

Letter of Amendment # 4 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: 07 April 2011

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.

Some of the following information affects the Sample Informed Consent. A Sample Informed Consent Addendum is attached. Your IRB/EC will be responsible for determining the process of informing subjects of the contents of this Letter of Amendment.

Upon receiving final IRB/EC and any other applicable Regulatory Entity (RE) approval(s) for this LoA, sites should implement the LoA immediately. Sites are still required to submit a LoA registration packet to the DAIDS Protocol Registration Office (PRO) at the Regulatory Support Center (RSC). Sites will receive a registration notification for the LoA once the DAIDS PRO verifies that all the required LoA registration documents have been received and are complete. A LoA registration notification from the DAIDS PRO is not required prior to implementing the LoA. A copy of the LoA registration notification along with this letter and any IRB/EC correspondence should be retained in the site's regulatory files.

Section 1: Summary of Revisions and Rationale

1. The protocol was changed to remove the requirement that participants selected for individual interviews be interviewed within 30 days of their study enrollment date. This change was made in order to meet the goal of achieving a balance of HIV positive and HIV negative interviewees.

The sampling method for qualitative interviews in the study asks each site to conduct at least 10 interviews for cross-site analysis, to be comprised of 5 HIV positive and 5 HIV negative participants, if possible, and to conduct those interviews within 30 days of participants' enrollment. Because few HIV positive participants were enrolling at the time that qualitative interviews began, it was necessary to interview some participants who had been enrolled earlier in the study, and therefore would fall outside of the 30 day limit.

This amendment of the protocol does not change the study's risk-to-benefit ratio, will not need to be reported to study participants, and does not require a change in the consent form.

2. The protocol was revised to provide alternative study procedures for participants who report co-enrollment in HPTN 061 and the HVTN 505 study at an HPTN 061 follow-up visit. The normal 061 HIV testing algorithm could disclose the participant's treatment arm in the vaccine trial and would result in HPTN 061 study staff providing preliminary HIV test results suggesting HIV infection to uninfected participants. Therefore, procedures for blood draw and HIV testing, and provision of test results and post-test counseling, have been modified for these participants. Procedures are also modified for CD4 and viral load testing for these participants. Informed consent will be obtained from co-enrolled participants for these modified procedures before implementation. The individual sites in HPTN 061 will decide whether or not to implement these procedures at their location. The changes in procedures for participants co-enrolled in HVTN 505 can be found in Appendix D of Section 11 of the HPTN 061 SSP Manual.

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.

Revision 1

2.4 Study Design: Qualitative Component

Trained study staff will conduct 60- to 90-minute individual qualitative interviews. The interviews will be audio recorded and transcribed for analysis. Interviews will ~~be conducted within 30 days of participants' study enrollment date and~~ will take place at a location identified by study staff to ensure adequate privacy and confidentiality. Participants will be provided with a separate reimbursement for participation in an interview.

Revision 2

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

Clinical/Counseling Procedures*

Laboratory Procedures*

***NOTE: Clinical/counseling and laboratory procedures will be different for participants reporting co-enrollment in HVTN 505. See note below and Appendix D of SSP Section 11 for additional information.**

5.4 Additional Information about Study Procedures

For participants who report co-enrollment in HPTN 061 and the HVTN 505 study at an HPTN 061 follow-up visit, following the normal 061 HIV testing algorithm could disclose their treatment arm in the vaccine trial and could cause site staff to provide preliminary HIV test results suggesting HIV infection to uninfected participants. Therefore, procedures for blood draw and HIV testing, including the laboratories where HIV testing will be conducted, provision of test results, and post-test counseling, have been modified for these participants. Procedures are also modified for CD4 and viral load testing for these participants. Informed consent will be obtained for these modified procedures before implementation. The changes in procedures for participants co-enrolled in HVTN 505 can be found in Appendix D of Section 11 of the HPTN 061 SSP Manual.

9.1 Local Laboratory Specimens

Note: Specification of specimens collected and testing performed for participants reporting co-enrollment in HVTN 505 can be found in Appendix D of the SSP Section 11.

9.2 HPTN Network Laboratory (NL) Specimens

Note: Specification of specimens collected and testing performed for participants reporting co-enrollment in HVTN 505 can be found in Appendix D of the SSP Section 11.

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
CLINICAL/COUNSELING PROCEDURES			
Provide HIV test results and post-test counseling, if applicable. ^{4, 12}	X	X	X
Collect venous blood draw for HIV rapid test. ^{6, 12}	X	X	X
Collect venous blood draw for syphilis test, WB, ⁷ CD4 cell count, ⁸ HIV viral load, ⁹ and plasma storage. ^{10, 12}	X	X	X
LOCAL LABORATORY PROCEDURES			
HIV rapid test ^{6, 12}	X	X	X
HIV WB ^{7, 12}	X	X	X
CD4 cell count ^{8, 12}	X	X	X
HIV viral load ^{9, 12}	X	X	X

¹² Clinical, Counseling and Laboratory procedures for HIV-related testing, including CD4 cell count and HIV viral load, will be different for participants who disclose co-enrollment in an HIV vaccine study at a follow-up visit. See SSP Section 11 Appendix D for details

[Note: All of Appendix VI is added content, but is not shown in bold text for ease of reading.]

APPENDIX VI: SAMPLE INFORMED CONSENT ADDENDUM FOR ALTERNATIVE HIV TESTING PROCEDURES FOR PARTICIPANTS DISCLOSING CO-ENROLLMENT IN HVTN 505

TITLE OF THE RESEARCH:

HPTN 061- A Feasibility Study of a Community-Level, Multi-Component Intervention for Black Men Who Have Sex with Men in Preparation for a Community-Level Randomized Trial to Test the Efficacy of the Intervention in Reducing HIV Incidence Among Black Men Who Have Sex with Men

HPTN 061, Version 2.0

02 April 2009

DAIDS ID: 10666

SPONSOR: NIAID, NIDA, NIMH, NIH

INVESTIGATOR OF RECORD: [insert name]

PHONE: [insert number]

INTRODUCTION:

You have informed the staff at this site that you are (or have been) a participant in the HIV vaccine study known as HVTN 505. As part of your participation in HVTN 505, you may have been injected with a trial vaccine for HIV. Neither you nor the HVTN 505 study staff will know until the end of that study if you have received the trial vaccine. If you have received the vaccine, then routine HIV tests, like the ones normally used in this study (HPTN 061), could be difficult to interpret. This is because the vaccine can make it look like you are HIV infected when you are not. For these reasons, we would like to test you for HIV in a slightly different way.

This is a consent form. It gives you information regarding the way we would test you for HIV infection and how it would be different from the way you were tested at previous study visits. We will discuss this information with you. We will also explain how your results may be affected if you do not agree to the new HIV testing approach.

Please ask us to explain anything that you do not understand. After we tell you about the new procedures, we will ask if you agree to them. If you agree, you will be asked to sign this consent form, or make your mark in front of a witness. You will be given a copy to keep; you do not need to take that copy if you do not want to. This process is called informed consent.

Please note that:

- You do not need to agree to these procedures. Even if you do not agree to them, you will still continue as a participant in this study.
- If you do not agree to these procedures, you can still join another study later, if one is available and you qualify.

REASON FOR DIFFERENT PROCEDURES

Some participants in the HVTN 505 study receive the trial vaccine. For these people, regular blood tests for HIV can make it look like they are HIV infected when they are not. This is because regular HIV tests look for signs that the body is fighting HIV infection, and the body's reaction to the vaccine can look like its reaction to HIV infection.

The regular way we test for HIV in HPTN 061 is to do a rapid (instant) HIV test. If the rapid test is positive, we tell the participant that the result suggests they may be infected and that we need to do more testing. If the follow-up test also shows that the person may be infected, we take one more blood sample and repeat the follow-up test to be sure of the result.

For people enrolled in both HPTN 061 and HVTN 505, a positive HIV rapid test could mean HIV infection, but it could also just be a reaction to the vaccine. We would have to wait for additional test results to know for sure what the rapid test result meant, and this could make you anxious. Also, some people might try to guess whether they got the vaccine, based on their rapid test results. But it's possible to have a false positive rapid test without the vaccine and to have a negative rapid test with the vaccine. So, we would prefer not to do the rapid test at your 061 study visits. Instead, we would like to collect a sample for a different test. It will take longer to get the result (about 1 to 2 weeks), but if the result is positive we will know it is because of the virus and not because of the vaccine.

PROCEDURES:

If you agree then here are the ways that your HIV tests will be different from what is usually done in this study:

- Instead of collecting about 40 mL of blood at a typical study visit, we will collect slightly more, up to about 48 mL.
- We will not perform an HIV rapid test at your study visit, and you will not receive rapid test results on that day. Instead, your blood sample will be sent for testing at a laboratory that can distinguish true HIV infection from your body's reaction to a trial vaccine. The laboratory will send the HIV test results to us in about 1 to 2 weeks.
- Whenever we request an HIV test for you, we will also request that the laboratory do another test. This test will show how your body is responding to infection if you are found to be infected with HIV. If you are infected with HIV we will tell you the results of this test too.
- When we receive the results back from the laboratory, we will contact you and arrange to provide the results and post-test counseling to you. If the results show that you may be infected with HIV, we will collect another sample from you to repeat the testing until we are sure that you either are or are not infected with HIV.

RISKS and DISCOMFORTS:

These alternative procedures should pose no greater risks or discomforts than the regular HIV testing in this study.

By agreeing to these procedures you will have to wait longer (about 1-2 weeks) before you receive any HIV test information.

POTENTIAL BENEFITS:

By agreeing to these testing procedures, you may avoid receiving rapid HIV test results that would suggest you might be infected with HIV when you are not. This may help you avoid a potentially stressful situation. However, not everyone in the vaccine study would receive a positive rapid result, even if the regular HIV testing procedures were used.

ALTERNATIVES TO PARTICIPATION:

If you choose not to agree to these alternative HIV testing procedures, you can still receive the regular HIV testing offered in this study. If you do not agree to the alternative testing procedures, it will not affect your ability to continue as a participant in HPTN 061.

SIGNATURE

If you have read this consent form (or had it explained to you), all your questions have been answered and you agree to the alternative HIV testing procedures for vaccine study participants, please sign your name or make your mark below.

Participant's Name (print)

Participant's Signature and Date

Participant's Legal Guardian
(As appropriate)

Legal Guardian's Signature and Date

Study Staff Conducting
Consent Discussion (print)

Study Staff Signature and Date

Witness' Name (print)
(As appropriate)

Witness' Signature and Date

Appendix D. Procedures for HVTN 505 Co-Enrolled Participants

Introduction

The procedures described in this Appendix applies only to HPTN 061 participants who self-disclose to HPTN 061 site staff (post-enrollment) that they are co-enrolled in HVTN 505. Each site implementing HPTN 061 will be allowed to decide whether or not they will implement these procedures, since some sites may reasonably assume that they will not have any participants co-enrolled in HVTN 505, or that establishment of these procedures is not worth the effort for the possibility of applying them in one or two cases.

The HPTN 061 study team acknowledges that some HPTN 061 participants who co-enroll in HVTN 505 may not disclose this to the HPTN 061 staff. Additional procedures, not included in this appendix, may be needed to address this issue, since such participants may have reactive HIV rapid tests and positive or indeterminate Western blots (WB), even though they are not HIV-infected. The HPTN 061 study team also acknowledges that if a participant does not disclose his co-enrollment status, testing performed in HPTN 061 may result in unblinding the participant's treatment arm in HVTN 505.

PROCEDURES

1. Procedures for determining if a participant is co-enrolled in HVTN 505

If the participant has not disclosed at a previous study visit that he was co-enrolled in HVTN 505, the participant will be asked if he is co-enrolled in HVTN 505. The participant's answer will be documented on the FUV-3 CRF and the following procedures should be followed. These procedures should also be followed for any participant who voluntarily disclosed that he was co-enrolled in HVTN 505 at a visit prior to the implementation of these procedures, even if the participant is no longer co-enrolled in HVTN 505.

2. Procedures for participants who disclose co-enrollment in HVTN 505 at a post-enrollment visit

Consent

- The procedures for co-enrolled participants that will be different from the standard procedures described in the main 061 consent form will be explained to the participant. If the participant agrees to the alternative procedures, they will be asked to sign a "consent addendum", documenting their consent. This consent process must be completed only one time per participant. If the participant refuses the alternative procedures, then the site staff will explain that the standard HPTN 061 HIV testing procedures will be followed, but that interpretation of the results may be difficult. As with any study procedure, the participant may refuse HIV testing at any time.

Blood Draw and Sample Processing

- The following procedures are expected to be followed regardless of the timing of the participant’s prior visits for HVTN 505, because results from one study will not be shared with the other study. Total blood volumes required for an HPTN 061 and an HVTN 505 visit on the same day would not exceed standard acceptable limits, but sites should always rely on their own clinical judgment for specific cases.
- Blood draw will proceed as described in the HPTN 061 Protocol and SSP Manual, with one exception: instead of drawing the 2 mL tube for HIV rapid testing, the site will draw a 10 mL tube EDTA-anticoagulated blood tube for testing at the HVTN. This 10 mL tube of blood is used to prepare plasma for shipment to the HVTN lab for HIV testing.
 - a. 10 mL tube for HIV testing to be kept at room temperature and delivered to processing lab within 4 hours of collection along with completed “HVTN 505 Co-Enrollment with HPTN 061 HIV Diagnostic Testing Requisition”. This form is included at the end of this appendix.
 - b. Lab to follow the current Plasma Processing SOP.
 - c. Aliquot the plasma into 3 cryovials of ~1.1 mL or greater volume, labeled with the standard HPTN 061 LDMS label and standard LDMS codes for EDTA plasma. (No HVTN identifiers will be used in labeling the specimens.) LDMS visit type should be entered as per the completed “Visit Type” item on the diagnostic testing requisition.
 - d. Samples to be stored at -65 to -90°C until shipped to UW-VSL for testing.

Sample Shipment

- HVTN HIV diagnostic specimens are to be shipped overnight on dry ice.
 - a. Ship as needed to arrive Monday through Thursday.
 - b. Do not ship on holidays or the day before a holiday.
- On the day the specimens are shipped, an Advance Notification email and an electronic LDMS shipping manifest need to be sent to:
VTN.Shipping.Notice.UWVSL@hvtn.org
 - c. The Advance Notification email must contain the following:

Shipper’s Name	
Address	
Telephone number	
Name of Courier	
Tracking or air bill number	
Shipping date	
Total volume of specimens shipped	

- d. The LDMS shipping manifest must be of type “LDMS Standard”
- Include a paper copy of the shipping manifest and a copy of the completed “HVTN 505 Co-Enrollment with HPTN 061 HIV Diagnostic Testing Requisition” with the shipment. Send to:
 - University of Washington, Virology
 - Specialty Laboratory
 - Attn: Joan Dragavon / Socorro Harb
 - Retrovirus Laboratory, Room 725
 - Research & Training Building
 - 300 Ninth Avenue
 - Seattle, WA 98104
 - Tel: 1-206-897-5210

Testing and Sample Storage

- The site will not perform HIV rapid testing and will not send samples for local WB or HIV RNA PCR (viral load, VL).
- The site will send samples to the Local Lab for CD4 cell count testing for each sample collected for ALL co-enrolled participants. CD4 count data will be needed in the event that a participant is found to be HIV-infected.
- Plasma samples will be stored for retrospective testing to be performed at the HPTN Network Lab.

Test Results- Sample 1

- The HVTN Lab will report the preliminary HIV infection status for Sample #1 to the HPTN 061 site and to the HPTN Network Lab within 5-7 working days via email. Possible results for Sample #1 are:
 - a. “HIV-1 NOT Detected”
 - b. “Further testing required. Please redraw and submit new EDTA plasma aliquots.”

Completion of HTR CRF- Sample #1

- HVTN test results for Sample #1 will be reported under item 7: Final HIV status.
 - a. Mark “negative” on the form for a lab result of “HIV-1 NOT Detected”
 - b. Mark “Additional testing needed” on the form for a lab result of “Further testing required. Please redraw and submit new EDTA plasma aliquots”.
- Indicate that testing was done at the HVTN for item 7a on the CRF.
- Sites should store plasma for each blood draw at each visit, regardless of HIV test results, so sites are expected to mark “stored” for item 1- Plasma Storage.

- For co-enrolled participants, there will be no local HIV rapid testing, Western blot testing, or viral load testing done from the Sample #1 visit, so items 2, 4 and 4a should be completed by marking “not done/not collected”.
- CD4 cell count testing should be performed for all co-enrolled participants at the time of Sample #1 collection; those results should be recorded in item 3.

Determining the Need for a Second Sample

- If the results from Sample #1 indicate that further testing is required, the participant will be called back to the site, ideally within 4 weeks, for collection of a second (confirmatory) sample (Sample #2), which will also be shipped to the HVTN Lab using the procedures described above.

Test Results- Sample #2 or Sample #3

- The HVTN Lab will report results from Sample #2 (or sample #3, if collected) to the HPTN 061 site and the HPTN Network Lab within 5-7 working days via email. Possible results for these samples are:
 - a. “HIV-1 NOT Detected”
 - b. “Infected, HIV-1”
 - c. “Further testing required. Please redraw and submit new EDTA plasma aliquots.”

The HVTN Lab will send results of VL testing to the HPTN 061 site with the HIV test report for a confirmatory sample that indicates HIV infection.

Completion of HTR CRF- Sample #2 or Sample #3

- HVTN test results for Sample #2 (or Sample #3, if indicated) will each be reported on a **NEW** HIV Test Report Form (HTR CRF) under item 7: Final HIV status. An interim visit CRF (IV) will also be required if Sample #2 (or Sample #3, if indicated) is not conducted at a regularly scheduled visit. Sites will need to be sure to write the correct visit code on the form.

Note: *This is different from the procedure of recording the results from the testing of multiple samples for one participant who completes HIV testing within 4 weeks on one CRF. It is the same procedure that is used for documenting the HIV results for a participant whose samples are collected outside of the 4 week window.*

- a. Mark “negative” on the form for a lab result of “HIV-1 NOT Detected”
- b. Mark “positive” on the form for a lab result of “Infected, HIV-1”
- c. Mark “Additional testing needed” on the form for a lab result of “Further testing required. Please redraw and submit new EDTA plasma aliquots”.

- Indicate that testing was done at the HVTN for item 7a on the CRF.
- Sites should store plasma for each blood draw at each visit, regardless of HIV test results, so sites are expected to mark “stored” for item 1- Plasma Storage.

Note: *Although this is a second (or third) sample drawn for this participant for this round off HIV testing, site will complete items 1-4a, not 5-5c or 6-6c, since a new form is being used to record these results,.*

- For co-enrolled participants, there will be no local HIV rapid testing or Western blot testing, so items 2 and 4 and 4a should be completed by marking “not done/not collected”.
- If a participant is confirmed to be HIV-infected based on testing of Sample #2 (or #3), the HVTN lab will include results from viral load testing on the test report for that sample; those results should be recorded in item 4b, otherwise mark “not done/not collected”..
- CD4 cell count testing should be performed for all co-enrolled participants at the time of sample collection; those results should be recorded in item 3.

Providing Results and Post-Test Counseling to the Participant

- Results will be sent in an email from the HVTN lab to the email address identified by the site in the diagnostic testing requisition sent with the samples. This email address needs to be confidential and secure, but should be accessible by more than one person in case that person is out of the office. Sites may wish to establish a limited-access address dedicated for this purpose.
- Once HIV status has been confirmed by the HVTN lab and results have been received at the HPTN site, the HPTN 061 site PI or designee will inform the participant of his HIV status. If the participant is infected, results from CD4 cell count testing and VL testing will also be provided. The HTPN 061 site will not request, receive, or provide to the participant results of HIV antibody testing. The staff working with co-enrolled participants should be those who have been thoroughly trained in these procedures and knowledgeable about how vaccines affect HIV test results. The site may wish to have only one or two staff members working with co-enrolled participants.
- Results of testing for co-enrolled participants from HPTN 061 will not be used for HVTN 505, and results from testing in HVTN 505 will not be used for HPTN 061. Separate test results will be obtained for each protocol, even if study visits for the two protocols are close in time.
- All non-HIV testing (syphilis, GC, CT) will be performed as usual by the HPTN 061 site at each study visit.

Questions

Sites are encouraged to contact the HPTN Network Laboratory, SCHARP and FHI representatives with any questions about these procedures or about working with co-enrolled participants. The best form of communication will be through an email to representatives from all three organizations. The HPTN Network Laboratory will be able to follow up with the HVTN Network Laboratory on the site's behalf if there are issues with sample shipment, processing or results.

HVTN 505 Co-Enrollment with HPTN 061 HIV Diagnostic Testing Requisition

Participant ID - - -

Collected by (initials): _____

Collection Date

Collection Time : 24-hour clock

Visit # _____

Visit Type* (mark one): -Routine(Vst) -Recent Exposure(Exp) -Redraw(RDW)

*See next page of this form for explanation of visit types

Email addresses for reporting results:

- To site: _____
- To HPTN Lab: vcummin1@jhmi.edu

SPECIMEN REQUIREMENTS FOR THIS VISIT

Tube Qty	Tube Type	Assay	CRS Phlebotomy Instructions
1	10mL EDTA	HIV Diagnostic	Mix tube immediately by gentle inversion. Keep at room temperature. Deliver to the processing lab within 4 hrs of collection.

If all required specimens are not collected, or are not submitted to processing lab, please explain below:

FOR PROCESSING LAB USE ONLY - Record Quantity Of Specimens Received In Boxes Below:

10mL EDTA	EDTA Plasma: 3 aliquots x 1.1 mL each (or more) .
	Store at -80C. Ship to UW-VSL for testing.

Receipt Date/Time: _____ Rec'd by (initials): _____

If specimens are received damaged, > 4 hours from time of collection, specimens rec'd do not match specimen requirements listed above, or other discrepancies exist, please document phone call to CRS below. If more space is needed, use reverse side:

Discrepancy Investigation/ Resolution:

Problem Description:

CRS Called (date/time): _____ Contact name: _____

Summary of discussion:

**Instructions re: Completing the “Visit Type” Section of the
HPTN 061/HVTN 505 Co-Enrollment Lab Requisition**

Visit Type is defined as:

Visit Type	LDMS Visit Type	When to Use
Routine	VST	Use this Visit Type when sending Sample #1 if this HIV test is being requested as part of routine study visit procedures (e.g. Visit 2.0 or 3.0)
Recent Exposure	EXP	Use this Visit Type when sending Sample #1 to the HVTN lab for testing if infection is suspected (e.g. symptomatic) or the participant has asked for an HIV test between visits because of a recent potential exposure.
Redraw	RDW	The Redraw Visit Type box must be marked <i>anytime</i> a sample is being sent after an HIV report of “Further Testing Required” has been received regardless of what the original visit type was.