; AE assessment, management and reporting; dispensing study products and documenting product accountability; and other study operations.

Study CRFs and other study instruments will be developed by the protocol team and HPTN SDMC. Data will be transferred to the HPTN SDMC for data entry, cleaning, reporting and analysis. Quality control reports and queries will be generated and distributed to the study sites on a routine schedule for verification and resolution.

Close coordination between protocol team members will be necessary to track study progress, respond to queries about proper study implementation, and address other issues in a timely manner. Rates of accrual, adherence, follow-up, and AE incidence will be monitored closely by the team as well as the HPTN Study Monitoring Committee (SMC). The Protocol Chair, DAIDS Medical Officer, Protocol Biostatistician, SDMC Project Manager, and LOC will address issues related to study eligibility and AE management and reporting as needed to assure consistent case management, documentation, and information-sharing across sites.

## Study Monitoring

On-site study monitoring will be performed in accordance with DAIDS policies. Study monitors will visit the site to:

* Verify compliance with human subjects and other research regulations and guidelines;
* Assess adherence to the study protocol, study-specific procedures manual, and local counseling practices; and
* Confirm the quality and accuracy of information collected at the study site and entered into the study database.

Site investigators will allow study monitors to inspect study facilities and documentation (e.g., ICFs, clinic and laboratory records, other source documents, CRFs), as well as observe the performance of study procedures. Investigators also will allow inspection of all study-related documentation by authorized representatives of the HPTN LOC, HPTN SDMC, HPTN LC, NIAID, (X), site IRBs/ECs, and US regulatory authorities (Office for Human Research Protections (OHRP) and US FDA). A site visit log will be maintained at each study site to document all visits.

## Protocol Compliance

The study will be conducted in full compliance with the protocol. The protocol will not be amended without prior written approval by the Protocol Chair and DAIDS Medical Officer. All protocol amendments must be submitted to and approved by the relevant IRB(s)/EC(s) and the RSC prior to implementing the amendment.

## Investigator’s Records

*(IND study)*

The Investigator will maintain, and store in a secure manner, complete, accurate, and current study records throughout the study. In accordance with FDA IND requirements, the Investigator will retain all study records for at least two years following the date of approval of any labeling change for this licensed product and at least three years after the completion of research. If no marketing application is filed, or if the application is not approved, the records must be retained for two years after the FDA is notified that the IND is discontinued, or longer if needed to comply with local regulations.

Completion of a clinical research study occurs when the following activities have been completed:

* All research-related interventions or interactions with human subjects (e.g., when all subjects are off study);
* All protocol-required data collection of identifiable private information described in the IRB/EC-approved research plan;
* All analysis of identifiable private information described in the IRB/EC-approved research plan;
* Primary analysis of either identifiable private or de-identified information.

Study records include administrative documentation — including protocol registration documents and all reports and correspondence relating to the study — as well as documentation related to each participant screened and/or enrolled in the study — including ICFs, locator forms, CRFs, notations of all contacts with the participant, and all other source documents.

*(Non-IND study)*

The Investigator will maintain, and store in a secure manner, complete, accurate, and current study records throughout the study. Under the US Department of Health and Human Services (DHHS) regulations, the Investigator is required to retain all study records relating to research for at least three [3] years after completion of the research, or longer if needed to comply with local regulations.

Completion of a clinical research study occurs when the following activities have been completed:

* All research-related interventions or interactions with human subjects (e.g. when all subjects are off study);
* All protocol-required data collection of identifiable private information described in the IRB/EC-approved research plan;
* All analysis of identifiable private information described in the IRB/EC-approved research plan;
* Primary analysis of either identifiable private or de-identified information.

Study records include administrative documentation — including protocol registration documents and all reports and correspondence relating to the study — as well as documentation related to each participant screened and/or enrolled in the study — including ICFs, locator forms, CRFs, notations of all contacts with the participant, and all other source documents.

## Use of Information and Publications

Publication of the results of this study will be governed by the HPTN Manual of Operations. Any presentation, abstract, or manuscript will be submitted by the author to the HPTN Manuscript Review Committee, DAIDS, and [treatment/product manufacturer] for review prior to submission.

# References

# SAMPLE appendices

## Appendix I: Schedule of Study Visits and Procedures

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Screening (up to Day -45)** | **Enrollment** | **Weeks 41 and 8** | **Week 13** | **Quarterly (Weeks 26, 39 and 52 )** |
| **Administrative and Behavioral Evaluations/Procedures** |  |  |  |  |  |
| Informed Consent | x |  |  |  | x2 |
| Locator information | x | x | x | x | x |
| Demographic information | x |  |  |  |  |
| Social harms |  |  | x | x | x |
| AE assessment |  | x | x | x | x |
| HIV/STI risk reduction counseling | x | x | x | x | x |
| Study product supply4 |  | x | x | x | x5 |
| Offer condoms and other prevention supplies | x | x | x | x | x |
| **Clinical Evaluations/Procedures** |  |  |  |  |  |
| Complete medical history including medications | x |  |  |  |  |
| Interim medical history including concomitant meds |  | x | x | x | x |
| Symptom-Driven Physical Examination | x | x |  | x | x |
| Blood collection | x | x | x | x | x |
| Urine collection | x | x | x | x | x |
| Rectal swab collection | x |  |  |  | x7 |
| Hepatitis vaccination or referral, if indicated |  | x8 |  |  | x8 |
| STI treatment if applicable: syphilis | x |  |  |  | x7 |
| STI treatment if applicable: gonorrhea and chlamydia | x |  |  |  | x7 |
| **Laboratory Evaluations/Procedures** |  |  |  |  |  |
| HIV diagnostic testing9 | x | x | x | x | x |
| Hematology (CBC with differential) | x |  |  |  |  |
| Renal function tests (BUN, creatinine) | x |  | x10 | x | x11 |
| Calculated creatinine clearance | x |  | x10 | x | x11 |
| Hepatic function tests (ALT/AST, bilirubin) | x |  |  |  |  |
| Hepatitis B status (HbsAg, HbsAb, HbcAb) | x |  |  |  | X8 |
| Urine dipstick for protein and glucose | x | x12 |  | x | x |
| STI testing: syphilis | x |  |  |  | X7 |
| STI testing: rectal swab and urine NAAT for gonorrhea and chlamydia | x |  |  |  | X7 |
| Plasma storage for Pharmacology testing14 |  | x | x14 |  | x15 |
| Lysed PBMC storage for Pharmacology testing14 |  |  | x14 |  | x15 |
| DBS storage for possible Pharmacology testing14 |  | x | x14 |  | x15 |
| Urine storage for substance use testing |  | x | x | x | x |
| Plasma storage for QC and Virology testing | x | x | x | x | x |

[Add footnote as appropriate here]

## Appendix II: Sample Informed Consent Forms

**Study Title**

(HPTN XXX)

Version X.0

Day Month Year

DAIDS Document ID:

**Sponsored by:** Division of AIDS, US National Institute of Allergy and Infectious Diseases, US National Institutes of Health. Study products are provided by X, Y, Z.

**PRINCIPAL INVESTIGATOR:** *[Insert Name*]

**PHONE:** *[Insert Number]*

INTRODUCTION

You are being asked to take part in a research study*.*  Joining this study is voluntary. You may refuse to join, or you may withdraw your consent to be in the study, for any reason. This research study is for men and women who may be at risk for getting Human Immunodeficiency Virus, or HIV. HIV is the virus that causes Acquired Immunodeficiency Syndrome, or AIDS.

Before you decided whether to join the study, we would like to explain the purpose of the study, the risks and benefits to you, and what is expected of you.

***(If applicable – refer to Food and Drug Administration Amendments Act of 2007 or FDAAA), Title VIII, Section 801)***A description of this clinical trial will be available on www.ClinicalTrials.gov, as required by US law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

YOUR PARTICIPATION IS VOLUNTARY

This consent form gives information about the study that will be discussed with you. We will help you understand the form and answer your questions before you sign this form. Once you understand the study, and if you agree to take part, you will be asked to sign your name or make your mark on this form. You will be offered a copy of this form to keep.

Before you learn about the study, it is important that you know the following:

Your participation is voluntary. You do not have to take part in any of the tests or procedures in the study.

You may decide not to take part in the study, or you may decide to leave the study at any time without losing your regular medical care.

If you decide not to take part in the study, you can still join another study at a later time if there is one available and you qualify.

You cannot join this study if you are taking part in another study of drugs or medical devices. You are asked to tell the study staff about any other studies you are taking part in or thinking of taking part in. This is very important for your safety.

PURPOSE OF THE STUDY

(Insert the Purpose of the study in terms the participant will understand, as well as any background research results from similar studies, how long the participant will be in the study, how many participants altogether, which sites/ countries, whether the FDA has approved, etc.).

You will be offered a copy of this form to keep.

STUDY GROUPS

(If applicable, list the differences between the groups).

STUDY PROCEDURES

If you decide to join the study, you will be asked to come to this clinic over the course of X for approximately X times.

Screening Visit

Your screening visit may happen after you read, discuss, understand, and sign this form, or we will schedule a screening visit with you. The procedures done at the Screening visit will take about X hours [*sites to fill in the amount of time].*

The study staff will: (These are examples. Amend as necessary)

(List out procedures for ascertainment of eligibility)

Collect ~XX mL (about x teaspoons) of blood for: X, Y, Z.

Confirm where you live and how to contact you.

Ask you questions about your sexual behavior

X

Y

Z

The results of the HIV test will be available [*site to insert timeframe of testing*]. You will be contacted about the results of your other tests when they are available. [If applicable: If you have gonorrhea, chlamydia, or syphilis, you will be referred for treatment (*sites to add specifics about this here as necessary*)]. A small amount of blood will be stored from this visit. No other samples collected at the time of screening will be kept or used for any other tests other than those listed above.

Confirmation of Eligibility:

Once all the results of the screening tests are known, the following will happen:

You will be told your test results and what they mean.

(If applicable): If you have a positive HIV test you will not be eligible for the study, and you will be referred for the appropriate medical care.

Give you referrals for other health services if you need them.

Enrollment Visit

If you are eligible for this study and decide to take part in the study, you will be asked to return for the enrollment visit. This visit will last about X hours. During the visit, the study staff will:

Examples below: (These are examples. Amend as necessary)

Confirm where you live and how to contact you.

Ask you some questions about yourself, like your age, and your ethnic group.

Ask you to answer questions on a computer about your sexual practices, and how you feel about how your life is going.

Talk with you about HIV and ways to protect yourself from getting it.

Give you a complete physical exam, to include measuring your height, weight, temperature, blood pressure, and ask you about any other medicines you are taking.

Collect ~XX mL (about x teaspoons) of blood for: X, Y, Z.

* For women of childbearing potential: Collect ~XX mL of [*blood or urine*] for pregnancy testing

Randomize you (if applicable).

(If applicable) Give you your study pills, and explain how to take them, and any side effects they may cause.

Give you the results of your tests (HIV, sexually transmitted infections, etc.).

Other procedures.

Offer you condoms.

Add all other visits and corresponding procedures here, e.g., Week or Month 2, Week or Month 4, Week or Month 12, etc.

Exit Visit

This visit will last about X hours [*site staff to insert amount of time]*. During this visit, the study staff will:

Talk with you about the end of the study, and when you will know what drugs (if applicable) you were taking, and when the results of the study will be available.

Give you a brief physical exam, ask you if you have experienced any side effects from the study drugs, and ask you about any other medicines you are taking.

Collect XX mL blood and XX mL urine for X, Y, Z.

Give you the results of your tests when they are available.

Give you condoms.

What will happen if you permanently stop taking your study drugs (if applicable):

If you permanently stop taking the study drugs during the study for any reason, we will ask you to continue to come for your regular study visits, but you will no longer have to undergo certain procedures, like answering questions about taking the study pills, talking to us about taking the study pills, etc. We will fully explain to you what will happen if you permanently stop taking your study drugs.

POSSIBLE FUTURE TESTS *( The protocol team should discuss before including this section to determine which, if any, sites are able to do this (particularly non-US sites). Protocols should include as many specified tests (via protocol objectives) as possible.)*

*(Sample language)* Some of your blood drawn for this study may be left over after all of the study tests are completed and will be stored (with usual protectors of identity) and used for future HPTN-approved research. (X) mL of blood will be drawn for this purpose. Your samples will be stored and tested at special laboratory facilities that may be located in the US and other countries outside of [insert site country]. Only approved researchers will have access to them. People who work at the facility will also have access to your samples to keep track of them. These people won’t have information that directly identifies you. Your samples will not be sold or directly used to produce commercial products. All proposed research studies using your samples will be reviewed by the National Institutes of Health (NIH). There is no time limit on how long your samples will be stored. You will be asked to sign at the end of this consent form to give permission for this. Even if you do not give permission to store your blood after the study, you can still be in this study. You may also withdraw your consent for specimen storage at any time.

RISKS AND/OR DISCOMFORTS

Pregnancy

(Insert risks)

Not all contraceptive choices can prevent HIV transmission, and some may actually increase the risk of getting HIV. We will talk with you throughout the study about ways to protect yourself from getting HIV. You should also discuss with your health care provider and the study clinic staff ways to maintain effective contraception during your participation in the study.

Blood Draws

Taking blood samples may cause some pain, bruise your arm, or make you feel lightheaded. In rare cases you may faint. There is also a slight chance of infection when blood is drawn. You may be nervous while you are waiting for your HIV test result. If the tests show that you have HIV, you may worry about your health and future. You will receive counseling before and after the test to help address your concerns. We will make every effort to protect your confidentiality during the study. However, it is possible that others may learn that you are part of this study and they may think that you are infected with HIV or are at high risk for infection with HIV. Because of this you could have trouble finding or keeping a job. You could also have problems with your family, friends and community.

Other Samples

(Insert risks)

Sensitive Questions

The questions we will ask you about your sexual behavior may make you feel uneasy. However, you do not have to answer any question that you do not want to and you can stop answering the questions at any time.

Other Genetic Testing (If applicable)

We also want to look at your genes that affect how your body changes and removes the drugs used in this study. Gene differences between people can lead to different amounts of drug in the body; this may affect how well a drug protects people from HIV infection. If you consent, we will test your blood to get information about how your genes may have affected the drug levels in your body. The tests we will use to look at your genes are research tests and will be performed in a research laboratory. All of the samples will be identified with a coded number. The laboratory doing the testing will not know who you are. The results obtained for individual study participants (like you) will not be reported to the study sites or back to you. However, the combined results of the testing from all of the study participants will be available to the study sites and to the study participants at their request, once the analysis has been completed.

Study Medications

The drugs used in this study may have side effects, some of which are listed below. Please note that these lists do not include all the side effects seen with these drugs. These lists include the more serious or common side effects with a known or possible relationship. If you have questions concerning the additional study drug side effects, please ask the medical staff at your site. It should be noted that these are the risks that are seen in HIV positive people taking these medications. It is not known if these side effects will occur as often and it could be that some of these side effects might be more or less serious HIV negative people.

(List out complete side effects for each drug)

Other Possible Risks

(These are examples. Amend as necessary) Example: We do not know if there are other risks if you use herbal treatments or supplements while you are using the tablets. Please tell study staff if you are using any herbal treatments or supplements.

We will perform an HIV test, which is routinely done before HIV drugs are tested in non-HIV subjects.  You will be counseled before and after this test is done.  [Sites to insert reporting responsibilities in the state the site is located in. Also include whether if a participant tests positive, the results will become part of public health records, or any other record (medical file, etc.)]

You will be tested for gonorrhea, chlamydia and syphilis. [*Note to sites: Insert here any reporting responsibilities for your state or local jurisdictions or reporting of these infections to public health authorities].*

In addition, there may be uncommon or previously unknown risks that might occur. You should report any problems to the researchers immediately.

There may also be some social risks to participating in this study. You may feel embarrassed or uncomfortable with some of the questions you will be asked, some of the procedures that will be done, or some of the test results that you will receive. You may also experience stigma as a result of being involved in a study about HIV because people may assume that you are HIV-infected.

If you test positive for HIV during the study you will be asked to stop taking your study medication. If you continue to take the study medication after HIV infection has occurred, there is a chance that drug resistance may occur.

BENEFITS

We will test you for HIV and other sexually transmitted infections throughout this study. The counseling you get during this study may help you to avoid HIV and other sexually transmitted infections. If you have or become infected with HIV, this counseling may help you to learn how to better care for yourself and avoid passing HIV to your sexual partners. If you become HIV infected, or have another sexually transmitted infection, we will refer you for care and/or treatment. At the screening visit we will also check if you have hepatitis B infection. If needed, we will refer you for hepatitis B vaccination. During the study you will have tests to check on the health of your blood, liver, and kidneys. If any health problems are found, you will be referred for care. At every visit you will receive condoms free of charge.

You may not receive any other direct benefit from being in this study; however, you or others in your community may benefit from this study later. The information gathered during this study may help to prevent HIV and other infections. This may be beneficial to you and your community.

NEW INFORMATION

You will be told any new information learned during this study that might affect your willingness to stay in the study. For example, if information becomes available that shows that the medication may be causing bad effects, you will be told about this. You will also be told when the results of the study may be available, and how to learn about them.

WHY YOU MAY BE WITHDRAWN FROM THE STUDY WITHOUT YOUR CONSENT

You may be withdrawn from the study without your consent if any of the following occur:

You are unable or unwilling to follow all of the study procedures or instructions.

You could be harmed by continuing to take tablets.

The study is stopped or canceled.

The study staff feels that staying in the study would be harmful to you.

You are not able to attend clinic visits or complete all of the study procedures.

Other reasons, as decided by the study staff.

ALTERNATIVES TO PARTICIPATION

[*Sites to include/amend the following if applicable:* There may be other studies going on here or in the community that you may be eligible for. If you wish, we will tell you about other studies that we know about. There also may be other places where you can go for HIV counseling and testing. We will tell you about those places if you wish.]

COSTS TO YOU

There will be no cost to you for study related visits, study products, physical examinations, laboratory tests, or other procedures.

REIMBURSEMENT

You will receive [$xx] for your time, effort, and travel to and from the clinic at each scheduled visit. [*Sites to insert information about local reimbursement for the study.*

CONFIDENTIALITY

To keep your information private, your samples will be labeled with a code that can only be traced back to your study clinic. Your name, where you live, and other personal information will be protected by the study clinic. The results of any tests done on these samples will not be included in your health records. Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

Efforts will be made to keep your study records and test results confidential to the extent permitted by law. However, we cannot guarantee absolute confidentiality. You will be identified by a code, and personal information from your records will not be released without your written permission. Any publication of this study will not use your name or identify you personally. However, your records may be reviewed, under guidelines of the US Federal Privacy Act, by the US Food and Drug Administration (FDA); the sponsor of the study (US National Institutes of Health [NIH]), the [*insert name of site*] Institutional Review Board (IRB), study staff, study monitors, the companies that make the drugs used in this study, and (*insert applicable local authorities*].

[*US sites only must add this section*]In addition to the efforts made by the study staff to help keep your personal information confidential, we have obtained a Certificate of Confidentiality from the U.S. Federal Government. This Certificate protects researchers from being forced to tell people who are not connected with this study, such as the court system, about your participation. The Certificate of Confidentiality does not prevent you from releasing information about yourself and your participation in the study. The Certificate cannot be used to resist a demand for information from personnel of the US Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the US FDA. Even with the Certificate of Confidentiality, if the study staff learns of possible child abuse and/or neglect or a risk of harm to you or others, we will tell the proper authorities.

The study staff will also use your personal information, if needed, to verify that you are not taking part in any other research studies. This includes other studies conducted by [site name] and studies conducted by other researchers that study staff know about. Any publication of this study will not use your name or identify you personally.

Your records may be reviewed by:

the US FDA

the US NIH

the US Department of Heath and Human Services (DHHS), Office of Human Research Protection (OHRP)

[insert names of applicable IRBs or other regulatory or local agencies]

study staff

study monitors

the companies that makes the study drugs (insert name if applicable)

*[Sites to include/amend the following if applicable:*] [*Local/state/national*] regulations require study staff to report the names of people who test positive for [*HIV and other infections*] passed during sex to the [*local health authority*]. Outreach workers from the [*health authority*] may then contact you about informing your partners, since they also should be tested. If you do not want to inform your partners yourself, the outreach workers will contact them, according to the confidentiality guidelines of the [*health authority*].

RESEARCH-RELATED INJURY

*[Sites to specify institutional policy:]* It is unlikely that you will be injured as a result of study participation. If you are injured, the [*institution*] will give you immediate necessary treatment for your injuries. You [*will/will not*] have to pay for this treatment. You will be told where you can get additional treatment for your injuries. There is no program to pay money or give other forms of compensation for such injuries either through this institution or the US NIH. You do not give up any legal rights by signing this consent form.

PROBLEMS OR QUESTIONS

If you ever have any questions about the study, or if you have a research-related injury, you should contact [*insert name of the investigator or other study staff*] at [*insert telephone number and/or physical address*].

If you have questions about your rights as a research participant, you should contact [insert name or title of person on the IRB or other organization appropriate for the site] at [insert physical address and telephone number].

If you have questions about who to contact at the research site, you should contact [insert name of the investigator or community educator or CAB member] at [insert physical address and telephone number]

**SIGNATURE PAGE**

**HPTN XXX, Study Title, Version X.0**

SCREENING AND ENROLLMENT CONSENT *(Modify as needed per protocol requirements)*

*Insert signature blocks as required by the local IRB*:] If you have read this consent form, or had it read and explained to you, and you understand the information, and you voluntarily agree to join the study, please sign your name or make your mark below. Also, please indicate by providing your initials in the spaces below the additional sample collection, genetic testing, or long-term storage that you agree to.

\_\_\_\_\_\_\_\_ I agree to take part in this study.

\_\_\_\_\_\_\_\_ I agree to have samples of my blood stored and used for future testing related to HIV infection.

\_\_\_\_\_\_\_\_ I do not agree to have samples of my blood stored and used for future testing related to HIV infection.

\_\_\_\_\_\_\_\_ I agree to allow my blood to be tested to see how my genes make the drugs work in my body.

\_\_\_\_\_\_\_\_ I do not agree to allow my blood to be tested to see how my genes make the drugs work in my body.

[If qualitative interviews add]:

\_\_\_\_\_\_\_ I agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded.

\_\_\_\_\_\_\_ I do not agree to participate in an interview where I will be asked questions about this research, and the interview will be recorded.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Participant Name (print) Participant Signature and Date

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Study Staff Conducting Study Staff Signature and Date

Consent Discussion (print)

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Witness Name (print) Witness Signature and Date

(As appropriate)