

Section 8. Clinical and Counseling Procedures

8.1 Overview of Section 8

This section presents general information related to the clinical assessments and counseling sessions performed for HPTN 061. Examples of clinical assessments include, but are not limited to, checking for circumcision, diagnosing sexually transmitted infections (STIs) and providing clinical care in accordance with the local standard-of-care. The protocol or SSP will NOT dictate the type of treatment provided for any condition noted during the course of the study. Sites are expected to follow their own procedures and standards of care. Counseling procedures include HIV and STI pre- and post-test counseling, HIV and STI risk reduction counseling, and counseling for issues raised during completion of the ACASI questionnaire. Detailed information on performing laboratory assessments to complement clinical assessments is provided in Section 11. Detailed information on completing data collection forms associated with these activities is provided in Section 9.

8.2 Clinical Procedures

The Schedule of Evaluations listed in Appendix I of the protocol indicates the clinical and counseling procedures to be performed at each study visit. This includes HIV and STI pre- and post-test risk reduction counseling, specimen collection for HIV, STI and research tests, post-ACASI counseling, confirmation of circumcision status through examination and HIV rapid testing.

While the protocol dictates the schedule for data capture, the Investigator of Record or their designee should perform clinical procedures at their discretion during any visit where they determine it to be clinically necessary, particularly if there are any on-going conditions that require closer follow-up. The participant's study chart should include source documentation of these procedures.

8.2.1 Clinical Assessment for Mental Health, Substance Use or Other Psychosocial Issues

At the conclusion of the ACASI session, all participants will meet with a counselor, and will be invited to discuss any issues that the interview session has raised. Provision of therapy and/or diagnosis of disease for psychosocial issues are not a part of the intervention being tested in HPTN 061. However, counselors will make all participants aware of locally-available resources for help with problems that have been identified during counseling and will offer to help arrange a referral. The counselor will provide the participant with a comprehensive locally-relevant list of available resources so the participant can follow-up on his own on any issues he may not have felt comfortable discussing. However, when site staff encounter a participant who seems to have mental health or substance use problems for which brief counseling and referral may not be adequate, the participant will be referred to a licensed mental health professional for assessment during the visit. Each site will have such a person available either on staff or on call so that this assessment can be made the same day.

Individual sites will have a procedure in place for making referrals for psychosocial assessment. Based on the outcome of this assessment, the participant will be triaged for care,

which could range from simple referral to local health services to immediate hospitalization (e.g. for acute suicide risk). Sites should also have an emergency plan in place for participants who appear seriously disturbed and/or possibly a threat to themselves or others.

It is the responsibility of the site to create and maintain a list of locally available resources for mental health, substance use and other psychosocial issues. Details of maintaining a local services inventory should be in the site-specific SOP on health navigation. In addition, the site should alert staff to the laws regarding what situations require a report to authorities and document these situations accordingly. Sites must make it clear to participants what, if anything, they would be obliged by law to report to authorities, before beginning counseling.

8.2.2 Specimen Collection

Specimens (including blood, urine and rectal swabs depending on participant consent and the visit number) will be collected at the enrollment, 6 and 12 months visits for clinical and research purposes per the Schedule of Evaluations listed in Appendix I of the protocol. Specific instructions for collecting and storing these samples are included in Section 11 of this SSP manual.

All specimens collected for research purposes during this study will be sent to HPTN Network Lab (NL) located in Baltimore, Maryland. The samples will be placed in short-term storage until they are used for analysis. If there are any samples left at the NL once the HPTN 061-related research is complete, these leftover samples will either remain at the NL for long-term storage and future testing or be destroyed. Only samples collected from participants who agree to long term storage of samples may be kept after analysis for HPTN 061 has concluded. The decision to keep or destroy any leftover sample will be made based on the content of each participant's enrollment informed consent form.

8.2.3 Confirmation of Circumcision

Circumcision will be confirmed by a visual examination of the participant completed by a clinician. The exceptions to this examination will be if the participant identifies they were female at birth or states that they have had gender reassignment surgery. Circumcision status will be determined by noting the degree of coverage of the corona (initial swelling of the head) of the glans penis by the foreskin when the penis is flaccid.

- Circumcised Penis: complete circumcision should be reported if the corona is fully visible.
- Uncircumcised Penis: the individual is considered uncircumcised if the glans is completely covered.
- Partially Circumcised Penis: the individual is considered partially circumcised if determined to be any status in between completely circumcised and completely uncircumcised; these individuals still have foreskin.

8.2.4 HIV Care

Individuals who are identified as HIV positive during screening, enrollment or follow-up should be referred for appropriate HIV care per the local standards of care at the participating site (this care may be provided at the study site, if available). If a participant being seen for follow-up visits initiates HAART after his enrollment visit, study staff should solicit consent to collect information from his medical provider about when he initiated treatment. See SSP Section 4.6.5 for more information on this topic.

Sites are expected to follow their own local standard-of-care in providing non-HIV related clinical care, which will not be dictated by the protocol or the SSP. However, as noted in the protocol, participants diagnosed with gonorrhea, Chlamydia, and/or syphilis will be offered treatment or referred for treatment. Participants will be encouraged to return to the clinic between study visits for testing and treatment (or referral for treatment) if they suspect they have acquired an STI. These will be documented as an interim visit. If a participant identifies a need for diagnosis or treatment during a health navigation visit, a PHN will refer the participant to the appropriate services and document this in the Referral Log (CRF RL) and Peer Health Navigation Encounter Form (CRF PHE)

8.2.5 SAE and Social Harms Reporting

The study site Investigator of Record is responsible for continuous close safety monitoring of all study participants, and for alerting the protocol team if unexpected concerns arise. However, because this study includes no biomedical interventions or study product, standard adverse event reporting will not be undertaken and no adverse event data will be collected in the study database.

SAEs that are determined to be related or possibly related to study procedures and/or participation will be reported within 3 business days of site awareness to the DAIDS HPTN Medical Officer and to the site's IRB/ECs, per the IRB's requirements. These SAEs will be reported to the Medical Officer using the HPTN 061 SAE reporting form provided in Appendix I of this SSP manual. No other adverse event reporting will be required for this observational study in which there are no interventions. This information will not be recorded on CRFs or entered into the study database. Serious adverse events will not be reported to the DAIDS Regulatory Compliance Center (RCC).

“Social Harms” will be monitored closely throughout the study including active solicitation from participants at health navigation encounters and follow-up visits. Social harms that are judged by the Investigator of Record to be serious or unexpected will also be reported to the responsible IRB/ECs at least annually, or according to their individual requirements. The CORE CRM will request a report of social harms from sites on a quarterly basis and will share a report compiling all sites' data with the protocol team and HPTN SMC.

8.3 Clinical Supervisors' Call

A conference call will be held on an as-needed basis among the clinical supervisors from the sites in order to maintain consistency in conduct of the clinical procedures in the study, and to work collaboratively to problem-solve issues as they arise in the conduct of the study. These calls may be held more frequently at study start up, as sites begin to implement study procedures.

8.4 Syphilis Diagnoses

There are several scenarios in which the interpretation of syphilis test results are expected to be straightforward. For example, a participant with a negative RPR test will be diagnosed as not infected with syphilis, and a participant with a high RPR titer, positive treponemal test, and no prior history of syphilis treatment will be diagnosed with untreated syphilis infection.

There are likely to be several syphilis scenarios, however, in which a diagnosis will be difficult to determine. For example, it may be difficult to diagnose a participant with a positive RPR and treponemal test, a low-to-intermediate titer, and who claims to have been treated for syphilis six months previously, but his previous medical records cannot be obtained to confirm treatment or to determine his titer when first diagnosed. In this case, it would not be obvious whether: 1) the participant has been successfully treated, but has not yet cleared the antibodies or is serofast, 2) whether the initial infection was not successfully treated, or 3) whether he was successfully treated previously, but has become re-infected. A study-specific syphilis advisory committee will be established to help site teams interpret more ambiguous data, and to ensure that diagnoses based on comparable data are consistent across participants and across sites. The committee will be composed of clinicians, experienced in diagnosing syphilis, drawn from the study team.

The guidance below is provided to assist study teams in interpreting syphilis results for reporting on the study case report form. Please note that clinical management of the participant will be directed by the on-site clinician according to their expertise and local policies and procedures.

8.4.1 Diagnosis by Site Clinician and Forms Completion

If the site clinician has enough information to confidently determine syphilis status, that diagnosis should be documented on the Enrollment STI Laboratory Results form (ELR-1) or Follow-Up STI Laboratory Results form (FLR-1) without referral to the syphilis advisory committee. Sites should solicit permission to obtain prior medical records from participants with positive confirmatory syphilis tests if the participant has (or suspects he has) been previously diagnosed and treated for syphilis. Since it is likely to take some time to obtain medical records, the site should record their preliminary diagnosis on the CRF and fax to the SDMC, and then update that diagnosis if necessary at a later date when more information is available. Forms with revised diagnosis must be re-faxed to the SDMC. Some scenarios in which sites would be expected to make unassisted diagnoses include:

- Participant has a positive RPR and confirmatory test at enrollment and reports no prior treatment for syphilis- new active infection
- Participant has a positive RPR and confirmatory test at enrollment but claims he was treated for syphilis recently at a local STI clinic. Site checks “self-report” for question 2a and “treated infection” for question 3 on ELR-1 and faxes in to SDMC. Medical records are obtained showing that the participant was indeed diagnosed and treated for syphilis prior to enrollment in HPTN 061 and his enrollment titers are consistent with successfully treated syphilis (for example, his enrollment titers have decreased by at least four fold). At this point, the answer to question 2a is changed to “documentation” and the CRF is re-faxed to the SDMC.
- Participant has a positive RPR and confirmatory test at enrollment and thinks he was treated for syphilis recently at a local STI clinic. Site checks “self-report” for question 2a and “treated infection” for question 3 on ELR-1 and faxes in to SDMC. Medical records are obtained showing that the participant was NOT diagnosed and treated for syphilis but rather for Chlamydia prior to enrollment in HPTN 061. At this point, the answer to question 2a is changed to “documentation”, the diagnosis in question 2 is changed to “new active infection” and the CRF is re-faxed to the SDMC.
- Participant is newly diagnosed with syphilis at enrollment and is treated. At 26 weeks his titer has dropped four fold or more, indicating successful treatment of infection.

This is not intended as a comprehensive list of scenarios in which the local clinicians could determine syphilis infection status on their own.

8.4.2 Scenarios in Which Syphilis Advisory Should be Consulted

Some scenarios in which a site should consult with the syphilis advisory committee include:

- Participant has a positive RPR and treponemal test, a low-to-intermediate titer, (for example, 1:1 to 1:8) and claims to have been treated for syphilis six months previously, but his previous medical records cannot be obtained to confirm treatment or to determine his titer when first diagnosed.
- Participant has a positive RPR and treponemal test, a low-to-intermediate titer, and claims to have been treated for syphilis six months previously. His previous medical records are obtained and show that he was treated, but also show that his current titer is only two fold lower than before he was treated.
- Participant has a positive RPR and treponemal test. His titer is 1:2, but he claims to have never been diagnosed with or treated for an STI.
- Participant has a positive RPR and treponemal test at baseline visit; his titer is

1:64. He is treated appropriately for syphilis. At 26 weeks he has an RPR titer of 1:32 (less than four fold decrease in titer from baseline).

This is not intended as a comprehensive list of scenarios in which the local clinicians should consult with the syphilis advisory committee

8.4.3 Procedures Concerning the Syphilis Advisory Committee

As noted above, the syphilis advisory committee will be composed of experienced clinicians drawn from the study team. When a site encounters a syphilis result that requires consultation with the committee, they should send an email to the alias 061Syphilis@HPTN.org providing all relevant information to the case, including:

- Participant PTID
- All relevant study-generated lab results
- Summary of participant self-report regarding prior STI diagnoses and/or treatment
- Whether prior medical records had been obtained and any relevant information from those records (if records are sent as an attachment, please ensure that all personal identifying information have been blacked out)
- Narrative summary of site investigation and discussion of the case

Sites should provide updates to the case if additional information becomes available using the same email alias.

The syphilis committee will discuss cases on a schedule either determined by the case load or at predetermined intervals. It is not anticipated that the syphilis committee will be consulted for clinical management of cases and so there should not be a need for expedited response from the committee. The committee will maintain a record of decisions on referred cases, to ensure consistent decisions in future, similar cases and for use in analysis at the end of the study. Once the committee has made its decision in a particular case, the decision will be communicated back the site via email.

8.5 Counseling Procedures

8.5.1 Pre-and Post-HIV Test Counseling

Each site is required to develop a local SOP for providing HIV pre- and post- test counseling whenever a participant is tested for HIV. Although this SOP will be site-specific and should at a minimum reflect the site's local requirements for HIV counseling and testing, the SOP should contain the following elements:

- Each individual should be provided with information that allows him to decide for himself whether to be tested (informed decision with informed consent).
- The HIV testing procedure should be organized to maximize confidentiality.
- All individuals being tested for HIV should be provided with information about HIV that allows them to understand the results of their HIV test.

- All individuals should be provided appropriate HIV post-test counseling including appropriate referrals and tailored risk reduction counseling according to the site-specific SOP on post-test counseling.
- Disclosing HIV status to others should be discussed with all participants.
- The need for additional and appropriate referrals should be addressed where possible.

Sites should refer to the HPTN 061 Counseling Manual (Appendix II of the SSP) in creating their counseling SOP. Sites may also wish to consider the guidelines set forth by the CDC in 2001 entitled, “Revised Guidelines for HIV Counseling, Testing, and Referral.” This document can be downloaded at

<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5019a1.htm>.

Another resource that may be useful for HIV pre- and post-test counseling is entitled, “HIV Voluntary Counseling and Testing (VCT): A Reference Guide for Counselors and Trainers,” which was developed by the Institute for HIV/AIDS at Family Health International and updated in January 2004. This document can be downloaded at

<http://www.fhi.org/en/HIVAIDS/pub/guide/vcttoolkitref.htm>

8.5.2 HIV Risk Reduction Counseling

In HPTN 061, a modified Project Respect-style counseling will be used for risk-reduction counseling. All participants are to be provided with HIV risk reduction counseling at each visit which should include provision of condoms and lubricant. It is required that each site develop a local SOP for providing this counseling, which can be combined with the HIV pre-and post-test counseling SOP. Although the HIV risk reduction SOP will be site-specific, it should contain the following elements:

- Assessing the participant’s knowledge of HIV/AIDS and providing appropriate information.
- On-going education about the transmission and prevention of HIV infection.
- Information on available treatments for HIV/AIDS in the community.
- Discussion of the participant’s current risk level and, if applicable, possible alternative behaviors that would lower their risk.
- Discussion of potential barriers the participant has (or may encounter) to changing his behavior.
- Demonstrating the proper use of condoms and offering free condoms and lubricant.
- Demonstration of needle cleaning techniques, if appropriate.
- Emphasizing good communication between any sexual and IDU partners.
- Discussion of family and community pressures and conflicts.
- A referral strategy for additional counseling, HIV treatment programs, drug or alcohol abuse, and domestic violence, as well as other social services.

Sites should refer to the HPTN 061 Counseling Manual (Appendix II of the SSP) in creating their risk-reduction SOP.

8.5.3 Post-ACASI counseling

Participants will also be administered an ACASI questionnaire at their enrollment visit. The ACASI format does not allow site staff to access a participant's answers, and is therefore well suited to collect data of a sensitive nature. This questionnaire will collect information on sexual risk behaviors, drug/alcohol use, health care/HIV testing history, incarceration history, mental health, structural and personal/cultural barriers to receipt of HIV care, experience of violence, unmet service needs, venues frequented, and attitudes toward race, sexual identity, other prevention strategies, research, and health care. **It is imperative that this questionnaire is done prior to risk reduction counseling so that the counseling will not bias results.** For participants who are eligible for follow-up, the ACASI will be repeated at their six and twelve month follow-up visit.