Letter of Amendment # 1 to:

HPTN 061: Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men, Version 2.0, dated 02 April 2009, DAIDS Document ID# 10666

Letter of Amendment Date: 22 September 2009

The following information impacts the HPTN 061 study and must be forwarded to all responsible Institutional Review Boards (IRBs)/Ethics Committees (ECs) as soon as possible for their information and review. This Letter of Amendment must be approved by all responsible IRBs/ECs before implementation.

The modifications in this Letter of Amendment include minor changes to the enrollment informed consent form. Your IRB(s)/EC(s) are responsible for determining how study participants are to be informed of the contents of this Letter of Amendment.

This Letter of Amendment and any IRB/EC correspondence must be filed in the site regulatory file and in other pertinent files. Any revised informed consent forms based on this LoA must be submitted to the DAIDS/RCC Protocol Registration Office for informational purposes.

Section 1: Summary of Revisions and Rationale

1. A correction was made to Sections 5.2, 5.4, and the Schedule of Study Visits and Procedures to remove a reference to a questionnaire about motivators and barriers for referring index partners. The instruction has been changed to discuss motivators and barriers with the participant instead of administering a questionnaire.
2. A change was made to shorten the window in which index participants may refer their partners to the study-- from 60 days to 30 days-- after the closure of community referred enrollment. This shortened window applies whether the community referral period has ended because the 12 month recruitment window has closed or because the site has enrolled 250 community recruited participants.
3. The CRS number was corrected for both New York sites. The name of the Harlem Prevention Center Clinical Research Site was also corrected.
4. An addition was made to Section 5.3, to the Schedule of Study Visits and Procedures, and to the Enrollment Informed Consent Form to ask participants whether they have enrolled in another HIV study since the last visit as part of follow-up visit procedures. This information will not be captured into the study database, but it will give sites the chance to discuss the burden of participating in more than one HIV study at a time and to discourage participants from doing so.
5. Several small changes have been made to Figure 4 and Sections 2.3, 3.3 and 3.5 to clarify the enrollment categories and caps that apply to this study.
6. Several small changes have been made to Sections 4.2, 5.4, 9.1, the Schedule of Study Visits and Procedures, and to the Enrollment Informed Consent Form to allow participants who have previously been diagnosed with HIV infection to provide documentation of their status, rather than having their status confirmed during the enrollment visit by HIV laboratory testing (and to correct one small

language inconsistency regarding HIV tests). Participants who report they are HIV positive but refuse HIV rapid testing may confirm their status by providing one or more items from the list of acceptable documentation listed in the SSP, such as:

- A letter from physician, provider, or agency (including a case manager) that states participant's name and positive HIV status
- AIDS Drug Assistance Program [ADAP] documentation
- A positive test result that includes the participant's name.
- Evidence that the participant has been prescribed anti-retroviral medications for treatment of HIV infection (e.g. a bottle of ARV drugs or a prescription with the participant's name on it)

7. A small change was made to Section 5.5 to clarify that site SOPs for conducting off-site visits will need to be reviewed by the local IRB if required by local policies.
8. Dr. Sheldon Fields was added to the protocol team roster.
9. A small correction was made to Section 9.1 to clarify laboratory procedures.

Section 2: Implementation of the Protocol Modifications
The modifications detailed below will be formally incorporated into the body of the protocol with the next full amendment. Deletions to the protocol text are indicated by strikethrough; additions are indicated in **bold**.

Implementation

Revision 1 A correction was made to Sections 5.2, 5.4 and the Schedule of Study Visits and Procedures to remove a reference to a questionnaire about motivators and barriers for referring index partners. The instruction has been changed to discuss motivators and barriers with the participant instead of administering a questionnaire.

5.2 Enrollment Visit

- ~~Administer questionnaire about~~ **Discuss** ~~referral~~ motivators & barriers **to referral**.

5.4 Additional Information about Study Procedures

- ~~A brief questionnaire will be administered to the index participants to assess motivators and barriers to referring network members to the study.~~ **Site staff will discuss with the participant the motivators and barriers that they perceive to referring their Black MSM sexual partners.**

APPENDIX I: SCHEDULE OF STUDY VISITS AND PROCEDURES FOR HPTN 061

PROCEDURES	Enroll Visit [1]	26 Week Follow-up Visit[1]	52 Week Follow-up Visit[1]
ADMINISTRATIVE, BEHAVIORAL, AND REGULATORY PROCEDURES			
For index participants, request referral of up to 5 Black MSM sexual network members. Provide training on techniques for motivating network members to come to the study site. ~~Administer questionnaire about~~ **Discuss** ~~referral~~ motivators & barriers **to referral**.	X		

Revision 2 A change was made to shorten the window in which index participants may refer their partners to the study-- from 60 days to 30 days-- after the closure of community referred enrollment. This shortened window applies whether the community referral period has ended because the 12 month recruitment window has closed or because the site has enrolled 250 community recruited participants.

SCHEMA
There will be no cap on the number of referred participants enrolled into the study, however enrollment of referred participants will stop ~~two months~~ **30 days** after closure of enrollment of community-recruited participants.

2.3 Study Design: Main (Quantitative) Component
This will continue until the waves of referral self-extinguish, or ~~two months~~ **30 days** after the last community-recruited participant has been enrolled.

3.5 Recruitment Process
Enrollment of referred partners will cease at a site ~~two months~~ **30 days** after the last community-participant has been enrolled

5.4 Additional Information about Study Procedures
Referral of sexual network members will continue through multiple waves until no more network members are referred, no more index participants are identified, or until ~~two months~~ **30 days** have passed since the enrollment of the last community-referred participant.

Revision 3 The CRS number was corrected for both New York sites. The name of the Harlem Prevention Center Clinical Research Site was also corrected.

SCHEMA
Study Sites:

- New York Blood Center (NYBC)/Union Square CRS (site ~~30913~~ **31605**) and ~~Harlem Hospital Center/Columbia University~~ **Harlem Prevention Center** CRS (site ~~31471~~ **30276**) in New York City, New York

Revision 4 An addition was made to Section 5.3, to the Schedule of Study Visits and Procedures, and to the Enrollment Informed Consent Form to ask participants whether they have enrolled in another HIV study since the last visit as part of follow-up visit procedures. This information will not be captured into the study database, but it will give sites the chance to discuss the burden of participating in more than one HIV study at a time and to discourage participants from doing so.

5.3 Follow-up Visits (26 and 52 Weeks After Enrollment)

Administrative, Behavioral, and Regulatory Procedures

- **Enquire with participant about participation in other HIV research studies and discuss time/study burden that co-enrollment in multiple studies could impose upon the participant**.

APPENDIX I: SCHEDULE OF STUDY VISITS AND PROCEDURES FOR HPTN 061

PROCEDURES	Enroll Visit [1]	26 Week Follow-up Visit[1]	52 Week Follow-up Visit[1]
ADMINISTRATIVE, BEHAVIORAL, AND REGULATORY PROCEDURES			
Enquire with participant about participation in other HIV research studies and discuss time/study burden that co-enrollment in multiple studies could impose upon the participant.		**X**	**X**

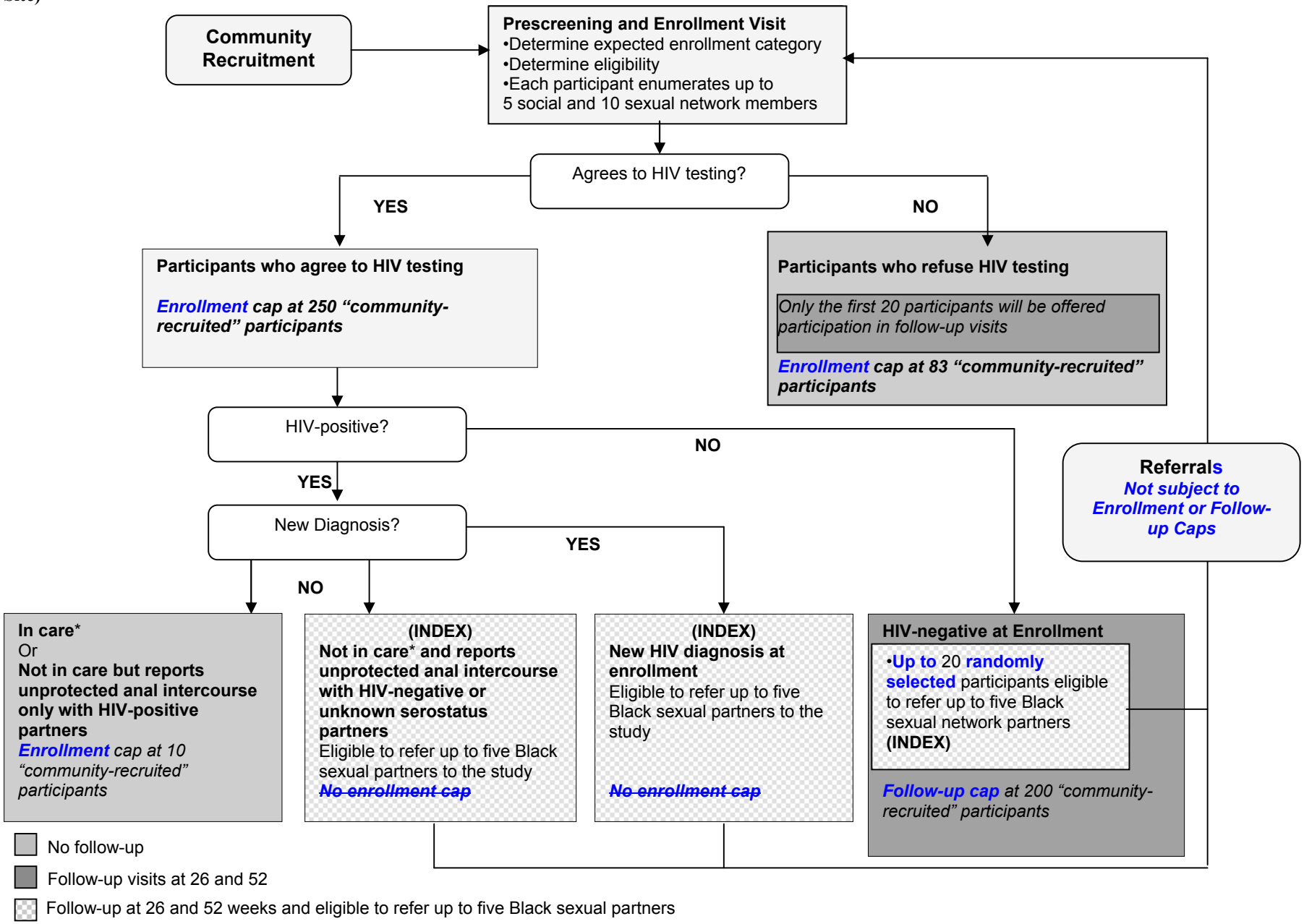
APPENDIX II: SAMPLE INFORMED CONSENT FOR ENROLLMENT

Six-Month Visit

- **We will ask you if you are participating in any other HIV research studies and talk with you about the difficulties of being in two studies at once**.

Revision 5 Several small changes have been made to Figure 4 and Sections 2.3, 3.3 and 3.5 to clarify the enrollment categories and caps that apply to this study.

Figure 4- Study Design of the Main (Quantitative) Component of HPTN 061 (Recruitment at One Site)



* "In care" = has engaged with health care provider for HIV care within the last six months

2.3 Study Design: Main (Quantitative) Component
Index participants meet one of the following criteria in addition to the study inclusion criteria listed in Section 3.1:

- Newly diagnosed with HIV infection at HPTN 061~~the~~ enrollment visit ~~(no cap)~~.
- Diagnosed with HIV prior to enrollment in HPTN 061, but are not in care (for this study, "not in care" means not having engaged with a health care provider for HIV-related care in the last six months) and have had unprotected anal sex with HIV uninfected partners or partners of unknown status in the last six months ~~(no cap)~~.
- Up to 20 HIV-negative participant~~s~~ randomly selected as eligible to refer partners~~(cap at 20 HIV-negative participants designated as index)~~.

Enrollment Visit
For participants meeting the criteria **above and therefore** ~~to be allowed~~ eligible to refer participants (i.e., "index" participants), the counselor will explain the referral process and will provide a brief training to the participant in techniques for motivating referred partners to come in for screening.

3.3 Participant Categories and Enrollment Caps
Figure 4 depicts graphically how the enrollment caps will be applied to participant categories at ~~one~~ **each** site. Recruitment of all community-recruited participants will cease when 250 community-recruited participants who agree to HIV testing have been enrolled. ~~In an effort to limit the number of HIV-uninfected participants, enrollment of this category will be capped at 200 participants. Because it will be impossible to identify uninfected participants who will be uninfected prior to enrollment and HIV testing, the enrollment cap in this case will mean exclusion from follow-up visits only HIV-negative participants who are enrolled after the 200-participant cap is reached will not count toward the overall cap of 250 community-recruited participants who agree to testing.~~ **Due to concerns that enrollment of large numbers of HIV negative participants could prevent the inclusion of other categories of men (HIV positive, unwilling to test, etc.), only the first 200 community-recruited, HIV-negative participants will count toward the overall 250 participant enrollment cap. Furthermore, the first 200 community-recruited, HIV-negative participants will have follow-up visits, but later participants in this category will have enrollment visits only.**

3.5 Recruitment Process
Recruitment will begin through outreach efforts of site staff to recruit community-recruited participants. Community-recruited participants meeting ~~certain~~ **the** criteria listed in Section 2.3 ("index" participants) will be asked to recruit members of their sexual network to the study ("referred" participants)…

…Therefore, the sites should expect to enroll approximately 333 ~~index~~ participants through community recruitment to reach 250 men who agree to testing, based on the assumption that approximately 25% of men will refuse HIV testing...

…Index participants (those who meet the criteria enumerated ~~above~~ in Section 2.3 for being eligible to refer partners to the study) will be asked to refer up to five of their Black MSM sexual network members for screening…

Revision 6 Several small changes have been made to Sections 4.2, 5.4, 9.1, the Schedule of Study Visits and Procedures, and to the Enrollment Informed Consent Form to allow participants who have previously been diagnosed with HIV infection to provide documentation of their status, rather than having their status confirmed during the enrollment visit by HIV laboratory testing (and to correct one small language inconsistency regarding HIV tests). Participants who report they are HIV positive but refuse HIV rapid testing may confirm their status by providing one or more items from the list of acceptable documentation listed in the SSP, such as:

- A letter from physician, provider, or agency (including a case manager) that states participant's name and positive HIV status
- AIDS Drug Assistance Program [ADAP] documentation
- A positive test result that includes the participant's name.
- Evidence that the participant has been prescribed anti-retroviral medications for treatment of HIV infection (e.g. a bottle of ARV drugs or a prescription with the participant's name on it)

Section 4.2 HIV Counseling, Testing and Referral for Care
A major component of this intervention is finding men with undiagnosed HIV infection. ~~Licensed~~ **FDA-cleared** HIV antibody tests (e.g., ~~licensed~~ **FDA-cleared** rapid HIV antibody tests with follow-up of reactive tests with WB assays) will be used to identify HIV-infected men who are unaware of their HIV status. **Participants who report a prior HIV positive diagnosis at their enrollment visit will have their status confirmed either through an FDA-cleared HIV antibody tests according to the algorithm in Section 11 of the SSP, or by providing acceptable documentation of prior diagnosis (see Section 4 of the SSP for a list of acceptable documentation).** Participants will be provided appropriate pre- and post-test counseling. Participants who are identified as being HIV-infected (whether this is a new diagnosis or confirmation of a prior diagnosis) will be assisted in obtaining care by a PHN.

Section 5.4 Additional Information about Study Procedures
Subject to the enrollment caps previously described, some participants will be enrolled into the study who refuse HIV and/or STI testing. **Participants who refuse HIV testing but identify as HIV positive will be asked for alternative documentation to verify status. A list of appropriate documentation is provided in Section 4 of the SSP. Participants who identify as HIV positive but refuse HIV testing and do not provide appropriate documentation of their diagnosis will be categorized as "participants refusing HIV testing"…**
~~…All p~~**P**articipants will be asked to either return to or expect contact from the study site to receive test results when they are available, about two weeks after the study visit…STI results for participants who have a negative HIV rapid test, **or who identified at enrollment as previously diagnosed with HIV infection,** may be provided over the telephone…

…These participants will be given instructions from the study team about options for receiving the results of the second WB, according to local procedures. If the reactive HIV rapid test is not confirmed by two positive WB tests (or an indeterminate and then two positive WB tests), the site should contact the NL to determine whether additional HIV testing is needed to determine the subject's HIV infection status, and should contact the study participant to discuss the test results

and to arrange for additional testing, if needed. **An exception to the procedures above is allowed when a participant identifies at enrollment as previously diagnosed with HIV infection. In this case, site staff may decide that WB results can be provided over the telephone, and per the HPTN 061 HIV testing algorithm, a second WB test need not be performed to confirm a positive rapid and positive WB**. Plasma specimens from each blood sample drawn for confirmatory testing will be stored for later use in incidence testing, if warranted.

Section 9.1 Local Laboratory Specimens

The following types of specimens will be collected for testing or processing at the local laboratory (LL):

~~Subjects who agree to testing:~~ **All Subjects**

- Blood for HIV rapid testing using an FDA-cleared kit ~~(~~**for** all subjects at enrollment, ~~including those reporting a history of HIV infection).*~~ **except**
    - **those who refuse HIV diagnostic testing**
    - **those who provide documentation of prior diagnosis of HIV infection in lieu of HIV testing***
- Sera for syphilis serology.
- Urine for GC/CT NAAT testing.
- Swab for rectal GC/CT testing.
- Plasma for future NL testing and storage.

Subjects with a reactive HIV rapid test:

- Plasma for WB testing using an FDA-cleared kit.*
- Blood for CD4 cell count* (CD4 cell counts must be performed at a laboratory that is CLIA-certified; laboratories that are certified through the DAIDS/Immunology Quality Assurance (IQA) program are preferred).
- Additional plasma for future NL testing and storage.

NOTE**: *HIV rapid testing and WB are not required at the 26- and 52- week visits if a subject was previously confirmed to be HIV ~~seropositive~~* ***infected either through on-study testing or documentation of prior diagnosis of HIV infection (if the subject refuses on-study testing).. *Consult SSP Section 11 for detailed algorithm. CD4 cell count is not required at the 26- week visit if subject was previously confirmed to be HIV seropositive.*

Subjects who report being HIV-infected but receive a non-reactive HIV rapid test result:

- **Site staff will alert the NL of the situation.**
- **Site staff will perform CD4 cell count testing locally, but will not perform WB testing.**
- **Plasma for VL, WB and plasma storage will be sent in real-time to the NL for testing to determine the subject's HIV status. At the NL's discretion, this may include additional serologic testing and/or NAAT testing.**
- **If results from NL HIV testing are clear, the NL will inform the site of the subject's HIV infection status. If the results do not yield a clear diagnosis, the NL will decide if more testing should be done, or will provide all testing results to HIV Endpoint Adjudication Committee (EAC), which will make a final determination of HIV status.**
- **Site staff will be informed of the NL's or EAC's decision, and will share that information with the subject.**

APPENDIX I: SCHEDULE OF STUDY VISITS AND PROCEDURES FOR HPTN 061

[4] HIV WB and STI test results will be provided at the post-test visit after the study visit, scheduled for a time soon after the results are expected to be available. **STI results, and WB results may be provided by telephone for participants who identify as HIV positive prior to on-study testing.**

[6] **An** HIV rapid test is performed at enrollment for all study subjects consenting to HIV testing, ~~even if~~ **unless** they provide ~~a history~~ **adequate documentation** of prior HIV diagnosis **or refuse testing**; HIV rapid testing is not performed at 26 or 52 weeks if HIV infection was confirmed at a prior visit. The HIV rapid test will be performed at the clinic site. Testing at the clinic site must be performed under the oversight of the study coordinator for the CRS.

APPENDIX II: SAMPLE INFORMED CONSENT FOR ENROLLMENT

We will draw a small amount of blood from you (up to about 40 ml, or about 3 tablespoons). If you agree, we will test your blood for HIV and syphilis. **If you already know that you are infected with HIV, and can document your HIV status, we would not ask you to have a blood test for HIV.** Some of your blood will be stored in case it is needed later for tests related to this study. These tests may not be done for a year or more after you have had your last study visit.

Revision 7 A small change was made to Section 5.5 to clarify that site SOPs for conducting off-site visits will need to be reviewed by the local IRB if required by local policies.

5.5 Off-Site Visits

To maximize retention for the study, provision has been made to conduct off-site visits for follow-up. An off-site visit should only be conducted after all other options for scheduling the visit at the clinic have been explored. Before off-site visits can be conducted, the site must have an SOP in place describing how this activity will be performed, and this SOP must be approved by ~~both~~ **the** HPTN Coordinating and Operations Center (CORE)**, and, if required locally,** by the local institutional review board (IRB) or ethics committee (EC).

Revision 8 Dr. Sheldon Fields was added to the protocol team roster.

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Revision 9 A small correction was made to Section 9.1 to clarify laboratory procedures.

Section 9.1 Local Laboratory Specimens

All subjects with **a** positive WB test result:

- HIV viral load (at time of on-study diagnosis, HAART initiation, and at 52 weeks)

A diagram of the HIV testing algorithm for HPTN 061 is provided in the SSP manual.

Each study site will adhere to standards of good clinical laboratory practice, the HPTN Manual of Laboratory Operations[102], and local SOPs for 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).