

Section 4. Participant Accrual

4.1 Overview of Section 4

This section provides an overview of requirements and procedures for recruiting, screening, and enrolling participants in the study. Additional procedure-specific detail can be found in the visit checklists in Section 6 as well as in Sections 8 and 11.

4.2 Target Enrollment

HPTN 061 is a multi-site, feasibility study of a community-level, multi-component intervention for Black men who have sex with men. The main study will enroll approximately 2418 participants at sites in six cities. Each of the six sites will have a target enrollment of 250 community-recruited participants who agree to HIV testing. It is expected that a further approximately 83 community-recruited participants will be enrolled, for a total of 333 community-recruited participants. A subset of community-recruited participants will be eligible to refer their partners to the study, so that overall, the enrollment at each site is expected to be approximately 403 participants. Because the focus of this study is on enrollment and uptake of the intervention components on a per-site basis, rather than the need for a specified number of clinical endpoints, failure to achieve the enrollment target at one site will not be cause to increase enrollment at other sites.

The qualitative component of the study will be conducted at each site among participants enrolled in the main study. Each site is expected to conduct 3-5 focus groups with a goal of 24 total focus group participants per site. Each site will decide whether to complete only 10 qualitative individual interviews (for cross-site analysis only) or 30 qualitative interviews (for both cross-site and intra-site analysis). Overall for all six sites then, between 204 and 324 main-study participants are expected to participate in the qualitative component of the study. Sites will be informed of their enrollment target as well as their actual enrollment via reports issued by SCHARP and FHI.

4.3 Recruitment Plan

Each site is responsible for establishing a recruitment plan/SOP for this study, and for updating the plan if needed to meet the targeted enrollment goals. At a minimum, the recruitment plan/SOP should contain the following elements:

- Site-specific accrual goals
- Methods for tracking actual accrual versus accrual goals
- Recruitment methods and venues
- Methods for identifying the recruitment source of participants who present to the site for screening
- Methods for timely evaluation of the utility of recruitment methods and venues
- Pre-screening activities
- Ethical and human subjects considerations

- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QC/QA procedures related to the above (if not specified elsewhere)
- Attached copies of recruitment worksheets, scripts, and other operational tools

4.4 Pre-Screening Activities

As described in the HPTN 061 protocol, there will be no separate screening visit for this study. Staff should ask potential participants a small number of questions (similar to those below) to determine potential eligibility prior to beginning an enrollment visit, for example at a recruitment venue, over the telephone, or at the site. In order to encourage honest responses from potential participants, staff should be careful not to reveal eligibility requirements. Prior to enrollment of a community-recruited participant in a category with an enrollment cap, staff must verify that there are spaces still available in that category at the site for the participant to be eligible. Table 4.1 below is a worksheet that can be used by sites to determine whether a participant will exceed the cap on an enrollment category (note that this worksheet is not intended to be used as a source document).

Table 4.1 Worksheet for Determining Eligibility Based on Enrollment Categories for HPTN 061

For community-recruited men interested in the study...

1) Have 250 community-recruited participants already enrolled in the study? If yes, then the study is closed to community-recruited men. If no, go to step 2.

2) What is the participant's situation regarding HIV testing/status as revealed during prescreening/enrollment procedures?

The participant reports he has previously been diagnosed as HIV positive...		
	not in care, and has UAI with men who are HIV negative or unknown status	Eligible
	not in care, only has UAI with HIV-positive partners or in care for HIV	Check to make sure 10-person cap for this category hasn't already been reached. If it hasn't, he can be eligible.
Participant reports he has not been tested before, or last prior test was HIV negative...		
	Not willing to have an HIV test at enrollment visit	Check to make sure 83-person cap for this category hasn't already been reached. If it hasn't, he can be eligible.
	Willing to have HIV test as part of the study	Eligible to enroll and complete enrollment visit. Once HIV test results are back, will need to see if eligible for follow-up visits.

For Index-referred men interested in the study...

Index-referred men are potentially eligible, regardless of enrollment category caps, up until two months after the 250th community-recruited participant has been enrolled.

Any records or log retained by the site of this pre-screening activity must not contain any personal identifiers, unless the local IRB has approved an independent protocol that allows the capture of such information. Sites may wish to develop a short text to be read to potential participant indicating that both HIV positive and negative participants will be eligible for this study. This may assist in ensuring honesty, particularly among long-term HIV positives who might believe that HIV status is an exclusionary criterion, and to avoid the perception in the community that all participants in the study are HIV positive.

Listed below are some questions that could be asked to determine a potential participant's eligibility as part of pre-screening. Sites may wish to use only a subset of these questions, or their own questions, for pre-screening, or may intersperse a number of questions unrelated to the study, to ensure that prescreening does not reveal the eligibility criteria to the community.

Pre-Screening Questions:

- Do you consider yourself to be a man, or were you male at birth? **{Must answer yes}**
- How do you identify your race or ethnicity? **{Must identify as Black, African American, Caribbean Black, or Multiethnic Black}**
- When did you last have anal intercourse with a man (as a top or a bottom)?
- Do you always use a condom when you have anal sex? **{Must have at least one act of unprotected anal intercourse within the last six months.}**
- How old are you? **{Must be 18 or older}**
- Where do you live? **{Must be within site's metropolitan area as defined in site SOPs}**
- Do you have any plans to move in the next two years? If so, to where? **{Must not have plans to leave site's metropolitan area during study participation, bearing in mind that some participants will not be seen for follow-up visits at all}**
- Are you a participant in any other studies?
[If yes:] Which study(/studies)?
{Must not be enrolled in other HIV interventional research study}
- Have you ever been in an HIV vaccine study?
[If Vaccine trial:] Did you receive the vaccine or placebo?
Must not have been enrolled in a vaccine trial in which they were either in the active arm or do not know which arm they were in}

- [As needed, if any enrollment caps for this site have already been met] Would you be willing to have an HIV test as part of your participation in this study?

{If “No” check against enrollment cap for this category}

[If “Yes”] Have you ever received a diagnosis of HIV infection?

[If “Yes”] Have you had sex with anyone in the last six months who you knew to be HIV negative or whose status you didn’t know?

{If “No” check against enrollment cap for this category}

[If “Yes”] When was the last time you saw a health care provider for care of your HIV? *{If within the last six months, check against enrollment cap for this category}*

4.5 Enrollment Activities

4.5.1 Eligibility Determination

Because there is no screening visit for HPTN 061 and participants do not sign a screening consent, documentation of participant eligibility should not begin until after the participant has provided consent to participate in the study. After consent is obtained, the staff can go through the criteria more carefully, documenting each eligibility criterion per the site’s table of source documentation for eligibility. Each site will need to determine its own procedures for documenting eligibility, which will be captured in an SOP on Determining Participant Eligibility, as described below. Sites may record some data regarding pre-screening (reason for ineligibility, method of recruitment, etc.) in order to assist in their recruitment efforts. However, no identifying information such as name or address should be associated with these data.

An HPTN 061 Eligibility Questionnaire has been provided below, which sites may choose to use and which may be used to document participant for eligibility.

For HPTN 061, it is expected that the age of a potential participant will be determined by self-report unless the person appears to the staff to be less than 18 years old. In these cases it will be the staff’s discretion to require proof of age prior to enrollment in accordance with local requirements or policies. Each site should determine site-specific procedures for how this will be done and what constitutes adequate documentation.

It is the responsibility of the site Investigator of Record, and other designated staff, to ensure that only participants who meet the study eligibility criteria are enrolled in the study. As a condition for study activation, study sites must establish an SOP that describes how study staff will fulfill this responsibility. At a minimum this SOP should contain the following elements:

- Eligibility determination procedures, including:
- Pre-screening procedures
- During-visit eligibility assessment procedures

- Post-visit eligibility assessment and confirmation procedures
- Final eligibility sign-off procedures
- Documentation
- Ethical and human subjects considerations
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QC/QA procedures related to the above (if not specified elsewhere)

Section 3 of this SSP manual (Documentation Requirements) includes a table that sites may use to identify the source documents that will be used to demonstrate participant eligibility.

HIV status for enrollment purposes will be based on self-report until confirmed by an HIV rapid test at the enrollment visit. Participants who report that 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 below. Participants who identify as HIV positive but refuse HIV testing and do not provide appropriate documentation of their diagnosis at the enrollment visit will be categorized as “participants refusing HIV testing”. The participant may bring back documentation within two weeks and his status will then be changed to “previously diagnosed”. Two weeks after the enrollment visit, the categorization as “refusing HIV testing” will be his final status. See Section 11 for more information on appropriate laboratory testing.

Acceptable Documentation of HIV Positive Status

- 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 (ARV) medications for treatment of HIV infection (e.g. a bottle of ARV drugs with the participant's name on it or an ARV prescription written for the participant).

Participants whose self-reported HIV status does not match with the results of their HIV rapid test will be re-categorized for enrollment based on the judgment of the site team. When a participant's HIV status (and therefore enrollment category) is changed, all CRFs should be corrected as appropriate, but the ACASI should not be re-administered.

HPTN 061 SAMPLE ELIGIBILITY QUESTIONNAIRE

PTID: _____

	Participant Response	To be eligible...	Meets eligibility for this criterion?	Enrollment Category Open?
Do you consider yourself to be a man, or were you male at birth?		<i>Must answer yes</i>		
How do you identify your race or ethnicity?		<i>Must identify as Black, African American, Caribbean Black or multiethnic Black</i>		
When was the last time you had anal sex with a man (top or bottom)?		<i>Must have been within the last six months</i>		
When did you last have unprotected anal intercourse with a man (top or bottom)? Did you use a condom during this last encounter?		<i>Must have been within the last six months</i>		
How old are you?		<i>Must be 18 or older</i>		
Where do you live?		<i>Must be within the metropolitan area as defined by the site SOP</i>		
(If participating in follow-up visits) Do you have any plans to move in the next year? If so, to where?		<i>Must not have plans to leave the metropolitan area during study participation</i>		
Are you a participant in any other studies? [If yes:] Which study(/studies)?		<i>Must not be enrolled in other HIV interventional research studies</i>		
Have you ever been in an HIV vaccine study? [If Vaccine trial:] Did you receive the vaccine or placebo?		<i>Must not have participated in an HIV vaccine trial in which he was in the active arm or does not know which arm.</i>		
Ask as needed, if any enrollment caps for this site have already been met				
Would you be willing to have an HIV test as part of your participation in this study?		<i>If "No" check against enrollment cap for this category</i>		
Have you ever received a diagnosis of HIV infection?		<i>If "yes" continue on to questions below</i>		
> Have you had sex with anyone in the last six months who you knew to be HIV negative, or whose status you didn't know?		<i>If "No" check against enrollment cap for this category</i>		
> When was the last time you saw a health care provider for care of your HIV infection?		<i>If within the last six months, check against enrollment cap</i>		

Initials of staff member documenting eligibility

Date

4.5.2 Enrollment Visit Timeframe, Enrollment Definition, Split Enrollment Visits

Enrollment procedures are expected to be completed during a single visit on a single day. If for some reason the enrollment visit must be split, sites should strive to complete that the following procedures during the initial encounter at the site:

- Obtaining informed consent
- Assignment of PTID (enrollment)
- Documentation of eligibility

If these procedures cannot be completed during a single encounter, a thorough review of the informed consent information should be conducted when the participant returns at the later date, prior to continuing to the remaining enrollment visit procedures. For the enrollment visit as well as follow up visits, completion of the ACASI and collection of clinical samples should be collected on the same date, if at all possible. If a split enrollment visit is necessary, all visit procedures should be completed with 72 hours of signing the Informed Consent.

A participant is considered enrolled once a participant ID (PTID) has been assigned. If a participant is assigned a PTID and then is found not to be eligible, their participation in the study will be terminated at that point. For more detailed instructions on assignment of a PTID, see Section 9 of this SSP.

4.5.3 Prescreening and Enrollment Logs

A log of prescreening attempts will be kept by each site using the template provided by the HPTN CORE and agreed upon by the study team (Appendix H- Pre-Screening and Enrollment Log template) This log is an adaptation of the requirements spelled out in the *DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-RA-03.00)* since HPTN 061 has no screening consent or true screening visit. Per agreement with DAIDS, this log will capture a site-generated prescreening number or other identifier for each person who prescreens, whether that prescreening takes place in the community, over the telephone, or at the clinic. For each person, the date of pre-screening, whether they were preliminarily eligible, and reason if found ineligible will also be documented. Sites may also wish to capture information such as recruitment venue or recruiter for their own assessment of site recruitment strategies, but this information will not be captured across study sites.

Sites must keep a log of participant enrollment, which will also be provided by the HPTN CORE, to capture PTID, date of enrollment, reason if unenrolled, enrollment category and documentation of whether participation eligible for a focus group or qualitative interview was offered this component, and whether it was accepted. See Appendix H for Pre-Screening and Enrollment Log template. The “reason if unenrolled” category is an unusual component for an enrollment log, but has been included in recognition of the fact that documentation of eligibility will take place

after assignment of a PTID, and could result in a consented and enrolled participant then turning out to be ineligible to remain in the study.

Sites may also choose to record participant initials on the enrollment log as specified by the *DAIDS Policy for Requirements for Essential Documents at Clinical Research Sites Conducting DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-RA-03.00)*. However, per HPTN policy and in agreement with DAIDS, participant initials need not be recorded on pre-screening and enrollment logs if doing so presents a potential threat to participant confidentiality. In such cases, a separate document must be available to document the link between a participant's name and PTID. It is assumed that all sites in HPTN 061 will maintain a link log.

4.5.4 Recruitment and Enrollment Tracking

Recruitment and enrollment information will be submitted to HPTN CORE on the frequency agreed upon by the protocol team (e.g. weekly or monthly) until all participants have been enrolled. This site-specific information will be consolidated and distributed as a report presenting accrual information to the Protocol Team as needed to monitor the accrual process. In addition, the SDMC will report to the team the number of participants enrolled monthly, based on data received and entered into the DataFax study database.

As noted above in Section 4.5.3, sites must capture basic data on pre-screening, but it is expected that sites will track additional pre-screening information that can be useful in assessing the effectiveness of various recruitment practices. Such information may include the number of contacts (“approaches”) outreach staff make for recruitment, the number of those contacts who are eligible and/or agree to come to the site for enrollment, etc., and should be evaluated on multiple parameters including recruiter, venue, and recruitment approach.

As noted in the protocol, twenty community-recruited participants at each site who test negative for HIV will be designated as index participants and asked to refer their sexual network partners to the study. The reason for offering index status to these HIV negative participants is in part so that HIV-positive participants recruiting their sexual network members in the community will not be automatically disclosing their status. Because of this, it will be helpful to offer index status to a small number of HIV-uninfected participants during several months of recruitment, rather than offering it to the first 20 uninfected participants to enroll. Therefore, sites should decide upon a mechanism that will designate index status to HIV uninfected participants over the course of the recruitment period and include this in the site's recruitment SOP. One mechanism would be to offer index status to the first HIV uninfected participant to enroll after the first and fifteenth of the month for the first ten months.

As the study accrual period comes to an end at each site, care must be taken to manage the recruitment and enrollment process in order not to exceed the protocol-specified sample size (see Section 4.2). Sites must establish a mechanism for

tracking enrollment into capped categories and follow it closely. As a category nears completion, potential participants must be informed that they may not be enrolled if the target sample size is reached before they are able to complete the screening and enrollment processes. This may be difficult to explain to potential participants — especially those who are very interested in taking part in the study — therefore all sites are advised to work with their local community advisory board (CAB) members to develop strategies to address this issue.

4.5.5 Referrals, Index partners, Follow-Up Visit Eligibility

Index participants must meet one of the following criteria:

- Newly diagnosed with HIV infection at HPTN061 enrollment visit.
- Diagnosed with HIV prior to enrollment, but are not in care and have had unprotected anal sex with HIV uninfected partners or partners of unknown status.
- For the purposes of this study, a participant who receives a diagnosis of HIV within six months prior to enrollment in the study, and who only sees a clinician for HIV care as part of their initial diagnosis (whether that takes place on the same day as diagnosis or shortly thereafter) is not considered “in care”. However, if such a participant sees a clinician for HIV care again after that initial consultation, they will be considered to be in care.
- One of twenty randomly selected HIV-negative participants. Random selection should occur in such a way as to spread out identification of HIV negative participants as indexes over the 12 months of recruitment. One way would be to specify that the first negative participant to enroll after the first and fifteenth of the month will be an index participant.

Site staff should work with index participants to refer up to five of their Black male sexual network members for enrollment. Referred partners (whether HIV positive or negative) will **not** be subject to enrollment caps. Study staff should provide counseling to the participant to minimize the potential for violence and protect the participant’s confidentiality. The site team should develop referral coupons for index participants to provide to the partners they attempt to refer to the study. The format and content of the coupons should align with the site’s referral procedures, but in general, the following approach is suggested:

- The site staff only distributes as many coupons to the index participant as he has potentially eligible partners to refer, as determined during prior discussions between the participant and the staff member. This is to prevent participants from getting additional coupons and distributing them to non-partners in the hope of receiving additional compensation.
- Each coupon should have a unique serial number. The site will record which coupons are distributed to which index participants. Staff members should note the serial number of the coupon used when a referred partner prescreens (whether that is by phone, at a venue, or in the clinic) and then cancel that

coupon's "eligibility" so that it can't then be passed on for someone else to use to try to enroll in the study.

- Staff should add an expiration date to each coupon at the time of issue. At a maximum that date should be approximately four months from the date of enrollment of the index participant, so that all referred-partner enrollments will be complete by the time of the index partner's six month visit and compensation can be provided then. Sites may choose a shorter time frame to encourage timely referrals. As the time to the end of enrollment at the site draws closer, this date-to-expiry window will need to be shortened so that referred partners do not come to the clinic expecting to enroll after recruitment has finished. The window for index participants to refer partners will close thirty days after the closure of community referred enrollment at that site.

Sites may find it useful to explain to index participants that they will receive their compensation for referred participants at the six month visit and not before, since in prior studies using respondent-driven-sampling, frequent telephone calls or drop-by visits to check on compensation have added significantly to site burden.

Additional tips on counseling index participants regarding referral of partners is provided in Appendix D.

Although only index participants will be compensated for referring their partners to the study, other participants should certainly be encouraged to refer their eligible partners to the study as well.

In this study only certain categories of participant are eligible for follow-up visits, as explained in the protocol. Table 4.2 provides a worksheet to help study staff determine whether a particular participant is eligible for follow-up during the enrollment visit.

Table 4.2 Worksheet for Determining Eligibility for Follow-Up Visits and Index Status for HPTN 061

The participant was diagnosed as HIV positive prior to study participation...		
	not in care, and has UAI with men who are HIV negative or unknown status	Follow-up, and index
	not in care, only has UAI with HIV-positive partners or in care for HIV	No follow up, not index
Participant not willing to have an HIV test at enrollment		
	Participant is among the first 20 enrolled who refuse HIV testing at enrollment	Follow up, not index
	Participant enrolls after 20 others are already in the study who refuse HIV testing at enrollment	No follow up, not index
Participant is diagnosed as HIV positive for the first time at enrollment visit		
		Follow-up, and Index
Participant tests HIV negative at enrollment visit		
	Has the site already enrolled 200 participants who were HIV-negative at enrollment?	If yes → No follow-up, not index If no → Follow up, see next question re: index status
	Is participant one of the 20 HIV-negatives selected at random to be index?	If yes → Index If no → Not index

Although it is possible that some index participants will have sexual partners from other cities where 061 is being conducted, the study team has decided that index participants will not receive “credit” for referred partners who enroll in a different city, and index participants should be informed of this. In cities where there are multiple clinics sharing a cohort of 061 participants (e.g. New York City and Atlanta), an index participant will be able to receive “credit” for a partner who enrolls at another clinic in the city. Sites will need to establish procedures for this activity that do not violate participant confidentiality.

If a participant is reactive on his HIV rapid test and it is a new diagnosis, the staff may need to postpone the conversation about being an index participant and referring his partners, and focus on providing support for the participant at this emotional time. In such cases, the index and referral conversation can be postponed until the follow-up visit in which he returns for his confirmatory HIV test results, expected to be approximately a week to ten days later.

4.5.6 Focus Groups and In-Depth Interviews

Some participants will be asked to participate in an in-depth interview or focus group after the enrollment visit. The procedures for selection of participants who will be asked to participate in these activities are covered in the HPTN 061 Qualitative Manual. Willing participants will be asked to sign a separate consent form when they return to the site to participate in these activities. Participants are not required to participate in an interview or focus group in order to remain in the rest of the 061 study. Sites are asked to track to whom participation in these activities is offered on the enrollment log. Additional information about conduct of the focus groups and in-depth interviews is provided in the HPTN 061 protocol and Qualitative Manual.

4.5.7 Enrollment Scenarios

4.5.7.1 Scenario 1

When reviewing the eligibility criteria with a potential participant prior to the informed consent discussion, he reports that he may remain living where he does now for the next year, but there's a chance that he will be moving in about six months, depending on a number of factors.

Question 1: Is he eligible?

Answer: Possibly. If he will not be receiving follow-up visits, his plans to move do not matter. If he will receive follow-up visits, the site should assess whether they think he is likely to move or not. Where he may move to is also important.

Question 2: What if he's thinking of moving within the city?

Answer: Then no problem, he is eligible

Question 3: What if he's thinking of moving to another city where HPTN 061 is being performed?

Answer: Per the protocol he should NOT be enrolled, but consult with protocol team.

4.5.7.2 Scenario 2

A potential participant wishes to join the study, but you know from prior history that he is a transgendered female to male who has not had "bottom" surgery yet. This person identifies as male.

Question 1: Is this person eligible?

Answer: Yes, because he self-identifies as male.

4.5.7.3 Scenario 3

A potential participant comes for an enrollment visit. He is HIV positive and is participating in an HIV treatment study of a new ART regimen which ends in two weeks. He reports that the last time he had unprotected anal sex was not quite six months ago, and it was with an HIV positive man.

Question 1: Is this person eligible?

Answer: The participant is not eligible because he is in an HIV interventional study. Also, he may not be eligible if the site already has reached its cap of HIV positive men in care or only having sex with other positive men.

Scenario Continued: The participant does not enroll today, but returns a month from now, and his participation in the ART study is now over. He has not had anal sex since his prior visit.

Question 2: Is this person eligible?

Answer: No. His participation in the ART study is no longer an issue, but he has not had unprotected anal sex in the last six months.

4.6 Informed Consent Procedures

This section provides an overview of requirements and procedures for obtaining informed consent from study participants for enrollment in the study. Given the ongoing nature of informed consent, key elements of informed consent also should be reviewed at study follow-up visits.

As a condition for study activation, each study site must establish an SOP for obtaining informed consent from potential study participants. This SOP should reflect all of the information provided in this section and the DAIDS SOP for Source Documentation (Appendix C).

Informed consent is a process by which an individual voluntarily expresses his willingness to participate in research after having been informed of all aspects of the research that are relevant to his decision. Informed consent is rooted in the ethical principle of respect for persons. It is not merely a form or a signature, but a process, with four key considerations — information exchange, comprehension, voluntariness, and documentation — as described below.

Informed consent must be obtained from participants prior to undertaking any study enrollment procedures. Informed consent is an ongoing process that continues throughout the study.

U.S. regulation 45 CFR 46 (Appendix A) specifies the elements of informed consent that must be conveyed to research participants through the informed consent process. It is the responsibility of the Investigator, and his/her assigned staff, to deliver all

required information to potential research participants. See Section 4.8 of the ICH GCP guideline and the informed consent section of the *DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00)* for detailed guidance on the informed consent process and documentation requirements.

Participants will be asked to provide informed consent for storage of blood specimens for possible future research testing. Selected participants will be asked to provide consent to participate in a focus group or qualitative interview. Participants who choose not to have their specimens stored for future testing or not to participate in a focus group or qualitative interview will still be eligible to enroll in the study.

Based on the technical and regulatory reviews that are completed as part of the HPTN protocol development and study activation processes, there is adequate assurance that once the HPTN CORE has “activated” a site for study implementation, the site-specific informed consent form specifies all information required by the regulations. However, responsibility for informed consent does not end with preparation of an adequate informed consent form. It also is the responsibility of the Investigator and designated study staff to perform the activities described in sections 4.7.1 through 4.7.5.

Deliver all required information in a manner that is understandable to potential participants.

Each study site is responsible for developing study informed consent forms for local use, (based on the templates in Appendices II through V in the Protocol), which describe 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 forms into other languages (if applicable) and verifying the accuracy of translations by performing an independent back-translation.

Sites should develop a process for determining participant literacy prior to beginning informed consent and should describe this process in their site specific SOP on Informed Consent. The protocol team has developed template language for this process that is designed to identify participants with low literacy without subjecting them to potentially stigmatizing literacy tests, and to make them aware of the purpose of a witness in the informed consent process:

We are going to go over the information in this document, called an informed consent form. It explains the reason we're doing this study, what would be expected of you if you participate in the study, and other information. Sometimes people find it difficult to read a long document like this one. In that case, we have a witness join us while we discuss the study. This witness would be here just to verify that what I'm explaining to you is the same as what's in this document. Would you like to have a witness present while we go over this

information, or do you feel you can read the consent form well enough on your own?

If the participant is literate, give him a copy of the informed consent form to read during the screening and enrollment visits. Also provide the participant with other (IRB/EC-approved) informational materials developed to complement the informed consent form, if any. If the participant is not literate, the materials may be read to him verbatim or summarized. After the participant has read the written material (or had it read to him), verbally review the information provided. A checklist or the informed consent form itself may serve as a useful guide for this. For example, you may note the main points described in each paragraph of the informed consent form, and ask if the participant has questions or concerns about each point. Listen carefully to the questions or concerns expressed by the participant, and discuss these thoroughly. Take as much time as needed to address each question and concern.

If the participant is illiterate, **an impartial witness must be present during the entire informed consent discussion**. The witness will be asked to sign and date the informed consent form to attest that the information in the consent form was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant. The participant may select a friend or family member as a witness. But if none is available, the HPTN MOP states that a witness can be a member of site staff who is identified as a Participant Advocate and does not necessarily need to be someone who is unaffiliated with the study. Each site must specify its procedures for obtaining informed consent from illiterate persons in its SOP for obtaining informed consent. The SOP should define who may serve as an impartial witness to the informed consent process. If the site plans to use a member of the site staff as a witness, the SOP should explain what steps are being taken to reduce any perception of coercion or influence by the witness. It is recommended that each site seek IRB/EC review and approval of these procedures.

Assure that informed consent is obtained in a setting free of coercion and undue influence.

During the informed consent discussion, take care to not overstate the possible benefits of the study, nor to understate the risks. Also emphasize to the participant that his medical care and any other services obtained from the recruitment site and/or research institution will not be affected by his decision whether or not to take part in the study. Encourage the participant to take as much time as he needs — and to talk about his potential participation with others, if he chooses — before making a decision.

If the participant is illiterate, and therefore a witness is present during the entire informed consent discussion, care should be taken to minimize the perception of coercion due to the presence of the witness. For example, the purpose of having the witness present should be clearly explained to the participant, with emphasis on the

fact that the witness is there as a protection for the participant, not as an agent of the study.

Confirm that the participant comprehends the information.

The participant must not be asked to agree to take part in the screening procedures or study, or sign the informed consent form, until he/she fully understands the study. Study staff are responsible for implementing procedures to ensure that each participant understands the screening process and the study prior to signing/marketing the screening and enrollment informed consent forms, respectively, and undertaking any screening or study procedures.

One approach to assessing comprehension is to use an assessment of understanding tool (either oral or written) that participants must complete prior to signing/marketing the informed consent form (see examples below). Another approach is to use open-ended questions to ascertain participant understanding during the informed consent discussion. It is possible to incorporate a scoring system into these assessment tools and to re-review the contents of the informed consent until the potential participant can answer a certain percentage of the questions correctly. Three types of informed consent assessment tools, one using specific and two using open-ended questions, are included at the end of this section. For sites that choose to adopt tools such as those included at the end of this section, detailed instructions for their use must be specified in the site SOP for obtaining informed consent.

Regardless of the method used to assess comprehension, if the assessment results indicate misunderstanding of certain aspects of the study, review those aspects again until the participant fully understands them. If after all possible efforts are exhausted, the participant is not able to demonstrate adequate understanding of the study, do not ask him to sign/mark the informed consent form or enroll in the study. Similarly, if the participant has concerns about possible adverse impacts on him if he were to take part in the study, or indicates that he may have difficulty adhering to the study requirements, do not ask him to sign the informed consent form to enroll in the study.

Sample Informed Consent Assessment Tool for Enrollment in HPTN 061

Question	Answers	√	Comments
1. Please describe your understanding of the purpose of this study.	Study is trying to test new ways to prevent HIV infection among Black MSM	<input type="checkbox"/>	
	Get Black MSM tested for HIV, get them into health care, recruit their sexual contacts into the study, find out more about Black MSM social world and feelings about HIV testing, research participation, other topics	<input type="checkbox"/>	
2. What do you understand that you are being asked to do in this study?	Asked to give blood and urine and get tested for HIV and other diseases. Provide rectal swab, answer questions.	<input type="checkbox"/>	
	Some will come back for follow up visits at 6 and 12 months	<input type="checkbox"/>	
	Some will be invited to participate in focus groups or qualitative interviews	<input type="checkbox"/>	
	Some will be asked to refer sexual partners	<input type="checkbox"/>	
3. What do you understand about possible risks that might happen as a result of being in the study?	May be upset if you receive a diagnosis of HIV or STI positive	<input type="checkbox"/>	
	Discomfort during questioning or blood draw or other visit procedures	<input type="checkbox"/>	
	possibility of social harms, especially with regard to STI/HIV reporting or partner recruitment	<input type="checkbox"/>	
4. What will happen to you if you decide not to join the study, or if you join and then dropout?	free to make own decision about joining	<input type="checkbox"/>	
	there will be no effect on access to care	<input type="checkbox"/>	
5. Describe what you understand about the possibility of visits outside of the clinic.	Can choose whether to agree to this or not...will not affect ability to join study	<input type="checkbox"/>	
	If the situation comes up, would staff would work with participants to identify a place to do this acceptable to participant and maintain confidentiality	<input type="checkbox"/>	
6. How will the information about you be protected?	information kept under lock and key or password protected computer	<input type="checkbox"/>	
	only certain people (those working on the study or the U.S. government) have access	<input type="checkbox"/>	
7. What are the benefits to you of participating in this study?	Everyone: can get health information/results including HIV and STI results, if agree to tests. Will also get counseling/info on how to reduce risk. Everyone can get care or referral for care for STIs/HIV. Participants in follow up will get assistance in accessing care (<i>should mention at least one</i>)	<input type="checkbox"/>	
8. What should you do if you have any questions about what is happening in this study?	knows contact information	<input type="checkbox"/>	
9. Is there anything else you'd like to ask or talk about?		<input type="checkbox"/>	
<p>Outcome: _____</p> <p>Notes: _____</p> <p>Proceed to enrollment _____</p> <p>Declined to consent _____</p> <p>Rescheduled for another consent visit _____</p> <p>Unable to consent _____</p>			

Sample Informed Consent Assessment Tool for Enrollment in HPTN 061

No.	Question	True	False
1	This study is part of the regular medical care offered here at [clinic name].	<input type="checkbox"/>	<input checked="" type="checkbox"/>
2	One purpose of this study is to test some new approaches to slowing down the spread of HIV among Black MSM.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
3	Each person in this study will be in the study for two years	<input type="checkbox"/>	<input checked="" type="checkbox"/>
4	Study participants must agree to have visits outside of the clinic when necessary.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
5	Some study participants will have follow up visits and some will only have this one enrollment visit.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
6	Study participants will be asked to provide a blood sample for HIV and STI testing.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
7	If you join this study, you must stay in the study for as long as the study staff says.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
8	If you join this study, you will automatically get to participate in other research studies done here in the future.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
9	If you join this study you will receive counseling on how to protect yourself or your partners from HIV and STIs.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
10	Participants' study records will be available to everyone at the [clinic name].	<input type="checkbox"/>	<input checked="" type="checkbox"/>
11	Whether you decide to allow your leftover samples to be used for future research after this study is over or not won't affect your eligibility for this study.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
12	If you decide not to join this study, it will not affect your options for receiving medical care here or anywhere else.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
13	Study participants can get condoms and HIV counseling from the study staff at any time.	<input checked="" type="checkbox"/>	<input type="checkbox"/>
14	Everyone in the study will also participate in a focus group or qualitative interview.	<input type="checkbox"/>	<input checked="" type="checkbox"/>
15	If the study staff determines that you have any medical problems, they will treat you or refer you to available sources of medical care for those problems.	<input checked="" type="checkbox"/>	<input type="checkbox"/>

Sample Open-Ended Discussion Questions for Assessing Comprehension of HPTN 061

Page 1 of 2

- 1. If you wanted to tell a friend or family member about this study, how would you describe it to them?**
 - Study objectives/purpose
 - Study population
 - Overall study design: duration, visit and procedures schedule, clinic- and community-based visit locations

- 2. How do you think it would affect your day-to-day life to be in this study?**
 - Study duration: one day or one year
 - Study visit schedule: one visit or visits every 6 months
 - Study visit duration: 3 ½ hours
 - Perceived risks and benefits of study participation
 - Potential social harms
 - No costs to participants

- 3. What do you think you will get out of being in this study?**
 - HIV/STI education, counseling, and testing
 - Condoms
 - May receive assistance in getting medical care
 - STI treatment
 - Personal satisfaction

- 4. Are there things about being in this study that you would be worried about?**
 - Embarrassment/worry/anxiety when answering interview questions about sexual activities or HIV/AIDS and risk behaviors
 - Embarrassment of having rectal swab/check for circumcision
 - Worry/anxiety while waiting for or after receiving test results
 - Social harms

- 5. What kind of clinical procedures will you undergo in this study?**
 - Blood collection
 - Urine collection
 - Rectal swab collection
 - Check for circumcision

Sample Open-Ended Discussion Questions for Assessing Comprehension of HPTN 061

Page 2 of 2

6. **Will everyone in the study have the same visits and procedures?**
 - Some will only have one visit (enrollment), some will have 3 visits over a year.
 - Some participants will be invited to participate in an extra activity (focus group or qualitative interview) but others will not.
 - Some participants will agree to all the procedures (HIV testing, STI testing) and some will not.

7. **What might the study staff do if you are scheduled for a follow up visit but miss it?**
 - Mail, phone, other contacts to re-schedule the visit
 - Work through locator contacts to reach the participant

8. **What are some reasons why the study staff might end your participation in the study?**
 - The study is stopped or cancelled
 - The staff feels that having you continue in the study would endanger the safety of you, other participants or the study staff

9. **What will the study staff do to protect your privacy and confidentiality during the study?**
 - Conduct visits in private
 - Keep information about study participation and all study records confidential
 - Maintain privacy and confidentiality when conducting locator activities
 - However some “outsiders” will review records

10. **What would you do if you joined the study and then you didn't feel comfortable about the way you were treated in the study?**
 - Role of IRB/EC and human subjects contact person
 - Voluntary participation — can leave the study at any time
 - Voluntary participation — can continue to receive other services at the study clinic

4.6.1 Documentation

U.S. regulations require that informed consent be documented by "the use of a written informed consent form approved by the IRB/EC and signed and dated by the subject or the subject's legally authorized representative at the time of consent."

To fulfill this requirement, complete all signature and date blocks on the informed consent form per local IRB/EC requirements. Per the *DAIDS Policy for Requirements for Source Documentation in DIADS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00)*, participants must sign the informed consent form using their complete last name (not just an initial); the SOP also recommends, but does not require, that the participant's complete first name (not just an initial or nickname) be used as well. It is essential that the date documented on the form either precedes or coincides with the (first) study screening date. In addition, enter a note in the participant chart documenting that informed consent was obtained prior to the initiation of any study procedures. Finally, regulations require that participants be offered a signed copy of the informed consent forms. If a participant opts not to receive a copy, document this in a chart note.

If the participant is illiterate, the impartial witness present during the informed consent discussion must sign and date the informed consent form to attest that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant. In addition, the participant's printed name, signature, and signature date blocks on the informed consent form should be completed as follows:

- The study staff member who completed the informed consent process with the participant should enter the participant's name below the "participant's printed name" block, together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.
- The participant should make his mark (thumbprint or "X") in the "participant's signature" block.
- If possible, the participant should write the date in the "participant signature date" block. If the participant is unable to do this, the study staff member who completed the informed consent process with the participant should enter the date below the "participant signature date" together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.

• **The DAIDS Policy for Requirements for Source Documentation in DIADS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00) provides detailed requirements and suggestions for documenting the informed consent process. All requirements listed in the DAIDS Policy must be met.** In order to also meet some of the suggestions listed in the DAIDS Policy, site staff may consider the use of an informed consent "coversheet" similar to the example included in this section. It is recommended that the comments indicate that the information in the

consent was described to, and apparently comprehended by, the participant, that all of his questions were answered, and that consent to participate in the study voluntarily given prior to the initiation of any other study procedures.

Sample Informed Consent Coversheet for HPTN 061

Participant name:	
Date of informed consent discussion:	
Time of informed consent discussion:	
Name of study staff person completing informed consent discussion (and this coversheet):	
Can the participant read?	<input type="checkbox"/> Yes <input type="checkbox"/> No ⇒ If no, an impartial witness should be present during the entire informed consent discussion. Refer to informed consent SOP for specific instructions.
In what language was informed consent obtained?	<input type="checkbox"/> English (written) <input type="checkbox"/> Spanish (written)
Did the participant accept a copy of the informed consent form?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Notes/Comments (not documented elsewhere):	

4.6.2 Ongoing Consent of Participants

Given the ongoing nature of informed consent, key elements of informed consent also should be reviewed at study follow-up visits. At these visits, study staff should review key elements of informed consent with the participant, focusing on the remainder of their study participation. For example, at study month 6, the discussion might focus on the fact that the participant is completing the first follow-up visit, and therefore has one more follow-up visit remaining.

4.6.3 ICF Requirements for Protocol Amendments

According to DAIDS policy (Protocol Registration Policy and Procedure Manual), the site's IRB/EC are ultimately responsible for determining whether study participants need to be re-consented for a protocol amendment.

4.6.4 Informed Consent SOP

As a condition for study activation, each study site must establish an SOP for obtaining informed consent from potential study participants. This SOP should reflect all of the information provided in this section and minimally should contain the following elements:

- The minimum legal age to provide independent informed consent in the study site locale
- Procedures for ascertaining participant identity and age
- Procedures for ascertaining participant literacy
- Procedures for providing all information required for informed consent to the participant
- Procedures for ascertaining participant comprehension of the required information
- Procedures to ensure that informed consent is obtained in a setting free of coercion and undue influence
- Procedures for documenting the informed consent process
- Considerations and requirements for illiterate participants, including specification of who may serve as an impartial witness to the informed consent process
- Storage locations for blank informed consent forms
- Storage locations and security for completed informed consent forms
- Procedures for implementing a change in the version of the informed consent form used
- Staff responsibilities for all of the above (direct and supervisory)
- Staff training requirements
- QC/QA procedures related to the above (if not specified elsewhere)
- Attached copies and instructions for use of all forms, worksheets, or checklists to be used during the informed consent process

For ease of reference, a summary of key instructions from the above sections related to obtaining informed consent from illiterate persons is presented in the box below.

Key Points to Consider when Obtaining Informed Consent from Illiterate Persons

- Each site must specify procedures for obtaining and documenting informed consent from illiterate persons in its SOP for obtaining informed consent. These procedures must be consistent with the *DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00)* and must be followed each time informed consent is obtained. It is recommended that each site seek IRB/EC review and approval of these procedures.
- An impartial witness must be present during the entire informed consent discussion with an illiterate participant. The witness must sign and date the informed consent form to attest that the information in the consent form was accurately explained to, and apparently understood by, the participant, and that informed consent was freely given by the participant.
- The site SOP for obtaining informed consent should define who may serve as the witness to the informed consent process.
- Take care to minimize the perception of coercion due to the presence of the witness.
- The study staff member who completed the informed consent process with the participant should enter the participant's name below the "participant's printed name" block, together with a signed and dated note documenting the name of the person who made the entry and the date of the entry.
- The participant should make her mark (thumbprint or "X") in the "participant's signature" block.
- If possible, the participant should write the date in the "participant signature date" block. If the participant is unable to do this, the study staff member who completed the informed consent process with the participant should enter the date below the "participant signature date" together with a signed and dated note directly on the ICF document documenting the name of the person who made the entry and the date of the entry.
- Refer to Section 4.8 of the ICH GCP guideline and the informed consent section of the *DAIDS Policy for Requirements for Source Documentation in DAIDS Funded and/or Sponsored Clinical Trials (DWD-POL-CL-04.00)* for additional information.

4.6.5 Authorization for Release of Medical Records

The protocol team would like to collect data about participants' HIV-related treatment from their health care providers (for those participants who are HIV infected and have received treatment). The team also will request medical records for syphilis diagnoses and treatments for those participants who have received same from non-study providers. Study staff should solicit consent to collect this protected health information from participants when appropriate (most likely at the first study visit at which they have a positive test result for HIV or report a prior syphilis infection). A template release form is provided below for adaptation by sites if they do not already have a release form. Sites may be required to use the provider's standard form instead. The only information that should be sought from prior medical records for this study collected is: prior syphilis diagnosis and treatment history, test results (including dates of testing), and HIV treatment and viral load history as requested on CRF MRR-1.

AUTHORIZATION FOR THE DISCLOSURE OF Protected Health Information

PATIENT NAME

ADDRESS

PHONE NUMBER

SOCIAL SECURITY NUMBER

DATE OF BIRTH

MOTHER'S MAIDEN NAME

I HEREBLY AUTHORIZE:

NAME, TITLE

ORGANIZATION/DEPARTMENT, ADDRESS, PHONE NUMBER

TO RELEASE INFORMATION FROM MY HEALTH RECORD TO:

NAME, TITLE

ORGANIZATION/DEPARTMENT, ADDRESS, PHONE NUMBER

INFORMATION REQUESTED

DATES OF SERVICE: _____

Results of HIV tests

Medication/Treatment History and/or Records

Laboratory Results, including _____

All available information

Other _____

This authorization is valid for this request only and will not be honored for any subsequent requests.

This authorization for disclosure (unless expressly revoked earlier) expires 6 months from the date last signed by the patient or authorized agent of the patient.

I understand that I may revoke this authorization at any time by making a request in writing to _____. However, it may not be possible to withdraw authorization for information that has already been used or disclosed.

I understand that information used or disclosed pursuant to this authorization could be subject to re-disclosure by the recipient and, if so, may not be subject to federal or state law protecting its confidentiality.

I hereby acknowledge that I have read, or have had read to me, and fully understand the above statements as they apply to me, and do voluntarily consent to disclosure.

PATIENT'S SIGNATURE OR IF AUTHORIZED AGENT SIGNATURE,
PLEASE SPECIFY RELATIONSHIP TO PATIENT.

DATE

WITNESSES SIGNATURE

DATE

4.7 Enrollment Procedures

A detailed listing of required study procedures is provided in the protocol Appendix I: Schedule of Study Visits and Procedures for HPTN 061. All procedures should be completed during one visit, if possible. Some lab results (giving participants' results from confirmatory tests for HIV diagnosis, for example) may take place several days later, but this will not be considered an interim visit.

The following notes describe particular enrollment considerations that bear highlighting:

- A participant should be assigned a PTID as soon as informed consent is obtained, prior to any other procedure, including documentation of eligibility
- Completion of the ACASI questionnaire should always precede pre-test and risk reduction counseling
- Staff should provide a brief counseling opportunity immediately after completion of the ACASI
- In case a visit must be split, collection of clinical samples should take place on the same day as completion of the ACASI
- For men who qualify as index participants, requesting referral of their sexual network partners may most logically follow completion of the Social and Sexual Networking survey. For participants who have just been given a reactive HIV result for the first time, postponing this conversation to when they return for their confirmatory results is advised.

More information can be found on clinical and counseling procedures in Section 8. More information can be found on laboratory procedures in Section 11.

4.7.1 ACASI

Each site should develop procedures for using the ACASI software. Computers should be positioned in a location that allows maximum confidentiality for the participant and participants should be provided with headphones. Headphones should be disposable or cleaned before each use.

Site staff should provide participants with a brief introductory lesson on how to use the computer and specific instructions on the use of the ACASI software. Site staff should work with the participant on the introductory piece to assess the participant's competency with the computer. The participant should be instructed on how to seek help from site staff if they encounter any problems with the software or computer while completing the survey. For participants who are uncomfortable with computers or otherwise unable to complete the ACASI survey independently, the site staff may assist the participant in completing the survey on the computer. This assistance will be documented at the end of the ACASI survey in the final question.

More information and instructions regarding use of the ACASI software can be found on the HPTN 061 Portal at <https://hptn.fhi.org/061/CRFs/Forms/AllItems.aspx>, as described in SSP Section 9.10.1.

4.7.2 Social and Sexual Networking

All participants will be asked to provide information on five of their social and ten of their sexual network members using the Social and Sexual Networking (SSN) tool during the enrollment visit. A counselor should work with the participant to complete this using a computer in a confidential space. Sites planning to use the same computers for completion of both the ACASI and the SSN surveys will need to coordinate their usage since confidentiality demands that the SSN not be completed at the same time and in the same space as other activities. For more information on completion of the survey, please refer to instructions provided on the ATLAS website portal, as described in SSP Section 9.11 at:

<https://atlas.ssharp.org/cpas/project/HPTN/061/Social%20and%20Sexual%20Network%20Questionnaire/begin.view?>